Medicines use in Italy

National Report Year 2023

OSSERVATORIO NAZIONALE SULL'IMPIEGO DEI MEDICINALI

AIFA
ITALIAN MEDICINES AGENCY

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Presentation of the OsMed Report 2023

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Since 1999, the Medicines Utilisation Monitoring Centre (OsMed) was introduced to develop and validate mechanisms for the collection, analysis and interpretation of data on the use of medicines in Italy. Over time, both the specific objectives and operational modalities of the OsMed have evolved significantly, in general and in particular, after the birth of the Italian Medicines Agency. The National Report on the Use of Medicines in Italy based on OsMed data, with its updated version to 2023, marks the tenth anniversary since it became a reference text for the Agency, in carrying out its administrative functions, in support of transparency. The technical complexities and the different perspectives of the actors involved in patient access to the drug require a focus that is no longer merely a summary of the use of medicines in Italy, but is also related to the analysis of the processes that characterise the organisation of pharmaceutical assistance and the provision by regions of medicines paid for by the National Health Service (SSN). The objective of the National Report is certainly ambitious as it seeks to balance, wherever possible, the need of a technical training on monitoring the use of medicines in clinical practice with that of direct information to the citizen. The result is an overview ranging from medicines delivered to patients by pharmacies open to the public, to those delivered by hospital pharmacies and/or administered within the framework of hospital facilities, to medicines purchased directly by citizens at their own charge. In the international context, the National Report on the Use of Medicines in Italy represents one of the rare experiences of national monitoring of the use of medicines and probably one of the most important in terms of data and depth of analysis. At a national level, the Report provides essential information for planning the various organisational levels of the NHS, supporting both the identification of care needs according to risk ranges, as well as the evaluation of performance, which is essential for the assessment of effectiveness and efficiency in the provision of pharmaceutical assistance by the NHS. In this edition of the Report, the use of drugs in the elderly population was analysed in greater detail because of the high number of comorbidities and the consequent high number of drugs taken. Specifically, chronic polypharmacy, i.e. the simultaneous administration of 5 or more drugs over time, was assessed; this is a very common condition in the over-65s that exposes them to a higher risk of adverse reactions and/or drug interactions. In view of the setting up of the technical roundtable for the revision of the AIFA Notes and Therapeutic Plans currently in force, an analysis has been introduced dedicated to drugs whose prescription at NHS charge is subject to an AIFA Note, providing time comparisons on expenditure, consumption and average cost per day of therapy, analysing both dispensing under the contracted care regime and dispensing through the direct distribution channel and on behalf. In addition, the impact on average costs per day of therapy resulting from the inclusion of drugs in the AIFA Transparency List was assessed, showing the 2019-2023 trend in the cost of substances that entered the list in the year 2021. Given the recent recognition of the importance of the environmental impact of the use of medicines, and in order to raise public awareness of the correct use and disposal of the medicines prescribed

to patients, there is a section dedicated to the analysis of the potential environmental impact of a series of active ingredients with a high use or high risk of environmental toxicity. The main objective of this section is to provide an informative overview of the emerging issue of the impact of drug consumption on the environment. Finally, in order to facilitate consultation of the Report, while still providing important information, useful mainly at local level, regional data on exposure, duration of therapy and detailed data on treatment adherence and persistence indicators stratified by age, gender and geographical area have been included in supplementary material published online. Overall, public pharmaceutical expenditure in 2023 amounted to EUR 24.9 billion, representing 68.7% of total pharmaceutical expenditure and 19.0% of public health expenditure, an increase compared to 2022 (+5.7%). The item that has the greatest impact on the increase is expenditure on drugs purchased by public health facilities, where new drugs never previously marketed are most prevalent, and in this area Italy is one of the European countries that makes the largest number of drugs available to patients after European centralised authorisation, with an availability rate of 63% in 2023. As might be expected, expenditure is more concentrated on the category of antineoplastics and immunomodulators, although there are other categories that have seen major changes, such as antidiabetic drugs, drugs of the respiratory system, drugs of the musculoskeletal system and drugs of the blood and haematopoietic organs; due to the recent entry of new products. The share of orphan drugs in expenditure on new medicines not previously marketed is also growing, reaching 31% in 2023. These data suggest even more the need for adequate planning and pricing tools and elements to ensure the sustainability of pharmaceutical care in Italy. With a view to a model of sharing instructional and decision-making paths with doctors, scientific societies and other actors involved, it is important to have a shared database capable of responding to the various information needs; the OsMed and the National Report are tools that contribute to this. In conclusion, the challenge for the NHS is to best meet the care needs of patients through the appropriate use of medicines. Diseases originate from a variable interplay between individual genetic constitutive factors and environmental factors; in this biological confrontation, unfortunately, many people, in the course of their lives, find themselves having to take medication, which in some cases contributes to prolonging their life expectancy, in many others to improving their quality of life. It is good to keep this reference in mind when seeking a balance, which is not easy and not banal, between pharmacological innovation, or even just between the essentiality of a drug, and the sustainability of public pharmaceutical expenditure. Enjoy the reading.

Pierluigi Russo
Scientific Technical Director

Summary

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This Report analyses pharmaceutical prescription data in Italy in 2023 by using the various information flows available, which allow to obtain a comprehensive picture of pharmaceutical care in the inpatient and outpatient settings, both when costs are borne by the National Health System (NHS) and when they are borne by the citizen through private purchases. OsMed flows have been used for analysing consumption under the approved care regime, whereas the medicine traceability flows have been used to analyse the consumption of medicines purchased by health facilities. In addition, for analysing prescriptions by age and gender and exposure and for estimating adherence and persistence, data from all Italian Regions, collected through the information flow of pharmaceutical prescriptions reimbursed by the NHS (Tessera Sanitaria) have been analysed. Finally, for assessing purchases by citizens, data collected through the medicine traceability flow for medicinal products delivered to public and private local pharmacies have been used. Finally, the relevant regional flows were used to analyse the expenditure and consumption of medicines dispensed through direct distribution and distribution 'per conto'

SECTION 1 - General characteristics of medicines use in Italy

In 2023 the overall pharmaceutical expenditure (both public and private) amounted to 36.2 billion euros, with an increase of 6.1% compared to 2022. It represents an important component of the national health expenditure, accounting for 1.9% of gross domestic product (GDP). Public expenditure, worth 24.9 billion euros, accounts for 68.7% of total pharmaceutical expenditure and 19.0% of public health expenditure, and has slighthly increased compared to 2022 (+5.7%) (Table 1.1.1). In 2023 the overall outpatient pharmaceutical expenditure, both public and private, amounted to 23.6 billion euros, with an increase of 4.9% over the previous year. Public outpatient expenditure, including expenditure on Class A medicines provided under approved care regime and direct and per conto distribution, was equal to 13.0 billion euros, with an increase of 3.0% compared to 2022, determined mainly by the increase in expenditure of class A medicines dispensed in direct distribution (+10.0%) and class A medicines dispensed per conto (+4.4%) (Table 1.2.1). The citizen pharmaceutical expenditure, including cost-sharing (regional tickets and difference between the price of patent-expired medicine and reference price), the private purchase of class A medicines and expenditure for class C medicines, totalled 10.6 billion euros, with an increase of 7.4% compared to 2022. This trend was influenced by the increase in expenditure on self-medication medicines (+10.5%), including medicines supplied in shops (+12.7%), and spending on class C prescription drugs (+9,0%), while private purchases of class A drugs showed a smaller increase (+5.9%). In 2023, 18 packs per citizen and 1128.1 doses per 1,000 inhabitants were consumed every day under approved care regime (-0.8% compared with 2022; Table 1.2.2).

Within local care, both public and private, about 1.9 billion packs were dispensed, stable compared to the previous year (+0.9%). It can be noted that the number of packages dispensed by direct distribution increased by +11.2%, while those dispensed "on behalf" grew by +5.7%. The main components of the variation in gross pharmaceutical expenditure under approved care regime show, with respect to the previous year, a reduction in the consumption of pharmaceuticals requiring prescription (-1.3% in terms of DDD), a slight decrease in average prices (-1.4%), related in part to an increasing use of patent-expired products and, finally, to the prescription of more expensive products (mix effect: +2.8%)

(Table 1.2.6). The region with the highest per capita gross expenditure for A-NHS medicines was Campania with 196.1 euros per capita, while the lowest value was found in the Province of Bolzano (116.3 euros per capita), with a 69% difference between the two regions (Table 1.2.4). As regards consumption, the region with the highest levels was Basilicata (1289.5 DDD/1000 inhabitants per day), while the lowest consumption was found in the Province of Bolzano (861.3 DDD/1000 inhabitants per day). Expenditure for the purchase of medicines by public health facilities amounted to approximately €16.2 billion (€275.14 per capita) and registered an increase of 8.4% compared to 2022, against an increase in consumption (+4.8%; 194.4 DDD/1000 inhabitants per day) and an increase in the average cost per DDD of 3.1% (Table 1.3.1). The Regions with the highest expenditure values are Campania (317.44 euros per capita) and Abruzzo (310.64 euros per capita); on the contrary, Valle d'Aosta (217.69 euros per capita) and the Province of Trento (234.28 euros per capita) have the lowest values. The increase in expenditure, compared to 2022, was recorded in all regions, with the largest variations in Friuli Venezia Giulia (+16.6%) and Valle d'Aosta (+15.0%). Overall, in 2023, 67.4% of the population received at least one pharmaceutical prescription, with a per capita expenditure of €207.41 and a consumption of 1182,7 DDD/1000 inhabitants per day; there is a difference in drug exposure between the two sexes, with prevalence reaching 63.0% in males and 72.0% in females (Table 1.4.1 and Figure 1.4.1). Per capita expenditure and consumption increase with age, especially regarding the population over 64 years of age, which accounts for about 60% of expenditure and doses. Generally, Northern Regions have a lower prevalence (64.2%) compared to Central (69.4%) and Southern (70.5%) ones (Table 1.4.2). More was spent per user in the South (EUR 324.5) than in the Centre (EUR 306.2) and the North (EUR 295.6). In 2023 almost 4.4 million children and adolescents received at least one pharmaceutical prescription, representing 48.6% of the general paediatric population, with a slightly higher prevalence in males than females (49.1% vs. 47.6%) (Table 1.5.1). Antiinfectives for systemic use continue to be the most consumed medicines in paediatric age, followed by medicines for the respiratory system. However, both categories register an increase in consumption compared to the previous year (Figure 1.5.3). In the elderly population, the average expenditure per user was equal to 563.4 euros (613.6 euros for men and 524.1 euros for women), a slight increase over 2022 (+1.5%), and almost the entire population (97.2%) received at least one drug prescription during the year (Table 1.6.1). On average, each user consumed more than 3.4 doses per day, with higher levels recorded among men than women. In addition, each user took 7.6 different substances, with the lowest rate (6.0 substances per user) recorded in the 65-69 age group, and the highest rate (8.7 substances per user) recorded in the ≥85 age group (Table 1.6.2). Both genders registered a progressive growth in the number of different active ingredients taken, which increased with age. During 2023, 68.0% of users aged ≥65 years received prescriptions for at least 5 different substances (i.e. polypharmacy) and approximately one out of three (28.5%) took at least 10 different active ingredients (Figure 1.6.2). This analysis shows that 33% of the elderly population (3 out of 10 patients) take at least 5 different medications for at least 6 months in the course of a year, with an upward trend with increasing age until age of 89, when it peaks at 44% (one out of two patients) (Table 1.6.4). The time trend of the monthly consumption of medicines shows a growth in class A medicines under approved care regime and in medicines purchased by public health facilities. Class C medicines requiring a prescription show a decreasing trend in the period 2004-2017, while in the last 6 years (2018-2023) an increase in consumption is observed (Figure 1.7.1, Figure 1.7.2 and Figure 1.7.3). The analysis of the time trend of prices for

medicines shows a reduction in the average price per dose for class A medicines under approved care regime (Figure 1.8.1) and an increase in outpatient class C medicines requiring prescription (Figure 1.8.3). An in-depth study of the trend in the average cost per DDD and per pack of drugs that entered the transparency list in 2021 showed that entry on the list leads to a reduction in both the cost per day of therapy and the cost per pack, even before 2021. When comparing the average cost recorded in January 2020 with the cost in December 2021, there is a reduction effect of 15.5% and 20.5% in the cost per package and per DDD, respectively. Thereafter, the average cost remains almost stable (Figura 1.8.2). The cost trend is found to be increasing from 2006 to 2009 and then stabilizing in the period 2010-2014 and increasing again since 2015, with a change from January 2015 to December 2023 of 41% corresponding to an average annual change (CAGR%) of 0.3%. In particular, in 2023 there was an increase of 3.1% over the previous year. The international comparison section compares the Italian pharmaceutical assistance with 9 other European countries, both for drugs distributed at local level and for those in the hospital setting. Considering these two different settings, a profound diversity emerges in the use of specific categories of medicines, which can also depend on the specific distribution regime used in Italy (Law No 405/2001). The total Italian pharmaceutical expenditure, including local public and private expenditure and hospital expenditure, was equal to 612 euros per capita, lower than in Germany (673 euros), Austria (672 euros), and Belgium (627 euros), while it is well above the values of Poland (276 euros), Portugal (439 euros), UK (502 euros), Sweden (455 euros) and the average of the European countries, which is equal to 384 euros (Figure 1.9.3). There is still a low incidence of expenditure on generic medicines (Figure 1.9.8) while it ranks first in the incidence of expenditure (80.8%) and consumption (66.9%) of biosimilar drugs compared to a European average of 64.7% for expenditure and 31.8% for consumption (Figures 1.9.10 and 1.9.11). Through the Herfindhal-Hirschman index, the penetration of biosimilars and the level of market concentration for single molecules were analysed (Tabella 1.9.20). Italy, with EUR 51.0 per capita, ranks 4th for orphan drug expenditure, after France (EUR 65.8), Belgium (EUR 59.4) and Austria (EUR 59.3). All countries show an increasing trend in spending in the years 2022 and 2023, with the exception of Great Britain (-1%) (Figura 1.9.12). Finally, a price comparison was made considering medicines that were identical or with the closest packaging to those marketed in Italy. In the case of Italy and Germany, countries for which they were available, the analysis was conducted using actual purchase prices. When considering outpatient drugs (Figure 1.9.13), it can be seen that all countries have higher average prices than Italy; when looking at medications dispensed in hospitals, Belgium, France, Portugal and Germany have lower prices than Italy, with differences ranging from -58.2% in Germany to -13.4% in Belgium (Figure 1.9.14). Considering the overall market, covering both medicines delivered at a local level and in hospital settings, Italy reports lower prices than Belgium (+85.9%), Germany (+77.9%), Austria (+33.2%), Sweden (+20.3%), Spain (+7.1%) and Great Britain (+4.2%), while the following countries have lower prices than Italy: France (-12.6%), Poland (-36.2%) and Portugal (-36.5%) (Figure 1.9.15).

SECTION 2 - Detailed analysis of expenditure and consumption of medicines

In 2023, patent-expired medicines accounted for 73.6% of expenditure and 86.0% of consumption of class A medicines under approved care regime. The percentage share of

generic medicines, excluding those with patent coverage, accounted for 22.8% of expenditure and 31.2% of consumption (Figures 2.1.1 e 2.1.2). The three therapeutic categories with a higher incidence of expenditure on patent-expired medicines are drugs active on the genito-urinary system (91.5%), cardiovascular medicines (91.4%), and anti-infectives for systemic use (89.4%) (Table 2.1.3). Citizen cost-sharing for the amount exceeding the reference price of patent-expired medicines (hereinafter "cost-sharing") was equal to 18.0 euros per capita (approximately 1.1 billion euros), representing 71% of the total citizen cost-sharing and showing a higher per capita value in the South and the Islands (23.5 euros) compared to the Centre (19.7 euros) and the North (13.3 euros) of Italy (Tabella 2.1.5). An analysis of the correlation between expenditure on citizen cost-sharing and regional per capita income shows that Regions with the lowest income are those with the highest citizen cost-sharing. With regard to biosimilars, wide regional variability is confirmed: Lombardy, the Province of Bolzano, Abruzzo, Molise, Calabria and Sardinia tend to consume larger quantities of ex-originators. Liguria, Marche, Tuscany, Emilia Romagna, Basilicata and Sicily are the Regions with a higher consumption of biosimilars than the national average (Figura 2.1.23). The total expenditure of class C-NN drugs reimbursed by the NHS and purchased by public health facilities in 2023 amounted to approximately EUR 47.5 million, corresponding to a per capita expenditure of EUR 0.81, which overall is reduced by 63.1% compared to the previous year (Table 2.2.1). Regarding class C medicines dispensed directly by public health facilities, per capita expenditure was equal to 12.04 euro, with a 6.1% increase compared to the previous year (Tabella 2.2.5). In 2023 expenditure for medicines dispensed via direct distribution (DD) and distribution "per conto" (DPC) equalled 10.2 billion euros (173.85 euro per capita), with 75.6% attributable to DD and 24.4% to DPC (Table 2.3.1). As far as direct distribution is concerned, class H medicines account for the largest share of expenditure (64.7%), while in the distribution "per conto" all expenditure is absorbed by class A medicines (Tables 2.3.2 and 2.3.3). In 2023, the total per capita expenditure for medicines dispensed in the context of inpatient and outpatent care amounted to 204.80 euro (12.05 billion euro), with an increase of 8.5% compared to 2022 (Tabelle 2.4.1). Pembrolizumab is the main active ingredient dispensed in inpatient and outpatient setting, followed by daratumumab and nivolumab (Table 2.4.4). Overall, this year's reimbursement for these medicines amounts to more than 660.6 million euro, with a per capita expenditure of 24,02 euro, up on the previous year's figure (+18.0%). Lombardy and Lazio recorded the highest amounts of expenditure, reporting a per capita value of 42.82 euro and 33.20 euro, up 20.1% and 15.7% compared to 2022 (Tabella 2.5.1). In 2023, expenditure on class C medicines exceeded 7.1 billion euro, an increase of 9.8% compared to 2022; 54% of the expenditure (3.8 billion euro) relates to prescription medicines, and the remaining 46% (3.3 billion euro) to self-medication medicines (SOP and OTC), including those dispensed in shops (Table 1.1.1). With regard to prescription drugs in class C, benzodiazepine derivatives with anxiolytic activity are the category with the highest expenditure with EUR 387.5 million, followed by anilides (ATC N02BE), which includes the active substances paracetamol, phenacetin and bucetin alone and in combination with EUR 275.3 million, and drugs used in erectile dysfunction with EUR 250.0 million (Table 2.6.1). Among class A medicines privately purchased by citizens, cholecalciferol, pantoprazole and amoxicillin in combination with clavulanic acid ranked in the top three places in 2023, all showing an increase in expenditure over the previous year (Table 2.6.13). Among self-medication medicines, propionic acid derivatives account for 12.6% of total expenditure and are worth EUR 416.3 million, up 6.9% compared to 2022; the first active ingredients by expenditure are confirmed

as ibuprofen and diclofenac, with an increase of 21.5% and 10.3% respectively (Tables 2.6.5 and 2.6.7). In 2023, the territorial expenditure (including expenditure under approved care regime and expenditure in DD and DPC) of medicines in AIFA Notes was EUR 5.5 billion, slightly up by 2.8% compared to 2022 (Table 2.7.1). This value is mainly attributable to the approved care regime (63.7%) and for a smaller share to direct and "on behalf" distribution (36.3%). Local expenditure was higher for medicines in Note 13 (lipid-lowering medicines) and Note 100 (antidiabetics), with absolute values of 981.6 and 953.6 million euro, respectively.

SECTION 3 - Consumption and expenditureby therapeutic class

In 2023, the NHS pharmaceutical expenditure, expressed as a per capita value, was 441.37 euros, with a 5.3% increase compared to the previous year (Table 3.1). This was entirely due to the increase in expenditure by public health facilities (+8.5%; 275.16 euros per capita, more than 62% of total expenditure) while expenditure on class A medicines under approved care regime remained stable (+0.3%; 166.22 euros per capita). Consumption remained at 1,322.9 DDD/1000 inhabitants per day, and was stable compared to 2022 (-0,1%), with consumption under approved care regime absorbing 85% of total doses (Table 3.2). Cardiovascular medicines represent the therapeutic category with the highest expenditure (52.25 euros per capita) and consumption (494.98 DDD) in the approved care regime, whereas, antineoplastic and immunomodulating agents as well as medicines for blood and blood forming organs show the highest expenditure (120.47 euros per capita) and consumption (54.70 DDD) among medicines purchased directly by public health facilities. Within the approved care regime, the active ingredients with the highest incidence on expenditure are atorvastatin (274.4 million), pantoprazole (265.5 million) and colecalciferol (198.0 million) (Table 3.11). Taking into account medicines purchased by public health facilities, the active ingredients with the highest incidence on expenditure are cancer drugs, such as pembrolizumab (456.5 million euros) and daratumumab (456.2 million euros) (Table 3.19). For each level I ATC, after presenting the overall data on expenditure, consumption and exposure, insights are given for the mostly prescribed therapeutic categories, including trends in consumption and expenditure, national and regional data and, where possible, indicators of exposure and of adherence and persistence to drug treatment in the Italian population are analysed. The assessment of adherence and persistence indicators was carried out using the flow data of the Tessera sanitaria for the following categories of pharmaceuticals: antidiabetics, anticoagulants, antiaggregants, lipid-lowering agents, antihypertensives, antidepressants, medicines for benign prostate hypertrophy, osteoporosis, and obstructive respiratory tract disorders (asthma COPD). The therapeutic category with the highest percentage of subjects with treatment coverage greater than or equal to 80% in the observed period is the treatment with medicines for osteoporosis (67.9%) followed, for the male population alone, by medicines for benign prostatic hypertrophy (64.8%) and finally by platelet aggregation inhibitors (62.0%). Conversely, the therapeutic categories with the highest percentages of subjects with treatment coverage lower than 40% of the observed period are the treatments with medicines for obstructive respiratory disorders (51.0%), antidepressants (27,5%) and antidiabetics (23.9%). As regards persistence, the therapeutic categories reaching the highest levels of persistence at 12 months are anticoagulants (67.0%), platelet aggregation inhibitors (54.2%) and antihypertensives (53.6%).

SECTION 4 - Monitoring registers and conditional reimbursability agreements

In the year 2023, 301 registers were active (at least 1 monitoring day), an increase of 6.4% compared to 2022 (Table 4.1.1). The number of registers activated in 2023 was 53, while the number of registers closed during the same period was 35, representing an increase of 18 new monitoring registers compared to 2022. It should be noted that, for ATC category A 'Gastrointestinal tract and metabolism', there is a much greater increase in the number of subjects treated than for the other categories, with patients started in 2023 almost three times as many as in 2022 (124,473 vs 43,518) (Table 4.1.2). Category B 'Blood and haemopoietic organs' remains the category with the highest number of patients included in the Monitoring Registers platform. Reimbursements paid by companies in the year 2023 as a result of the application of conditional reimbursability agreements, both for those managed through the Registries (i.e. the payment by result agreement) and those managed through the expenditure and consumption monitoring information flows (i.e. the caps on expenditure per product and the price/volume agreements) amounted to EUR 217.6 million, 72% of which was generated as a result of the application of the caps on expenditure and the price/volume agreements. SECTION 5 - New therapeutic entities and orphan drugs. The new therapeutic entities, selected from class A and H medicines marketed in the period 2014-2023, increased from 203 to 304 (incident and prevalent). There were 37 new therapeutic entities marketed as from 2023 (accidents) (Table 5.1.1 and Table 5.1.2) with an expenditure of EUR 184.3 million. Expenditure of new incident and prevalent therapeutic entities increased from about €5160,2 million in 2014 to about €9625,4 million in 2023; the incidence of expenditure of new therapeutic entities on total NHS expenditure also increased over the years, from a share of 25.9% in 2014 to 38.6% in 2023 (Table 5.1.2). The category ATC L 'Antineoplastic and immunomodulatory medicines' is not only the one with the highest number of new therapeutic entities, but also the one with the highest expenditure, increasing over the period 2014-2023 (from €2,621 million to €5,212 million, increasing by 99%,CAGR 2014-2023: +7,1%), the second category, ATC A, is also increasing from 2014 to 2023 (CAGR 2014-2023: +4.5%), reaching €704 million in 2023 (Table 5.1.3 and Figure 5.1.4). Orphan medicines are medicinal products used for the diagnosis, prevention and treatment of rare diseases. During 2023, the European Medicines Agency (EMA) granted the authorisation to a total of 12 new orphan medicines. As of 31 December 2023, out of a total of 155 orphan medicines authorised by the EMA, 146 were available in Italy of which 85 in class H (58.2%) and 25 in class A (17.1%). (Figure 5.2.1 and Figure 5.2.2) The expenditure for orphan medicines, including purchase by public health facilities and the provision under the approved care regime, showed for 2023 an increase of 12.5% compared to 2022, reaching a value of €2.23 billion, corresponding to 8.5% of pharmaceutical expenditure borne by the NHS (Table 5.2.1). The therapeutic category that ranks first in both expenditure and consumption is antineoplastic and immunomodulatory medicines (47.6% and 51.2%, respectively) (Figure 5.2.3).

The highest incidence of expenditure concerns drugs used in lymphomas and myelomas as well as in genetic diseases (32.8% and 25.4% respectively), reconfirming the same trend as last year. As regards the consumption, the medicines used in lymphomas, myelomas and other onco-haematological diseases top the list, followed by those for genetic diseases and pulmonary arterial hypertension, with significantly lower values (Table and Figure 5.2.9). SECTION 6 - Environmental Impact of Medicines. This section, dedicated to analysing the potential environmental impact of a number of high-use or highly toxic active ingredients,

aims to provide an informative overview and raise awareness of the emerging issue of the impact of medicines on the environment. The environmental impact was assessed for 109 active ingredients, selected on the basis of criteria of environmental toxicity, included in the Watch List programme for monitoring European waters, and highest consumption in Italy. The active substances estimated high risk are 10, while those at moderate risk sono 25. Despite low environmental toxicity, amoxicillin, diclofenac and ibuprofen showed a high environmental risk due to their high use (Figure 6.1). With regard to the analysis by geographical area, differences in use, and thus environmental risk, were observed between North, Centre and South, suggesting that differences in territorial consumption may lead to different environmental risks in different geographical areas.

Section 1

General characteristics of medicines use in Italy

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1.1 General data on expenditure and consumption

In 2023 the overall pharmaceutical expenditure (both public and private) amounted to 36.2 billion euros, with an increase of 6.1% compared to 2022. This expenditure represents an important part of healthcare expenditure, accounting for 1.9% of the gross domestic product (GDP) at current prices. Gross public pharmaceutical expenditure, equal to 24.9 billion euros, accounts for 68.7% of total pharmaceutical expenditure and for 19.0% of public health expenditure, it has increased compared to 2022 (+5.7%). The most impacting item is referred to local health authorities, hospitals, healthcare residences and prisons (44.8% of public health expenditure). Private expenditure, including citizen cost-sharing, amounts to 10.7 billion euros, and mainly concern class C prescription medicines (36.0% of private expenditure). The increase in total pharmaceutical expenditure recorded in comparison with 2022 is mainly due to the trend in expenditure on medicines supplied by the local health authorities, hospitals, healthcare residences and prisons (+8.5%), accounting for 30.8% of total expenditure. An increase was also recorded for class A medicines supplied in direct distribution (+10.0%), drugs used for self-medication (+10.5%) and class Class C medicines with prescription (+9.0%) Net expenditure under approved care regime is stable (+0.3%), whereas a reduction in expenditure on imported medicines (-3.4%) continues to be recorded and expenditure on non-tariff drugs is rising sharply (+17.8%) (Table 1.1.1). Similar trends are found when looking at the period 2020-2023 (Figure 1.1.2). As regards public expenditure, € 2,228 million refer to expenditure that does not contribute to the pharmaceutical expenditure ceiling, which is mainly related to class C medicines, including C-NN (€ 783 million), vaccines (€ 711 million) and non-tariff drugs (€ 661 million) (Figure 1.1.1). Table 1.1.2 shows the composition of the total regional pharmaceutical expenditure by distribution channel and reimbursement regime. In Central and Southern Regions, a higher incidence of gross expenditure under approved care regime and of medicines purchased by public health facilities is observed, whereas expenditure for self-medication medicines and class C medicines requiring a medical prescription is smaller compared to Northern Regions. The share of class A medicines purchased privately by citizens is higher in the Centre than in the South and in the North (Table 1.1.2 and Figure 1.1.2).

Figure 1.1.4 shows that public territorial expenditure has decreased over the period 2017-2020, whereas slight increases have been recorded over the last two years; conversely, hospital expenditure as well as expenditure for class A medicines purchased privately by citizens are constantly growing. Figure 1.1.5 shows the comparison between the National Healthcare Fund (NHF), current public health expenditure, public pharmaceutical expenditure, pharmaceutical expenditure borne by the NHS calculated for the purpose of monitoring compliance with the pharmaceutical ceilings (hereafter, NHS pharmaceutical expenditure) and the planned funding for pharmaceutical care, which is the sum of the pharmaceutical expenditure ceilings as defined by the various regulations (including funds for innovative medicines), over the period 2014-2023. To cope with the emergency situation related to the spread of the SARS-COV-2 virus, there was a 6.1% increase in healthcare expenditure in 2020 compared to 2019, whereas until 2019 the rates of change had not exceeded 2%. Health expenditure was also on the rise in the next two years, increasing by 4.0% in 2021 and 3.2% in 2022 compared to the previous year. In 2023, healthcare expenditure amounted to EUR 131,119 million, with a rate of decrease of 0.4% compared to 2022. This development is driven by two important components of healthcare expenditure, which are employee income

(EUR 40,073 million) and intermediate consumption expenditure (EUR 44,356 million). The employee income component showed a decrease of 1.8% compared to 2022. This decrease is mainly due to the failure to grant, in 2023, the arrears resulting from the signing, in the previous year, of the contract for non-managerial staff covering the three-year period 2019-2021. Expenditure on intermediate consumption, including the purchase of medicines, was stable (+0.3%) compared to 2022. This was due to the increase in expenditure on pharmaceutical products by 13.1%, whereas non-pharmaceutical intermediate consumption expenditure decreased by 5%. Expected healthcare expenditure in 2024 is EUR 138,776 million, with a growth rate of 5.8%; for the employee income component, growth of 9.7% is estimated due to contractual renewals, and for the intermediate consumption component, growth of 2.9% is estimated compared to 2023, mainly attributable to pharmaceuticals, for which growth of 7.1% is estimated. The cross-time comparison between the NHF and health expenditure shows that the greatest differences between the two values were found in 2022, the year in which the NHF was EUR 5,694 million lower than health expenditure.[1]

Comparing, on the other hand, the financing of pharmaceutical expenditure and NHS pharmaceutical expenditure, we see that the greatest difference was found in 2016, then decreased sharply in 2017 and increased again in 2018, remaining stable in the following years. In 2023, an excess of NHS expenditure over funding of 10.8% was observed, higher than the average for the period 2014-2023, which was 8%. However, it should be stressed that this figure could deviate from the reference value, especially for direct purchases, given the presence of separate ceilings for approved care regime and purchases from public facilities. In addition, it is possible to compare the trend of NHS pharmaceutical expenditure and public pharmaceutical expenditure that includes other components of pharmaceutical care charged to the NHS that do not fall within the definition of the ceilings (class C and C-non-negotiated medicines purchased by public health facilities, foreign medicines, vaccines, galenic preparations, and extra fee drugs). Public pharmaceutical expenditure in 2023 amounted to EUR 24.9 billion compared to EUR 22.6 billion of NHS expenditure for the purposes of monitoring pharmaceutical expenditure ceilings; both show a slight increase compared to 2022, by 5.7% and 5.5% respectively.L'incidenza della spesa sanitaria rispetto al PIL ha registrato un picco nel 2020 pari al 7,4%, per effetto sia di un incremento della spesa sanitaria del 6% sia di una riduzione del PIL del 7% circa (Figura 1.1.6). A partire dal 2021 l'incidenza si riduce fino ad arrivare ad una previsione per il 2026 del 6,3%. Sia l'incidenza della spesa farmaceutica pubblica sia quella della spesa farmaceutica ai fini del monitoraggio rimangono pressoché stabili nel periodo 2019-2023, con un lieve incremento nel 2020. L'incidenza del finanziamento della spesa farmaceutica sul PIL mostra un andamento stabile nel periodo 2023-2026, pari circa all'1%.

The incidence of health expenditure in relation to GDP peaked in 2020 at 7.4%, due to both an increase in health expenditure of 6% and a reduction in GDP of about 7% (Figure 1.1.6). From 2021 onwards, the incidence decreases to a forecast for 2026 of 6.3%. Both the incidence of public pharmaceutical expenditure and of pharmaceutical expenditure for monitoring purposes remain almost stable in the period 2019-2023, with a slight increase in 2020. The impact of pharmaceutical expenditure financing on GDP shows a stable trend over the period 2023-2026, amounting to about 1%.

[1] Financial Document 2024 Section II Public Finances Analysis and Trends
https://www.rgs.mef.gov.it/_Documenti/VERSIONE-I/Attivit—i/Contabilit_e_finanza_pubblica/DEF/2024/Sez-II-AnalisiETendenzeDellaFinanzaPubblica.pdf

The incidence of public pharmaceutical expenditure over GDP is higher in Southern Regions (2.3%) compared to the Centre (1.4%) and the North (1.1%) of Italy, with a national percentage of 1.4%. The incidence of public pharmaceutical expenditure over GDP in Calabria (2.7%) is more than 3 times higher than in the Autonomous Province (AP) of Bolzano (0.7%; Table 1.1.3).

By analysing the correlation between regional per capita income and pharmaceutical expenditure borne by the NHS, Regions with lower per capita income appear to have higher pharmaceutical expenditure (Figure 1.1.7). Analysing, instead, the correlation between regional per capita income and private per capita expenditure, no real correlation between the two variables emerges. Moreover, it can be seen that Campania, among the Regions with the lowest income, has the highest private expenditure, and, on the contrary, the Province of Bolzano, the one with the highest income, records after Molise, Basilicata and Friuli Venezia Giulia the lowest expenditure (Figure 1.1.8).

With regard to consumption, an upward trend can be observed for class A-NHS pharmaceuticals supplied under the approved care regime until 2020, when a 4% reduction in consumption was recorded with respect to 2019 (1,096.0 DDD/1000 inhabitants per day in 2020 compared to 1,140.7 in 2019), probably attributable to the effect of the pandemic, while in 2021 and 2022 an increase was observed that brought consumption levels back to pre-pandemic levels (1,131 DDD in 2021 and 1,141 in 2022). In 2023, consumption was reported to be stable (-0.8%). Drugs purchased by public health facilities show an upward trend in consumption from 2006 to 2012, which becomes stable in the following years, and then increases again in 2022 and 2023, by 6.7% and 4.8%, respectively, over the previous year. Regarding consumption of class C medicines with prescription, no significant changes were recorded in the period 2004-2020. In the years 2020-2023, an upward trend is recorded with a change of 4% (Figure 1.1.9).

Table 1.1.1 Composition of pharmaceutical expenditure: 2023-2022 comparison (Table and Figure)

	Expenditure *(million)*	Δ % 23-22	%°	%°°
Net expenditure under approved care regime^	7,700.7	0.3	21.3	31.0
of which oxygen and vaccines	73.9	-13.3	0.2	0.3
Direct distribution Class A	2,793.3	10.0	7.7	11.2
Class A - distribution "on behalf"	2,504.0	4.4	6.9	10.1
Local health authorities, Hospitals, Healthcare residences and prisons*	11,149.7	8.5	30.8	44.8
of which oxygen and vaccines	966.4	8.9	2.7	3.9
Import	40.3	-3.4	0.1	0.2
Galenic preparations	32.4	5.1	0.1	0.1
Extra DRG	660.6	17.8	1.8	2.7
Public expenditure	**24,881.0**	**5.7**	**68.7**	**100.0**
Fixed co-payment (ticket)	424.4	1.7	1.2	4.0
Reference price share	1,056.8	-2.5	2.9	9.9
To private	2,021.3	5.9	5.6	19.0
C with prescription	3,839.3	9.0	10.6	36.0
OTC	2,940.6	10.5	8.1	27.6
Shops	367.6	12.7	1.0	3.5
Private expenditure	**10,650.0**	**7.4**	**29.4**	**100.0**
Discounts	690.3	-2.0	1.9	
Total	**36,221.3**	**6.1**	**100.0**	

^ including expenditure for class C reimbursed medicines (17 million euros)
* Does not include expenditure for class A medicines under direct and "on behalf" distribution
° calculated on the total
°° calculated on subtotals (public and private expenditure)

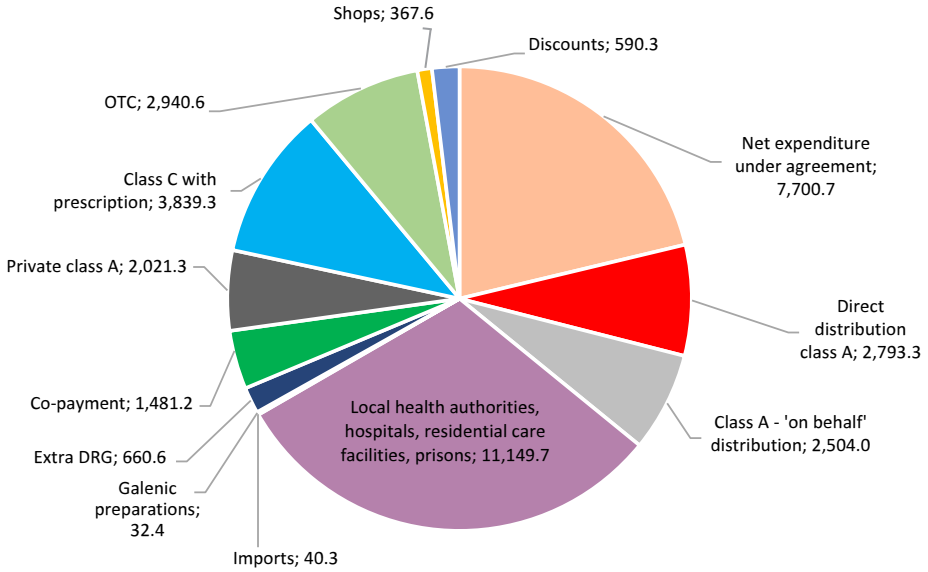


Figure 1.1.1 Breakdown of public pharmaceutical expenditure and public pharmaceutical expenditure not related to the ceiling of pharmaceutical expenditure (2023)

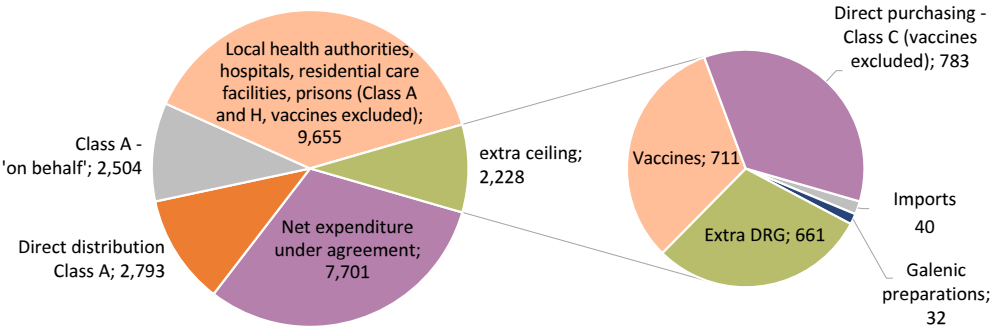


Figure 1.1.2 2023-2020 % change in pharmaceutical expenditure components

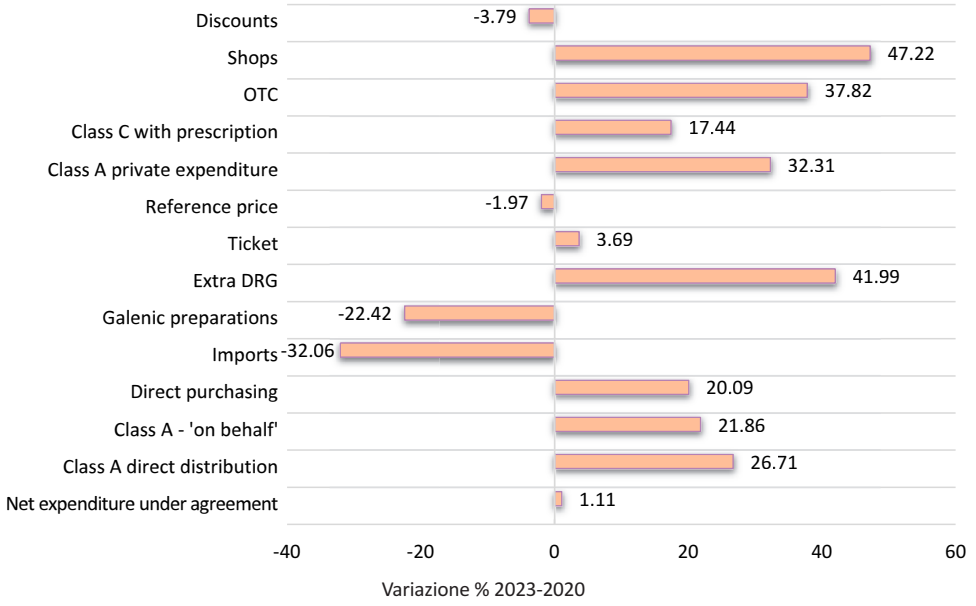


Table 1.1.2 Composition of total pharmaceutical expenditure by Region (year 2023)

Region	Expenditure under approved care regime lorda1		Classe A private		Classe C with prescription		Self-medication pharmaceuticals (public and private pharmacies)		Shops commerciali		Public health facilities		Total
	€°	%*	€°	%*	€°	%*	€°	%*	€°	%*	€°	%	€°
Piedmont	624	24.3	175	6.8	303	11.8	227	8.8	25	1.0	1,210	47.2	2,564
Valle d'Aosta	17	23.8	9	13.5	8	10.9	8	10.9	1	0.8	28	40.0	70
Lombardy	1,859	32.0	272	4.7	681	11.7	517	8.9	81	1.4	2,403	41.3	5,813
Province of Bolzano	57	21.9	12	4.4	26	10.0	30	11.4	0	0.2	136	52.0	262
Province of Trento	77	28.2	9	3.4	28	10.4	31	11.4	2	0.7	125	45.8	273
Veneto	652	24.7	126	4.8	289	11.0	253	9.6	23	0.9	1,294	49.1	2,636
Friuli VG	184	25.7	21	3.0	69	9.7	61	8.5	6	0.8	376	52.4	717
Liguria	240	23.4	58	5.7	130	12.8	100	9.7	9	0.9	486	47.5	1,023
Emilia R.	595	23.1	87	3.4	281	10.9	227	8.8	34	1.3	1,358	52.6	2,582
Tuscany	520	23.7	100	4.6	278	12.6	205	9.3	30	1.4	1,064	48.4	2,198
Umbria	134	25.0	28	5.2	63	11.8	40	7.4	5	0.9	266	49.6	535
Marche	251	26.9	42	4.5	99	10.6	71	7.6	7	0.7	464	49.7	933
Lazio	1,032	28.6	323	8.9	404	11.2	313	8.7	20	0.6	1,521	42.1	3,613
Abruzzo	239	29.1	28	3.5	76	9.3	59	7.2	7	0.9	410	50.0	820
Molise	52	31.0	5	3.1	16	9.4	10	6.3	1	0.8	83	49.5	167
Campania	1,035	28.9	153	4.3	377	10.5	289	8.1	48	1.3	1,674	46.8	3,576
Puglia	724	30.7	91	3.9	222	9.4	167	7.1	21	0.9	1,131	48.0	2,355
Basilicata	107	31.6	20	5.8	27	7.9	21	6.3	4	1.3	160	47.1	339
Calabria	354	30.2	79	6.7	109	9.3	73	6.3	11	1.0	545	46.5	1,172
Sicily	831	31.0	192	7.2	247	9.2	169	6.3	15	0.6	1,228	45.8	2,683
Sardinia	289	24.9	192	16.6	105	9.1	69	6.0	16	1.4	486	42.0	1,158
Italy	**9,872**	**27.8**	**2,021**	**5.7**	**3,839**	**10.8**	**2,941**	**8.3**	**368**	**1.0**	**16,447**	**46.3**	**35,488**
North	4,305	27.0	768	4.8	1,816	11.4	1,453	9.1	182	1.1	7,416	46.5	15,940
Centre	1,937	26.6	493	6.8	844	11.6	629	8.6	61	0.8	3,314	45.5	7,278
South and Islands	3,630	29.6	760	6.2	1,179	9.6	858	7.0	124	1.0	5,717	46.6	12,270

[1] The expenditure refers to class A-NHS medicines and class C medicines reimbursed by the NHS. Expenditure on reimbursed class C medicines is EUR 17 million.

° Million euros

* Calculated on overall regional expenditure

Figure 1.1.3 Regional variability in expenditure and consumption under approved care regime, direct purchasing and private purchasing (year 2023)

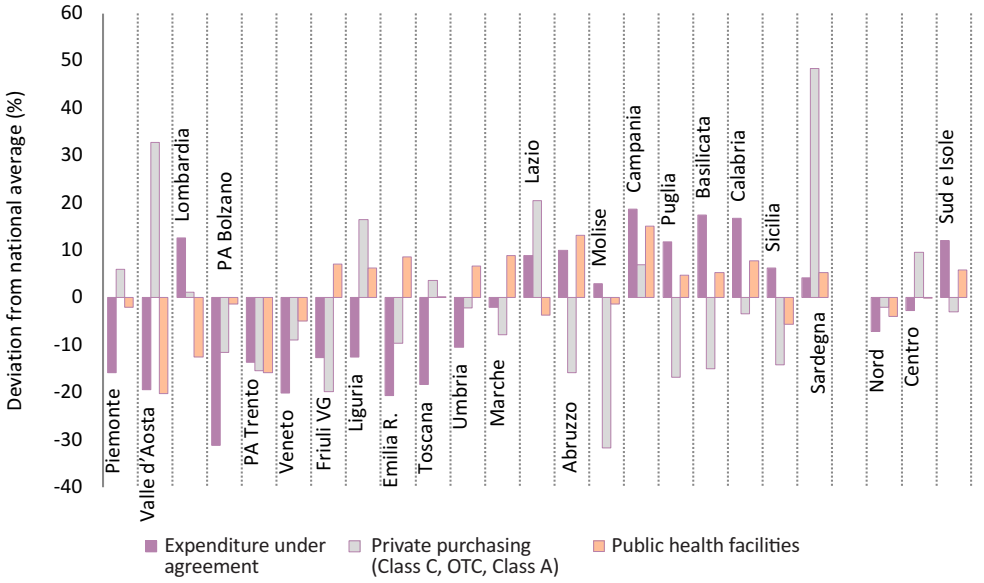
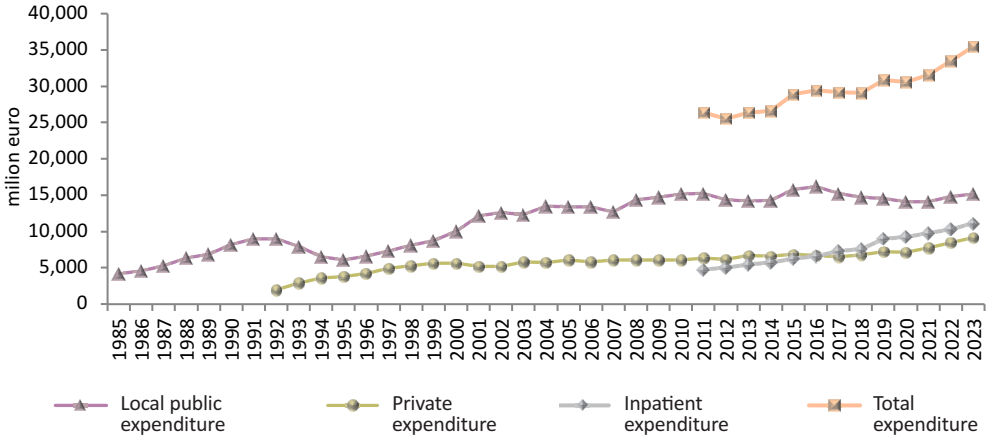


Figure 1.1.4 Pharmaceutical expenditure in the period 1985-2023 (Figure and Table)



Year	Expenditure under approved care regime gross expenditure*	Direct and "on behalf" distribution of class A medicines	Public local expenditure^ (1)	Private expenditure (2)	Public health facilities	Hospital expenditure^^ (3)	Total Expenditure (1+2+3)
1995	6,087		6,087	3,785			
1996	6,638		6,638	4,216			
1997	7,321		7,321	4,919			
1998	8,113		8,113	5,332			
1999	8,760		8,760	5,640			
2000	10,041		10,041	5,684			
2001	12,154		12,154	5,232			
2002	12,644		12,644	5,204			
2003	12,354		12,354	5,849			
2004	13,491		13,491	5,694			
2005	13,408		13,408	6,046			
2006	13,440		13,440	5,814			
2007	12,712		12,712	6,046			
2008	12,724	1,651	14,375	6,088			
2009	12,928	1,767	14,695	6,122			
2010	12,985	2,144	15,129	6,046			
2011	12,387	2,832	15,219	6,346	7,606	4,774	26,339
2012	11,488	2,837	14,325	6,152	7,892	5,055	25,532
2013	11,226	3,003	14,229	6,732	8,425	5,421	26,383
2014	10,988	3,250	14,238	6,648	8,994	5,744	26,630
2015	10,863	4,921	15,784	6,859	11,203	6,282	28,926
2016	10,638	5,556	16,194	6,681	12,143	6,587	29,461
2017	10,499	4,792	15,291	6,526	12,124	7,332	29,149
2018	10,141	4,620	14,761	6,771	12,214	7,594	29,126
2019	10,089	4,481	14,570	7,261	13,461	8,980	30,811
2020	9,820	4,259	14,080	7,180	13,544	9,284	30,544
2021	9,772	4,295	14,067	7,734	14,089	9,794	31,595
2022	9,881	4,940	14,821	8,418	15,221	10,281	33,519
2023	**9,872**	**5,297**	**15,170**	**9,169**	**16,447**	**11,150**	**35,488**

^ inclusive of the reimbursed pharmaceutical expense (gross of the pay-back and discount) and of the direct distribution and *per conto* of the class A, including the share paid by the citizen;

^^ expenditure on public health facilities (gross of pay-back) net of direct distribution and *per conto* of class A;

Figure 1.1.5 Trend of the National Health Fund, health expenditure, pharmaceutical expenditure and pharmaceutical expenditure borne by the NHS over the period 2014-2023

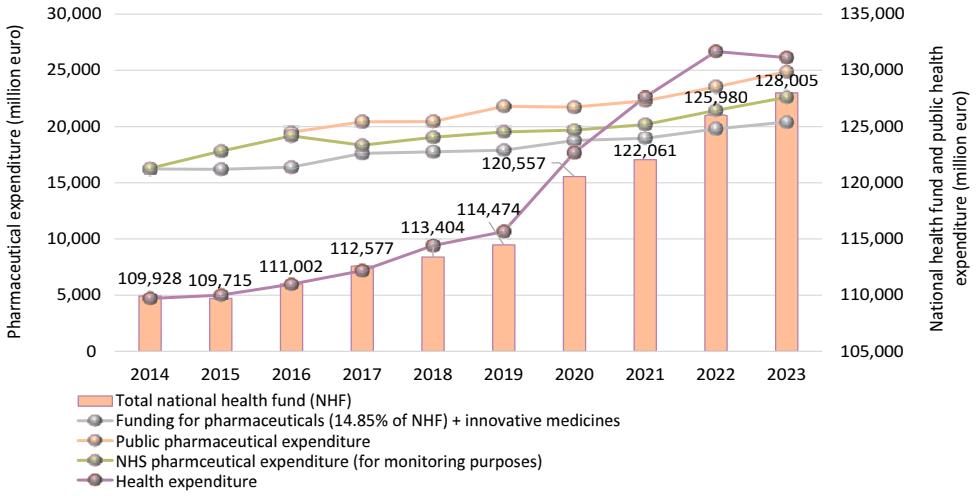
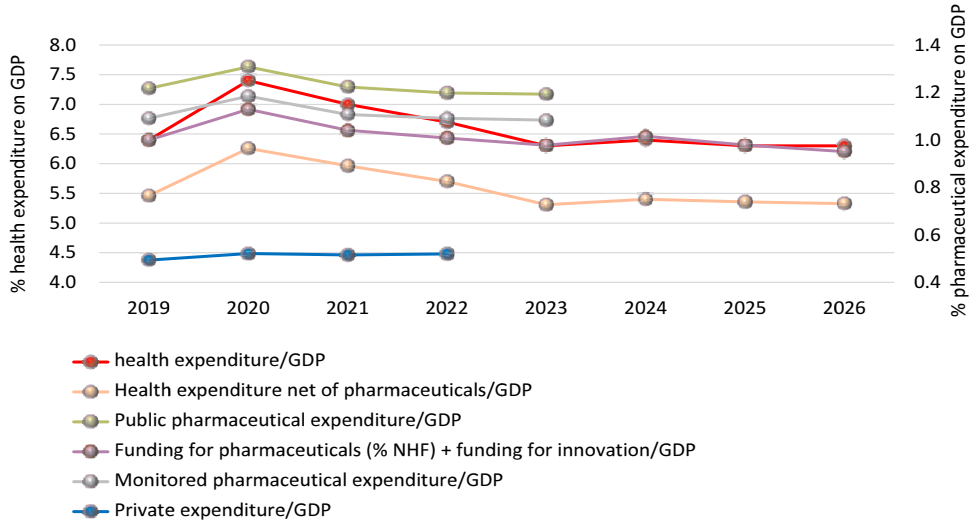


Figure 1.1.6 Trend in the ratio of healthcare expenditure to GDP and pharmaceutical expenditure to GDP (2019-2026)



Source: Source: For healthcare expenditure 2014-2018 AIFA processing of data from: MEF-Monitoraggio della spesa sanitaria-Rapporto N.9. For the years 2019-2026 the data published in DEF 2024 was used.

For national healthcare fund (FSN) AIFA processing of data from: MEF-Monitoraggio della spesa sanitaria-Rapporto N.8

NHS pharmaceutical expenditure for the purposes of monitoring includes: net expenditure under approved care regime, that is, net of discounts paid by pharmacies, of the 1.83% payback paid to the regions gross of regional co-payments; of the expenditure for direct purchases of band A and H medicines net of vaccines and paybacks, including expenditure on innovative medicines.

Public pharmaceutical expenditure includes net contracted expenditure, purchases by public health facilities including oxygen and vaccines, class C and C-NN medicines, medicines imported from abroad, galenic preparations and extra tariff expenditure.

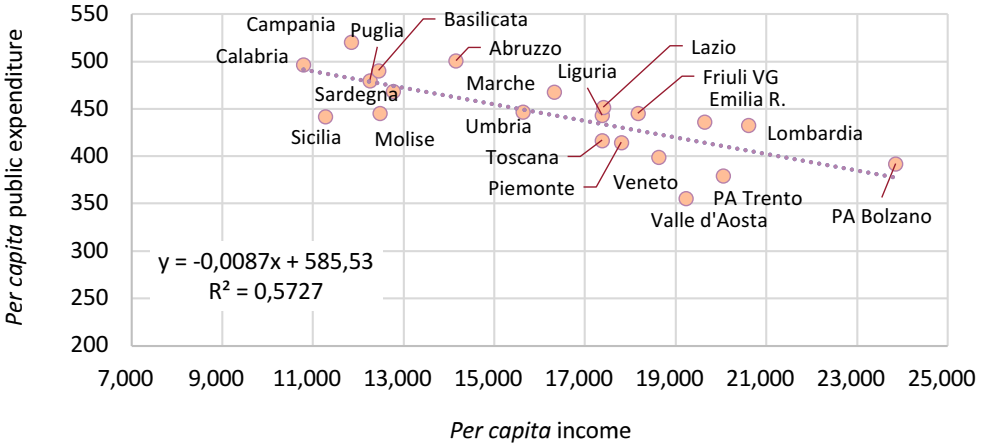
Table 1.1.3 Regional incidence of public pharmaceutical expenditure^ over GDP*: period 2017-2023

Region	Incidence (%)						
	2017	2018	2019	2020	2021	2022	2023
Piedmont	1.15	1.11	1.18	1.27	1.26	1.25	1.32
Valle d'Aosta	0.77	0.76	0.80	0.86	0.84	0.86	0.94
Lombardy	0.90	0.87	0.93	1.00	1.01	0.97	1.02
Province of Bolzano	0.64	0.61	0.65	0.71	0.69	0.69	0.75
Province of Trento	0.80	0.78	0.82	0.89	0.89	0.88	0.93
Veneto	1.00	0.96	1.01	1.11	1.13	1.12	1.16
Friuli VG	1.26	1.19	1.27	1.36	1.31	1.26	1.38
Liguria	1.23	1.24	1.25	1.36	1.38	1.39	1.46
Emilia R.	0.99	0.98	1.01	1.08	1.15	1.11	1.16
Tuscany	1.25	1.17	1.21	1.34	1.30	1.27	1.34
Umbria	1.60	1.59	1.64	1.79	1.84	1.71	1.73
Marche	1.53	1.47	1.52	1.64	1.63	1.61	1.66
Lazio	1.16	1.14	1.18	1.25	1.26	1.23	1.29
Abruzzo	1.66	1.68	1.71	1.85	1.86	1.85	1.95
Molise	1.84	1.80	1.94	2.07	1.98	1.96	2.04
Campania	2.16	2.11	2.25	2.38	2.37	2.31	2.43
Puglia	2.38	2.30	2.32	2.45	2.45	2.31	2.37
Basilicata	1.91	1.80	1.91	2.04	2.08	1.95	2.03
Calabria	2.40	2.39	2.46	2.56	2.62	2.57	2.67
Sicily	2.08	2.02	2.12	2.22	2.25	2.12	2.25
Sardinia	2.14	1.93	1.95	2.13	2.13	2.07	2.20
Italy	**1.30**	**1.26**	**1.32**	**1.41**	**1.42**	**1.38**	**1.44**
North	0.99	0.96	1.01	1.09	1.11	1.08	1.13
Centre	1.26	1.21	1.25	1.35	1.35	1.31	1.37
South and Islands	2.15	2.09	2.17	2.29	2.30	2.21	2.32

^ Inclusive of pharmaceutical expenditure under approved care regime (gross of pay-back and discount) and expenditure for pharmaceuticals purchased by public health facilities

*Production-side gross domestic product, at market prices-current prices, extracted from Istat (National Institute of Statistics)

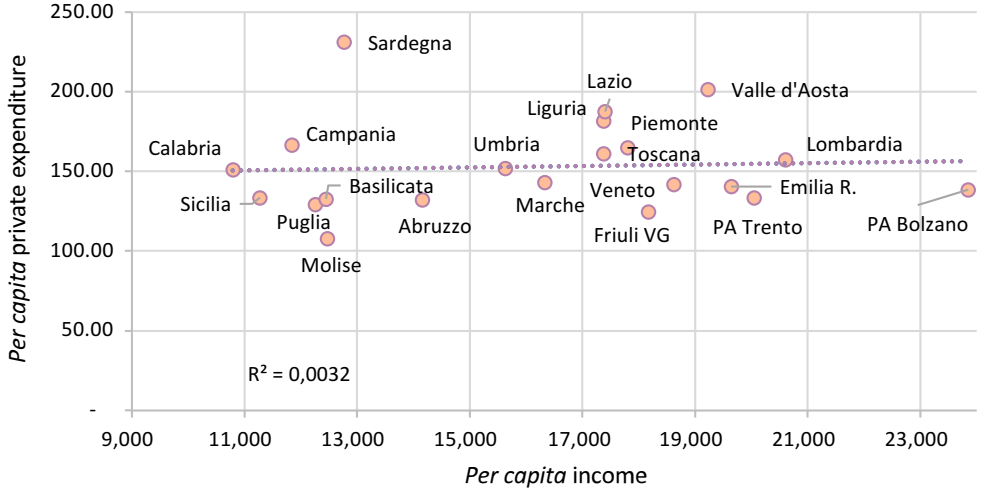
Figure 1.1.7 Relationship between per capita public pharmaceutical expenditure^ and per capita regional income* in 2023



^Inclusive of pharmaceutical expenditure under approved care regime (gross of pay-back and discount) and expenditure for pharmaceuticals purchased by public health facilities

*Source: Ministry of Economy and Finance (MEF)-Department of Finance-Statistical Analysis

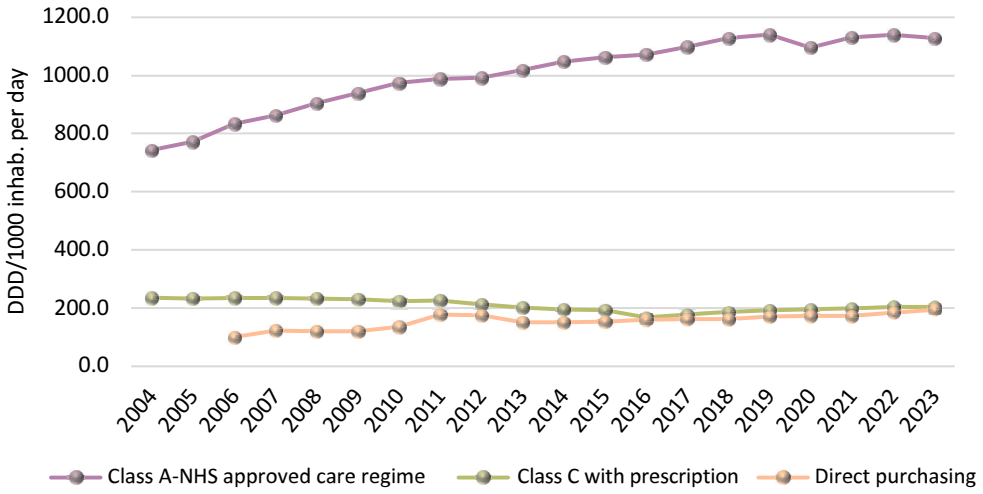
Figure 1.1.8 Relationship between per capita private pharmaceutical expenditure^ and per capita regional income* in 2023



^Including the private purchase of Class A drugs, prescription C drugs, and OTCs

*Source: Ministry of Economy and Finance (MEF)-Department of Finance-Statistical Analysis

Figure 1.1.9 Consumption (DDD/1000 inhabitants per day) in the period 2004-2023 (Figure and Table)



Year	DDD/1000 inhabitants per day					
	Approved care regime Class A-NHS	Δ % vs previous year	Class C with prescription	Δ % vs previous year	Direct purchases	Δ % vs previous year
2004	743.6		235.9			
2005	771.9	3.8	231.7	-1.8		
2006	833.0	7.9	235.4	1.6	100.6	
2007	861.6	3.4	235.0	-0.2	121.7	21.0
2008	904.9	5.0	231.9	-1.3	120.4	-1.1
2009	939.4	3.8	229.6	-1.0	120.9	0.4
2010	973.9	3.7	223.8	-2.5	136.5	12.9
2011	987.0	1.3	225.7	0.8	178.8	31.0
2012	992.3	0.5	212.2	-6.0	175.1	-2.1
2013	1019.2	2.7	202.4	-4.6	150.9	-13.8
2014	1047.9	2.8	195.8	-3.3	151.2	0.2
2015	1062.4	1.4	193.0	-1.4	154.3	2.1
2016	1071.5	0.9	168.2	-12.8	160.0	3.7
2017	1098.0	2.5	178.8	6.3	163.1	1.9
2018	1127.9	2.7	186.8	4.5	162.6	-0.3
2019	1140.7	1.1	192.1	2.9	171.5	5.5
2020	1096.0	-3.9	195.9	1.9	173.0	0.9
2021	1130.8	3.2	200.3	2.2	173.7	0.4
2022	1140.6	0.9	203.9	1.8	185.4	6.7
2023	**1128.1**	**-0.8**	**204.2**	**0.1**	**194.4**	**4.8**

1.2 Outpatient pharmaceutical expenditure and consumption

In 2023 the overall outpatient pharmaceutical expenditure, both public and private, amounted to 23,648 million euros, with an increase of 4.9% compared to the previous year (Table 1.2.1). The NHS outpatient pharmaceutical expenditure includes medicines supplied under the approved care regime (7,701 million) and class A medicines supplied through direct and "on behalf" distribution channels (2,793 million and 2,504 million euro respectively) (Table 1.2.1). Public outpatient expenditure amounted to 12,998 million euros (221 euros per capita), which, compared to 2022, showed an increasing trend (+3.0%), in the face of a slight increase in expenditure under approved care regime (+0.3%), a strong increase in expenditure on class A medicines supplied in direct distribution (+10.0%) and, although to a lesser extent, class A medicines supplied "on behalf" (+4.4%). In 2023 public local expenditure represented 55.0% of the total local pharmaceutical expenditure; this incidence over the last 6 years has shown a decreasing trend due to the increase in private expenditure.

The expenditure borne by the citizen (Table 1.2.1 and Figure 1.2.1), comprising expenditure for citizen cost-sharing (regional co-payments and the difference between the price of the expired patent medicine and the corresponding reference price), expenditure for class A medicines purchased privately and expenditure for class C medicines amounted to €10,650 million, with an increase of 7.4% compared to 2022. This trend was influenced by the increase in expenditure on self-medication medicines (+10.5%), including medicines supplied in shops (+12.7%), and spending on class C prescription drugs (+9,0%), while private purchases of class A drugs showed a smaller increase (+5.9%). There is also a slight decrease in expenditure for citizen cost-sharing (-1.3%) with a value of €1,481 million (about €25.0 per capita) and an incidence on gross pharmaceutical expenditure under approved care regime of 15.0%. Compared to 2022, the change in expenditure related to total citizen cost-sharing (-1.3%) was mainly driven by the reduction in citizen cost-sharing for the share exceeding the reference price of patent expired medicines (-2,5%), whereas expenditure related to the per-prescription/package cost-sharing recorded a slight increase (+1.7%). The incidence of citizen cost-sharing on gross expenditure, after increasing in 2018 compared to 2017, showed a decreasing trend in the years 2018-2020 and then remained stable at about 15% in the last three years. The incidence of citizen cost-sharing for the share exceeding the reference price remained stable in the years 2019-2023, at around 11% (Figura 1.2.2).

During 2023, an average of 1128.1 daily doses per 1000 inhabitants (hereinafter DDD) of NHS reimbursed class A medicines were consumed, with a stable trend compared to 2022 (-0.8%) (Table 1.2.2). The average cost per day of therapy, EUR 0.40 in 2023, is stable compared to the previous year. As for the purchase of class C drugs, prescription drug packages remain stable (-0.2%), although spending is increasing (+9.0%), probably due to an increase in average prices or the purchase of higher-cost drugs. Consistent with spending, packages of self-medication drugs (+5.0%), and those dispensed by shops (+4.6%) increased sharply (Tables 1.2.1 and 1.2.2).

At national level, net expenditure amounted to €7,701 million (Table 1.2.3), with the highest levels, in absolute terms, recorded in Lombardy (€1,439.8 million), Lazio (€798.4 million) and Campania (€756.3 million). The Regions with the highest expenditure in absolute terms for fixed co-payments (ticket) are Lombardy (€131.0 million), Campania (€78.1 million) and Veneto (€58.9 million). The major increases in the fixed co-payment compared to the previous year were recorded in Tuscany (+13.6%), Umbria (+11.8%), Emilia Romagna (+11.3%)

and Piedmont (+11.2%), while Calabria (-7.7%), Basilicata (-7.6%), Abruzzo (-6.3%), Sardinia (-3.8%) and Latium (-2.9%) recorded decreases in the fixed co-payment. With regard to citizen cost-sharing for the portion exceeding the reference price, Lazio (€ 140.0 million), Lombardy (€ 135.0 million), Campania (€ 127.5 million) and Sicily (€ 108.6 million) show the highest expenditure in absolute terms. All regions observed a decrease from the previous year, with the largest changes in Umbria (-6.2%) and Tuscany (-5.9%).

The region with the highest per capita gross expenditure for A-NHS medicines was Campania with 196.1 euros per capita, while the lowest value was found in the Province of Bolzano (116.3 euros per capita), with a 69% difference between the two regions (Table 1.2.4). In terms of consumption, the Region that shows the highest levels is Basilicata with 1,289.5 DDD/1000 inhabitants per day, while the lowest consumption is found in the Province of Bolzano (861.3 DDD/1000 inhabitants per day). In general, on average, Southern Regions consume and spend more than Northern and Central Regions as regards medicines provided under approved care regime. Analyzing the trend in spending and consumption compared to the previous year, it can be seen that the North (+0.4% in spending and +0.0% in consumption) shows a stable trend compared to the Central and Southern Regions, which show slightly decreasing values of consumption and spending. The out-of-pocket expenditure for self-medication drugs, Class C with prescription and Class A, was 155.8 euros per capita at national level. Some variability across Italian Regions emerges, with Campania registering the highest value with 231.4 euros per capita and Molise registering the minimum value (107.9 euros) (Table 1.2.4). Contrary to what was found for class A medicines reimbursed by the NHS, Regions in the centre of Italy showed higher private expenditure than Northern and Southern Regions. The Center and the South show the largest increase in terms of spending compared to the previous year (+13.5% and +12.2% respectively), well above the Italian average (+9.2%); the North shows a more moderate increase (+5.3%) both compared to the Italian average and to other geographical areas.

An analysis of the relationship between average cost and consumption under approved care regime (Table and Figure 1.2.5) shows that Campania, Basilicata, Puglia, Calabria, Lazio, Abruzzo and Sicily are the regions with a consumption and an average cost per DDD higher than the national average. Conversely, Tuscany,the Province of Trento, Friuli Venezia Giulia, Veneto, Piedmont, Valle d'Aosta and the Province of Bolzano are those with the lowest consumption and average cost compared to the national average.

While gross spending at the national level was stable in 2023 compared to the previous year, there were heterogeneous trends among the regions, with Sardinia (+2.2%), Marche (+2.1%) and Basilicata (+2.0%) observing the largest increases, while Umbria (-4.7%) and Tuscany (-1.7%) showed the largest reductions (Table 1.2.6). The main components of the variation in gross pharmaceutical expenditure under approved care regime (i.e. quantity, prices and mix effect) (Figure 1.2.3 and Table 1.2.6) show, with respect to the previous year, a reduction in the consumption of pharmaceuticals requiring prescription (-1.3% in terms of DDD), a slight decrease in average prices (-1.4%), linked in part to an increasing use of patent-expired products, and finally to the prescription of more expensive products (mix effect: +2.8%). In contrast to 2022, 2023 shows an increase of the average DDD cost (+1.4%). Against these national average values, regional variability is very broad: change in prices compared to the previous year ranges between -5.5% in Valle d'Aosta to -1.4% in Emilia Romagna. The mix effect varies between +2.2% in Lombardy to +6.3% in Valle d'Aosta. The variation in consumption ranges between -4.6% in Umbria and +1.5% in the Province of Bolzano. Compared to

2022, there is also wide variability in the change of the average DDD cost, ranging from +2.2% in Sardinia to -1.2% in the Province of Bolzano.

Table 1.2.7 shows data on class A local expenditure (approved care regime and direct and "on behalf" distribution) and private expenditure (class A, class C, self-medication). Valle d'Aosta has the lowest territorial public spending (147.4 euros per capita), while Campania, Calabria and Lazio have the highest territorial public spending (254.2, 242.8 and 242.0 euros per capita, respectively). Considering also private expenditure, the Province of Bolzano and Lazio are, respectively, the regions with the lowest and highest level of expenditure (287.0 and 429.6 euros per capita) (Table and Figure 1.2.7).

Table 1.2.1 Public and private local pharmaceutical expenditure: comparison 2017-2023

		2017 (million)	2018 (million)	2019 (million)	2020 (million)	2021 (million)	2022 (million)	2023 (million)	Δ % 18-17	Δ % 19-18	Δ % 20-19	Δ % 21-20	Δ % 22-21	Δ % 23-22
1	**Gross outpatient NHS expenditure**	**10,499**	**10,141**	**10,089**	**9,820**	**9,772**	**9,881**	**9,872**	**-3.4**	**-0.5**	**-2.7**	**-0.5**	**1.1**	**-0.1**
2	Citizen cost-sharing	1,549	1,608	1,582	1,487	1,481	1,501	1,481	3.8	-1.6	-6.0	-0.4	1.4	-1.3
3	Fixed co-payment (ticket)	499	482	459	409	398	417	424	-3.4	-4.7	-10.9	-2.7	4.8	1.7
4	Reference price (euro)	1,050	1,126	1,123	1,078	1,083	1,084	1,057	7.2	-0.3	-4.0	0.4	0.1	-2.5
5	Discount^	830	751	743	717	709	704	690	-9.5	-1.1	-3.4	-1.2	-0.7	-2.0
6=1-2-5	**Net outpatient expenditure**	**8,120**	**7,781**	**7,764**	**7,616**	**7,583**	**7,675**	**7,701**	**-4.2**	**-0.2**	**-1.9**	**-0.4**	**1.2**	**0.3**
7	Direct distribution of Class A pharmaceuticals	3,171	2,829	2,541	2,205	2,181	2,540	2,793	-10.8	-10.2	-13.2	-1.1	16.5	10.0
8	"On behalf" distribution of class A medicines	1,622	1,794	1,939	2,055	2,114	2,400	2,504	10.6	8.1	6.0	2.9	13.5	4.4
9=6+7+8	**Public local expenditure**	**12,913**	**12,404**	**12,244**	**11,875**	**11,878**	**12,615**	**12,998**	**-3.9**	**-1.3**	**-3.0**	**0.0**	**6.2**	**3.0**
10	Citizen cost-sharing*	1,549	1,608	1,582	1,487	1,481	1,501	1,481	3.8	-1.6	-6.0	-0.4	1.4	-1.3
11	Private purchase of class A medicines	1,317	1,360	1,544	1,528	1,644	1,908	2,021	3.3	13.5	-1.1	7.6	16.1	5.9
12	Class C medicines with prescription	2,813	2,875	3,066	3,269	3,466	3,523	3,839	2.2	6.6	6.6	6.0	1.6	9.0
13	Self-medication pharmaceuticals	2,109	2,270	2,392	2,134	2,337	2,661	2,941	7.6	5.4	-10.8	9.5	13.9	10.5
14	Shops	286	266	259	250	287	326	368	-7.0	-2.5	-3.7	14.9	13.7	12.7
15=10+11+12+13+14	**Total private expenditure**	**8,074**	**8,379**	**8,843**	**8,668**	**9,215**	**9,919**	**10,650**	**3.8**	**5.5**	**-2.0**	**6.3**	**7.6**	**7.4**
16=9+15	**Total pharmaceutical expenditure**	**20,987**	**20,783**	**21,087**	**20,543**	**21,093**	**22,535**	**23,648**	**-1.0**	**1.5**	**-2.6**	**2.7**	**6.5**	**4.9**
9/16	**Share (%) borne by the NHS**	**61.5**	**59.7**	**58.1**	**57.8**	**56.3**	**56.0**	**55.0**						

^Including the discount per price ranges charged to pharmacies, the extra-discount following AIFA Resolution of June 15, 2012 and art. 15, paragraph 2 of Law 135/2012 and, charged to the industry, both the discount from AIFA Resolution of 30 December 2005, and the pay-back under the approved care regime under art. 11, paragraph 6, of Law 122/2010, temporarily modified by Law 135/2012; ° Expenditure for Class A medicines by direct and "on behalf" distribution, including - in the case of Regions with missing data - the value of 40% of pharmaceutical expenditure outside the approved care regime recorded through the flow of the "Traceability of medicines", pursuant to Law 222/2007. In 2023 this condition was not applied to any Region; *Source: OsMed analysis from NSIS data*

Figure 1.2.1 Composition of local pharmaceutical expenditure: comparison 2014-2023

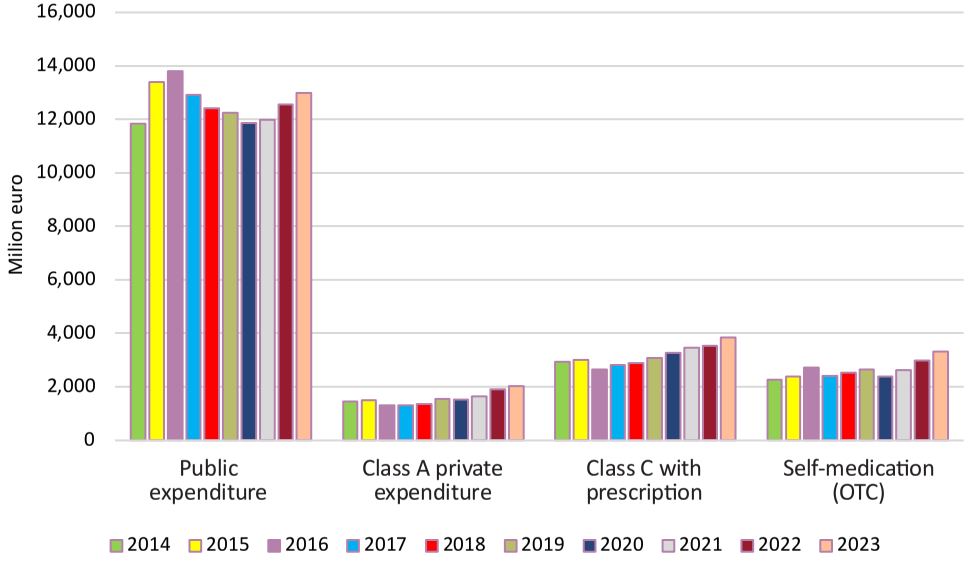


Table 1.2.2 Consumption for public and private local pharmaceutical care: comparison 2017-2023

		2017 *(million)^*	2018 *(million)^*	2019 *(million)^*	2020 *(million)^*	2021 *(million)^*	2022 *(million)^*	2023 *(million)^*	Δ % 18-17	Δ % 19-18	Δ % 20-19	Δ % 21-20	Δ % 22-21	Δ % 23-22
1	Approved care regime	1,110	1,102	1,083	1,034	1,029	1,039	1,035	-0.7	-1.7	-4.6	-0.4	1.0	-0.4
2	Class A medicines paid by citizens*	216	162	190	215	227	232	231	-25.0	17.4	13.3	5.3	2.1	-0.3
3	Direct distribution of class A medicines	66	175	64	50	44	41.2	45.8	164.7	-63.2	-22.9	-12.0	-6.4	11.2
4	"On behalf" distribution of class A medicines	38	44	47	52	55	58	61	15.2	7.3	8.7	7.1	5.1	5.7
5=1+2+3+4	**Total packages class A**	**1,431**	**1,484**	**1,385**	**1,350**	**1,355**	**1,370**	**1,373**	**3.7**	**-6.6**	**-2.5**	**0.4**	**1.1**	**0.3**
6	Class C medicines with prescription	222	229	234	243	244	247.9	247.5	3.2	2.1	4.1	0.4	1.6	-0.2
7	Self-medication pharmaceuticals OTC	231	241	242	248	215	256.4	269.3	4.3	0.6	2.2	-13.4	19.3	5.0
8	Shops	30	29	28	27	28	31.7	33.2	-3.3	-4.0	-1.9	2.0	13.4	4.6
9=6+7+8	**Total packages class C**	**484**	**498**	**504**	**519**	**487**	**536**	**550**	**2.9**	**1.2**	**2.9**	**-6.1**	**10.1**	**2.6**
10=5+9	**Total packages**	**1,915**	**1,982**	**1,889**	**1,869**	**1,842**	**1,906**	**1,923**	**3.5**	**-4.6**	**-1.1**	**-1.4**	**3.5**	**0.9**
	DDD/1000 inhab. per day#	1,101.6	1,130.8	1,143.9	1,098.4	1,130.8	1,140.6	1,128.1	2.7	1.2	-4.0	2.9	0.9	-0.8
	Average DDD cost#	0.43	0.41	0.40	0.41	0.39	0.40	0.40	-5.7	-1.5	0.9	-2.6	0.7	1.4
	Prescriptions #	581	576	570	541	552	564	567	-0.9	-1.0	-5.2	2.2	2.2	0.6

^ only the number of recipes and packages is expressed in millions of units

* the data relating to the private expenditure of medicines reimbursable by the NHS is obtained by the difference between total expenditure (estimated through the data from the "Traceability of medicines" flow) and the expense borne by NHS (obtained from OsMed data)

related to the consumption of Class A medicines provided under the approved care regime

Table 1.2.3 Expenditure and consumption of medicines supplied under approved care regime in 2023

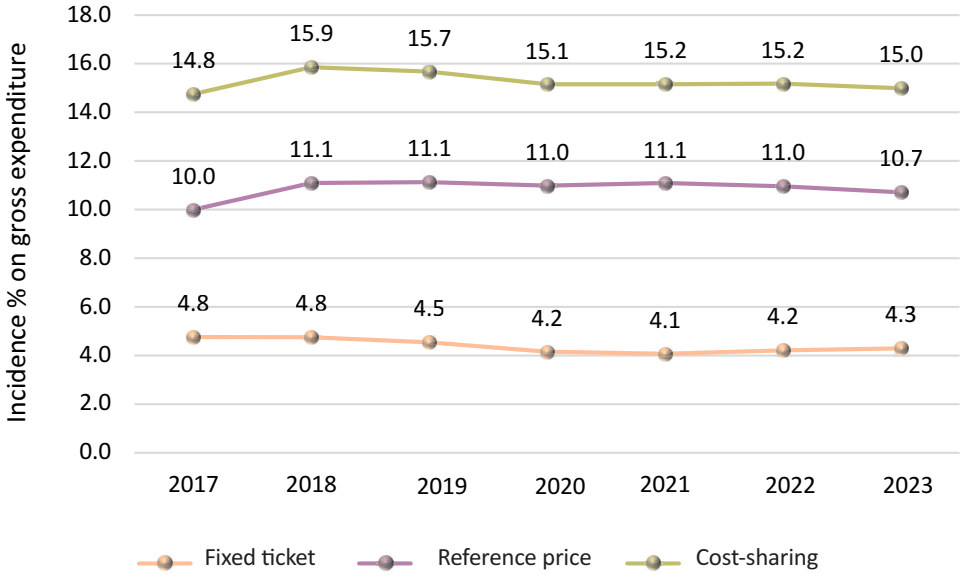
Region	Gross expenditure *(million)*	Citizen cost-sharing				Discount^ *(million)*	Net expenditure^^ *(million)*
		Fixed co-payment (ticket) *(million)*	Δ % 23-22	Prezzo di riferimento *(milioni)*	Δ % 23-22		
Piedmont	624.0	0.5	11.2	58.7	-4.8	38.3	526.6
Valle d'Aosta	16.7	1.5	2.2	1.6	-3.7	1.0	12.7
Lombardy	1859.4	131.0	2.6	135.0	-2.4	153.5	1,439.8
Province of Bolzano	57.5	4.6	2.6	5.9	-1.8	3.8	43.2
Province of Trento	76.9	0.1	9.7	6.7	-2.8	4.8	65.2
Veneto	651.8	58.9	0.9	66.9	-3.0	40.2	485.9
Friuli VG	184.1	-	-	17.8	-2.4	11.5	154.8
Liguria	239.7	19.7	3.8	23.9	-3.6	14.5	181.5
Emilia R.	595.1	0.4	11.3	64.9	-2.5	35.2	494.5
Tuscany	520.2	0.4	13.6	49.4	-5.9	34.0	436.4
Umbria	133.7	0.1	11.8	16.0	-6.2	8.0	109.6
Marche	250.7	-	-	28.7	-1.4	16.5	205.5
Lazio	1,032.0	18.8	-2.9	140.0	-2.2	74.9	798.4
Abruzzo	239.1	6.7	-6.3	27.3	-0.5	15.3	189.8
Molise	51.6	2.7	2.5	6.5	-0.5	2.7	39.7
Campania	1,034.9	78.1	5.6	127.5	-2.5	73.1	756.3
Puglia	723.8	43.9	-0.1	82.9	-2.6	51.6	545.3
Basilicata	106.9	0.1	-7.6	13.1	-0.4	7.0	86.8
Calabria	354.0	9.7	-7.7	47.3	2.6	21.8	275.1
Sicily	831.5	47.0	0.0	108.6	-2.3	63.8	612.0
Sardinia	288.6	0.2	-3.8	28.1	-2.0	18.7	241.6
Italy	**9,872.2**	**424.4**	**1.7**	**1,056.8**	**-2.5**	**690.3**	**7,700.7**
North	4,305.1	216.8	2.3	381.4	-3.0	302.8	3,404.2
Centre	1,936.6	19.2	-2.6	234.1	-3.2	133.4	1,549.9
South and Islands	3,630.4	188.4	1.6	441.3	-1.7	254.1	2,746.6

^including the discount per price ranges charged to pharmacies, the extra-discount following AIFA Resolution of June 15, 2012 and art. 15, paragraph 2 of Law 135/2012 and -charged to the industry- both the discount from AIFA Determination of 30 December 2005, and the pay-back under the approved care regime under art. 11, paragraph 6, of Law 122/2010, temporarily modified by Law 135/2012

^^ Net expenditure is obtained by subtracting the discount and the patient's co-payment from gross expenditure

Source: Italian Medicines Agency DCR (Distinte Contabili Riepilogative - Summary Accounting Statement)

Figure 1.2.2. Time trend (2017-2023) of the incidence of citizen total citizen cost-sharing, fixed co-payment (ticket) and reference price share on gross expenditure



The data in the following tables are calculated net of oxygen

Table 1.2.4 Regional variability of pharmaceutical consumption supplied through local, public and private pharmacies: year 2023 (Table and Figure)

Region	Class A medicines reimbursed by the NHS					Class A medicines - private purchase (A, C, and OTC)	
	Gross expenditure A-NHS^	Weighted gross *per capita* expenditure	Δ % 23-22	DDD 1000 inhab. per day	Δ % 23-22	Per capita expenditure	Δ % 23-22
Piedmont	623,0	140,9	0,1	1042,5	-0,6	165,0	4,6
Valle d'Aosta	17,0	132,5	0,4	932,2	0,5	201,6	3,2
Lombardy	1845,0	187,4	0,4	1102,6	0,6	157,6	7,8
Province of Bolzano	57,0	116,3	0,3	861,3	2,3	138,6	9,0
Province of Trento	77,0	144,1	1,7	1075,8	0,9	133,6	-3,7
Veneto	650,0	133,5	0,2	997,5	-0,4	141,8	4,0
Friuli VG	183,0	146,0	0,3	1104,8	0,3	124,9	2,5
Liguria	239,0	145,9	-0,5	984,3	-1,5	181,6	4,5
Emilia R.	593,0	132,7	1,3	1128,0	-0,3	140,5	3,7
Tuscany	516,0	135,9	-1,7	1065,2	-2,4	161,3	14,2
Umbria	133,0	148,8	-4,7	1140,5	-3,7	152,0	9,1
Marche	250,0	164,0	2,1	1137,1	1,2	143,3	2,2
Lazio	1024,0	181,2	-0,2	1165,5	-1,4	187,6	16,2
Abruzzo	238,0	183,4	-0,8	1194,2	-1,4	132,2	-22,6
Molise	51,0	169,5	1,0	1171,6	0,5	107,9	11,2
Campania	1021,0	196,1	-0,6	1259,7	-2,3	166,6	4,8
Puglia	718,0	185,7	-0,3	1232,8	-1,7	129,5	10,1
Basilicata	106,0	195,6	2,0	1289,5	0,8	132,8	46,6
Calabria	342,0	189,0	0,6	1203,7	-0,9	151,0	24,2
Sicily	812,0	174,2	-0,3	1168,1	-1,4	133,7	18,4
Sardinia	288,0	174,1	2,2	1198,6	0,3	231,4	36,5
Italy	**9782,0**	**166,2**	**0,0**	**1128,1**	**-0,8**	**155,8**	**9,2**
North	4284,0	154,9	0,4	1066,1	0,0	152,6	5,3
Centre	1923,0	162,0	-0,6	1127,9	-1,5	170,8	13,5
South and Islands	3575,0	184,9	-0,1	1216,8	-1,5	151,2	12,2

Amounts in million euros

^Expenditure for class A medicines net of class C reimbursed medicines (17 million euros) and oxygen including expenditure for vaccines

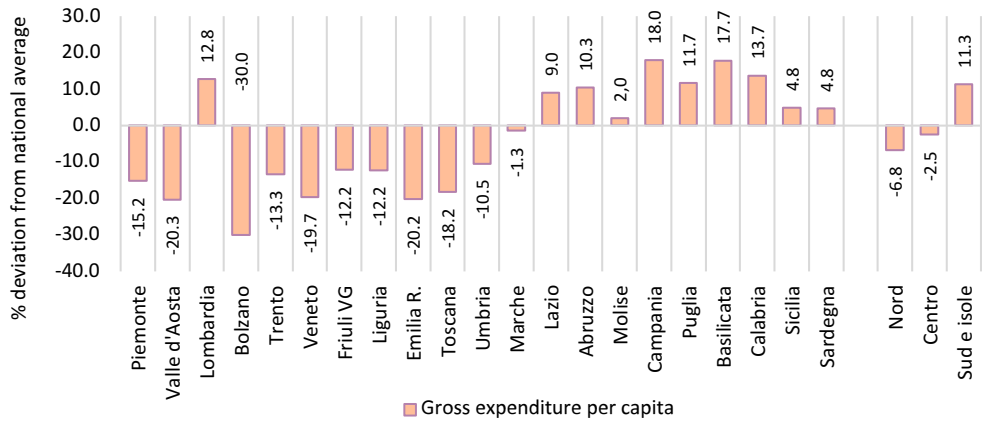


Table 1.2.5 Regional variability of 2023 pharmaceutical consumption under approved care regime by quantity, average cost per day of therapy and expenditure (% deviations from national average) (Table and Figure)

Region	% deviation from national average			Expenditure rank 2023
	DDD/1000 inhab. per day	Average cost DDD	Gross expenditure expenditure	
Campania	12	6	18	1
Basilicata	14	3	18	2
Calabria	7	6	14	3
Lombardy	-2	16	13	4
Puglia	9	2	12	5
Abruzzo	6	4	10	6
Lazio	3	6	9	7
Sicily	4	1	5	8
Sardinia	6	-1	5	9
Molise	4	-2	2	10
Marche	1	-2	-1	11
Umbria	1	-12	-11	12
Friuli VG	-2	-10	-12	13
Liguria	-13	1	-12	14
Province of Trento	-5	-9	-13	15
Piedmont	-8	-8	-15	16
Tuscany	-6	-14	-18	17
Veneto	-12	-9	-20	18
Emilia R.	0	-20	-20	19
Valle d'Aosta	-17	-4	-20	20
Province of Bolzano	-24	-8	-30	21
North	-5	-1	-7	
Centre	0	-3	-3	
South and Islands	8	3	11	

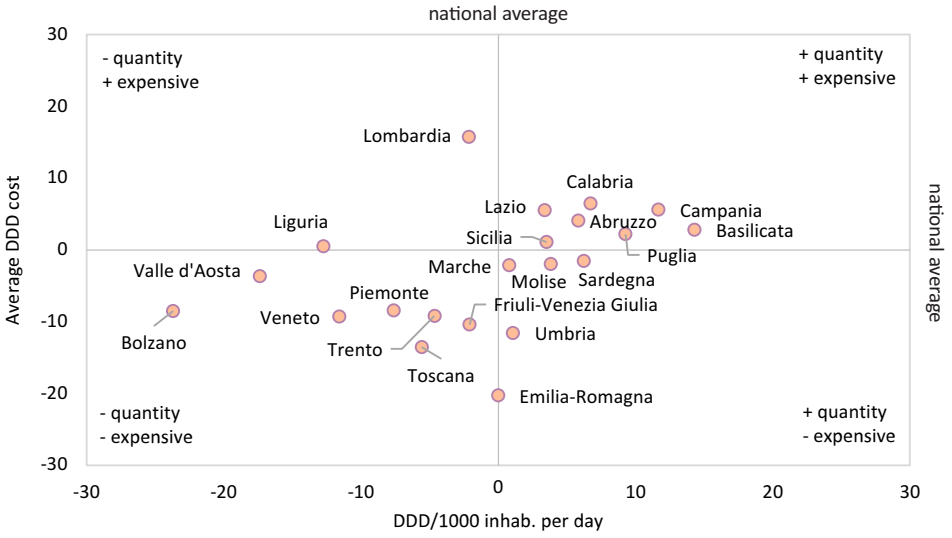


Figure 1.2.3 Trend of class A-NHS pharmaceutical expenditure under approved care regime in the period 2010-2023: consumption, price and mix effect

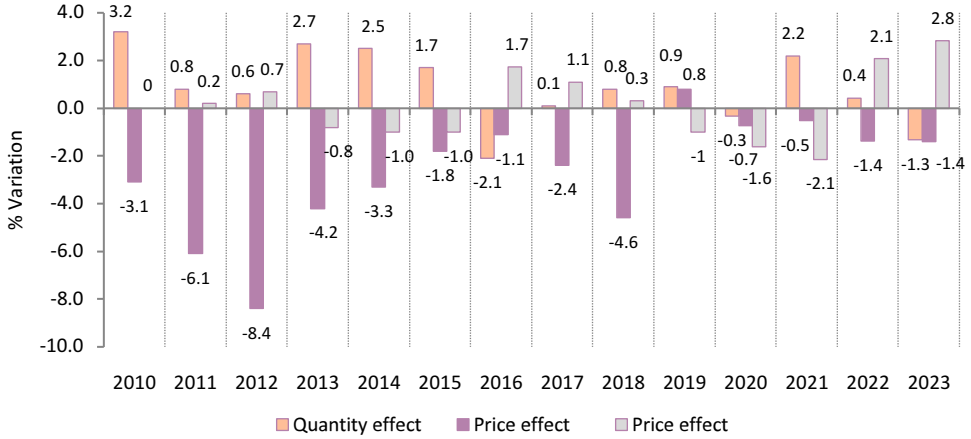


Table 1.2.6 Consumption, price and mix effect on the variation in class A-NHS pharmaceutical expenditure under approved care regime: comparison 2023-2022

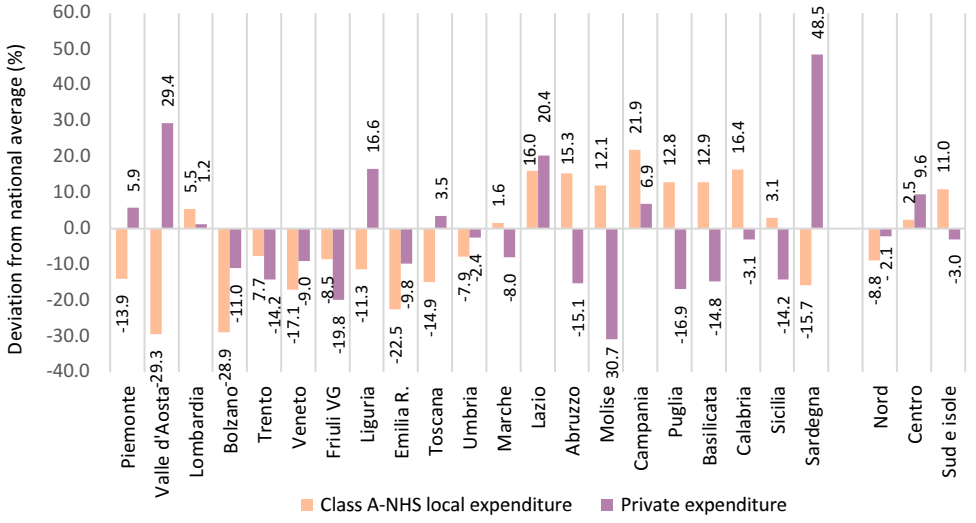
Region	Gross expenditure 2023 *(million)*	Δ % 2023-2022				Average cost DDD 2023	Δ % average cost DDD
		expenditure	DDD	prices	mix		
Piedmont	622.8	0.1	-1.3	-1.8	3.3	0.37	1.4
Valle d'Aosta	16.7	0.4	-0.1	-5.5	6.3	0.39	0.5
Lombardy	1844.8	0.4	0.0	-1.8	2.2	0.47	0.4
Province of Bolzano	57.4	0.3	1.5	-3.4	2.3	0.37	-1.2
Province of Trento	76.6	1.7	0.8	-2.6	3.6	0.37	1.0
Veneto	649.9	0.2	-1.0	-1.8	3.0	0.37	1.2
Friuli VG	183.5	0.3	-0.6	-2.4	3.3	0.36	0.9
Liguria	238.8	-0.5	-2.6	-2.0	4.2	0.41	2.1
Emilia R.	593.5	1.3	-0.8	-1.4	3.5	0.32	2.1
Tuscany	516.2	-1.7	-3.3	-2.1	3.8	0.35	1.6
Umbria	132.8	-4.7	-4.6	-2.4	2.4	0.36	-0.1
Marche	250.4	2.1	0.2	-1.7	3.6	0.40	1.9
Lazio	1023.9	-0.2	-1.7	-1.7	3.3	0.43	1.5
Abruzzo	237.6	-0.8	-2.0	-2.0	3.3	0.42	1.3
Molise	51.1	1.0	-0.2	-3.9	5.3	0.40	1.2
Campania	1020.6	-0.6	-2.4	-1.5	3.3	0.43	1.8
Puglia	717.9	-0.3	-2.0	-1.7	3.4	0.41	1.7
Basilicata	106.3	2.0	0.1	-2.4	4.5	0.42	1.9
Calabria	341.8	0.6	-1.2	-2.1	4.0	0.43	1.8
Sicily	811.7	-0.3	-1.7	-1.7	3.2	0.41	1.4
Sardinia	287.9	2.2	0.1	-2.1	4.3	0.40	2.2
Italy	**9,782.0**	**0.0**	**-1.3**	**-1.4**	**2.8**	**0.40**	**1.4**
North	4,283.9	0.4	-0.6	-1.6	2.7	0.40	1.1
Centre	1,923.2	-0.6	-2.2	-1.6	3.3	0.39	1.6
South and Islands	3,574.9	-0.1	-1.7	-1.5	3.2	0.42	1.7

Note: expenditure is net of reimbursed class C medicines, vaccines and oxygen

Table 1.2.7 Per capita local pharmaceutical expenditure (public and private) in 2023 (weighted population) (Table). % deviation from national average (Figure)

Region	Local expenditure^ class A-NHS per capita(A)	Private expenditure per capita (A, C, and OTC)(B)	Total local expenditure^ per capita(C=A+B)
Piedmont	179.6	165.0	344.7
Valle d'Aosta	147.4	201.6	349.0
Lombardy	220.0	157.6	377.6
Province of Bolzano	148.4	138.6	287.0
Province of Trento	192.6	133.6	326.2
Veneto	173.0	141.8	314.9
Friuli VG	190.9	124.9	315.8
Liguria	185.1	181.6	366.7
Emilia R.	161.7	140.5	302.2
Tuscany	177.6	161.3	338.9
Umbria	192.2	152.0	344.2
Marche	211.9	143.3	355.1
Lazio	242.0	187.6	429.6
Abruzzo	240.5	132.2	372.8
Molise	233.8	107.9	341.7
Campania	254.2	166.6	420.8
Puglia	235.4	129.5	364.9
Basilicata	235.6	132.8	368.4
Calabria	242.8	151.0	393.8
Sicily	215.0	133.7	348.7
Sardinia	175.8	231.4	407.3
Italy	**208.6**	**155.8**	**364.4**
North	190.3	152.6	342.9
Centre	213.8	170.8	384.6
South and Islands	231.5	151.2	382.6

^Gross class A expenditure under approved care regime, net of reimbursed class C medicines, to which expenditure for direct and "on behalf" distribution of class A medicines has been added. It does not include oxygen and vaccines



1.3 Medicines purchased by public health facilities

Expenditure for the purchase of medicines by public health facilities (hospitals, direct and "on behalf" distribution) amounted to approximately €16.2 billion (€275.14 per capita) (Table 1.3.1) and registered an increase of 8.4% compared to 2022, against an increase in consumption (+4.8%; 194.4 DDD/1000 inhab. die) and an increase in the average cost per DDD of 3.1%. It should be highlighted that, although the DDD approach allows a useful parameterization at different levels (geographical and temporal) of the consumption of medicines purchased by public health facilities, it does not represent the actual pharmaceutical dose administered to the patient. Although this assumption is also valid in cases where DDD is used to parametrize local consumption (for example in the paediatric population), it becomes even more valid in a hospital setting, where the dose of a medicine can vary considerably depending on the patient's care needs. The southern regions have the highest per capita expenditure (289.93 euros) and the lowest consumption (176.2 DDD). Therefore, the higher expenditure is mainly attributable to the higher average DDD cost of 4.5 euro, compared to the North (3.5 euros) and the Centre (3.9 euros).

The regions where the highest expenditure values were found were Campania (317.44 euros per capita), Abruzzo (310.64 euros per capita) and Marche (300.30 euros); on the contrary, the lowest values were found in Valle d'Aosta (217.69 euros per capita), the Province of Trento (234.28 euros per capita) and Lombardy (240.60 euros). The increase in expenditure, compared to 2022, was recorded in all regions, with the largest variations in Friuli Venezia Giulia (+16.6%) and Valle d'Aosta (+15.0%).

In terms of consumption, Emilia Romagna (320.8 DDD) and Lombardy (123.2 DDD) represent the regions with the highest and lowest levels of consumption, respectively. The regions with the largest increases in consumption compared to the year 2022 are Sicily (+15.0%) and Campania (+7.8%), while Calabria and Marche are the only regions with decreases (-6.7% and -2.7%, respectively).

An analysis of the relationship between average cost per DDD and the purchase of pharmaceuticals by public health facilities (Table and Figure 1.3.2) reveals that no Region consumes fewer quantities at a lower cost than the national average. Lombardy, Abruzzo, Puglia, Lazio, Calabria, Basilicata, Molise, Campania, and Sicily registered lower consumption, but with an average cost per DDD higher than the national average. Emilia Romagna, Valle d'Aosta, Friuli Venezia Giulia, Marche, Veneto, Tuscany, Umbria, Liguria, Piedmont, A.P. of Bolzano and A.P. of Trento consumed higher quantities but with a lower average cost per DDD. Table 1.3.3 analyses the elements that contributed to the change in expenditure for purchases by public health facilities. In 2023, nationwide spending showed an increase of 8.1%, driven by a shift to more expensive molecules (mix effect: +8.1%), and increased consumption (+4.9%), while prices continued to fall by 4.6%. However, the average cost per DDD increased by 3.1%, with the largest changes recorded in Valle d'Aosta (+10.5%) and Friuli Venezia Giulia (+10.0%), while it decreased in Sicily (-3.0%), Puglia (-2.4%) and Veneto (-1.7%).

Table 1.3.1 Expenditure and consumption for medicines purchased by public health facilities: comparison 2023-2022 (weighted population) (Table and Figure)

Region	NHS Expenditure *(million)*^	NHS Expenditure per capita		DDD/1000 inhab. per day		Average cost DDD	
		€	Δ % 23-22	N.	Δ % 23-22	€	Δ % 23-22
Piedmont	1,187	268.51	9.7	233.4	7.0	3.1	2.2
Valle d'Aosta	27	217.69	15.0	206.5	3.8	2.9	10.5
Lombardy	2,368	240.60	9.7	123.2	3.6	5.3	5.6
Province of Bolzano	135	274.16	12.6	221.3	2.2	3.4	9.8
Province of Trento	125	234.28	7.9	208.8	2.8	3.1	4.7
Veneto	1,284	263.76	4.9	242.4	6.3	3.0	-1.6
Friuli VG	372	296.21	16.6	216.1	5.2	3.7	10.5
Liguria	482	294.55	9.9	231.0	2.8	3.5	6.6
Emilia R.	1,338	299.18	6.7	320.8	1.3	2.5	5.0
Tuscany	1,052	276.88	10.4	222.6	6.2	3.4	3.7
Umbria	262	293.11	5.9	247.5	4.9	3.2	0.6
Marche	459	300.30	4.1	227.1	-2.7	3.6	6.6
Lazio	1,496	264.74	7.7	152.7	5.2	4.7	2.1
Abruzzo	403	310.64	9.9	165.0	2.7	5.1	6.7
Molise	81	267.56	6.3	161.7	4.4	4.5	1.6
Campania	1,652	317.44	9.3	193.3	7.8	4.5	1.1
Puglia	1,109	286.83	4.2	167.4	6.5	4.7	-2.4
Basilicata	156	287.18	6.5	168.9	1.5	4.6	4.6
Calabria	531	293.52	6.5	152.9	-6.7	5.2	13.8
Sicily	1,196	256.63	11.7	171.7	15.0	4.1	-3.1
Sardinia	478	289.20	9.0	195.1	1.4	4.1	7.2
Italy	**16,192**	**275.14**	**8.4**	**194.4**	**4.8**	**3.9**	**3.1**
North	7,320	264.71	8.7	208.2	4.1	3.5	4.1
Centre	3,268	275.33	7.9	191.8	4.2	3.9	3.3
South and Islands	5,605	289.93	8.4	176.2	6.6	4.5	1.4

Source: OsMed analysis on NSIS data related to the "Traceability of medicines" - Ministerial Decree 15 July 2004
^ expenditure on drugs in each reimbursable class including vaccines and net of oxygen

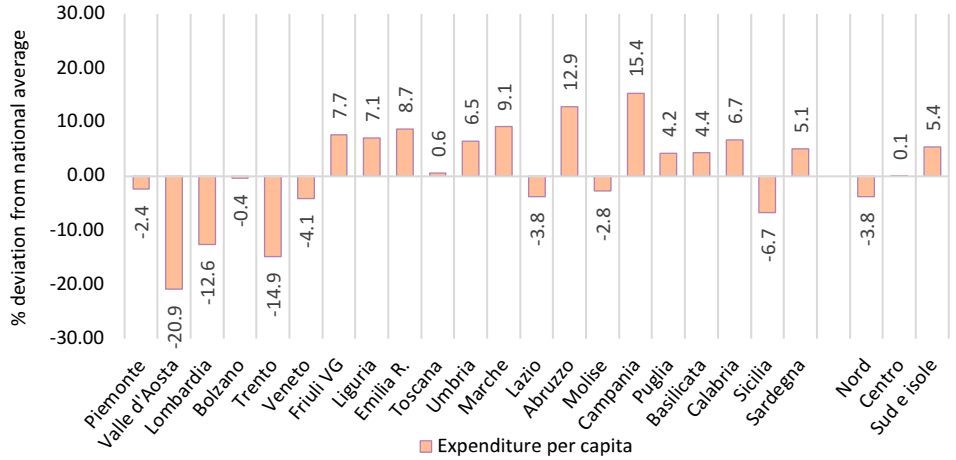


Table 1.3.2 Regional variability of consumption of medicines purchased by public health facilities in 2023 by quantity, average cost per day of therapy and expenditure (% deviations from national average) (Table and Figure)

Region	% deviation from national average			Rank expenditure 2023
	DDD/1000 inhab. per day	Average cost DDD	Gross expenditure per capita	
Campania	-1	16	15	1
Abruzzo	-15	33	13	2
Marche	17	-7	9	3
Emilia R.	65	-34	9	4
Friuli VG	11	-3	8	5
Liguria	19	-10	7	6
Calabria	-21	36	7	7
Umbria	27	-16	7	8
Sardinia	0	5	5	9
Basilicata	-13	20	4	10
Puglia	-14	21	4	11
Tuscany	15	-12	1	12
Province of Bolzano	14	-12	0	13
Piedmont	20	-19	-2	14
Molise	-17	17	-3	15
Lazio	-21	22	-4	16
Veneto	25	-23	-4	17
Sicily	-12	6	-7	18
Lombardy	-37	38	-13	19
Province of Trento	7	-21	-15	20
Valle d'Aosta	6	-26	-21	21
North	7	-10	-4	
Centre	-1	1	0	
South and Islands	-9	16	5	

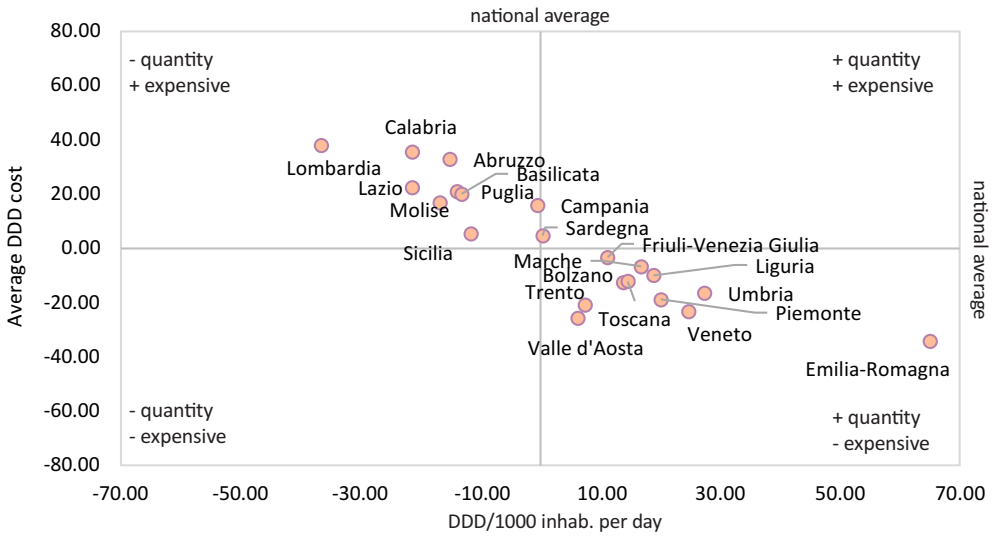


Table 1.3.3 Consumption, price and mix effect on the variation of expenditure for medicines purchased by public health facilities: comparison 2023-2022

Region	Gross expenditure 2023*(million)*	Δ % 2023-2022				Average cost DDD 2023	Δ % 23-22
		expenditure	DDD	prices	mix		
Piedmont	1,187	9.2	7.0	-9.5	12.8	3.1	2.0
Valle d'Aosta	27	14.6	3.7	-27.7	52.7	2.9	10.5
Lombardy	2,368	9.5	3.7	-7.4	14.0	5.3	5.5
Province of Bolzano	135	11.9	2.0	-21.9	40.3	3.4	9.6
Province of Trento	125	8.0	3.3	-24.0	37.7	3.1	4.6
Veneto	1,284	4.5	6.4	-9.2	8.3	3.0	-1.7
Friuli VG	372	15.4	4.9	-23.3	43.3	3.7	10.0
Liguria	482	9.1	2.3	-9.9	18.4	3.5	6.7
Emilia R.	1,338	6.3	1.3	-8.2	14.3	2.5	5.0
Tuscany	1,052	9.3	5.6	-10.4	15.4	3.4	3.4
Umbria	262	5.0	4.5	-15.3	18.6	3.2	0.5
Marche	459	3.3	-3.1	-12.0	21.2	3.6	6.6
Lazio	1,496	7.6	5.5	-7.6	10.3	4.7	2.0
Abruzzo	403	9.3	2.5	-10.1	18.6	5.1	6.6
Molise	81	5.3	4.3	-20.3	26.7	4.5	0.9
Campania	1,652	9.5	8.3	-8.8	10.9	4.5	1.1
Puglia	1,109	4.2	6.8	-10.0	8.5	4.7	-2.4
Basilicata	156	6.1	1.6	-16.0	24.3	4.6	4.4
Calabria	531	5.9	-7.3	-12.7	30.9	5.2	14.3
Sicily	1,196	11.7	15.2	-9.8	7.6	4.1	-3.0
Sardinia	478	9.0	0.5	-16.6	30.1	4.0	8.5
Italy	**16,192**	**8.1**	**4.9**	**-4.6**	**8.1**	**3.9**	**3.1**
North	7,320	8.2	4.1	-5.0	9.4	3.5	3.9
Centre	3,268	7.3	4.1	-5.8	9.4	3.9	3.1
South and Islands	5,605	8.3	6.6	-5.4	7.3	4.5	1.6

1.4 Pharmaceutical consumption by age and gender

The use of pharmaceuticals in the population may depend on different factors, including socio-demographic characteristics, epidemiological profiles of the populations, a variety of healthcare settings and the different prescribing attitudes of physicians. The aim of this section is to provide, within the approved care regime and the "on behalf" distribution, a description of consumption and expenditure, as well as of the prevalence of use of medicines by age and sex in the general population. Data for this analysis derive from the information flow of prescriptions of medicines charged to the NHS (*tessera sanitaria*) and provided through public and private pharmacies. This flow covers the whole Italian population.

Overall, in 2023, 67.4% of the population received at least one pharmaceutical prescription, with a per capita expenditure of €207.41 and a consumption of 1182,7 DDD/1000 inhabitants per day (this suggests that on average every Italian citizen received slightly more than one dose of medicine every day of the year) (Tables 1.4.1 and 1.4.2).

There is a slight difference in the exposure to medicines between the two sexes, with a prevalence of 63% in males and of 72% in females. As far as consumption and expenditure are concerned, the number of doses registered are 1126,1 DDD in males and 1236,8 in females, whereas pharmaceutical expenditure is equal to 206.08 euros *per capita* in males and 208.69 euros *per capita* in females (Table 1.4.1 and Figure 1.4.1).

As expected, the trend of pharmaceutical expenditure and consumption increases with the ageing of population. The per capita pharmaceutical expenditure borne by the NHS is over 3 times higher in the +75 age group compared to the national average value. Moreover, for citizens older than 64, the pharmaceutical expenditure is over 6 times higher than the average expenditure for people younger than 40 (Table 1.4.1). This result is due to change both in the prevalence of use and in consumption. The prevalence of use ranges from about 50% in children and adults up to 49 years of age, to over 90% in the elderly population up to 74 years, and to 100% in the population aged +74 years. Consumption is between 290.7 and 489.4 DDD/1000 inhabitants per day in the 40-49 age group and reaches over 4,000 in the population over 75 years of age (Figure 1.4.1 and 1.4.2, Table 1.4.1). This shows that each person in this age group has taken at least 4 doses of medicine every day of the year. The population over 64 years of age accounts for more than 60% of expenditure and DDD (Table 1.4.1).

Sex differences can be seen especially in the 15-69 age group, where females show a higher prevalence of use than male (Figure 1.4.1). Compared to a prevalence of use of 67.4% at a national level in 2023, the values of the different Regions vary between 54.7% in the Province of Bolzano and 75.1% in Basilicata (Table 1.4.2). Generally, Northern Regions have a lower prevalence (64.2%) compared to Central (69.4%) and Southern (70.5%) ones. An expenditure of €324.5 per user was incurred in the South (+5.4% compared to the national average of €307.9), compared to €295.6 in the North and €306.2 in the Centre. These differences are mainly due to increased consumption, to the prescription of more expensive products and to a reduced use of generic medicines. As a matter of fact, more doses per user are dispensed in the South (648.8 DDD) than in the Centre (634.3 DDD) and in the North (637.7 DDD), which could reflect a different epidemiological distribution of the pathologies, both in terms of severity and the presence of comorbidity, and a different prescriptive attitude of doctors. Compared to 2022, the prevalence of use increased (+1,5%), while doses per user observed a 1.7% decrease, with the greatest reductions in the Centre (-2.8%). In relation to the two sexes (Table 1.4.3), there are no differences in the average age of users, which is equal to 51 and

53 years in men and women respectively, while there are differences in consumption, which is higher in men in terms of DDD per user (652.7 in men and 631.0 in women) and in terms of packages per user (28.1 in men and 26.6 in women). At the regional level, Friuli Venezia Giulia records the highest DDDs per user in males (715.0 DDDs), while Sardinia in females (692.7 DDDs); the Province of Bolzano observes the lowest number of doses and packages per user in both males and females (Table 1.4.3).

This consumption trend is also reflected in the expenditure sustained per user, which is equal to €327.5 in males and €291.7 in females; with with the highest value for both sexes in Calabria (387.3 euros and 330.6 euros, respectively; Table 1.4.3).

An analysis of the distribution of consumption by ATC level I in the various age groups (Figure 1.4.3 and Figure 1.4.4) shows that in both males and females in the age group 0-14 years, drugs belonging to ATC A-Gastrointestinal tract and metabolism, R-Respiratory system, and J-Antimicrobials for systemic use account for the largest share of total consumption in the age group. In the 15-24 age group, the incidence of these ATCs decreases and the percentage of consumption of drugs belonging to ATC N-Central Nervous System increases, especially in females. In the later age groups, it is observed that the incidence of cardiovascular system drugs gradually increases, with the highest percentage of 52% in the male population of the 55-64 age group and 42.5% in the female population of the 75-84 age group. In males there is also evidence of an increasing trend with age in the consumption of blood and hematopoietic organ drugs. In females, there is evidence of 12.3% consumption of these drugs in the 25-34 age group, which decreases in the intermediate age groups and increases again to 14% in the population aged 85 years and older.

The greatest differences in prevalence of use between the two sexes are found in the ATCs A-Gastrointestinal system, G-Genitourinary system, H-Systemic hormonal preparations, excluding sex hormones and insulin, J-Antibacterials for systemic use and N-Central nervous system (Table 1.4.4).

With the exception of ATC G, the prevalence of use of these ATCs is higher in women than in men. These differences are also reflected in the indicators of consumption and expenditure per capita. For example, for ATC N, where the prevalence of use is 16.7% in the female population and 10.3% in the male population, while consumption is 93.7 DDD/1000 inhabitants per day in the former and 59.7 DDD/1000 inhabitants per day in the latter. Similarly, per capita spending is higher in females at 28.37 euros compared to 20.43 euros in males. Conversely, analysing the indicators by user, both higher consumption and expenditure are observed in males than in females.

Assessing the highest-consumption ATC level IV categories, the greatest differences between the two sexes in terms of consumption are recorded for the group relating to vitamin D and analogues, thyroid hormones, selective serotonin reuptake inhibitors, alpha-adrenergic receptor antagonists, and other antidepressants. For all these groups, consumption is higher in females than in males, with the exception of alpha-adrenergic receptor antagonists, which are used almost exclusively in males (Table 1.4.5); these differences in consumption are also reflected in expenditure (Table 1.4.6) In addition, it is observed that for the male population there is usually a higher intensity of medication use, especially for categories related to chronic diseases, probably due to the higher dosages used that take into account weight diversity compared to the female population.

Among the top 20 active ingredients by consumption, important gender differences are ob-

served for cholecalciferol and levothyroxine, used more in females, and for tamsulosin, used almost exclusively in males. Higher consumption in the male population is also reported for ramipril, atorvastatin, acetylsalicylic acid, amlodipine, metformin, and furosemide (Table 1.4.7). Also for rosuvastatin and the combination rosuvastatin/ezetimibe, higher consumption is found in males than in females. Among the top 20 active ingredients by expenditure (Table 1.4.8), there are important differences in the two sexes, on the one hand, for dulaglutide, semaglutide, omega-3, and respiratory medications (formoterol/beclomethasone and vilanterol/fluticasone) which show higher expenditure among males and, on the other hand, for cholecalciferol, esomeprazole, enoxaparin which record the highest expenditure among females.

Table 1.4.1 Breakdown of local expenditure and consumption by age group and sex (year 2023)

Age group	*Per capita* gross expenditure			Total expenditure		DDD/1000 inhabitants per day			Total DDD	
	M	F	T	%	cum. %	M	F	T	%	cum. %
0-4	25.16	21.76	23.51	0.4	0.4	112.7	104.2	108.6	0.3	0.3
5-9	30.43	26.69	28.62	0.6	1.0	75.9	67.1	71.6	0.3	0.6
10-14	32.06	25.55	28.90	0.7	1.6	69.4	61.4	65.5	0.3	0.8
15-19	39.30	27.80	33.76	0.8	2.4	87.7	97.6	92.5	0.4	1.2
20-24	32.98	36.40	34.61	0.8	3.3	104.4	138.2	120.5	0.5	1.7
25-29	39.46	44.48	41.87	1.0	4.3	122.4	168.0	144.4	0.6	2.4
30-34	44.38	56.20	50.18	1.3	5.6	145.6	209.7	177.0	0.8	3.2
35-39	55.08	74.82	64.88	1.8	7.4	198.9	268.2	233.3	1.1	4.3
40-44	69.86	88.06	78.96	2.4	9.8	290.7	346.4	318.6	1.7	6.0
45-49	96.26	104.18	100.24	3.7	13.5	455.5	489.4	472.6	3.1	9.1
50-54	138.87	143.18	141.05	5.5	19.1	726.7	765.0	746.1	5.1	14.2
55-59	203.93	192.14	197.93	7.8	26.8	1,129.3	1,130.2	1,129.8	7.8	22.0
60-64	303.77	266.78	284.66	9.7	36.5	1,725.9	1,631.6	1,677.2	10.0	32.0
65-69	424.67	357.54	389.56	11.5	48.0	2,447.1	2,254.5	2,346.4	12.1	44.1
70-74	533.25	443.79	485.64	13.1	61.1	3,103.3	2,832.0	2,958.9	14.0	58.1
75-79	682.00	567.61	619.26	14.0	75.1	3,982.0	3,644.6	3,797.0	15.0	73.2
80-84	723.01	600.37	652.00	12.1	87.2	4,214.8	3,848.0	4,002.4	13.0	86.1
85+	812.48	642.23	700.62	12.8	100.0	4,744.9	4,079.9	4,308.0	13.9	100.0
Total	**206.08**	**208.69**	**207.41**	**100.0**		**1,126.1**	**1,236.8**	**1,182.7**	**100.0**	

Figure 1.4.1 Trend in prevalence of use of local pharmaceuticals by age and sex (year 2023)

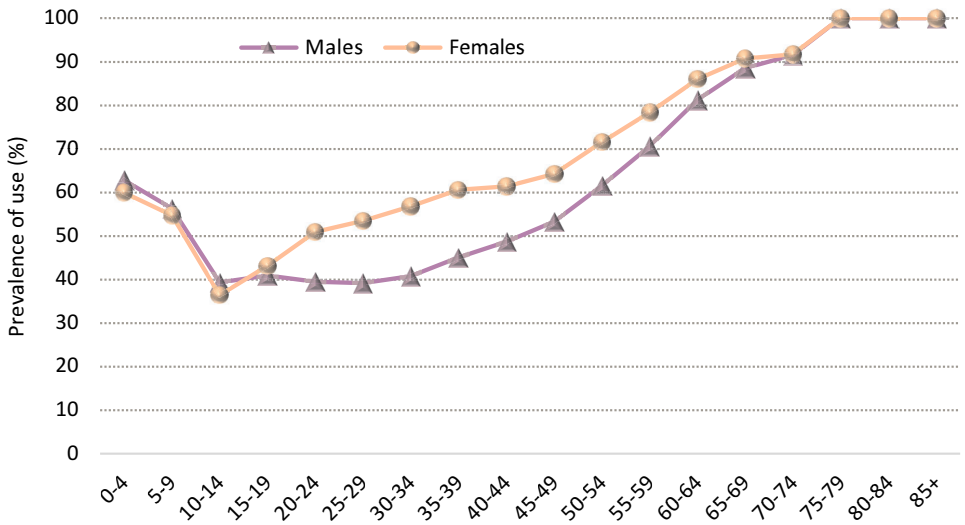


Figure 1.4.2 Trend in local DDD/1000 inhabitants per day by age and sex (year 2023)

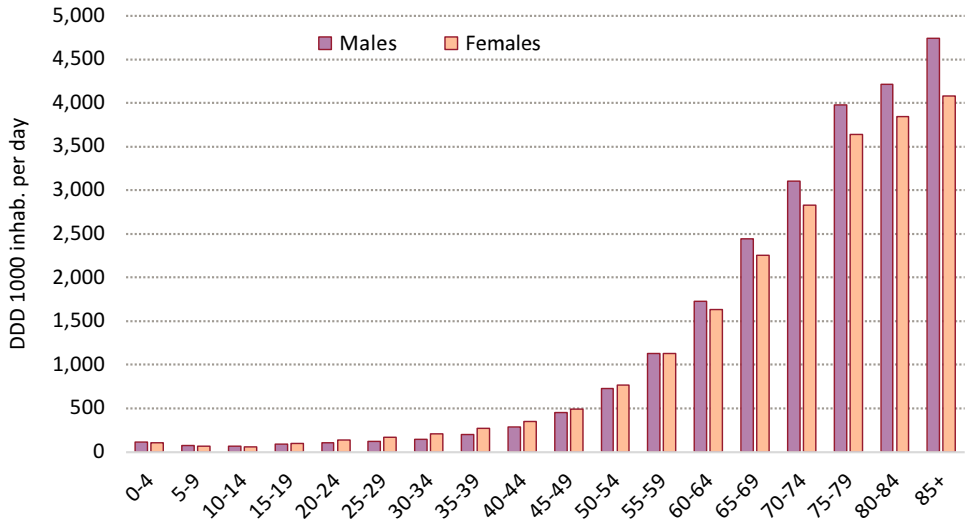


Table 1.4.2 Prevalence and intensity of use in local setting by Region (2021-2023)

Region	Prevalence of use (%)				Expenditure per user				DDD per user			
	2021	2022	2023	Δ % 23-22	2021	2022	2023	Δ % 23-22	2021	2022	2023	Δ % 23-22
Piedmont	61.7	65.4	66.4	1.6	292.9	284.8	287.3	0.9	678.4	650.1	637.5	-1.9
Valle d'Aosta	57.7	60.7	62.1	2.2	275.0	265.7	270.5	1.8	615.9	590.1	588.5	-0.3
Lombardy	57.9	61.4	62.8	2.3	347.9	332.1	342.9	3.3	686.6	638.1	646.4	1.3
Province of Bolzano	48.1	52.8	54.7	3.6	268.3	252.0	248.9	-1.2	605.4	570.8	563.1	-1.3
Province of Trento	62.1	66.0	67.1	1.7	264.0	258.8	265.5	2.6	617.7	594.2	594.6	0.1
Veneto	57.3	61.2	62.1	1.4	280.7	271.2	272.0	0.3	673.2	635.6	625.1	-1.6
Friuli VG	61.1	64.2	65.7	2.2	312.5	305.6	305.3	-0.1	717.1	700.2	687.7	-1.8
Liguria	60.8	65.2	65.4	0.2	317.6	303.2	299.9	-1.1	692.3	656.0	635.2	-3.2
Emilia R.	62.5	66.7	67.8	1.6	229.6	230.2	233.6	1.5	659.9	644.3	633.8	-1.6
Tuscany	62.8	66.9	67.6	1.0	277.6	263.9	264.6	0.3	695.7	651.8	629.7	-3.4
Umbria	67.0	70.5	71.6	1.5	338.6	298.8	287.6	-3.8	747.5	685.9	656.9	-4.2
Marche	66.9	70.7	72.7	2.8	306.8	294.8	297.9	1.0	668.1	638.4	633.0	-0.9
Lazio	64.8	68.9	69.5	0.8	356.4	340.8	337.2	-1.1	687.4	651.5	634.0	-2.7
Abruzzo	69.7	74.0	73.3	-1.0	320.4	308.6	311.8	1.0	658.4	623.8	600.7	-3.7
Molise	69.0	71.4	72.3	1.3	332.4	309.3	292.2	-5.5	683.8	648.5	620.0	-4.4
Campania	66.9	69.1	70.1	1.5	353.7	339.6	339.0	-0.2	712.5	668.9	655.4	-2.0
Puglia	69.4	72.3	73.4	1.5	341.5	360.0	319.1	-11.4	676.9	648.6	629.1	-3.0
Basilicata	69.4	73.0	75.1	2.9	335.7	326.2	325.3	-0.3	696.7	675.3	661.1	-2.1
Calabria	63.2	66.1	67.5	2.0	366.4	247.7	356.6	44.0	720.9	693.6	679.2	-2.1
Sicily	64.0	67.2	68.1	1.5	324.4	312.0	309.8	-0.7	692.1	663.3	650.0	-2.0
Sardinia	67.1	69.6	71.0	2.0	317.3	307.9	310.9	0.9	706.3	681.7	679.7	-0.3
Italy	**62.8**	**66.4**	**67.4**	**1.5**	**319.5**	**305.9**	**307.9**	**0.7**	**687.0**	**651.8**	**640.9**	**-1.7**
North	59.3	49.5	64.2	1.8	300.8	300.8	295.6	1.7	677.1	796.1	637.7	-0.7
Centre	64.6	55.0	69.4	1.2	324.5	324.5	306.2	-0.7	691.9	797.9	634.3	-2.8
South and Islands	66.7	56.7	70.5	1.5	339.5	339.5	324.5	0.3	696.2	798.6	648.8	-2.2

Table 1.4.3 Prevalence and intensity of use in local setting by Region and sex (year 2023)

Region	Prevalence of use (%)		Average age		Expenditure per user		DDD per user		Packages per user	
	M	F	M	F	M	F	M	F	M	F
Piedmont	62	71	53	55	305.8	272.0	659.7	619.1	27.9	25.7
Valle d'Aosta	57	67	53	55	296.0	249.6	613.1	568.4	26.6	24.0
Lombardy	58	67	51	53	371.8	318.5	660.4	634.6	27.4	25.3
Province of Bolzano	50	59	50	52	268.9	232.5	572.4	555.4	22.7	20.7
Province of Trento	63	72	50	52	280.9	252.5	608.7	582.6	26.1	24.4
Veneto	58	66	52	54	292.7	254.3	651.7	602.4	26.5	23.7
Friuli VG	61	71	54	56	328.9	286.0	715.0	665.3	29.5	26.8
Liguria	61	70	55	57	315.0	287.7	641.9	629.7	27.4	26.3
Emilia R.	63	72	51	53	246.0	223.2	643.6	625.6	26.7	25.5
Tuscany	63	72	53	55	283.7	248.6	651.6	611.5	27.3	25.8
Umbria	67	76	53	55	308.9	269.9	690.9	628.6	29.0	26.9
Marche	69	77	51	54	316.1	282.3	655.2	613.9	28.5	26.6
Lazio	65	74	51	53	364.7	314.5	642.4	627.1	28.7	27.8
Abruzzo	69	77	51	53	325.2	300.4	607.4	595.0	27.2	26.4
Molise	68	77	52	54	305.3	280.9	620.8	619.4	28.3	27.5
Campania	66	74	48	51	350.4	329.1	657.3	653.8	29.4	28.6
Puglia	69	77	50	52	332.4	307.8	632.0	626.6	28.5	27.7
Basilicata	71	79	51	53	340.1	312.5	650.2	670.6	29.6	29.2
Calabria	63	71	51	53	387.3	330.6	692.5	667.9	32.0	30.5
Sicily	64	72	50	53	322.2	299.5	656.5	644.6	28.7	27.9
Sardinia	66	76	53	55	322.6	301.1	664.0	692.7	28.5	28.1
Italy	**63**	**72**	**51**	**53**	**327.5**	**291.7**	**652.7**	**631.0**	**28.1**	**26.6**
North	60	68	52	54	317.3	277.5	654.6	623.5	27.2	25.2
Centre	65	74	52	54	329.3	286.9	650.6	620.7	28.3	27.0
South and Islands	66	74	50	52	338.5	312.6	651.5	646.5	29.1	28.2

Figure 1.4.3 Distribution of local consumption by age group and ATC 1st level (Males - year 2023)

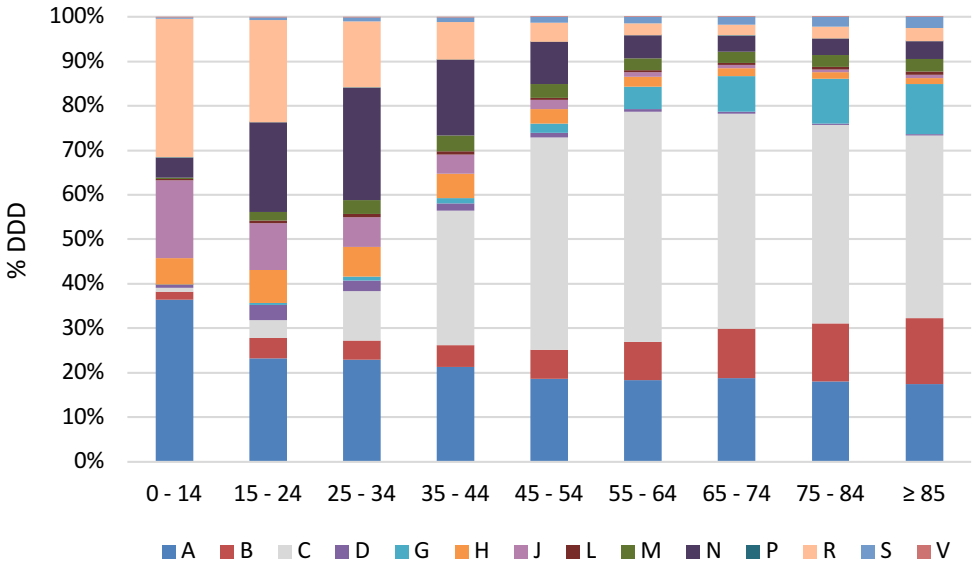


Figure 1.4.4 Distribution of local consumption by age group and ATC 1st level (Females - year 2023)

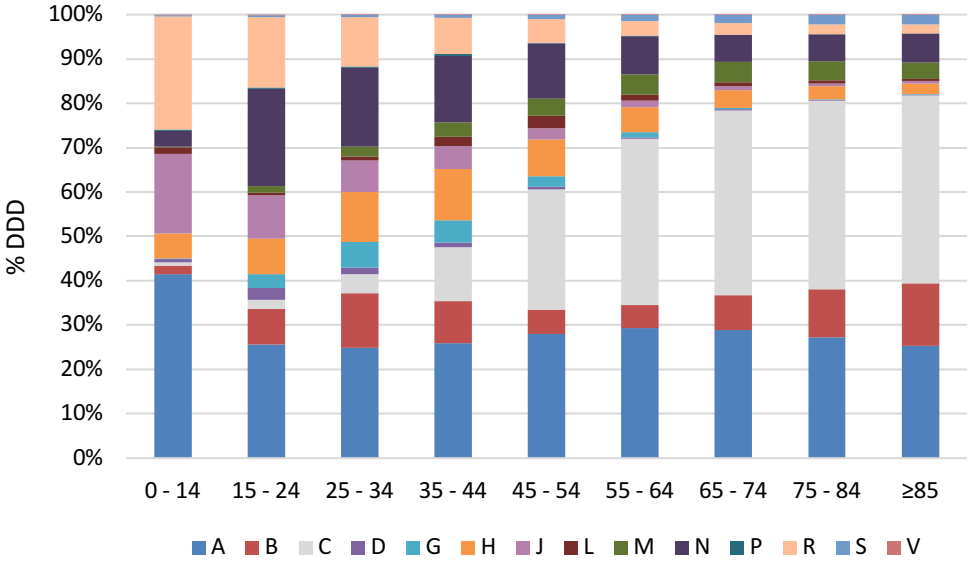


Table 1.4.4 Prevalence, expenditure, consumption and intensity of use in local setting by ATC 1st level and sex (year 2023)

1st level ATC	Prevalence of use (%)			*Per capita* expenditure			DDD/1000 inhab. per day			Expenditure per user			DDD per user		
	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
A	25.3	34.0	29.7	45.78	43.94	44.84	210.4	343.7	278.6	181.24	129.40	150.93	304.0	369.5	342.3
B	16.2	18.5	17.3	24.14	20.18	22.12	121.7	112.6	117.0	149.20	109.33	127.50	274.5	222.7	246.3
C	29.7	31.6	30.7	55.59	50.65	53.07	509.1	470.7	489.5	187.05	160.48	173.06	625.2	544.4	582.6
D	1.6	1.4	1.5	1.84	1.20	1.51	5.9	4.3	5.1	112.25	83.04	98.22	132.1	109.0	121.0
G	9.1	2.4	5.7	10.14	3.09	6.53	84.1	9.7	46.0	111.19	130.40	115.30	336.6	149.2	296.5
H	13.1	21.0	17.1	4.38	7.09	5.77	23.7	54.9	39.7	33.53	33.71	33.65	66.3	95.2	84.5
J	34.8	42.0	38.5	10.90	12.51	11.72	15.0	17.4	16.3	31.36	29.75	30.46	15.8	15.1	15.4
L	1.2	2.1	1.6	7.24	10.86	9.09	5.5	13.1	9.4	610.21	519.82	551.59	170.2	228.3	207.8
M	15.7	20.6	18.2	3.65	9.12	6.45	30.3	51.6	41.2	23.20	44.25	35.37	70.3	91.5	82.6
N	10.3	16.7	13.6	20.43	28.37	24.49	59.7	93.7	77.1	197.65	169.40	179.87	211.0	204.3	206.8
P	0.7	1.2	1.0	0.13	0.34	0.23	0.4	1.6	1.0	18.43	27.66	24.42	23.9	47.7	39.3
R	14.1	15.8	15.0	16.65	15.85	16.24	39.6	40.8	40.2	117.71	100.18	108.25	102.2	94.1	97.8
S	2.1	2.4	2.3	3.51	3.89	3.71	20.4	22.6	21.5	169.01	159.59	163.82	357.9	337.7	346.8
V	0.6	0.6	0.6	1.74	1.64	1.69	0.4	0.2	0.3	300.58	267.75	283.31	22.2	12.1	16.9

Table 1.4.5 Prevalence, expenditure, consumption and intensity of use at local level by sex for the top 20 ATC 4th level by consumption (year 2023)

ATC 4th level	Prevalence of use (%)			Per capita per capita			DDD/1000 inhab. per day			Expenditure per user			DDD per user		
	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
Vitamin D and analogues	4.7	16.3	10.6	1.57	6.21	3.95	46.8	184.68	117.34	33.37	38.21	37.16	363.4	414.5	403.5
HMG-CoA reductase inhibitors	11.2	11.8	11.5	8.08	7.86	7.97	87.4	74.46	80.76	72.48	66.72	69.45	286.0	230.6	256.9
Ace inhibitors, not in combination	6.5	5.5	6.0	3.69	3.08	3.38	87.0	68.26	77.43	56.41	55.51	55.99	485.6	449.2	468.4
Proton pump inhibitors	16.1	19.5	17.8	10.08	11.72	10.92	69.8	80.95	75.48	62.47	60.27	61.24	157.7	151.9	154.5
Platelet aggregation inhibitors, excl. heparin	9.7	8.5	9.1	5.03	3.12	4.05	75.5	59.84	67.49	51.57	36.76	44.51	282.7	257.6	270.7
Angiotensin II receptor blockers(ARBs), not in combination	5.9	6.2	6.0	4.78	5.07	4.93	57.0	58.25	57.66	81.43	81.82	81.63	354.8	342.8	348.5
Dihydropyridine derivatives	5.7	5.5	5.6	4.01	3.79	3.90	52.1	45.18	48.56	70.42	68.46	69.43	334.2	297.7	315.8
Beta blockers, selective	9.6	11.2	10.4	4.53	5.49	5.02	37.1	45.21	41.23	47.09	48.87	48.07	140.5	146.9	144.0
Angiotensin II receptor blockers (ARBs) and diuretics	3.6	4.7	4.1	3.12	4.18	3.66	26.4	35.06	30.82	87.56	89.49	88.68	270.4	273.9	272.4

continued

Table 1.4.5 - *continued*

ATC 4th level	Prevalence of use (%)			Per capita per capita			DDD/1000 inhab. per day			Expenditure per user			DDD per user		
	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
Selective serotonin reuptake inhibitors	2.7	5.9	4.4	2.06	4.59	3.35	19.0	41.67	30.60	75.13	77.70	76.91	253.5	257.4	256.2
Alpha adrenergic receptor antagonists	8.0	0.1	4.0	6.12	0.02	3.00	59.9	0.14	29.32	76.39	17.36	75.69	272.8	56.5	270.2
HMG-CoA reductase inhibitors w/other lipid modifiers	4.2	3.4	3.8	4.58	3.52	4.04	27.4	20.95	24.11	109.93	103.15	106.80	240.3	223.8	232.7
Sulfonamides, not in combination	3.9	5.1	4.5	0.73	0.81	0.77	23.1	23.20	23.14	18.50	15.96	17.04	213.3	167.6	187.1
Thyroid hormones	1.8	8.2	5.1	0.56	2.38	1.49	9.2	36.39	23.13	30.92	29.20	29.50	187.7	162.7	167.1
Biguanides	4.7	3.9	4.3	1.82	1.49	1.65	25.5	19.85	22.61	38.72	37.78	38.28	197.7	183.4	191.0
ACE inhibitors and diuretics	2.2	2.7	2.5	1.98	2.44	2.21	15.9	19.07	17.51	87.96	90.03	89.11	257.9	257.0	257.4
Direct factor Xa inhibitors	2.4	2.3	2.4	9.64	9.00	9.31	15.9	13.74	14.79	393.72	398.84	396.24	236.9	222.2	229.7
Glucocorticoids	11.3	14.2	12.8	1.34	1.67	1.51	13.0	15.88	14.48	11.83	11.77	11.79	41.9	40.9	41.4
Other antidepressants	1.8	3.5	2.7	2.35	4.71	3.55	8.2	17.02	12.70	128.00	135.36	132.90	163.0	178.6	173.4
Vitamin B12 (cyanocobalamin and derivatives)	0.5	0.7	0.6	0.09	0.12	0.10	10.8	14.21	12.54	16.83	15.85	16.25	755.6	713.7	730.7

Table 1.4.6 Prevalence, expenditure, consumption and intensity of use at local level by sex for the top 20 ATC 4th level by expenditure (year 2023)

ATC 4th level	Prevalence of use (%)			Per capita per capita			DDD/1000 inhab. per day			Expenditure per user			DDD per user		
	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
Proton pump inhibitors	16.1	19.5	17.8	10.08	11.72	10.92	69.8	81.0	75.5	62.47	60.27	61.24	157.7	151.9	154.5
Direct factor Xa inhibitors	2.4	2.3	2.4	9.64	9.00	9.31	15.9	13.7	14.8	393.72	398.84	396.24	236.9	222.2	229.7
HMG-CoA reductase inhibitors	11.2	11.8	11.5	8.08	7.86	7.97	87.4	74.5	80.8	72.48	66.72	69.45	286.0	230.6	256.9
GLP-1 (glucagon-like peptide-1) receptor analogues	1.2	0.8	1.0	9.63	6.22	7.88	9.0	5.8	7.4	817.22	797.48	809.14	279.1	270.8	275.7
Adrenergics in combination with corticosteroids or others, excluding anticolinergics	3.2	3.6	3.4	6.24	6.79	6.52	11.6	12.5	12.1	196.91	190.16	193.26	133.2	127.8	130.3
Beta blockers, selective	9.6	11.2	10.4	4.53	5.49	5.02	37.1	45.2	41.2	47.09	48.87	48.07	140.5	146.9	144.0
Angiotensin II receptor blockers (ARBs), not in combination	5.9	6.2	6.0	4.78	5.07	4.93	57.0	58.2	57.7	81.43	81.82	81.63	354.8	342.8	348.5
Other lipid modifying agents	2.6	2.0	2.3	4.92	3.26	4.07	10.8	8.4	9.6	188.63	165.06	178.19	150.7	155.6	152.8
Platelet aggregation inhibitors, excl. heparin	9.7	8.5	9.1	5.03	3.12	4.05	75.5	59.8	67.5	51.57	36.76	44.51	282.7	257.6	270.7
HMG-CoA reductase inhibitors w/other lipid modifiers	4.2	3.4	3.8	4.58	3.52	4.04	27.4	21.0	24.1	109.93	103.15	106.80	240.3	223.8	232.7
Vitamin D and analogues	4.7	16.3	10.6	1.57	6.21	3.95	46.8	184.7	117.3	33.37	38.21	37.16	363.4	414.5	403.5
Dihydropyridine derivatives	5.7	5.5	5.6	4.01	3.79	3.90	52.1	45.2	48.6	70.42	68.46	69.43	334.2	297.7	315.8

continued

Table 1.4.6 – *continued*

ATC 4th level	Prevalence of use (%)			Per capita per capita			DDD/1000 inhab. per day			Expenditure per user			DDD per user		
	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
Angiotensin II receptor blockers (ARBs) and diuretics	3.6	4.7	4.1	3.12	4.18	3.66	26.4	35.1	30.8	87.56	89.49	88.68	270.4	273.9	272.4
Other antidepressants	1.8	3.5	2.7	2.35	4.71	3.55	8.2	17.0	12.7	128.00	135.36	132.90	163.0	178.6	173.4
ACE inhibitors, not in combination	6.5	5.5	6.0	3.69	3.08	3.38	87.0	68.3	77.4	56.41	55.51	55.99	485.6	449.2	468.4
Selective serotonin reuptake inhibitors	2.7	5.9	4.4	2.06	4.59	3.35	19.0	41.7	30.6	75.13	77.70	76.91	253.5	257.4	256.2
Insulins and injectable analogues, long-acting	1.5	1.2	1.4	3.83	2.80	3.30	7.2	5.3	6.2	247.87	226.80	238.28	169.7	158.0	164.4
Other antiepileptics	0.6	0.9	0.8	3.08	3.51	3.30	4.2	4.8	4.5	478.01	390.70	426.20	237.1	195.6	212.4
Combination of penicillins, incl. beta-lactamase inhibitors	17.4	19.3	18.4	2.98	3.26	3.12	5.7	6.3	6.0	17.08	16.87	16.97	11.8	11.9	11.9
Alpha adrenergic receptor antagonists	8.0	0.1	4.0	6.12	0.02	3.00	59.9	0.1	29.3	76.39	17.36	75.69	272.8	56.5	270.2

Table 1.4.7 Prevalence, expenditure and intensity of use by sex for the top 20 substances by consumption (year 2023)

Substance	Prevalence of use (%)			Per capita per capita			DDD/1000 inhab. per day			Expenditure per user			DDD per user		
	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
cholecalciferol	3.8	13.4	8.7	1.25	5.28	3.31	45.6	181.2	115.0	33.36	39.27	38.02	443.8	491.7	481.7
ramipril	4.5	3.6	4.0	2.12	1.63	1.87	68.6	51.3	59.7	47.26	45.33	46.38	558.9	520.1	541.2
atorvastatin	6.7	6.2	6.5	5.04	4.17	4.60	58.2	41.9	49.9	74.84	67.38	71.18	315.3	247.3	281.9
acetylsalicylic acid	7.1	5.8	6.5	1.32	1.05	1.18	51.0	39.8	45.2	18.48	18.01	18.27	261.1	248.6	255.3
pantoprazole	7.9	9.0	8.4	4.30	4.56	4.44	28.1	29.7	28.9	54.76	50.71	52.55	130.7	120.4	125.1
amlodipine	3.8	3.3	3.5	1.78	1.38	1.57	32.1	23.9	27.9	47.47	41.95	44.83	312.1	266.3	290.2
levothyroxine	1.8	8.1	5.0	0.54	2.33	1.46	9.2	36.3	23.1	30.22	28.60	28.88	187.7	162.7	167.0
metformin	4.7	3.9	4.3	1.82	1.49	1.65	25.5	19.8	22.6	38.72	37.78	38.28	197.7	183.4	191.0
furosemide	3.7	4.6	4.1	0.65	0.67	0.66	22.3	21.9	22.1	17.68	14.64	15.96	220.4	174.7	194.6
olmesartan	2.5	2.6	2.6	1.96	2.11	2.04	17.3	18.1	17.7	79.21	79.44	79.33	255.1	249.1	251.9
nebivolol	2.2	3.2	2.7	1.25	1.86	1.56	13.7	20.0	16.9	57.44	58.33	57.98	229.0	229.5	229.3
omeprazole	3.5	4.4	3.9	1.83	2.22	2.03	15.3	18.4	16.9	53.07	50.85	51.81	161.5	154.1	157.3
rosuvastatin	2.3	2.6	2.4	1.51	1.61	1.56	16.7	16.3	16.5	66.60	62.95	64.62	270.1	232.6	249.8
esomeprazole	3.2	4.3	3.7	1.86	2.51	2.20	13.3	18.0	15.7	58.62	59.00	58.84	153.0	154.2	153.7
ezetimibe/rosuvastatin	2.8	2.2	2.5	2.61	1.89	2.24	17.9	13.3	15.5	94.19	84.24	89.63	235.5	216.1	226.6
bisoprolol	6.0	6.5	6.2	2.71	3.01	2.87	12.7	13.3	13.0	45.56	46.51	46.07	77.9	74.9	76.3
lansoprazole	2.6	3.2	2.9	1.84	2.10	1.98	11.6	13.0	12.3	70.11	66.59	68.15	161.0	150.0	154.8
tamsulosin	3.7	0.1	1.8	2.35	0.01	1.15	23.3	0.1	11.4	64.07	12.50	63.16	231.4	44.0	228.1
cyanocobalamin	0.5	0.7	0.6	0.07	0.09	0.08	9.5	12.7	11.1	14.26	13.81	13.99	716.2	685.9	698.2
clopidogrel	1.8	1.4	1.6	1.49	1.19	1.34	12.4	9.6	11.0	83.62	86.36	84.85	253.5	254.8	254.1

Table 1.4.8 Prevalence, expenditure, consumption and intensity of use at local level by sex for the top 20 substances by expenditure (year 2023)

Active ingredient	Prevalence of use (%)			Per capita per capita			DDD/1000 inhab. per day			Expenditure per user			DDD per user		
	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
atorvastatin	6.7	6.2	6.5	5.04	4.17	4.60	58.2	41.9	49.9	74.84	67.38	71.18	315.3	247.3	281.9
pantoprazole	7.9	9.0	8.4	4.30	4.56	4.44	28.1	29.7	28.9	54.76	50.71	52.55	130.7	120.4	125.1
dulaglutide	0.6	0.3	0.5	4.89	2.95	3.90	5.3	3.2	4.2	854.90	844.01	850.65	339.4	331.5	336.3
apixaban	0.9	0.9	0.9	3.72	3.64	3.68	5.9	5.4	5.6	394.20	397.38	395.80	229.9	213.5	221.6
semaglutide	0.6	0.4	0.5	4.33	2.94	3.62	3.2	2.2	2.7	752.32	727.17	741.67	203.4	199.5	201.7
cholecalciferol	3.8	13.4	8.7	1.25	5.28	3.31	45.6	181.2	115.0	33.36	39.27	38.02	443.8	491.7	481.7
rivaroxaban	0.9	0.7	0.8	3.59	2.85	3.21	6.1	4.8	5.5	398.62	406.39	402.11	249.2	250.4	249.7
amoxicillin/clavulanic acid	17.4	19.3	18.3	2.84	3.14	2.99	5.6	6.3	6.0	16.39	16.28	16.33	11.9	11.9	11.9
bisoprolol	6.0	6.5	6.2	2.71	3.01	2.87	12.7	13.3	13.0	45.56	46.51	46.07	77.9	74.9	76.3
enoxaparin	2.4	3.0	2.7	2.20	2.86	2.54	4.1	5.3	4.7	91.89	94.00	93.09	62.6	63.4	63.1
edoxaban	0.6	0.7	0.7	2.33	2.52	2.42	3.8	3.6	3.7	360.26	367.47	364.05	214.5	191.0	202.1
ezetimibe/rosuvastatin	2.8	2.2	2.5	2.61	1.89	2.24	17.9	13.3	15.5	94.19	84.24	89.63	235.5	216.1	226.6
formoterol/beclomethasone	1.2	1.4	1.3	2.02	2.37	2.20	3.8	4.4	4.1	174.95	167.44	170.73	118.6	112.7	115.3
esomeprazole	3.2	4.3	3.7	1.86	2.51	2.20	13.3	18.0	15.7	58.62	59.00	58.84	153.0	154.2	153.7
omega-3	1.6	0.9	1.2	2.95	1.44	2.18	3.6	1.7	2.6	186.57	160.79	176.97	82.6	70.3	78.0
mesalazine	1.0	1.0	1.0	2.33	1.93	2.12	5.9	5.0	5.4	239.62	188.47	212.78	220.9	177.1	197.9
vilanterol/fluticasone furoate	0.8	0.9	0.8	2.03	2.13	2.08	3.5	3.7	3.6	263.67	249.49	256.05	167.8	158.8	162.9
olmesartan	2.5	2.6	2.6	1.96	2.11	2.04	17.3	18.1	17.7	79.21	79.44	79.33	255.1	249.1	251.9
omeprazole	3.5	4.4	3.9	1.83	2.22	2.03	15.3	18.4	16.9	53.07	50.85	51.81	161.5	154.1	157.3
lansoprazole	2.6	3.2	2.9	1.84	2.10	1.98	11.6	13.0	12.3	70.11	66.59	68.15	161.0	150.0	154.8

1.5 Use of pharmaceuticals in the paediatric age

This section presents an analysis of the use of pharmaceuticals in the paediatric age taking into consideration data from all Italian regions, with a resident paediatric population (age <18 years) of 9.1 million individuals in 2023.

In 2023 almost 4.4 million children and adolescents received at least one pharmaceutical prescription, representing 48.6% of the general paediatric population, with a slightly higher prevalence in males than females (49.1% vs. 47.6%) (Table 1.5.1). Furthermore, in the same year, 19.3 million prescriptions were issued, for a total of 19.6 million packages (approximately 2.2 packs per user) and a total expenditure of €258.5 million euros (€28.5 per capita and €58.6 per user). As in previous years, 2023 will see an increase in consumption in terms of prescriptions (+13.9%) and packages (+12.9%), and per capita spending (+6.7%), while spending per user will decrease slightly (-1.2%).

During the year, each child received 2 prescriptions and 2.2 packages of pharmaceuticals, without significant differences between males and females (Table 1.5.1).

At regional level there is marked variability in the use of paediatric mediciations, with an increasing North-South gradient in the prevalence of use; in particular, the prevalence level varies from a minimum of 39% in the Province of Bolzano to a maximum of 57% in Marche and Abruzzo (Figure 1.5.1).

The prevalence of use peaks in the pre-school age group (1-5 years) (66.3%), and then gradually decreases in the following years to reach a value of 38.2% in the 12-17 age group (Figure 1.5.2). A similar trend by age concerns consumption, with the number of packs per capita going from 3.1 in pre-school children (1-5 years) to 2.1 in school children (6-11 years) to 1.8 in adolescents (12-17 years), with a negligible difference by sex: 2.3 packages for males versus 2.0 packages for females (Table 1.5.2). Compared to the year 2022, there was an increase in the number of packages per capita in both males and females and, when analysing the age groups, it can be noticed that the increase is more concentrated in children between 6 and 11 years old, while, in contrast to previous years, in 2023 there is a decrease (-12.7%) in consumption in the child's first year of life (Table 1.5.2).

As expected, antimicrobials for systemic use are the medicines with the highest consumption (45.2% of the total number of packages prescribed in the Italian paediatric population), followed by medicines for the respiratory system (24.5%) (Figure 1.5.3).

The analysis of distribution of consumption by sex shows a higher use in males than in females for all therapeutic categories, with the exception of medicines for the genito-urinary system and sexual hormones (females 65.5% vs males 34.5%), anti-neoplastic and immunomodulatory medicines (females 62.1% vs males 37.9%), anti-parasitics, insecticides and repellents (females 53.3% vs males 46.7%) and medicines belonging to the blood and haemopoietic organs category (females 50.3% vs males 49.7%) (Figure 1.5.4).

Anti-infectives for systemic use are confirmed as the therapeutic category with the highest pediatric consumption, at a prevalence of 482.0 per 1,000 children and a number of packages of 977.3 per 1,000 children, increasing by 29.9% compared to 2022 (Table 1.5.3), and confirming the recovery in antibiotic consumption already observed in 2022 (+53.3%), after the downward trend in previous years (2021-2020: -4.0% and 2020-2019: -46.0%). The prescribing pattern of the previous year was also confirmed in 2023: the combination

amoxicillin/clavulanic acid was the most prescribed drug in the category (409.7 packs per 1,000 children), up by 45.4% compared to 2022, confirming it as the top 30 active ingredient with the highest consumption in 2023 (Table 1.5.4). This is followed by amoxicillin alone (149.8 packs per 1,000 children, up 27.7% from 2022), the first-choice antibiotic in the treatment of the most common pediatric infections according to the guidelines (and therefore to be preferred over the combination with clavulanic acid), which ranks second in the top 30 active ingredients by consumption. Within the category cefixime, a third-generation cephalosporin, follows in fourth place, with 123.3 packs per 1,000 children (up 36.1% from 2022), and azithromycin in sixth place, with 100.2 packs per 1,000 children (up 8.7% from 2022) (Table 1. 5.4).

In the list of most prescribed categories, respiratory system drugs follow with a prevalence of 261.8 per 1000 children and a consumption of 529.0 packs per 1000 children. After the significant reduction in packaging observed in 2020 (-30.3%), the recovery in consumption observed in 2021 (+13.4%) and 2022 (+36.9%) is confirmed in 2023 as well, although the increase is much smaller than in previous years (+1.1% compared to 2022). Drugs indicated for the treatment of bronchial asthma, such as the inhaled corticosteroids, budesonide and beclomethasone, and salbutamol, a beta-2 adrenergic receptor agonist, are the drugs with the highest prevalence of use within the category; however, while budesonide and salbutamol continue to register further increases in consumption in 2023 compared to the previous year (+7.0% and +12.7%, respectively), beclomethasone, after the strong increase recorded in 2022 (+43.2%) inverts the trend by registering a 9.5% decrease compared to the previous year (Table 1. 5.3). In fourth place among respiratory drugs is the antihistamine cetirizine with a prevalence of use of 32.1 per 1,000 children and by number of packs per 1,000 children of 66.2 (+5.0% compared to 2022); all four drugs in this category rank in the top 10 positions among the active ingredients with the highest consumption in 2023 in the pediatric population (Tables 1.5.3 and 1.5.4).

The third category by consumption is systemic hormone preparations, excluding sex hormone preparations and insulins, with a prevalence of 124.3 per 1,000 children and consumption of 194.8 packs per 1,000 children, noting an increase in consumption in 2023 as well (+2.6% over 2022), although smaller than that observed in the previous year (+33.2 % over 2021). Betamethasone, a corticosteroid indicated in the treatment of complications related to upper respiratory tract infections in children, is the most prescribed medicine (125.0 packs per 1000 children), followed by growth hormone somatropin, with 23.6 packs per 1000 children. Both active ingredients rank among the top 30 for paediatric consumption in 2023, in second and seventeenth place respectively (Table 1.5.3 e 1.5.4).

The fourth most prescribed category is central nervous system drugs, with a prevalence of 13.6 per 1,000 children and consumption of 177.5 packs per 1,000 children, up from the previous year (+5.9%). Valproic acid appears to be the most prescribed active ingredient in the category, with a prevalence of 2.4 per 1000 children and a consumption of 53.2 packs per 1000 children, followed by two other antiepileptic drugs (carbamazepine and levetiracetam); these active ingredients rank thirteenth, twenty-second and twenty-third, respectively, in the list of the top 30 active ingredients by pediatric consumption in 2023 (Tables 1.5.3 and 1.5.4).

If along with these three active ingredients, we also consider other antiepileptic drugs such as lamotrigine, ethosuximide and phenobarbital, ranking sixth, ninth and tenth in terms of

consumption within the category, these active ingredients cover more than half of the consumption of the nervous system drug category. Ranking fourth in terms of consumption within the category is aripiprazole -with 12.2 packs per 1,000 children- which is indicated for the treatment of schizophrenia from the age of 15 years and bipolar disorder from the age of 13 years, followed by sertraline -with 9.5 packs per 1,000 children- a serotonin reuptake inhibitor antidepressant (SSRI) licensed for the treatment of obsessive-compulsive disorder (OCD) in children and adolescents aged between 6 and 17 years. Almost stable consumption is observed for all drugs in this category compared to the previous year. For methylphenidate and risperidone -both active ingredients with prevalence levels of use of 1.0 and 1.2 per 1,000 children, respectively- higher levels of use are reported in males than in females (M/F ratios of 5.4 and 3.0, respectively), consistent with epidemiological data in literature showing a higher prevalence of certain neuropsychiatric disorders in males than in females. In particular, the use of methylphenidate, a psychostimulant considered to be the drug therapy of choice, in cases where psycho-social interventions or psycho-behavioral therapies alone have proven insufficient, is found to be used more in males in a ratio of 5:1, as well as risperidone, which appears to be used more in males in a ratio of 3:1. This is an antipiscotic licensed in the short-term (up to 6 weeks) treatment of persistent aggression in conduct disorder in children as young as 5 years old and adolescents with below-average intellectual functioning or intellectual disability and in children and adolescents with autism spectrum disorders. In 2023, methylphenidate also ranks 30th among the highest consumed medications in the pediatric population (Table 1.5.4).

The category that ranks fifth in terms of consumption is gastrointestinal tract and metabolism drugs, with 154.3 packs per 1,000 children, half of which is attributable to cholecalciferol, although consumption has decreased by 4.1% since 2022. Ranking second in the category is insulin lispro for the treatment of diabetes mellitus, with 11 packs per 1,000 children, increasing by 15.5% in 2023 and 14.4% in 2022.

As for blood and hematopoietic organ drugs, one-fifth of consumption is accounted for by enoxaparin, with 8 packs per 1,000 children, more used by males than females. They are followed in consumption by anti-anemic drugs, such as ferrous sulfate (5.8 packs per 1,000 children) and folic acid (5.2 packs per 1,000 children), which, on the contrary, are found to be used more by females (Table 1.5.3).

The use of cardiovascular medicines, indicated in the treatment of congenital or acquired paediatric heart disease, is slightly higher in males than in females, although for some active ingredients the use is greater in females, as in the case of propranolol, whose greater use in females could be associated with the treatment of infantile haemangiomas, which occur more frequently in females.

Among the antineoplastics and immunomodulators, triptorelin, a medicine indicated in the paediatric population in the treatment of precocious puberty, appears to be the most widely used drug, with a ratio of 10:1 in favour of females over males. The other active ingredients in this group are instead used mainly in the treatment of paediatric rheumatological diseases.

There is also evidence of twice as much use in the male population as in the female population of isotretinoin, a drug licensed for the treatment of prepubertal acne, the use of which in females is limited because of the molecule's known teratogenic effects.

Among the top 30 active ingredients with the highest level of consumption in the paediatric

population in 2023 (Table 1.5.4), we find 10 belonging to the category of respiratory system medicines, 7 antibiotics, 6 of the central nervous system (3 antiepileptics, an antipsychotic, an antidepressant and a psychostimulant), 4 in the category of hormones (excluding sex hormones), 2 belonging to the category of gastrointestinal tract drugs (cholecalciferol and insulin lispro) and one belonging to the category of pesticides, insecticides and repellents (mebendazole).

After amoxicillin/clavulanic acid and amoxicillin combination, betamethasone and cefixime rank in the top positions by consumption with 125.0 and 123.3 packs per 1000 children, respectively; however, while there is only a slight increase in consumption for betamethasone (+1.1%), for cefixime the increase is quite marked (+36.1% compared to 2022), as well as for cefpodoxime (+53.2%), another third-generation cephalosporin, which ranks 12th in terms of consumption. The only active ingredients showing a reduction in 2023 are cholecalciferol (-4.1%), beclomethasone (-9.5%), and salbutamol/hypratropium (-41.0%). The latter finding could be a consequence of AIFA's restriction of use following a review of efficacy and safety data of medicinal products containing this combination, used in the treatment of bronchospasm in adult patients (>18 years of age) with chronic obstructive pulmonary disease (COPD), who require regular therapy with both ipratropium bromide and salbutamol.

Of all the highest consumed active ingredients, only for cholecalciferol, mebendazole, levothyroxine (a drug indicated in forms of hypothyroidism), levetiracetam and sertraline there is higher consumption in females than in males (Table 1.5.4).

Table 1.5.1 General prescription data in the paediatric population in 2023

	Males	Females	Total
Users	**2,312,460**	**2,096,426**	**4,408,886**
Prevalence (%)	49.1	47.6	48.6
Prescriptions	**10,458,907**	**8,797,779**	**19,256,686**
Per capita	2.2	2.0	2.0
Δ % 22-21	31.7	31.9	31.9
Δ % 23-22	12.5	13.9	13.9
Packages	**10,651,347**	**8,954,502**	**19,605,849**
Per capita	2.3	2.0	2.2
Δ % 22-21	31.0	31.2	31.1
Δ % 23-22	12.3	13.6	12.9
Per capita	**148,010,003**	**110,518,393**	**258,528,396**
Per capita	31.7	25.1	28.5
Δ % 22-21	18.1	23.1	20.2
Δ % 23-22	5.8	7.9	6.7
Per user	64.0	52.7	58.6
Δ % 22-21	-8.1	-3.7	-6.3
Δ % 23-22	-1.4	-0.7	-1.2

Figure 1.5.1 Regional trend in prescriptions in the paediatric population in 2023

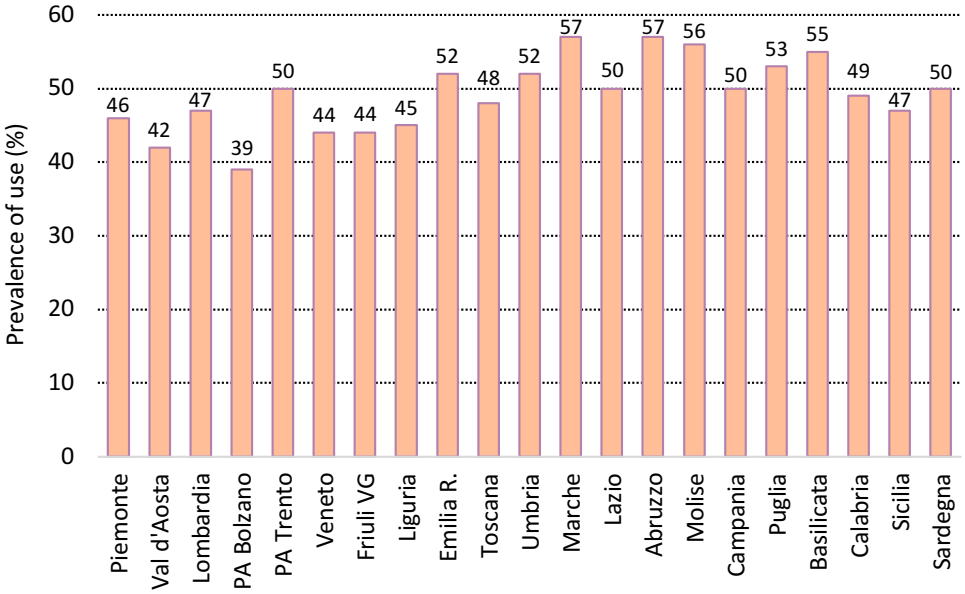


Figure 1.5.2 Trend in the prevalence of use and prescriptions in the paediatric population by age in 2023

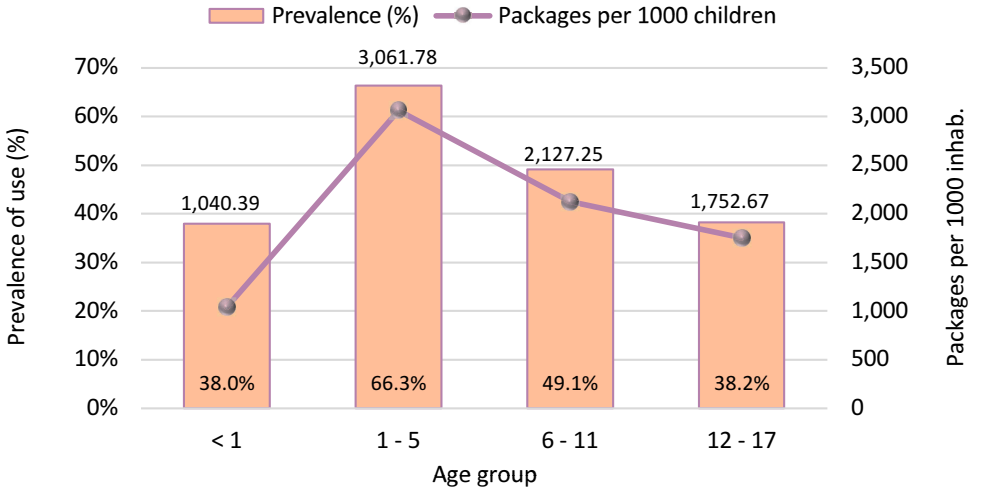


Table 1.5.2 Distribution of consumption (packages) by age and gender in the paediatric population in 2023

Age group	*Per capita* packages					
	Males	Δ % 23-22	Females	Δ % 23-22	Total	Δ % 23-22
< 1	1.13	-13.1	0.95	-12.3	1.04	-12.7
1 - 5	3.23	12.8	2.88	13.5	3.06	13.1
6 - 11	2.25	28.4	1.99	32.4	2.13	30.2
12 - 17	1.84	1.0	1.66	1.1	1.75	1.1
Total	**2.28**	**12.3**	**2.03**	**13.6**	**2.16**	**12.9**

Figure 1.5.3 Percentage distribution of consumption (packages) in the paediatric age by ATC I level in 2023

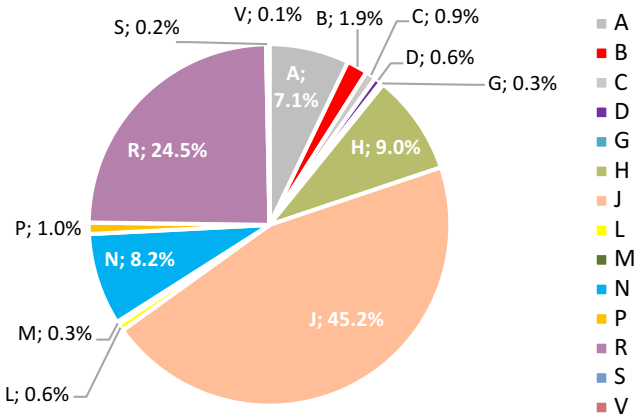
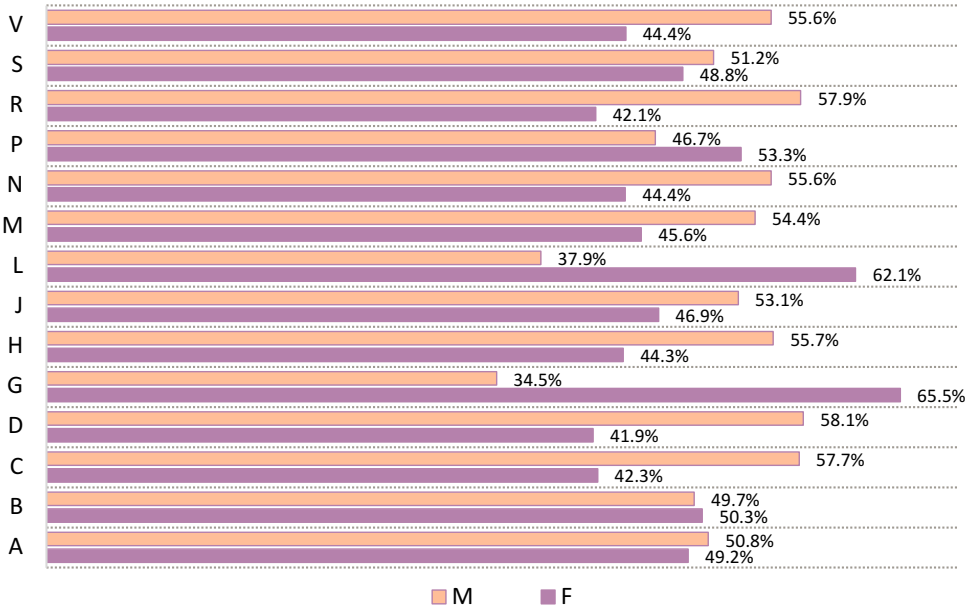


Figure 1.5.4 Percentage distribution of consumption (packages) in the paediatric age by ATC I level in 2023



A	Gastrointestinal tract and metabolism	H	Hormones (excl. sex hormones)	N	Nervous system
B	Blood and blood-forming organs	J	Antimicrobials for systemic use	P	Antiparasitic products
C	Cardiovascular system	L	Antineoplastic and immunomodulating agents	R	Respiratory system
D	Dermatologicals	M	Musculo-skeletal system	S	Sensory organs
G	Genito-urinary system and sex hormones			V	Various

Table 1.5.3 Most prescribed substances in the paediatric age by therapeutic category (75% of packages) in 2023

Therapeutic category/ substance	Packages Per 1000 children	Δ % 23-22	Δ % 22-21	Prevalence Per 1000 children	Ratio M/F
J - Anti-infectives for systemic use	**977.3**	**29.9**	**53.3**	**482.0**	**1.1**
amoxicillin/clavulanic acid	409.7	45.4	57.3	210.4	1.1
amoxicillin	149.8	27.7	67.6	72.5	1.1
cefixime	123.3	36.1	69.7	79.3	1.1
azithromicyn	100.2	8.7	28.9	66.2	1.1
R- Respiratory system	**529.0**	**1.1**	**36.9**	**261.8**	**1.2**
budesonide	107.9	7.0	77.0	72.7	1.2
salbutamol	93.9	12.7	37.2	65.0	1.4
beclomethasone	91.4	-9.5	43.2	67.2	1.2
cetirizine	66.2	5.0	10.6	32.1	1.4
fluticasone	34.6	3.4	26.4	19.6	1.6
montelukast	27.4	7.9	5.7	8.4	1.6
H - Systemic hormonal preparations, excl. sex ones and insulins	**194.8**	**2.6**	**33.2**	**124.3**	**1.2**
betamethasone	125.0	1.1	52.4	82.8	1.2
somatropin	23.6	10.7	1.5	0.9	1.5
N- Central nervous system	**177.5**	**5.9**	**6.9**	**13.6**	**1.2**
valproic acid	53.2	3.2	0.0	2.4	2.1
carbamazepine	15.8	3.3	2.9	0.8	1.2
levetiracetam	14.9	5.1	5.1	1.2	0.8
aripiprazole	12.2	15.5	29.2	1.3	1.0
sertraline	9.5	10.2	33.2	1.3	0.5
lamotrigin	8.0	5.7	6.2	0.4	0.5
methylphenidate	9.0	25.7	14.9	1.0	5.4
risperidon	5.3	12.6	7.4	1.2	3.0
ethosuximide	4.9	5.5	6.9	0.3	0.7
phenobarbital	4.3	-7.4	-5.0	0.2	1.2
A - Gastrointestinal tract and metabolism	**154.3**	**-1.9**	**-0.6**	**65.6**	**1.0**
cholecalciferol	76.7	-4.1	-5.1	35.8	1.0
insulin lispro	11.0	15.5	14.4	1.1	1.1
lansoprazole	8.0	-3.8	-0.3	1.9	1.0
insulin aspart	7.2	1.1	3.5	0.6	1.2
esomeprazole	6.5	3.0	4.1	2.0	1.0
ursodeoxycholic acid	5.2	3.4	0.4	0.4	1.0
mesalazine	4.3	5.0	1.4	0.4	1.2
B - Blood and blood-forming organs	**40.3**	**0.8**	**6.5**	**17.8**	**0.7**
enoxaparin	8.0	7.1	11.2	2.6	1.8
ferrous sulfate	5.8	10.1	7.6	3.0	0.3
folic acid	5.2	8.0	5.5	3.1	0.5
electrolytes for intravenous solutions	5.2	17.1		0.8	1.2
tranexamic acid	2.5	4.8	8.7	1.5	1.0
sodium ferric gluconate	2.2	47.9	4.1	1.1	1.3
polymaltosate iron	1.7	-59.1	1.0	0.9	1.3

continued

Table 1.5.3 – *continued*

Therapeutic category/ substance	Packages Per 1000 children	Δ % 23-22	Δ % 22-21	Prevalence Per 1000 children	Ratio M/F
P - Antiparasitic, insecticide and repellent pharmaceuticals	**21.9**	**23.4**	**-2.4**	**16.5**	**0.9**
mebendazole	19.9	31.5	7.6	12.1	0.9
C - Cardiovascular system	**20.0**	**-0.1**	**0.8**	**2.9**	**1.2**
ramipril	1.9	-1.4	2.4	0.2	1.6
enalapril	1.9	-2.1	-2.9	0.2	1.4
flecainide	1.7	3.9	4.1	0.2	1.1
bisoprolol	1.5	5.2	5.5	0.2	1.2
furosemide	1.4	-0.9	-4.6	0.2	1.1
losartan	1.4	6.4	1.5	0.1	2.1
carvedilol	1.2	-0.7	-4.1	0.1	1.5
amlodipine	1.2	9.1	9.4	0.2	1.4
propranolol	0.9	9.3	-2.4	0.2	0.6
spironolactone	0.9	-11.9	4.4	0.1	0.9
omega-3	0.5	5.6	-2.7	0.1	1.4
adrenaline	0.5	-18.5	70.3	0.3	1.5
atorvastatin	0.4	6.5	-9.0	0.1	1.1
L - Antineoplastic and immunomodulating agents	**13.6**	**0.3**	**0.7**	**1.8**	**0.5**
triptorelin	3.7	-7.4	10.9	0.5	0.1
methotrexate	2.9	3.1	-7.0	0.4	0.5
tacrolimus	2.3	4.7	-1.9	0.1	1.1
azathioprine	1.2	5.2	9.0	0.2	1.0
ciclosporin	0.7	-1.5	-12.4	0.1	1.1
D - Dermatologicals	**13.4**	**0.0**	**-0.3**	**6.2**	**1.3**
isotretinoin	7.1	-7.4	1.1	1.6	1.8
calcipotriol/betamethasone	1.2	5.9	-3.9	0.6	0.9
methylprednisolone	1.1	12.0	3.9	0.8	1.1
clobetasol	1.0	14.2	-1.0	0.5	0.9
G - Genito-urinary system and sex hormones	**6.0**	**-0.3**	**2.0**	**1.8**	**0.3**
oxybutynin	2.2	1.1	5.4	0.3	1.8
cyproterone/ethinylestradiol	0.7	-12.0	-8.7	0.1	0.0
estradiol	0.5	6.5	6.5	0.1	0.0
dydrogesterone	0.5	11.5	-6.0	0.2	0.0
cabergoline	0.2	-9.3	-7.2	0.1	0.1
nomegestrol	0.2	-14.2	1.8	0.1	0.0
progesterone	0.2	-17.2	1.5	0.1	0.0
M - Musculo-skeletal system	**5.6**	**-12.7**	**29.1**	**4.5**	**1.1**
ibuprofen	1.5	-21.2	111.5	1.3	1.1
ketoprofen	1.1	-18.5	30.9	0.9	1.0
baclofen	0.7	-0.1	1.9	0.1	1.5
allopurinol	0.4	0.1	4.7	0.1	2.0
diclofenac	0.4	0.5	7.0	0.3	1.2
colchicine	0.3	7.1	15.0	0.1	1.4

continued

Table 1.5.3 – *continued*

Therapeutic category/ substance	Packages Per 1000 children	Δ % 23-22	Δ % 22-21	Prevalence Per 1000 children	Ratio M/F
S-Sensory organs	**4.4**	**9.4**	**-2.4**	**0.6**	**0.8**
acetazolamide	1.4	24.9	-6.5	0.1	1.0
timolol	0.7	6.6	-1.3	0.2	0.6
dorzolamide/timolol	0.6	12.9	-0.3	0.1	1.2
dorzolamide	0.2	-1.2	8.6	<0.05	1.4
latanoprost	0.2	18.2	6.1	<0.05	1.2
timolol/brinzolamide	0.2	-11.8	-7.5	<0.05	1.4
bimatoprost	0.2	0.5	-2.6	<0.05	1.1
V - Various	**2.2**	**14.3**	**-2.2**	**0.5**	**1.4**
oxygen	0.6	7.4	-2.6	0.2	1.0
grass pollen (phleum pratense)	0.4	45.0	47.0	0.1	2.0
deferasirox	0.4	10.2	8.5	0.0	1.1
grass pollen (phleum pratense/dactylis glomerata/ Anthoxanthum odoratum/lolium perenne/poa pratensis)	0.3	19.7	16.6	0.1	1.9

Table 1.5.4 Top 30 active ingredients by consumption in the paediatric age in 2023

ATC I liv	Active ingredient	Packages Per 1000 children	Δ % 23-22	Δ % 22-21	Consumption (%)*		Inc. % tot**%
					males	females	
J	amoxicillin/clavulanic acid	409.7	45.4	57.3	53.7	46.3	22.7
J	amoxicillin	149.7	27.7	67.6	52.5	47.5	31.0
H	betamethasone	125.0	1.1	52.4	56.4	43.6	37.9
J	cefixime	123.3	36.1	69.7	51.5	48.5	44.7
R	budesonide	107.9	7.0	77.0	55.1	44.9	50.7
J	azithromicyn	100.2	8.7	28.8	53.5	46.5	56.3
R	salbutamol	93.9	12.7	37.2	58.8	41.2	61.5
R	beclomethasone	91.4	-9.5	43.2	54.8	45.2	66.5
A	cholecalciferol	77.0	-4.1	-5.1	49.4	50.6	70.8
R	cetirizine	66.2	5.0	10.6	60.2	39.8	74.4
J	clarithromycin	58.2	4.6	86.7	54.0	46.0	77.6
J	cefpodoxime	55.8	53.2	72.7	53.6	46.4	80.7
N	valproic acid	53.2	3.2	0.0	67.8	32.2	83.7
R	fluticasone	34.6	3.4	26.4	61.6	38.4	85.6
R	montelukast	27.4	7.9	5.7	62.4	37.6	87.1
H	somatropin	23.6	10.7	1.5	61.0	39.0	88.4
R	flunisolide	21.1	2.0	55.0	54.2	45.8	89.6
R	salbutamol/ ipratropium	20.3	-41.0	33.4	55.0	45.0	90.7
J	ceftriaxone	20.0	15.4	35.9	55.5	44.5	91.8
P	mebendazole	19.9	31.5	7.6	46.6	53.4	92.9
H	levothyroxine	16.1	2.4	1.7	39.0	61.0	93.8
N	carbamazepine	15.8	3.3	2.9	56.8	43.2	94.7
N	levetiracetam	14.9	5.1	5.1	44.1	55.9	95.5
H	prednisone	14.7	3.4	24.7	55.9	44.1	96.3
R	levocetirizine	12.5	5.0	5.6	62.0	38.0	97.0
N	aripiprazole	12.2	15.5	29.2	52.0	48.0	97.7
R	salmeterol/ fluticasone	12.1	20.7	14.8	65.2	34.8	98.4
A	insulin lispro	11.0	15.5	14.4	53.5	46.5	99.0
N	sertraline	9.5	10.2	33.2	32.0	68.0	99.5
N	methylphenidate	9.0	25.7	14.9	85.9	14.1	100.0
	Total top 30	**1,805.9**	**15.6**	**38.4**	**54.9**	**45.1**	**100.0**
	Total	**2,160.2**	**12.9**	**32.0**	**54.3**	**45.7**	**100.0**

* calculated with reference to the overall consumption of the molecule in the paediatric age

** calculated with reference to the overall consumption in the paediatric age

1.6 Pharmaceutical use in the geriatric age

In Italy, the population aged 65 and over reached about 14.1 million people in 2023, or 24% of the Italian population. Women are about 7.9 million, representing 56.0% of this age group.

As expected, medicines use increases with age up to the 80-84 ys group and then slightly decreases among those aged 85 and over (Figure 1.6.1). The highest level of pharmaceutical consumption was recorded in the 80-84 and ≥85 age groups (4065,4 and 3869,3 DDD/1000 users per day, respectively), with an expenditure per user equal to 662.3 euros and 629.3 euros, respectively (Table 1.6.1).

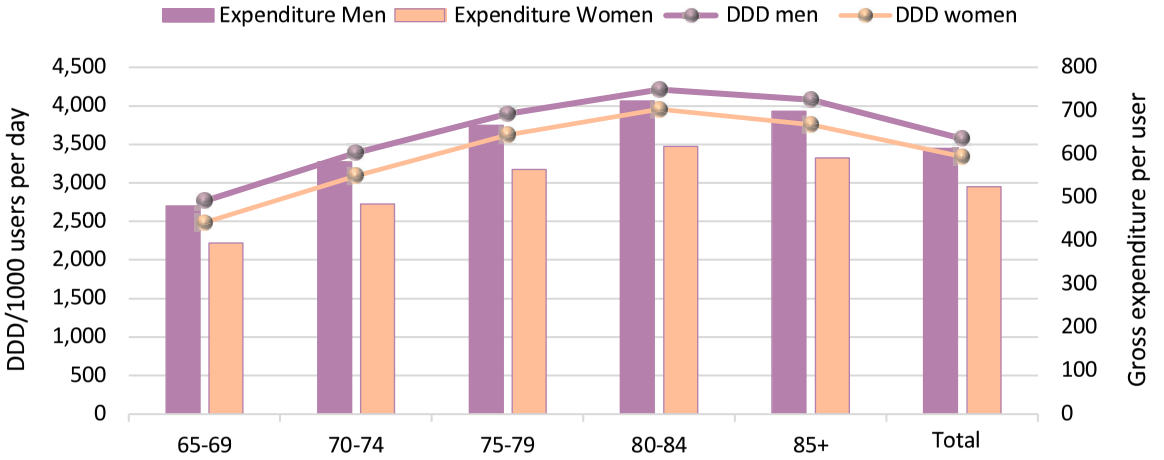
Overall, the average expenditure per user was 563.4 euros (613.6 in men and 524.1 in women), up slightly from 2022 (+1.45%). The analysis of drug consumption in patients who received at least one drug prescription in 2023 showed a higher number of DDD/1000 users per day in males than in females (3,569.7 vs 3,341.6) and a general stability of doses dispensed per user in 2023 compared to 2022 (-0.86%) (Table 1.6.1).

When the prevalence of use is analyzed, it is observed that almost the entire population (97.2%) received at least one drug prescription during the year, with no differences in the two sexes and slightly decreasing (-1.15%) compared to 2022. The incidence of use also decreased by 7.3% in 2023 compared with the previous year. After the observed positive trend in the number of incident patients of previous years that showed a probable recovery of new diagnoses from the years of health emergency (2019-2020), there is a reduction in incident patients for all age groups in 2023.

Table 1.6.1 Distribution by age and sex of pharmaceutical prescription in the population aged ≥65 years in 2023

Age group	Expenditure per user				DDD/1000 users per day				Prevalence of use (%)				Incidence of use (%)			
	M	F	T	Δ % 23-22	M	F	T	Δ % 23-22	M	F	T	Δ % 23-22	M	F	T	Δ % 23-22
65-69	479.7	394.2	434.5	1.41	2,764.5	2,485.3	2,616.8	-1.67	88.5	90.7	89.7	-1.77	6.1	5.4	5.7	-7.97
70-74	582.5	484.4	530.3	1.37	3,389.7	3,091.3	3,230.8	-1.64	91.6	91.6	91.6	1.33	3.8	3.3	3.6	-4.51
75-79	666.8	563.9	610.8	1.10	3,893.5	3,621.1	3,745.2	-1.17	102.3	100.7	101.4	-4.23	2.7	2.4	2.6	-9.59
80-84	722.4	617.3	662.3	1.63	4,211.2	3,956.3	4,065.4	-0.27	100.1	97.3	98.5	-1.88	2.0	1.8	1.8	-8.03
85+	698.4	590.7	629.3	1.90	4,078.7	3,752.4	3,869.3	0.58	116.3	108.7	111.3	0.12	2.2	2.1	2.1	-8.53
Total	**613.6**	**524.1**	**563.4**	**1.45**	**3,569.7**	**3,341.6**	**3,441.9**	**-0.86**	**97.2**	**97.2**	**97.2**	**-1.15**	**3.7**	**3.2**	**3.4**	**-7.30**

Figure 1.6.1 Prescription trend in the population aged ≥65 years (DDD/1000 users per day and gross expenditure per user) in 2023



Polypharmacy in the elderly population

In order to assess polypharmacy in the elderly population, two analyses were conducted to evaluate "polypharmacy" and "chronic polypharmacy," using the number of drugs prescribed per user as a proxy.

The first analysis assessed "polypharmacy" defined as the "administration of an average number of substances (ATC Level V) per user over the course of the year, regardless of the duration of prescription."

Based on this in-depth study, in 2023 each user over 65 years old took an average of 7.6 different pharmacological substances (Table 1.6.2), with the lowest value (6.0 substances per user) in the 65-69 age group and the highest value (8.7 substances per user) recorded in the over 85s. For both sexes, there is a gradual increase in the number of different active ingredients (pharmacological substances) taken as age increases: in males, there is an increase from 5.9 substances in the 65-69 age group to 8.9 taken in the over-80s, while in females, there is an increase from 6 different substances taken in the 65-69 age group to 8.5 different active ingredients taken in the 85+ age group. When analyzing the distribution of users by number of different active ingredients (Figure 1.6.2), it can be seen that about 68.0% of elderly users (nearly 7 out of 10 users) received prescriptions for at least 5 different substances (definition of polypharmacy) during the reporting year and that even about one in three (28.5%) aged 65 years or older took at least 10 different active ingredients during the year.

An analysis of the prevalence of use by region and geographical area (Table 1.6.3) shows a prevalence higher than the national average, relating to the use of more than 10 substances, for the regions of the Centre (29.3%) and the South (38.1%). For a number of less than 7 substances, on the other hand, a higher prevalence of use can be noted in the northern regions, compared to the national average.

Table 1.6.2 Average number of substances by age and sex in 2023

Age group	Average number of substances			Average last 5 years
	Males	Females	Total	
65-69	5.9	6.0	6.0	6.0
70-74	7.0	7.0	7.0	6.9
75-79	7.9	7.8	7.8	7.8
80-84	8.5	8.4	8.5	8.4
≥85 years	8.9	8.5	8.7	8.6
Total	**7.6**	**7.5**	**7.6**	**7.5**

Figure 1.6.2 Percentage distribution of users in the population ≥ 65 years by number of different substances in 2023

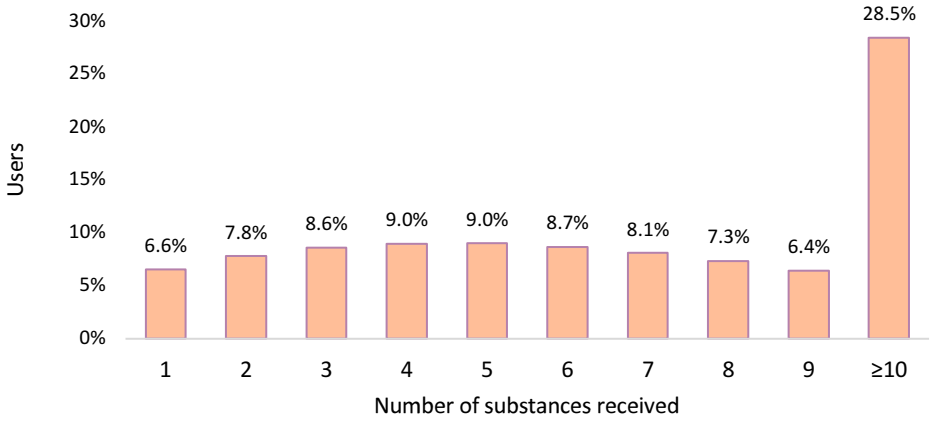


Table 1.6.3 Prevalence of use by Region and number of different substances (year 2023)

Regione	Number of different subtances				
	1	2-4	5-7	8-9	10+
Piedmont	7.3	27.3	26.0	13.0	22.5
Valle d'Aosta	8.9	30.0	24.5	11.5	18.9
Lombardy	7.7	28.3	25.5	12.1	19.7
Province of Bolzano	11.0	31.7	23.9	10.3	13.8
Province of Trento	8.6	28.1	25.5	12.3	20.4
Veneto	8.9	31.1	25.7	11.4	16.4
Friuli VG	8.1	28.9	26.3	12.5	19.3
Liguria	7.4	26.7	25.3	12.6	22.3
Emilia R.	7.1	27.3	27.2	13.5	21.6
Tuscany	7.1	26.5	25.9	13.1	24.7
Umbria	5.8	25.2	26.8	14.5	26.7
Marche	5.7	24.2	26.7	14.7	28.4
Lazio	5.3	21.6	24.7	14.5	33.2
Abruzzo	5.7	21.6	24.4	14.4	32.0
Molise	5.4	21.6	24.2	14.1	32.1
Campania	3.8	17.8	22.8	14.7	42.2
Puglia	4.6	20.6	24.8	14.8	35.8
Basilicata	4.4	19.8	24.8	15.1	36.9
Calabria	4.2	17.4	21.0	13.7	43.3
Sicily	4.3	18.6	22.9	14.4	40.5
Sardinia	6.2	25.4	26.7	14.2	25.9
Italy	**6.4**	**24.7**	**25.1**	**13.4**	**27.7**
North	7.8	28.4	25.9	12.4	20.0
Centre	6.0	23.8	25.5	14.1	29.3
South and Islands	4.5	19.6	23.6	14.5	38.1

The second analysis aimed to assess "chronic polypharmacy" defined as the "administration of 5 or more drugs (ATC Level IV) taken in the same month for at least 6 months, including non-consecutive months, during the year."

For this purpose, a cohort of patients (≥65 years old) who received at least one pharmaceutical prescription during the last quarter of 2022 (index date) and were alive in the last quarter of 2023 was selected, excluding patients >95 years old as they were frequently hospitalized or admitted to RSA.

All subjects so identified were followed for an observation period (follow-up) of 12 months, assuming that treatment began on the day the prescription was issued and that the subject took the drug for the duration of therapy. For each prescription, drug treatment, i.e., the number of days of therapy (calculated from the DDDs dispensed in each prescription) was calculated, and for each subject, the number of drugs taken in the same month for 6 or 9 months, including non-consecutive months, in a year was calculated. ATC level IV was considered for calculating the number of drugs taken in order to avoid considering two active ingredients belonging to the same drug class as two different therapies (e.g., atorvastatin and simvastatin prescribed during 6 months) in order to minimize the effect of drug switch within the same therapeutic class, a frequent event in clinical practice, especially in the management of chronic diseases.

This analysis shows that 33% of the elderly population (3 out of 10 patients) take at least 5 different medications for at least 6 months in the course of a year (definition of chronic polypharmacy), with an upward trend with increasing age until age 89, when it peaks at 44% (one out of two patients); then, from age 90 onward, this percentage decreases to 38% (Table 1.6.4). The trend by age is similar in both sexes, although the percentage of males in polypharmacy appears to be higher than females for all age groups. These trends are maintained even when considering a longer period (9 months, also non-consecutive), although the percentage of subjects on polypharmacy is lower, standing at 22.1% (one out of 5 patients).

Table 1.6.4 Percentage of users in the population aged ≥65 years in chronic polypharmacy (prescription of 5 drugs or more for at least 6 and 9 months, including non-consecutive, during 2023)

	6 months			9 months		
	Females %	Males %	Total %	Females %	Males %	Total %
65 - 69	18.4	23.3	20.7	11.2	15.3	13.2
70 - 74	26.4	31.6	28.8	16.9	21.5	19.0
75 - 79	34.4	38.9	36.5	22.7	27.0	24.7
80 - 84	40.4	43.9	41.9	27.0	30.8	28.7
85 - 89	42.5	45.1	43.6	28.2	31.3	29.4
90 - 94	36.6	40.0	37.7	23.0	26.5	24.1
Total	**31.7**	**35.1**	**33.2**	**20.6**	**24.0**	**22.1**

The increase in life expectancy of the population has led to an increase in the number of patients with multiple chronic diseases (multimorbidity) and the consequent co-prescription of multiple related drugs (polypharmacy), especially among the elderly.

Recent literature data indicate a prevalence of polypharmacy in the elderly population that varies, depending on the definition used, from 2.6% to 86.6% globally. Data obtained in the Italian population also indicate a frequent use of polypharmacy in the over-65s (68.0% and 33% chronically), consequently exposing this segment of the population to a high risk of drug interactions and adverse drug reactions, and thus a higher likelihood of hospitalization and death. Pharmacological burden reduction and optimization of treatment regimens in elderly patients through reevaluation of medication prescriptive appropriateness, medication reconciliation, and deprescribing are therefore crucial activities to be implemented, especially within general practice, in order to improve health outcomes and quality of life of elderly patients.

References

- Carollo M, Boccardi V, Crisafulli S, Conti V, Gnerre P, Miozzo S, Omodeo Salè E, Pieraccini F, Zamboni M, Marengoni A, Onder G, Trifirò G; Italian Scientific Consortium on medication review, deprescribing. Medication review and deprescribing in different healthcare settings: a position statement from an Italian scientific consortium. Aging Clin Exp Res. 2024;36(1):63.
- Fincke BG, Snyder K, Cantillon C, Gaehde S, Standring P, Fiore L, Brophy M, Gagnon DR. Three complementary definitions of polypharmacy: methods, application and comparison of findings in a large prescription database. Pharmacoepidemiol Drug Saf 2005; 14:121–8
- Franchi C, Marcucci M, Mannucci PM, Tettamanti M, Pasina L, Fortino I, Bortolotti A, Merlino L, Nobili A. Changes in clinical outcomes for community-dwelling older people exposed to incident chronic polypharmacy: a comparison between 2001 and 2009. Pharmacoepidemiol Drug Saf. 2016;25(2):204-11.
- Franchi C, Cartabia M, Risso P, Mari D, Tettamanti M, Parabiaghi A, Pasina L, Djignefa Djade C, Fortino I, Bortolotti A, Merlino L, Nobili A. Geographical differences in the prevalence of chronic polypharmacy in older people: eleven years of the EPIFARM-Elderly Project. Eur J Clin Pharmacol. 2013;69(7):1477-83.
- Haider SI, Johnell K, Weitoft GR, Thorslund M, Fastbom J. The influence of educational level on polypharmacy and inappropriate drug use: a register-based study of more than 600,000 older people. J Am Geriatr Soc 2009; 57:62–9
- Hallas J. Drug utilization statistics for individual-level pharmacy dispensing data. Pharmacoepidemiol Drug Saf 2005; 14:455–63
- Johnell K, Fastbom J, Rosen M, Leimanis A. Inappropriate drug use in the elderly: a nationwide register-based study. Ann Pharmacother 2007; 41:1243–8

- Johnell K, Klarin I. The relationship between number of drugs and potential drug-drug interactions in the elderly: a study of over 600,000 elderly patients from the Swedish Prescribed Drug Register. Drug Saf 2007; 30:911–8
- Mantel-Teeuwisse AK, Klungel OH, Verschuren WM, Porsius A, de Boer A. Comparison of different methods to estimate prevalence of drug use by using pharmacy records. J Clin Epidemiol 2001; 54:1181–6
- Nicholson K, Liu W, Fitzpatrick D, Hardacre KA, Roberts S, Salerno J, Stranges S, Fortin M, Mangin D. Prevalence of multimorbidity and polypharmacy among adults and older adults: a systematic review. Lancet Healthy Longev. 2024;5(4):e287-e296.
- Pazan F, Wehling M. Polypharmacy in older adults: a narrative review of definitions, epidemiology and consequences. Eur Geriatr Med. 2021;12(3):443-452.
- Viktil KK, Blix HS, Moger TA, Reikvam A. Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems. Br J Clin Pharmacol 2007; 63:187–95

Consumption and expenditure trend by age group

The trend of drug consumption in the elderly population (≥65 years), expressed as DDD/1000 population per day (Figure 1.6.3), shows increases as the age of patients rises to a maximum value of 4.784 DDD in patients aged 85-90 years, although it is the over-90s who show the greatest increase in consumption over time, rising from a value of 3,797 DDD in 2019 to one of 4,612 DDD in 2023 (CAGR: +3.8%). The percentage incidence of the number of doses (Figure 1.6.4) shows how the weight of the ultra-sixty-five-year-aged in the general population increased by one percentage point over the period, from 67.0% in 2019 to 68.0% in 2023. Patients aged 70-79 years old will have the greatest impact on the consumption of the over-65 population in 2023 (15.0%).

In addition, there is a gender difference in consumption (expressed as number of doses) in all years considered, with females consuming more doses than males in the older age groups (≥80 years), while in the younger age groups (65-79 years), it is males who consume more doses than females (Figures 1.6.5 and 1.6.6). In 2023, it is found that the largest difference between the two sexes is among those over the age of 90, where females consume more doses than males (4.6% vs. 2.5%). Despite the increase in doses used that is observed in all age groups over the period from 2019 to 2023, in the over-65s, the average cost per DDD is lower than that observed in younger individuals (<64 years old), as well as remaining almost constant over time (Figure 1.6.7). These trends indicate that the elderly show higher consumption of lower-cost drugs per DDD than individuals younger than 64 years of age.

The analysis of per capita spending reflects consumption trends. Analyzing the trends over the past five years (2019-2023 period), stratified by age group (Figure 1.6.8), it is clear that the over-65 population registers significantly higher per capita expenditure values than younger individuals (≤64 years old) and that they tend to increase with age, reaching the highest values in the 85-90 age group (725.13 euros in 2023), and then decreasing in the over-90s (638.95 euros in 2023). This trend can be observed for all the years considered. Of particular interest is the average annual rate of increase (CAGR: +3.0%) recorded in the over-90s, the highest ever observed during the period under consideration. Patients aged 75-79 years, while experiencing a lower annual rate of increase, record the largest reduction in per capita expenditure in 2023 when compared to other age groups. In contrast, patients aged 70 to 74 years old, while registering a not particularly high annual rate of increase (CAGR: +0.9%), experience the highest increase in per capita spending in 2023 compared to the previous year, ranging from 472.79 euros in 2022 to 485.68 euros in 2023. The incidence of gross local pharmaceutical expenditure by age group (Figure 1.6.9) shows that in 2023, the over-65s account for more than 63% of the total, with a rather steady trend over time. The highest incidence is found in the 75-79 age group (14 % in 2023), increasing slightly from the previous year (13.5 % in 2022), while the lowest incidence was observed in the over-90s (3.3 % in 2023), a value that remained stable from the previous year.

Analyzing the differences by sex in the incidence of spending in the over-65 population (Figures 1.6.10 and 1.6.11), you see that in all years considered females show higher percentage values than males in the older age groups (≥80 years), excluding the younger age groups (65-79 years). Specifically, in 2023 the incidence for females was 64.3% and for males 62.6%; the age group that absorbs largest expenditure is 75 to 79 years of age in both sexes (13.6% for females and 14.3% for males).

Analyzing the trend in spending per user in 2023 (Figure 1.6.12), it is seen an increase in values with advancing age, up to the 80-84 age group (662.3 euros), while thereafter a decrease is observed, which is more pronounced in the over-90s (564.62 euros). Looking at the period 2019-2023, the largest increases are observed in the 85-90 age group (CAGR: +0.8%), only slightly smaller than those observed in the under-64 population (CAGR: +1.0%), although in the under-64 age group spending per user remains almost steady compared to 2022 and increases in all other age groups, particularly in the 85-90 age group (+2.0%).

The time series of the number of users over the age of 65 in 2019-2023 (Figure 1.6.13) shows that the number of people taking drugs decreases in the 70-74 years (CAGR: -0.76%), 80-84 years (CAGR: -0.24%) and 85-89 years (CAGR: -0.4%), and increases, on the other hand, in the 65-69 year olds (CAGR: +0.7%) and 75-79 year olds (CAGR: +1.5%), and especially in the over-90s (CAGR: +5.3%), where the number of users increased from 556,406 users in 2019 to 721,356 users in 2023. Since spending per user in the over-90s remains fairly stable over time, the increase in the number of users is likely to justify the increase in per capita expenditure observed in this age group.

Overall, throughout the period considered, per capita spending and drug consumption in the elderly population tends to increase with age up to 90 years. Expenditure per user also tends to increase with age, peaking in the 80-84 age group and then declining in the older age groups.

Looking at the period 2019-2023, it can be seen that per capita spending attributable to subjects over the age of 90 and 75-79 is on the rise, however, intensive use, expressed as spending per user, tends to remain stable over the period. Therefore, the growth in spending per capita could be due to the increase in the number of users, which is particularly marked in these populations.

The average DDD cost of the over-65s, on the other hand, tends to remain steady over time, despite an increase in the doses used. These trends indicate that the elderly show a higher consumption of medicines with a lower DDD cost than those under 64 years of age.

Figure 1.6.3 Trend in the consumption of medicines (DDD/1000 inhabitants per day) by age in the period 2019-2023

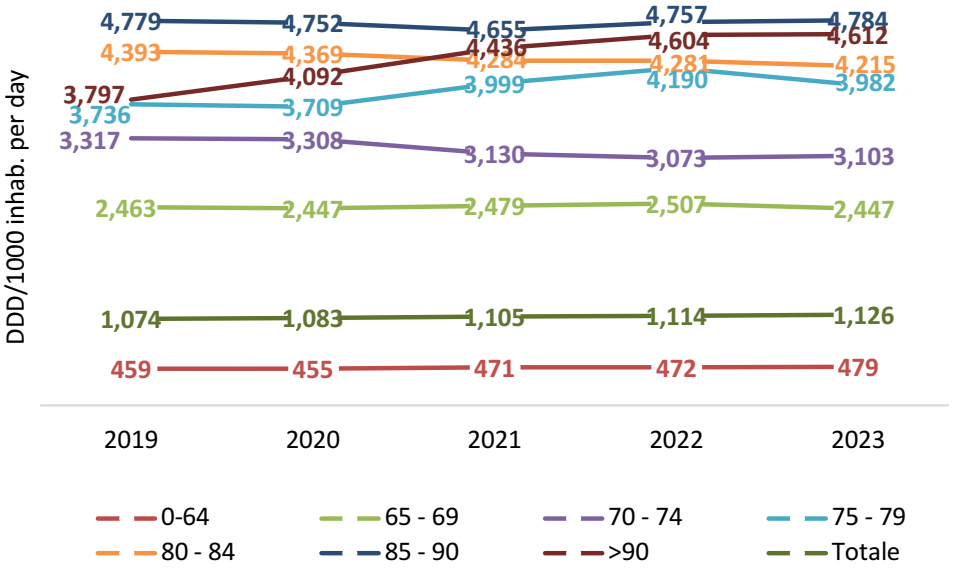


Figure 1.6.4 Incidence of local consumption (number of doses) of medicines by age in the period 2019-2023

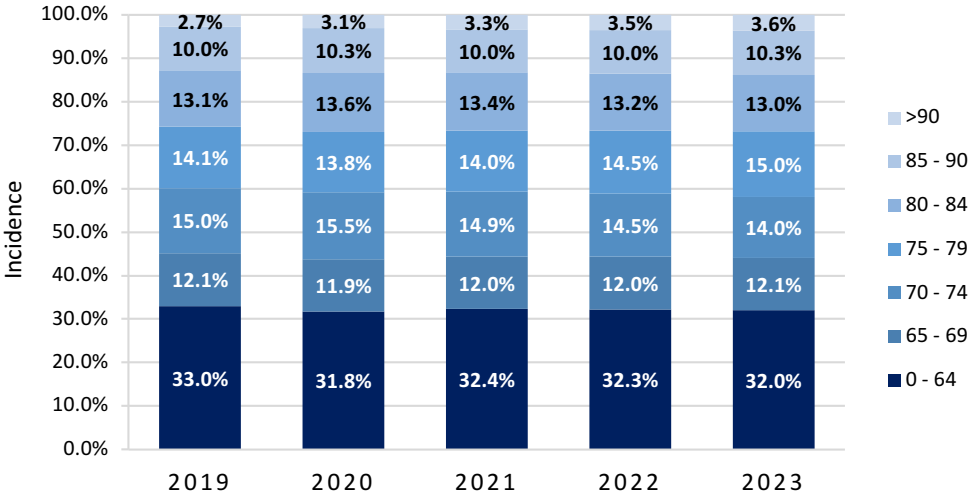


Figure 1.6.5 Incidence of local consumption (number of doses) of medicines by age of females in the period 2019-2023

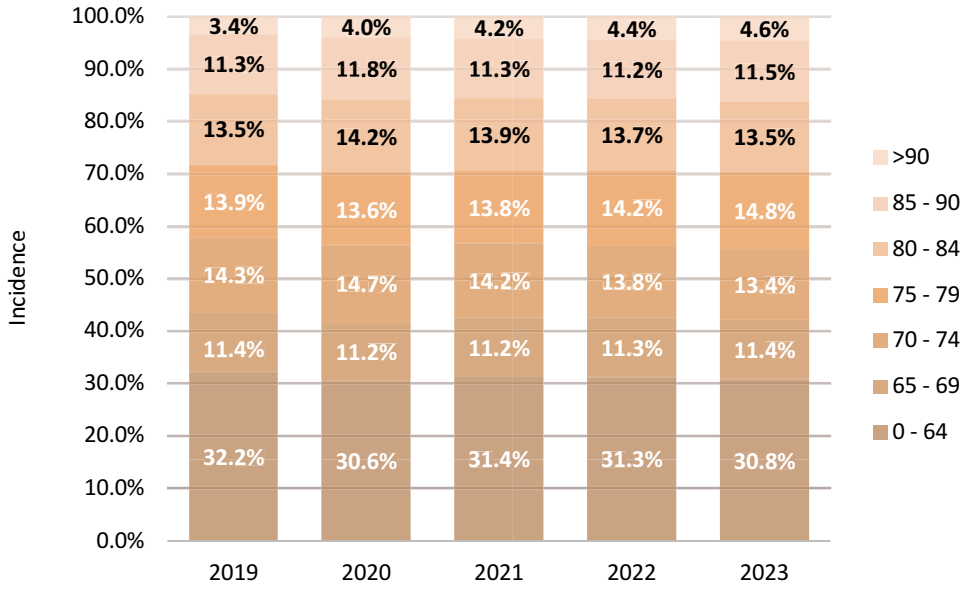


Figure 1.6.6 Incidence of local consumption (number of doses) of medicines by age of males in the period 2019-2023

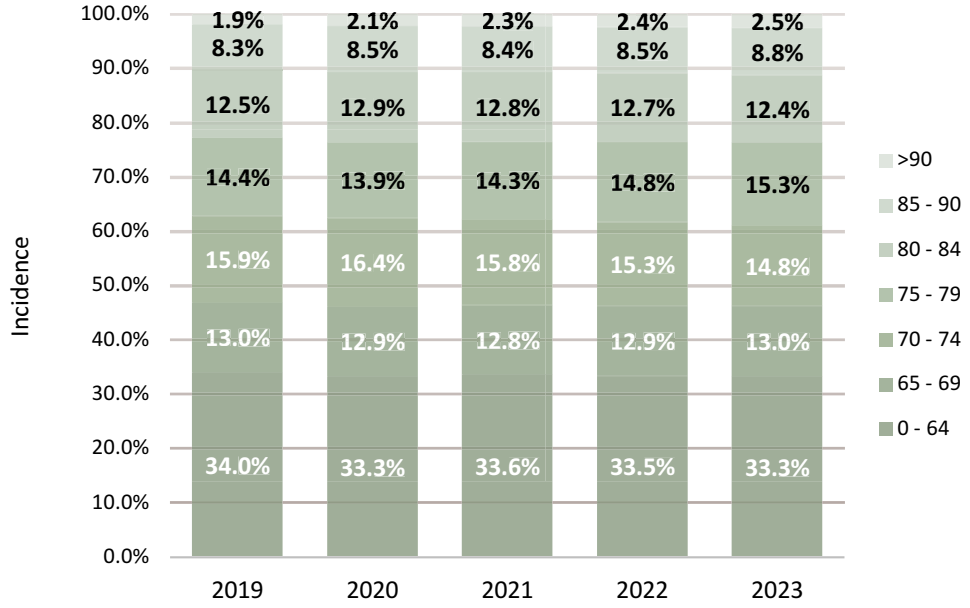


Figure 1.6.7 Trend of average cost for day of therapy by age group in the period 2019-2023

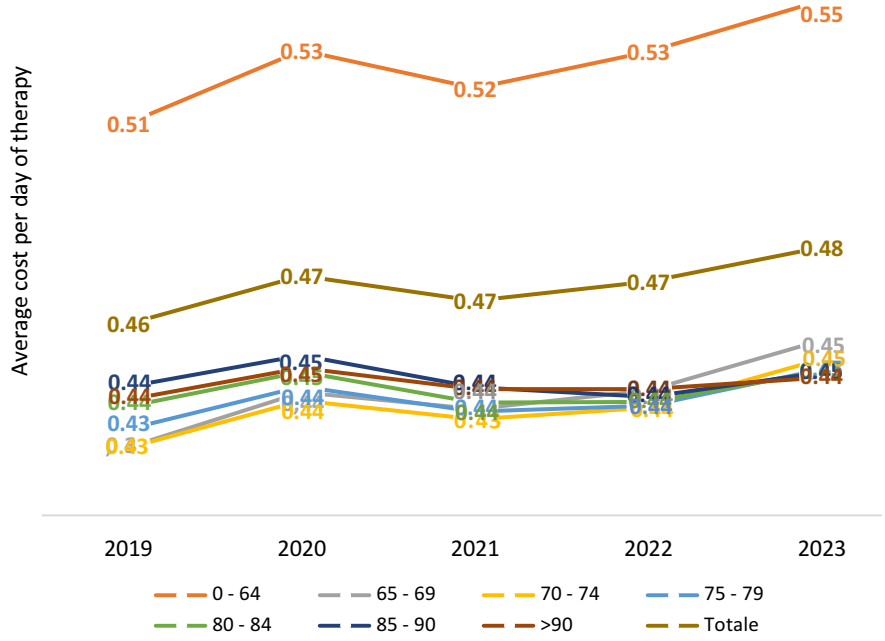


Figure 1.6.8 Trend in per capita expenditure by age over the period 2019-2023

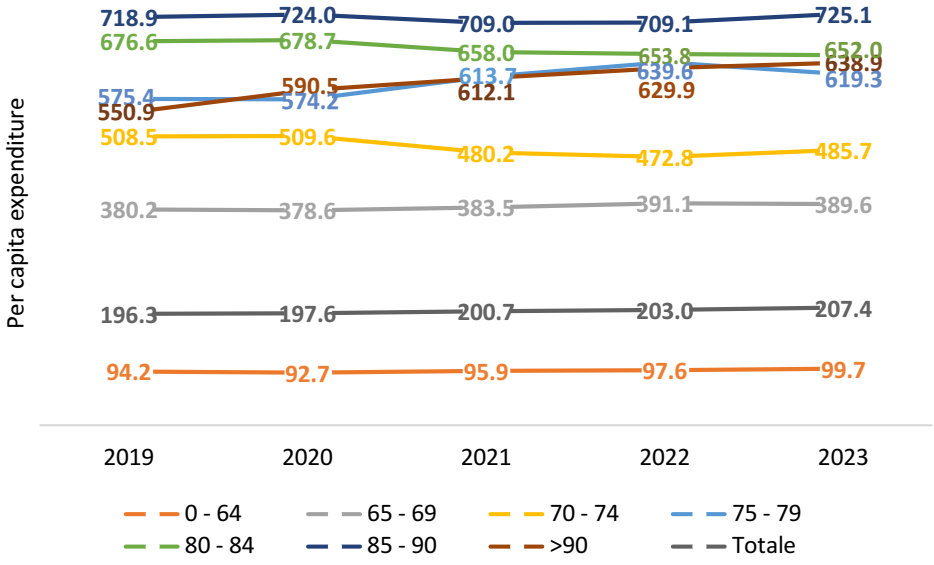


Figure 1.6.9 Incidence of local gross pharmaceutical expenditure by age over the period 2019-2023

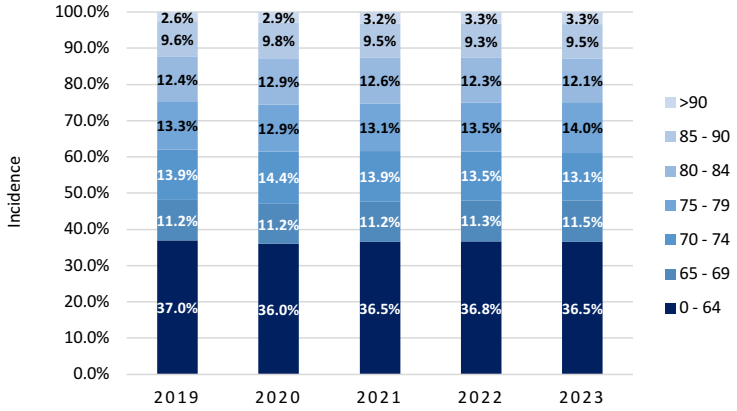


Figure 1.6.10 Incidence of local gross pharmaceutical expenditure by age over the period 2019-2023

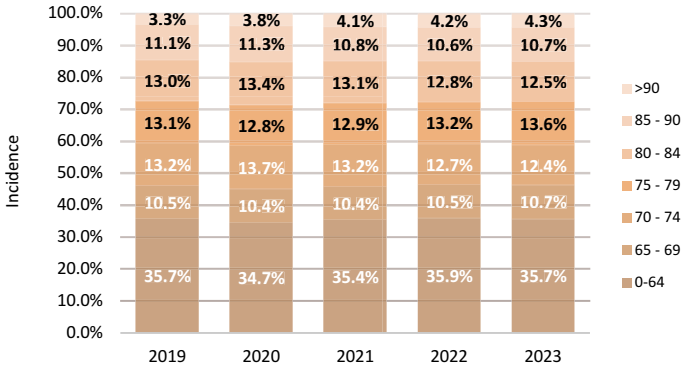


Figure 1.6.11 Incidence of local gross pharmaceutical expenditure by age over the period 2019-2023

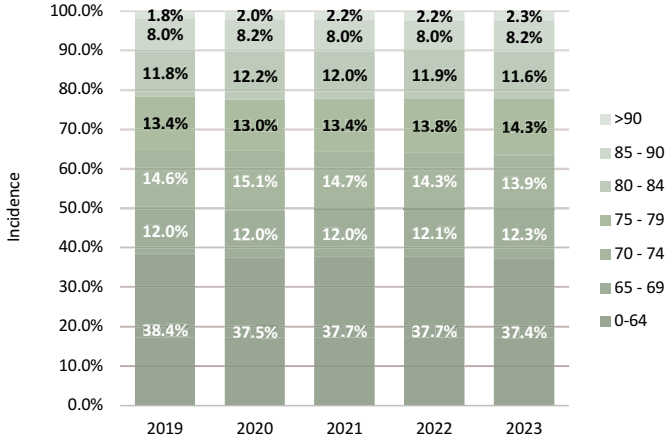


Figure 1.6.12 Trend in per user expenditure by age over the period 2019-2023

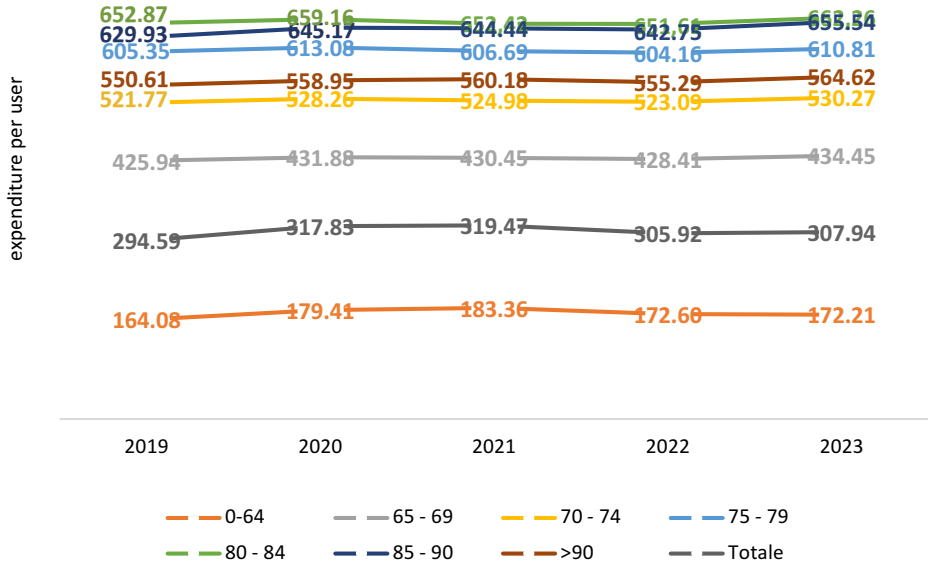
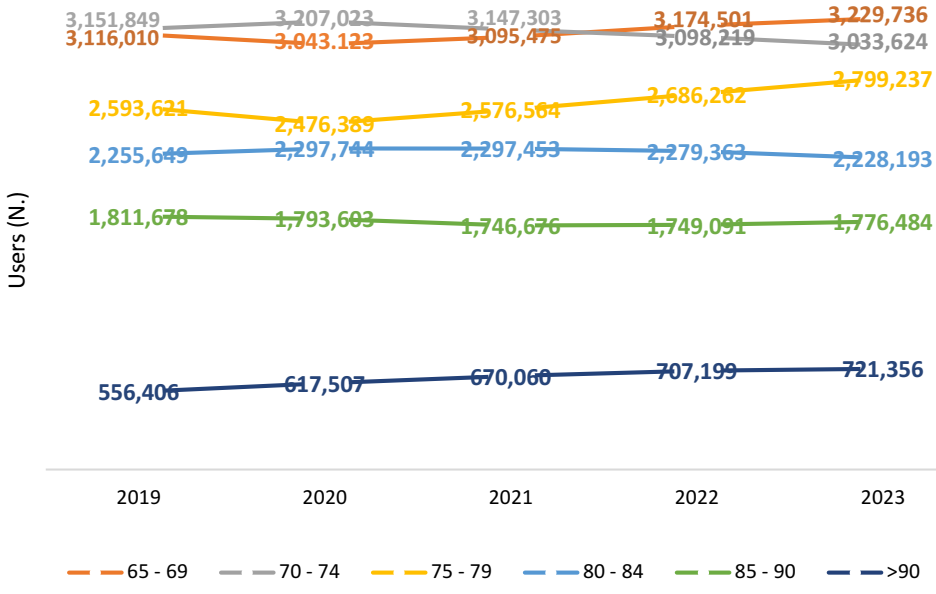


Figure 1.6.13 Number of users over 65 per age group in the period 2019-2023



1.7 Temporal trend of monthly pharmaceuticals consumption

Approved care regime Class A-NHS

Figure 1.7.1 shows the consumption trend, expressed in DDD/1000 inhabitants per day, of class A-SSN medicines over the period 2002-2023.

The consumption of medicines in this period showed an increasing trend, rising from 751.7 DDD/1000 inhabitants per day in January 2003 to 1087.8 DDD in December 2023.

Besides being characterised by an increasing trend, the consumption of medicines is associated with a seasonal periodicity, as shown by the regularity of the monthly consumption peaks shown in Figure 1.7.1. Generally, systemic antimicrobials and respiratory medicines are the therapeutic categories on which consumption seasonality has the highest impact.

It is observed that consumption has been slightly decreasing in the last period (CAGR 2019-2023: -0.3%). The trend in the last period was influenced by the reduction in consumption recorded in 2020 following the SARS-CoV-2 pandemic, which led to a reduction in the consumption of certain categories of medicines that are mainly supplied under approved care regime, such as antibiotics. In 2023, the highest consumption was in March and May (1211 and 1214 DDD, respectively), while the lowest consumption was in August and June (989 and 1071 DDD, respectively).

Class C medicines with prescription

Figure 1.7.2 shows the temporal trend of DDD/1000 inhabitants per day of class C medicines with prescription starting from January 2004. It should be taken into account that trends in consumption might be influenced by regulatory decisions that over time have resulted in the inclusion or exclusion of medicines from compulsory prescription and price updating every two years. Over the period 2004-2017, consumption is found to be decreasing, while the last 7 years show an increase; in fact, it goes from an annual average of 178.8 DDD in 2017 to an average of 204.2 DDD in 2023, with an increase of 14.2 % and an average annual change of 2% (for further details see Section 2.6). In 2023, the months with the highest average consumption are February and March (220.0 and 222.2 DDD); in contrast, August has the lowest consumption (173.1 DDD).

Medicines purchased by public health facilities

Figure 1.7.3 shows the trend in consumption of medicines purchased by public health facilities in the period 2006-2023. Consumption shows an increasing trend from an average of 100.6 DDD in 2006 to an average of 194.4 DDD in 2023 (+93%). The chart shows that the largest increase in consumption was recorded in the period 2010-2011; while in later periods increases are smaller. In 2023, when an increase compared to 2022 of 4.8% was recorded, the lowest consumption levels were observed in August with 130.3 DDD and December with 149.9 DDD, while July with 230.6 DDD and November with 224.6 DDD show the highest consumption levels. For a correct interpretation of monthly consumption of medicines purchased by public health facilities, it should be noted that, unlike annual consumption trends, such trend cannot be strictly interpreted in terms of monthly consumption and seasonality since it is impacted by the purchase procedures of public health facilities. This clarification can be verified on the basis of irregularities in the size of monthly purchases made by public health facilities in the past 17 years.

Figure 1.7.1. Time series 2002-2023 of total DDD/1000 inhabitants per day of class A-NHS medicines under approved care regime

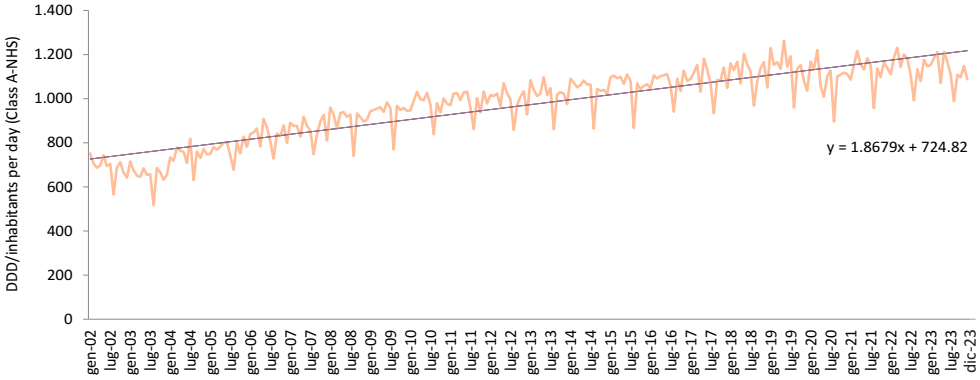


Figure 1.7.2 Time series 2004-2023 of total DDD/1000 inhabitants per day of class C medicines with prescription

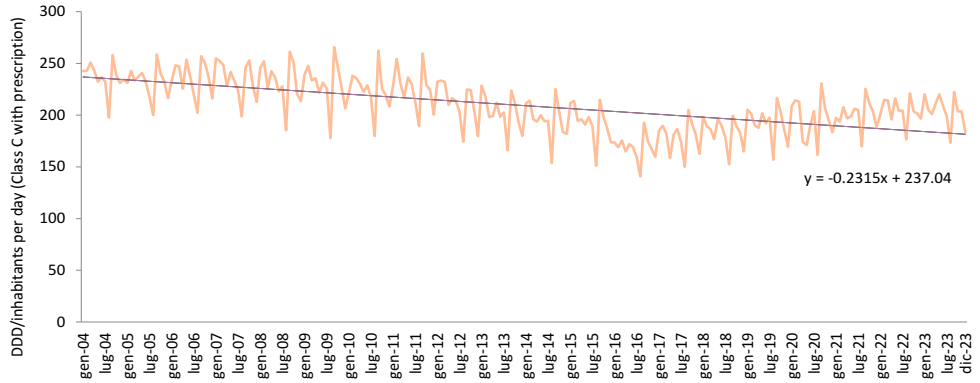
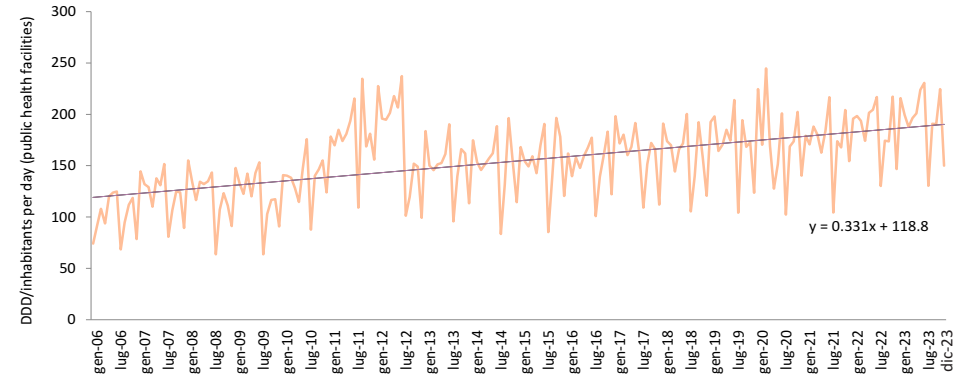


Figure 1.7.3 Time series 2006-2023 of DDD/1000 inhabitants per day of medicines purchased by public health facilities



1.8 Temporal trend of medicines prices

Approved care regime - Class A-NHS

The data in Figure 1.8.1 show the development of the weighted average price per DDD for class A-NHS medicines over the period from January 2002 to December 2023. The time series shows a decreasing trend up to December 2017 (CAGR% January 2022-December 2017: -0.4%) mainly due to patent expirations of important molecules that occurred during that period (e.g. valsartan and atorvastatin), price reduction maneuvers implemented during the years of renegotiations, and activities to promote the Transparency List. In the latest period (2018-2023), the trend has remained substantially stable (CAGR: -0,1%). A 2019-2023 trend analysis of the average cost per DDD of the drugs that entered the transparency list in 2021 was conducted in order to investigate the cost-reducing effect of entering the transparency list. It can be seen from Figure 1.8.2 that entry on the transparency list results in a reduction in both cost per DDD and per pack even before 2021. When comparing the average cost recorded in January 2020 with the cost in December 2021, there is a reduction effect of 15.5% and 20.5% in the cost per package and per DDD, respectively. Thereafter, the average cost remains almost stable.

Figure 1.8.1 2002-2023 trend of average price of class A-NHS medicines under approved care regime

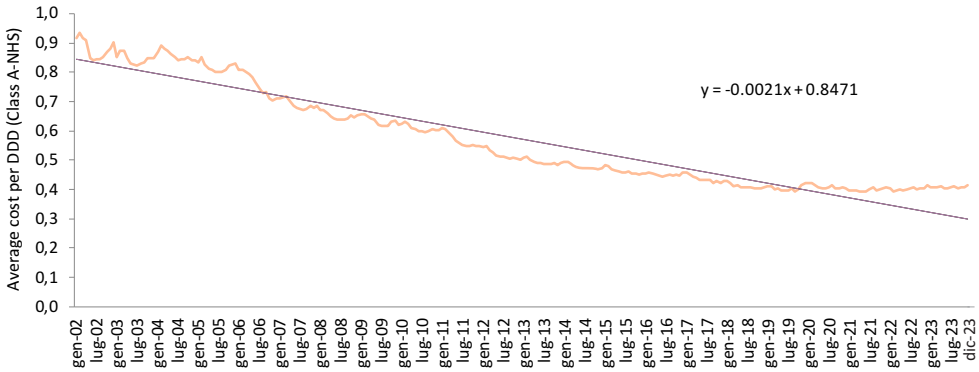
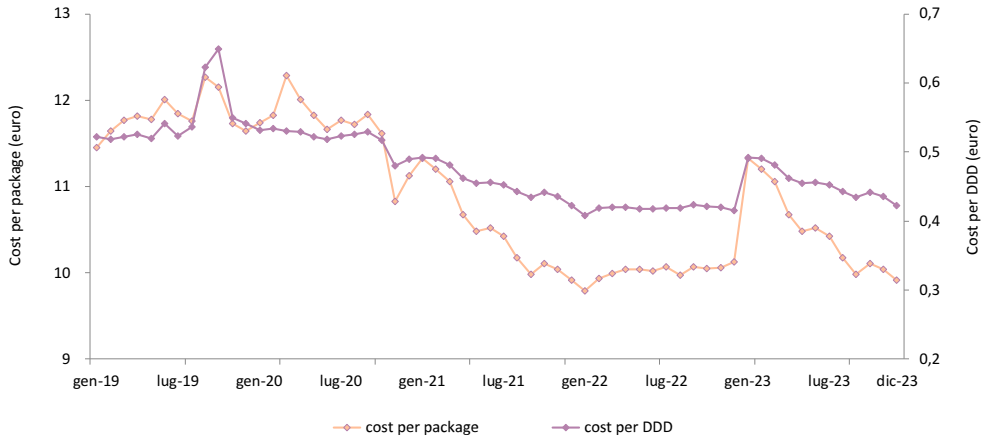


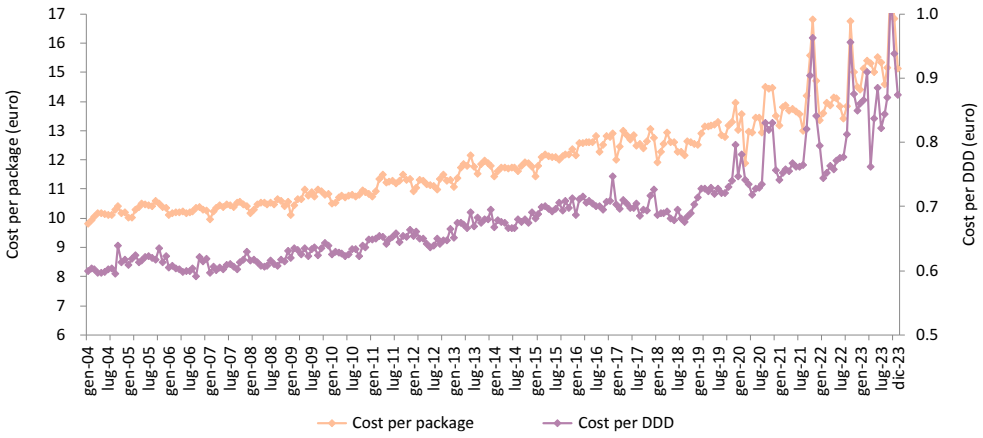
Figure 1.8.2 2019-2023 trend of average price for medicines included in the transparency list after 1 January 2021 (approved care regime)



Class C medicines with prescription

Figure 1.8.3 shows the trend in average weighted price per package and per DDD of class C medicines with prescription in the period 2004-2023. Looking at the monthly data of the time series, trends between these two indexes show regular growth from 9.82 euros per package (and 0.60 euros per DDD) in 2004 to 15.13 euros per package (and 0.87 euros per DDD) in 2023, up by respectively 54.1% and 45.8%, compared to 2004. In 2023, an even year when pharmaceutical companies could not change the price of these medicines, a stability of prices was recorded compared to the previous year, when prices had increased by 9% (see Section 2.6 for further details).

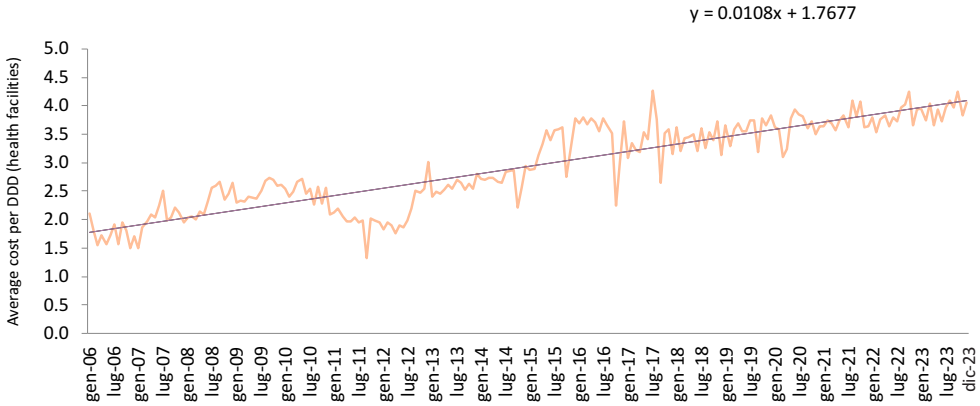
Figure 1.8.3 2004-2023 trend of average price for class C medicines with prescription (local pharmacies)



Medicines purchased by public health facilities

Figure 1.8.4 shows the trend of average cost per package and DDD of medicines purchased by public health facilities in the period 2006-2023. The cost trend is found to be increasing from 2006 to 2009 and then stabilizing in the period 2010-2014 and increasing again since 2015, with a change from January 2015 to December 2023 of 41% corresponding to an average annual change (CAGR%) of 0.3% in the period 2015-2023 and, in particular, in 2023 there was an increase from the previous year of 3.1%.

Figure 1.8.4 2006-2023 trend of average price per DDD for medicines purchased by public health facilities



1.9 International comparison

This section presents an international comparison of pharmaceutical consumption and expenditure. Several in-depth studies have been carried out on:

- impact of pharmaceutical expenditure on Gross Domestic Product (GDP);
- the relationship between *per capita* GDP and *per capita* expenditure;
- distribution of consumption and expenditure in the different supply channels, by therapeutic category and by active ingredient;
- the international comparison in the average cost per Standard Unit;
- penetration of generic and biosimilar medicines;
- level of market concentration in relation to patent-expired biological medicinal products;
- expenditure for orphan medicines;
- a price comparison analysis in 2023;
- a time analysis (2016-2023) comparing ex factory prices against the European average for products covered and not covered by patents;
- a comparison analysis of ex factory prices in Italy during 2016-2023 against the European average for baskets of pharmaceuticals, defined on the basis of their launch date.
- a comparison analysis of ex factory prices in Italy against the European average by therapeutic category.

The source of the international comparison is the IQVIA MIDAS® database. The data collected in the different countries, both in the inpatient and outpatient settings, are standardised (language, currency, company name, product name and packaging). Information was gathered on launch dates, patent coverage, specialty, biological/biosimilar classification and orphan drug designation. Community data include private purchases by citizens, net of direct and "on-behalf" distribution. Data on inpatient treatments include accredited private health care facilities. Territorial expenditure was calculated by valuing movements at the realized industry price. Fifty percent of the public price net of VAT or the price published in the Official Gazette for sale to NHS facilities is used to calculate hospital spending. Therefore, so calculated spending does not take into account the effect of purchasing by health facilities, which on average has a 40% impact on drug prices. Besides Italy, 9 countries were considered for the purposes of the international comparison: Germany, Belgium, Austria, Spain, France, Sweden, Portugal, UK, Poland (EU 10) and the average of European countries (Europe).

Comparison of expenditure and consumption

In Italy in 2023 the incidence of total pharmaceutical expenditure on GDP was 1.7%, lower only to Spain (2.0%) and in line with Portugal (1.7%). Significantly lower percentages were recorded in Sweden (0.9%) and UK (1.1%) (Figure 1.9.1). All countries showed an increase from 2019 to 2020 in GDP percentage related to pharmaceutical expenditure. This trend is essentially due to a decrease in GDP recorded in all countries, against an increase in pharmaceutical expenditure. In the period 2021-2023 a substantial stability is instead recorded in the incidence of total pharmaceutical expenditure on GDP. No correlation emerges between expenditure and GDP *per capita*, although there is a tendency for expenditure per capita to rise as GDP *per capita* increases (Figure 1.9.2).

Figure 1.9.1 International comparison: incidence of total pharmaceutical expenditure as a percentage of GDP in 2019-2023

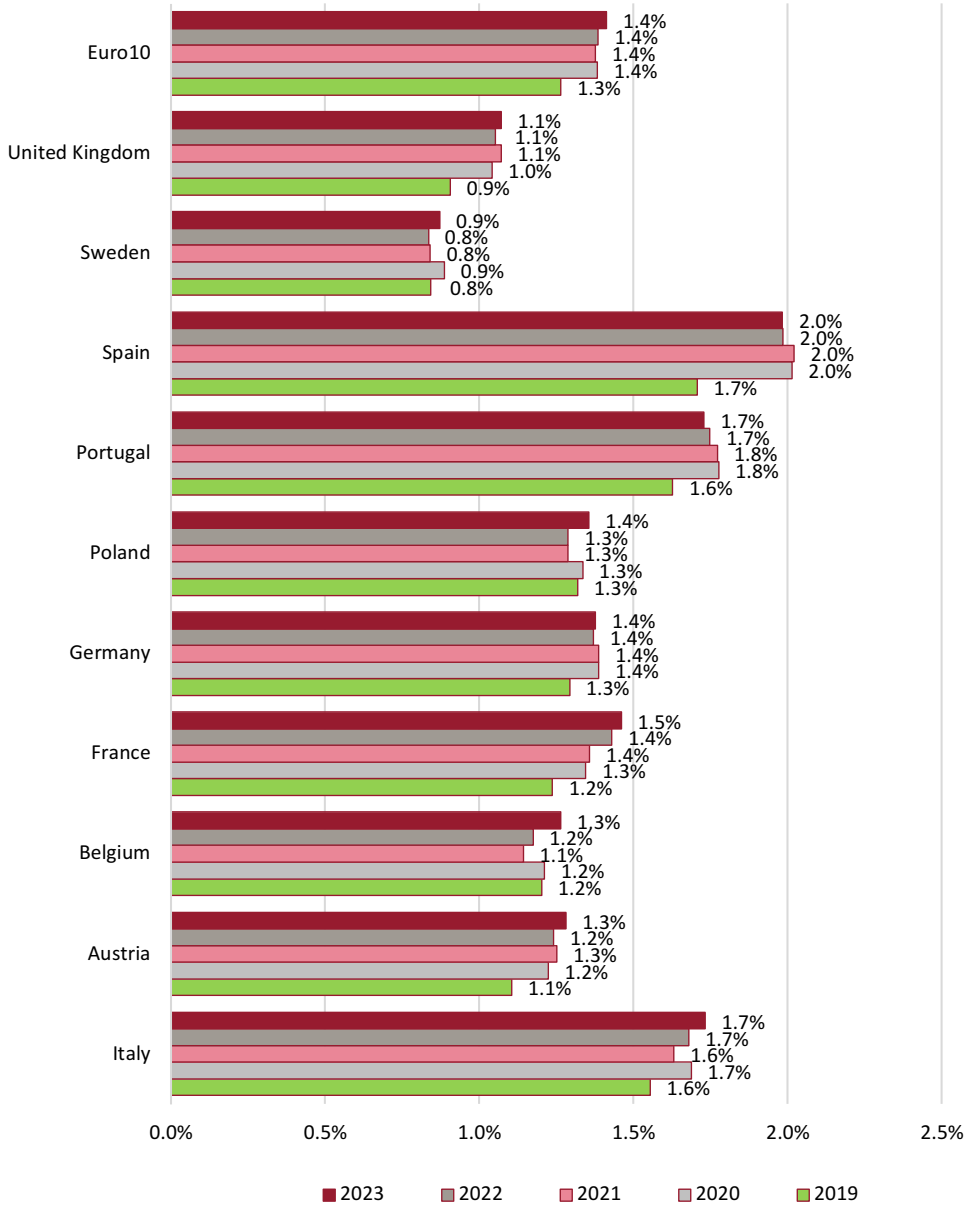
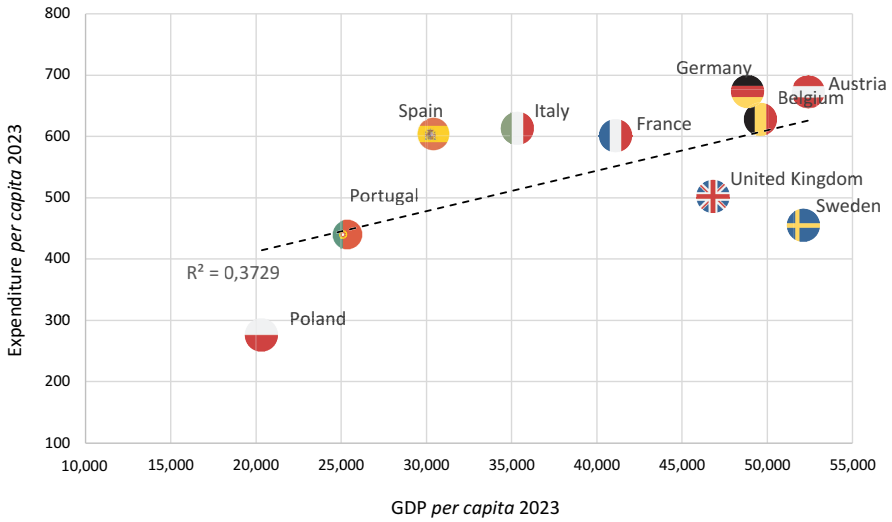


Figure 1.9.2 Relationship between *per capita* pharmaceutical expenditure and per capita GDP (Year 2023)



The total Italian pharmaceutical expenditure, including local public and private expenditure and hospital expenditure, was equal to 612 euros per capita, lower than that Germany (673 euros), Austria (672 euros), Belgium (627 euros) and Spain (520 euros), while it is well above the values of Poland (276 euros), Portugal (439 euros), UK (502 euros), Sweden (455 euros) and the average of the European countries, which is equal to 384 euros (Figure 1.9.3).

The international comparison was also made in terms of Standard Unit (standard unit - SU), i.e. the elementary units contained in each package. Standard units can be easily defined in the case of solid forms (typically tablets, capsules, etc.) or liquid forms that have been already pre-packaged in minimum units (e.g. pre-filled syringes). In the case of other forms (e.g. syrups or aerosols), criteria are identified for the identification of the minimum standard minimum unit (e.g. inhalation).

The comparison by Standard Unit shows a per capita consumption of 836 SU in Italy (Figure 1.9.4), lower than all countries considered (average countries analysed (EU 10) 1.088 SU per capita and average Europe 1.078 SU). It is worth highlighting that consumption refers to supplied Standard Units and not to those actually consumed by the patient, therefore the different packaging or the number of dose units within the individual packages may have an impact on the consumption levels detected. If the treatment adherence is the same, a country that has on average a smaller number of dose units per package will report a lower consumption than a country with higher number of dose units per package, given by the lower number of dose units not taken by the single patient. The difference found in consumption in Italy compared to the European average can therefore also be attributed to the fact that in Italy the packages delivered at a local level contain on average a lower number of SU and DDD than the European average. In addition, unlike DDD which represents the average daily dose, SU does not take into account the dosage used. Therefore, for the same prescribed dosage, countries where lower-dose dosage units are used more frequently may experience higher consumption and higher cost per SU. Finally, higher SU prices, when linked to higher con-

sumption of higher-dose SUs, do not take into account the impact of factors such as individual patient's different exposure to the drug or different organization in its administration (e.g., drug preparations for a larger number of subjects).

Figure 1.9.3 International comparison of total *per capita* pharmaceutical expenditure 2016-2023

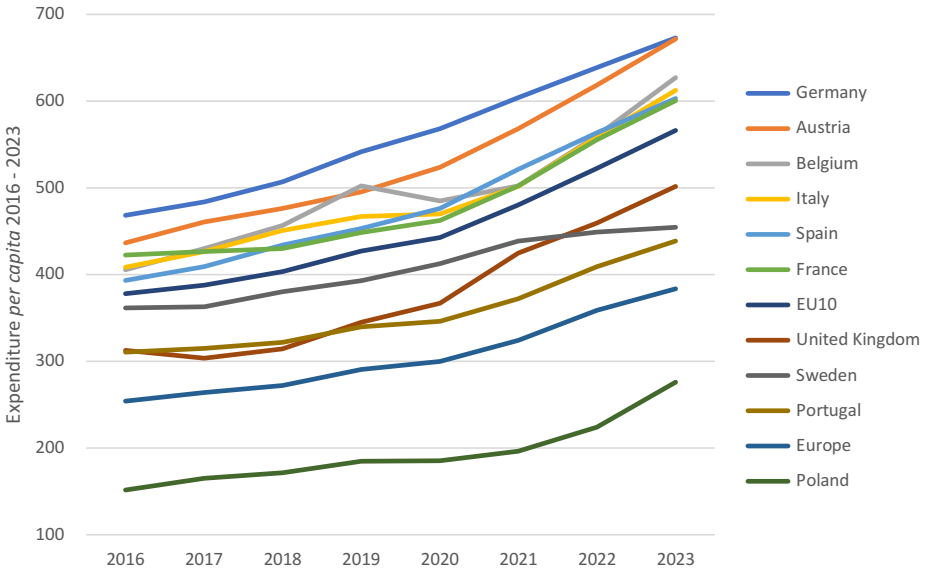
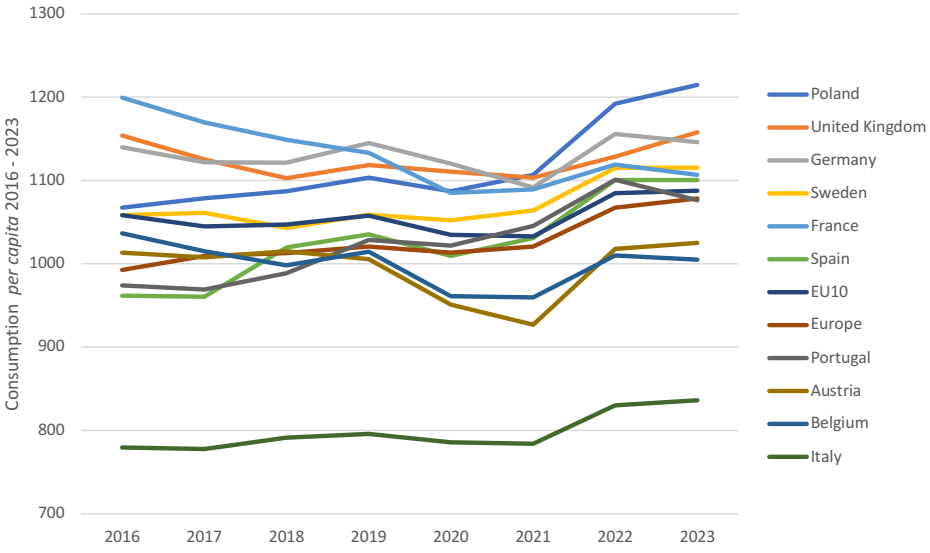
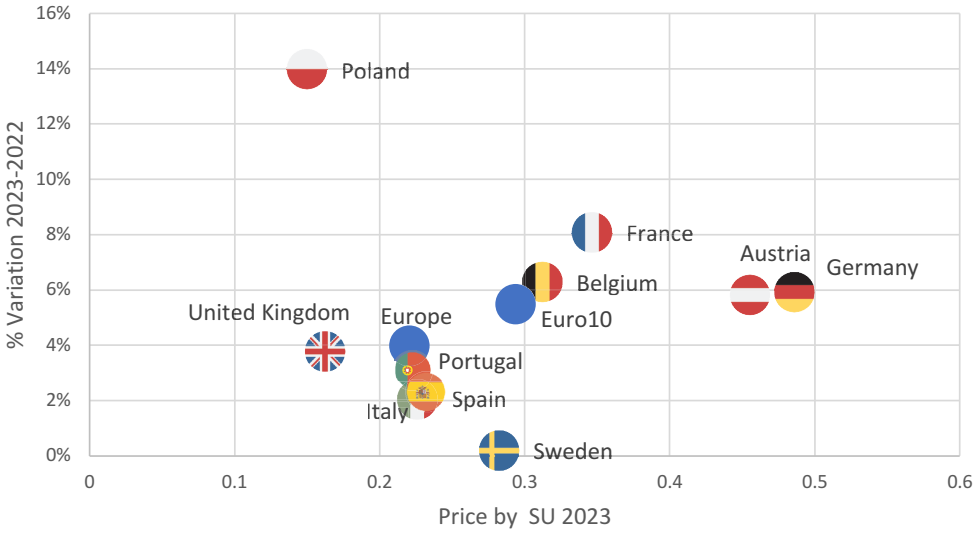


Figure 1.9.4 International comparison of total *per capita* consumption (standard unit per inhabitant) 2016-2023



When looking at the average cost per posological unit, Italy with 0.23 euros presents a value in the territorial area 23% lower than the average (0.29 euros) of the 10 countries analyzed (Figure 1.9.5). In Italy, the average cost is fairly stable compared with 2022, with the largest variation found in Poland (+14.0%) and France (+8.1%).

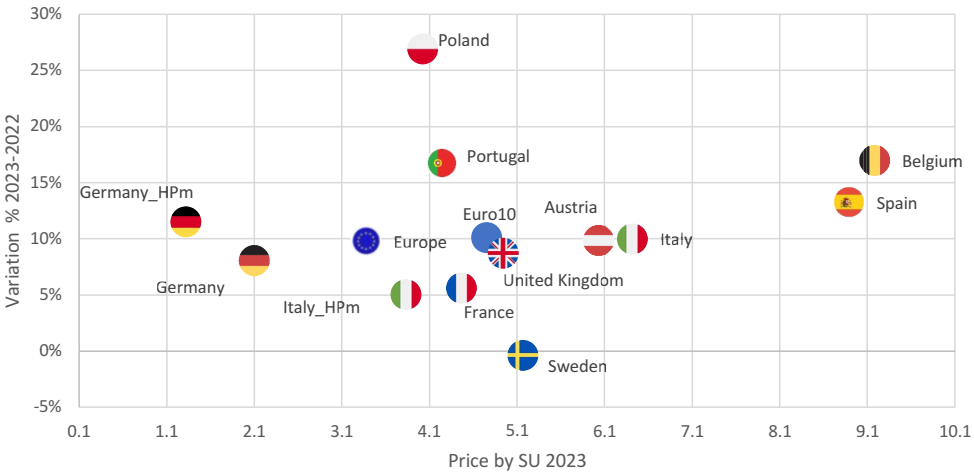
Figure 1.9.5 International comparison of the average cost by standard unit at local level in 2023 and 2023-2022 variation



In hospital settings (Figure 1.9.6), Italy has an average cost for Standard Unit (6.42 euros) higher than the average of the countries analysed (4.74 euros), with a 35% percentage difference. It is important to underline that the comparison is not carried out on a common basket of medicines and that the different packaging (number of dose units contained) could affect the definition of the cost per dose unit, due to a potential price/volume effect. In all the countries analyzed there is an increase over 2022, with the highest values in Poland (+26.9%), Belgium (+17.0%) and Portugal (+16.7%). When considering the purchase prices of public health facilities for Italy and Germany, the only countries for which such a price is available, a price per SU of 3.83 euros and 1.32 euros, respectively, is obtained.

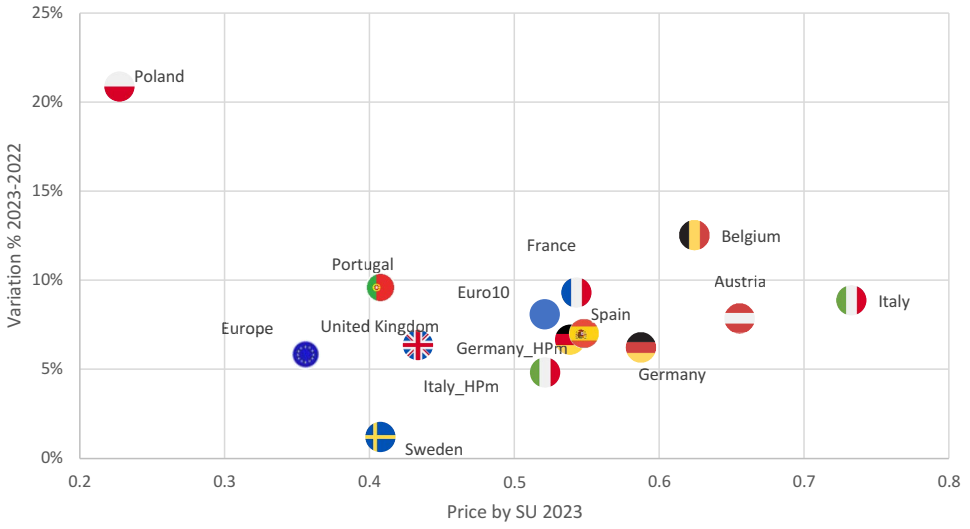
Considering altogether the territorial and hospital setting and the purchase price, the values for Italy and Germany are aligned with each other (respectively 0.52 and 0.54 euro per SU; Figure 1.9.7).

Figure 1.9.6 International comparison of the average cost by Standard Unit in hospital setting in 2023 and 2023-2022 Variation with Tender Price in hospital setting (HPm)



For Italy and Germany both the cost per standard unit was included using the base auction price and the tender price (HPm).

Figure 1.9.7 International comparison of the average cost by Standard Unit in local and hospital care in 2023 and 2023-2022 variation with Tender Price in hospital setting (HPm)



For Italy and Germany both the cost per standard unit was included using the base auction price and the tender price (HPm).

In the context of local care, in Italy the largest share of expenditure, equal to 20.2%, is represented by medicines of the cardiovascular system, which is higher than that recorded in the other countries; for example, in Sweden, only 6.7% of the local expenditure is represented by this category of medicines. Great Britain and Spain, with a value of 20.9% and 22.5% respectively, have the highest incidence of expenditure on central nervous system medicines. Finally, gastro-intestinal medicines account for a very large share of expenditure in Portugal (24.4%), Great Britain (23.7%) and Spain (22.0%). Poland (14.6%) and Great Britain (12.6%) are the countries with the highest incidence of expenditure on respiratory system medicines. Sweden (11.0%), France (8.9%), Germany (8.9%), Belgium (8.0%) and Austria (5.6%) report a considerably higher proportion of antimicrobial expenditure than Italy (4.9%) (Table 1.9.1).

Table 1.9.1 International comparison of the percentage distribution of local pharmaceutical expenditure* 2023 by ATC 1st level

ATC 1 level	Italy	Austria	Belgium	France	Germany	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	EU10
C - Cardiovascular	20.2	10.0	11.5	10.4	7.5	15.3	19.2	15.4	6.7	12.7	11.7	11.3
N - SNC	19.3	15.4	16.8	12.0	13.1	14.2	18.2	22.5	16.2	20.9	14.7	15.5
A - Gastrointestinal	17.8	10.2	15.5	11.0	12.6	22.0	23.7	21.7	15.3	24.4	16.4	15.5
R - Respiratory	12.8	10.6	11.0	9.9	9.2	14.6	9.2	10.9	8.3	12.6	10.6	10.5
G - Genitourinary and sex hormones	7.4	2.0	4.3	2.9	2.3	5.9	5.5	5.8	3.8	6.3	4.2	3.9
M - Musculoskeletal	6.0	4.6	3.7	2.8	3.8	4.7	5.7	4.6	3.2	1.9	4.3	3.8
J - Antimicrobial	4.9	5.6	8.0	8.9	8.9	4.6	3.7	2.8	11.0	2.9	7.0	7.0
D - Dermatological	3.3	2.7	3.5	1.8	3.5	2.5	2.2	2.1	1.7	2.4	2.7	2.7
B - Haematological	3.0	7.9	10.1	9.3	9.2	11.7	9.5	7.4	9.0	9.8	8.5	8.7
H - Systemic hormones	2.1	1.3	2.0	2.2	1.8	1.2	1.0	1.8	2.8	2.2	1.8	1.9
L - Antineoplastic	1.5	28.0	12.4	23.8	24.2	1.4	0.4	3.4	20.6	2.4	15.1	16.1
S - Sense Organs	1.3	0.2	0.6	4.2	1.9	0.6	0.7	0.7	0.7	0.9	1.6	1.9
V - Various	0.3	1.4	0.5	0.5	1.8	1.0	0.8	0.6	0.6	0.2	1.2	1.0
P - Antiparasitic	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.1	0.2	0.2	0.2

*Medicines supplied by local pharmacies, excluding distribution “on behalf”

Table 1.9.2 shows the average annual change (CAGR) in local expenditure for ATC 1st level over the period 2020-2023. In Italy, the largest increases were recorded for ATC P (pesticides), S (sense organs), R (respiratory) and J (antimicrobials), while there was a decrease in spending on hematological drugs. The increase in pesticides and respiratory drugs is also confirmed at the level of the 10 countries analyzed, where there is also significant growth in hematological, antineoplastic, dermatological and gastrointestinal drugs.

Table 1.9.2 International comparison of the 4-year CAGR on local pharmaceutical expenditure* 2023 by ATC 1st level

ATC 1 level	Italy	Austria	Belgium	France	Germany	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	EU10
P - Antiparasitic	21.8%	-10.6%	22.7%	3.3%	4.2%	13.4%	6.5%	35.1%	9.8%	9.8%	9.6%	7.9%
S - Sense Organs	5.6%	7.0%	2.8%	4.0%	2.4%	10.7%	7.7%	3.7%	-1.1%	5.2%	5.0%	3.7%
R - Respiratory	5.0%	12.0%	5.5%	8.6%	9.2%	10.6%	4.5%	4.8%	0.1%	1.7%	7.3%	7.0%
J - Antimicrobial	4.2%	1.9%	0.1%	2.9%	5.9%	8.3%	-0.5%	1.7%	3.9%	3.6%	4.4%	4.5%
M - Musculoskeletal	3.6%	4.7%	0.7%	5.9%	5.3%	6.6%	4.2%	4.8%	0.1%	-2.5%	5.6%	4.5%
G - Genitourinary and sex hormones	3.1%	1.6%	1.0%	0.8%	0.1%	7.7%	2.4%	2.3%	-0.8%	6.8%	3.4%	2.6%
H - Systemic hormones	2.2%	-4.2%	0.2%	0.3%	0.4%	2.7%	4.4%	1.6%	5.3%	-0.9%	1.2%	0.8%
A - Gastrointestinal	1.9%	4.6%	5.4%	3.3%	5.5%	13.2%	5.4%	5.3%	5.9%	7.1%	6.0%	5.5%
D - Dermatological	1.8%	17.4%	10.7%	9.6%	11.3%	7.8%	3.2%	3.5%	7.4%	3.0%	8.6%	8.4%
N - SNC	1.8%	6.4%	1.1%	0.2%	1.0%	5.3%	1.5%	1.1%	-1.4%	-1.0%	2.0%	1.1%
C - Cardiovascular	1.4%	3.5%	3.7%	10.6%	3.8%	4.5%	3.3%	2.1%	6.5%	3.4%	4.5%	4.3%
V - Various	0.4%	5.5%	20.9%	0.6%	-0.1%	16.4%	5.2%	6.4%	5.4%	-3.4%	2.5%	1.6%
L - Antineoplastic	0.2%	6.2%	3.8%	7.2%	4.3%	3.3%	-0.4%	1.2%	-0.7%	-0.9%	5.8%	5.1%
B - Haematological	-2.5%	4.7%	3.2%	7.8%	6.2%	6.9%	2.9%	2.8%	2.6%	3.6%	5.4%	5.4%

*Medicines supplied by local pharmacies, excluding distribution “on behalf”

Italy ranks first in terms of the incidence of local consumption of cardiovascular system medicines (27.4%) (Table 1.9.3), followed immediately by Germany (24.3%) and Portugal (23.8%). The percentage of SU consumed for medicines of the central nervous system (14.9%) is lower in almost all the countries considered with the exception of Poland (14.8%). The percentage of consumption of respiratory system drugs also shows a low value in Italy (14.9%), lower than all the other countries analyzed, with the exception of Portugal (12.1%). As for antimicrobials for systemic use, represented at the local/community level mainly by antibiotics (J01), Italy shows the largest share of consumption, lower only than France. Analysing the CAGR of local consumption over the period 2020-2023 (Table 1.9.4), it is noted that the largest changes in Italy were observed for pesticides (+10.8%), antimicrobials (+6.6%) and respiratory drugs (+5.4%); also in the European countries analyzed, the largest increases were recorded for pesticide drugs (+6.7%) and antimicrobials (+4.9%). Both in Italy and at the level of all countries analyzed, the largest decreases were in miscellaneous drugs (-4.6% in Italy and -4.2% in the 10 countries analyzed).

Table 1.9.3 International Comparison of the percentage distribution of local/community consumption* in 2023 by ATC 1st Level

ATC 1 level	Italy	Austria	Belgium	France	Germany	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	EU10
C - Cardiovascular	27.4	18.9	18.4	16.9	24.3	21.8	23.8	18.5	18.6	18.3	19.1	20.9
A - Gastrointestinal	16.8	14.2	15.5	18.1	14.1	22.9	15.6	15.5	18.1	18.1	17.1	17.1
R - Respiratory	14.9	28.3	21.9	16.9	20.1	18.1	12.1	16.1	17.6	20.1	22.4	18.2
N - SNC	14.9	16.1	22.6	23.7	15.2	14.8	24.5	27.9	26.3	22.6	16.8	20.2
M - Musculoskeletal	6.7	7.2	4.6	5.0	5.8	6.9	8.0	6.3	3.7	3.2	5.8	5.5
B - Haematological	5.4	4.7	5.4	4.8	5.5	4.7	4.6	4.4	5.0	4.5	4.6	4.9
H - Systemic hormones	4.1	3.2	2.4	2.9	4.2	2.6	2.3	2.8	3.1	2.9	2.6	3.2
G - Genitourinary and sex hormones	3.0	1.9	2.7	2.3	2.7	2.7	2.9	2.2	2.2	3.2	2.4	2.7
S - Sense Organs	2.4	1.2	2.1	4.3	2.4	1.7	1.7	2.1	2.2	1.6	2.7	2.4
D - Dermatological	2.1	2.2	1.7	1.9	2.6	1.6	2.3	1.7	1.1	3.1	3.4	2.2
J - Antimicrobial	1.8	1.1	1.6	1.9	1.0	1.7	1.3	1.7	1.0	1.6	1.8	1.5
L - Antineoplastic	0.4	0.6	0.7	0.6	0.6	0.3	0.2	0.5	0.8	0.5	0.6	0.5
V - Various	0.2	0.4	0.1	0.5	0.9	0.3	0.3	0.1	0.1	0.1	0.5	0.4
P - Antiparasitic	0.0	0.1	0.1	0.1	0.6	0.1	0.2	0.1	0.1	0.2	0.2	0.2

*Medicines supplied by local pharmacies, excluding distribution "on behalf"

Table 1.9.4 International comparison of the 4-year CAGR on local consumption* in 2023 for ATC 1st level

ATC 1 level	Italy	Austria	Belgium	France	Germany	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	EU10
P - Antiparasitic	10.8%	-8.4%	18.7%	1.3%	7.5%	3.3%	0.5%	27.1%	5.3%	-0.3%	7.8%	6.7%
J - Antimicrobial	6.6%	6.7%	6.0%	2.1%	7.3%	4.9%	6.2%	6.4%	3.4%	4.3%	3.4%	4.9%
R - Respiratory	5.4%	6.9%	4.7%	2.9%	2.8%	7.2%	4.3%	4.8%	1.5%	-0.5%	3.9%	3.2%
S - Sense Organs	3.2%	2.5%	4.2%	1.7%	1.0%	5.5%	3.3%	4.1%	2.6%	4.2%	4.6%	2.7%
M - Musculoskeletal	2.5%	-1.0%	-1.3%	-0.5%	-1.4%	2.5%	0.0%	1.4%	0.3%	0.9%	1.2%	0.4%
G - Genitourinary and sex hormones	2.3%	0.7%	1.4%	0.7%	1.1%	3.0%	2.0%	3.4%	2.1%	10.2%	3.1%	3.3%
H - Systemic hormones	1.8%	-0.4%	-0.9%	1.0%	-1.2%	1.6%	1.9%	3.1%	4.1%	0.5%	2.0%	0.7%
C - Cardiovascular	1.1%	0.1%	0.6%	-0.1%	0.7%	1.3%	0.5%	0.9%	1.6%	1.7%	1.1%	0.9%
N - SNC	1.1%	1.5%	0.7%	-0.4%	0.9%	2.4%	1.4%	2.1%	1.4%	0.1%	0.8%	0.9%
D - Dermatological	0.6%	-2.2%	-1.8%	-2.6%	-2.0%	-1.2%	-0.9%	0.4%	-0.1%	-0.9%	-0.5%	-1.2%
L - Antineoplastic	-0.3%	2.4%	-0.3%	1.5%	2.4%	2.5%	-1.6%	0.1%	0.9%	-0.5%	-2.1%	1.1%
B - Haematological	-0.6%	0.4%	-1.9%	1.8%	0.1%	1.8%	-0.2%	1.2%	0.5%	0.9%	0.9%	0.7%
A - Gastrointestinal	-0.7%	-0.4%	-0.8%	-0.7%	-0.3%	1.9%	1.4%	1.3%	1.2%	1.2%	0.4%	0.4%
V - Various	-4.6%	-5.3%	0.0%	0.2%	-6.2%	-6.4%	-0.2%	-0.6%	4.2%	-2.7%	-4.8%	-4.2%

*Medicines supplied by local pharmacies, excluding distribution "on behalf"

On the hospital care side (Table 1.9.5), in Italy the first expenditure item is represented by antineoplastic drugs (44.0%), although higher percentages are observed in almost all the countries considered, with the exception of Germany (42.0%) and Portugal (42.6%). In Germany (21.6%), Portugal (17.3%) and Spain (15.8%), expenditure for antimicrobials has a greater impact than in other countries. This incidence in Italy is gradually decreasing, in fact in 2019 it was 22.8%, in 2020 17.7%, in 2021 15.7%, in 2022 14.7% and in 2023 13.7%. In contrast, the incidence of spending on antineoplastics continues to grow, rising from 36.9% in 2019 to 44.0% in 2023. For hematology drug spending, Sweden has the highest incidence (12.0%) followed by Italy (11.6%). For these drugs the European average stands at 8.1% and for the countries considered in the analysis 8.3%. Also for ATC A (gastrointestinal system and metabolism) Italy presents the highest incidence of expenditure (8.0% compared to the EU10 average of 5.4%); this could be attributable to the different supply of antidiabetics, which in Italy are mainly supplied "on behalf". The highest increases (CAGR 2020-2023) were observed for Italy for dermatological drugs (+46.8%), respiratory system agents (+21.7%), cardiovascular drugs (+16.5%), gastrointestinal medications (+12.4%), sensory organ drugs (+12.1%) and antineoplastics (+10.8%; Table 1.9.6). The increase recorded in Italy for ATC A, which is higher than the EU10 average (+8.6%), could be driven by the trend in antidiabetics. At the level of the 10 countries analysed, the largest increases were for dermatological drugs (+28.1%), respiratory system agents (+16.3%), antineoplastics (+11.1%), sensory organ drugs (+10.9%) and cardiovascular drugs (+10.6%).

Table 1.9.5 International comparison of the percentage distribution of hospital pharmaceutical expenditure in 2023 by ATC 1st level

ATC 1 level	Italy	Austria	Belgium	France	Germany	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	EU10
L - Antineoplastic	44.0	61.2	58.0	56.1	42.0	53.8	42.6	50.2	47.4	48.2	48.7	48.6
J - Antimicrobials	13.7	13.9	7.1	10.8	21.6	8.2	17.3	15.8	11.6	13.3	14.4	14.1
B - Haematological	11.6	7.6	7.2	8.7	9.5	4.2	5.8	5.9	12.0	6.4	8.1	8.3
N - SNC	9.1	6.1	6.6	10.8	12.5	13.5	14.0	8.7	8.0	7.8	9.6	9.5
A - Gastrointestinal	8.0	3.2	3.9	5.7	4.3	3.5	6.0	4.1	5.2	4.6	5.4	5.4
R - Respiratory	4.2	0.8	3.9	1.0	1.1	6.0	4.6	5.2	0.8	8.0	3.9	4.2
C - Cardiovascular	3.4	2.0	7.1	1.9	2.0	2.8	2.4	1.9	1.4	1.5	2.3	2.4
M - Musculoskeletal	1.6	1.3	1.3	1.6	1.8	2.8	1.8	1.9	4.3	2.4	2.0	1.9
H - Systemic hormones	1.2	0.6	0.6	0.7	0.9	1.6	0.9	1.0	0.6	0.9	1.0	1.0
D - Dermatological	1.2	0.3	0.1	0.9	1.0	0.7	1.8	1.5	0.1	1.0	1.0	1.1
S - Sense Organs	1.1	2.1	3.4	0.5	1.4	2.1	2.0	3.3	7.5	4.9	2.4	2.4
V - Various	0.5	0.5	0.3	0.5	1.5	0.3	0.7	0.2	0.8	0.4	0.6	0.6
G - Genitourinary and sex hormones	0.4	0.5	0.6	0.8	0.4	0.3	0.2	0.3	0.3	0.5	0.5	0.5
P - Antiparasitic	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0

Table 1.9.6 International comparison of the 4-year CAGR on hospital pharmaceutical expenditure in 2023 by ATC 1st level

ATC 1 level	Italy	Austria	Belgium	France	Germany	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	EU10
D - Dermatological	46.8%	24.2%	5.6%	7.1%	10.0%	60.3%	38.2%	45.5%	3.8%	29.5%	27.4%	28.1%
R - Respiratory	21.7%	0.1%	34.6%	8.4%	2.5%	49.9%	23.1%	13.7%	-8.2%	14.1%	16.1%	16.3%
C - Cardiovascular	16.5%	3.4%	66.3%	-1.7%	2.7%	15.8%	21.7%	4.1%	-1.4%	8.6%	10.1%	10.6%
A - Gastrointestinal	12.4%	-1.2%	6.2%	5.8%	-0.3%	17.5%	5.6%	8.4%	1.9%	12.1%	8.9%	8.6%
S - Sense Organs	12.1%	18.9%	5.8%	11.3%	0.3%	14.2%	16.8%	22.1%	2.7%	9.2%	9.9%	10.9%
L - Antineoplastic	10.8%	11.0%	8.6%	13.6%	7.1%	16.9%	8.7%	9.1%	8.0%	13.1%	10.9%	11.1%
M - Musculoskeletal	7.6%	2.6%	12.3%	-0.5%	1.4%	42.2%	12.4%	10.3%	6.1%	9.2%	7.6%	7.3%
P - Antiparasitic	7.5%	-11.4%	12.3%	-2.6%	5.5%	5.4%	-1.8%	3.4%	-0.2%	10.7%	0.1%	4.9%
N - SNC	7.0%	2.4%	6.2%	3.2%	-1.5%	6.7%	13.3%	7.2%	-2.9%	13.5%	6.1%	5.6%
G - Genitourinary and sex hormones	6.3%	1.0%	13.7%	20.3%	15.3%	16.2%	2.4%	12.0%	0.3%	8.2%	9.7%	11.4%
B - Haematological	5.6%	2.7%	9.7%	3.5%	-1.6%	14.1%	9.4%	9.5%	1.6%	12.3%	5.2%	5.5%
J - Antimicrobial	2.2%	4.3%	6.0%	7.5%	3.1%	8.2%	5.4%	3.4%	1.3%	6.1%	3.4%	4.2%
H - Systemic hormones	-0.7%	0.4%	5.3%	1.5%	2.2%	6.5%	-6.4%	1.1%	-0.9%	6.1%	1.3%	1.7%
V - Various	-2.8%	-0.8%	-7.8%	4.6%	13.2%	22.3%	11.7%	7.3%	6.4%	9.9%	6.0%	5.9%

In Italy blood medicines rank first in terms of incidence on hospital consumption (25.9%), much higher than the average of the countries considered in the analysis (8.0%) and the European average (6.3%; Table 1.9.7). These differences may be attributable to the different methods of supplying certain medicines belonging to this category, such as the new oral anticoagulants, which in Italy are mainly supplied by direct distribution and "on behalf". Also for gastrointestinal drugs, Italy has the highest incidence on hospital consumption (20.4% vs EU10 average: 15.3% and European average: 13.9%), mainly due to dispensing of antidiabetics 'on behalf' in Italy. On the other hand, the percentage of SUs consumed in hospital for respiratory system medicines is low, amounting to 2.9%, compared to the percentage of consumption in all countries under analysis (EU10 average: 11.7% and European average: 10.0%). Increases in hospital consumption (CAGR 2020-2023) were recorded for Italy, in addition to pesticides (+11.0%), gastrointestinal drugs (+5.1%), hematological drugs (+4.8%), and antineoplastics (+3.6%). The largest reductions are recorded for drugs of the genito-urinary system (-5.4%) and the cardiovascular system (-4.1%). At the level of the 10 countries analyzed, antineoplastics (+5.6%), antiparasitics (+5.1%), hematological drugs (+3.6%) and gastrointestinal drugs (+3.5%) showed increases in consumption (Table 1.9.8). When taking into consideration territorial and hospital expenditures together, it is observed that, for Italy and for all countries considered, antineoplastics and central nervous system drugs are first and second, respectively, in terms of incidence. In Italy the third in terms of incidence are antimicrobials with a value of 11.6% on total expenditure, higher than that of the 10 countries analysed (10.3%) and than the European average (10.0%) (Table 1.9.9). Increases in total expenditure (CAGR 2020-2023) were recorded for Italy, in addition to pesticides (+19.6%), dermatological drugs (+14.2%), respiratory drugs (+11.1%), and antineoplastics (+10.7%). At the level of the 10 countries, there was a similar increase for antineoplastics (+12.0%), dermatological medicines (+9.2%) and for respiratory medicines (+9.0%) (Table 1.9.10).

Table 1.9.7 International comparison of the percentage distribution of hospital consumption in 2023 by ATC 1st level

ATC 1 level	Italy	Austria	Belgium	France	Germany	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	EU10
B - Haematological	25.9	4.8	4.7	4.5	3.1	6.4	2.2	3.2	5.0	5.3	6.3	8.0
N - SNC	25.0	27.7	36.3	35.6	18.6	29.3	15.1	27.4	42.4	23.5	21.5	25.3
A - Gastrointestinal	20.4	14.1	12.3	15.8	13.9	17.8	7.5	8.5	15.2	16.0	13.9	15.3
C - Cardiovascular	8.8	12.9	8.8	8.4	9.1	14.5	5.5	7.0	9.2	6.9	10.0	8.5
L - Antineoplastic	5.3	0.7	4.8	0.9	0.3	3.8	9.8	4.9	1.2	5.9	2.7	3.2
J - Antimicrobial	4.4	4.5	5.1	3.5	2.7	6.5	7.7	7.8	5.9	8.8	6.9	5.2
R - Respiratory	2.9	16.3	12.8	12.2	9.8	7.2	24.7	17.0	6.8	15.3	10.0	11.0
D - Dermatological	1.7	5.1	4.0	5.1	26.5	1.5	15.8	10.4	1.5	5.4	17.1	10.8
S - Sense Organs	1.6	3.1	5.6	4.9	3.2	3.9	5.9	8.1	3.0	4.2	3.3	3.9
H - Systemic hormones	1.4	2.2	1.8	2.0	1.6	2.5	1.9	2.4	5.6	3.7	2.0	2.2
M - Musculoskeletal	1.1	6.1	2.3	1.9	4.0	4.9	1.5	2.4	2.3	2.1	2.5	2.6
V - Various	1.0	1.5	0.4	4.2	6.6	0.5	1.6	0.2	0.6	0.9	2.8	2.9
G - Genitourinary and sex hormones	0.6	1.0	1.0	0.9	0.6	1.2	0.7	0.6	1.3	1.8	0.9	0.9
P - Antiparasitic	0.0	0.0	0.1	0.1	0.1	0.1	0.2	0.0	0.0	0.1	0.1	0.1

Table 1.9.8 International comparison of the 4-year CAGR on hospital consumption in 2023 by ATC 1st level

ATC 1 level	Italy	Austria	Belgium	France	Germany	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	EU10
P - Antiparasitic	11.0%	-6.9%	27.6%	1.2%	4.5%	0.5%	3.3%	14.7%	-9.6%	6.4%	-10.8%	5.1%
A - Gastrointestinal	5.1%	1.2%	1.1%	3.6%	2.2%	4.7%	3.8%	0.1%	-1.6%	4.4%	2.0%	3.5%
B - Haematological	4.8%	0.4%	1.1%	2.6%	1.4%	5.4%	3.3%	1.3%	-2.3%	3.8%	2.6%	3.6%
L - Antineoplastic	3.6%	2.2%	12.4%	7.8%	0.6%	11.6%	2.9%	8.5%	1.2%	6.2%	-1.4%	5.6%
N - SNC	0.3%	1.5%	3.9%	2.7%	0.5%	4.5%	5.3%	3.0%	2.5%	3.2%	1.4%	2.1%
R - Respiratory	0.2%	4.4%	2.4%	0.1%	-3.8%	6.8%	4.0%	2.4%	1.8%	2.9%	-0.1%	0.7%
S - Sense Organs	0.1%	3.0%	2.6%	5.4%	0.1%	7.7%	6.5%	-0.3%	4.8%	6.0%	2.9%	2.9%
M - Musculoskeletal	-0.1%	-0.4%	4.1%	3.6%	1.1%	4.4%	5.9%	-1.7%	3.5%	4.7%	1.4%	2.0%
V - Various	-0.1%	-5.8%	-0.8%	23.0%	-12.5%	-16.2%	3.0%	3.1%	-5.4%	-5.8%	-7.8%	-6.6%
D - Dermatological	-0.2%	3.7%	3.9%	-0.7%	-1.4%	-1.9%	-11.1%	-1.2%	0.2%	2.8%	-0.7%	-1.1%
H - Systemic hormones	-0.5%	1.0%	8.3%	4.0%	0.8%	0.4%	3.0%	2.4%	5.3%	4.6%	-0.1%	2.7%
J - Antimicrobial	-1.6%	1.9%	3.9%	2.3%	1.0%	3.7%	-0.1%	0.3%	3.4%	4.4%	-6.1%	1.9%
C - Cardiovascular	-4.1%	-0.5%	-3.6%	2.3%	1.3%	4.6%	-0.1%	1.4%	4.3%	4.2%	2.2%	0.8%
G - Genitourinary and sex hormones	-5.4%	-0.9%	-2.1%	3.7%	1.0%	0.2%	2.4%	1.4%	4.2%	4.3%	0.0%	1.7%

Table 1.9.9 International comparison of the percentage distribution of total expenditure in 2023 by ATC 1st Level

ATC 1 level	Italy	Austria	Belgium	France	Germany	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	EU10
L - Antineoplastic	31.9	39.0	36.0	36.5	28.2	19.9	20.6	31.1	29.3	32.0	28.8	31.2
N - SNC	12.0	12.3	11.5	11.5	13.0	14.0	16.2	14.3	13.5	12.5	12.6	12.7
J - Antimicrobial	11.2	8.4	7.5	9.6	11.7	5.9	10.2	10.5	11.2	9.7	10.0	10.3
A - Gastrointestinal	10.8	7.9	9.5	8.9	10.7	15.5	15.2	11.3	12.0	11.6	11.9	10.8
B - Haematological	9.1	7.8	8.6	9.1	9.2	9.1	7.7	6.5	9.9	7.6	8.3	8.5
C - Cardiovascular	8.2	7.3	9.2	7.1	6.3	10.9	11.2	7.4	5.0	5.4	7.9	7.2
R - Respiratory	6.6	7.3	7.3	6.4	7.4	11.6	7.0	7.5	5.9	9.6	7.9	7.6
M - Musculoskeletal	2.9	3.5	2.5	2.4	3.4	4.1	3.8	3.0	3.5	2.2	3.4	2.9
G - Genitourinary and sex hormones	2.4	1.5	2.4	2.1	1.8	3.9	2.9	2.5	2.6	2.6	2.7	2.3
D - Dermatological	1.8	1.9	1.7	1.4	2.9	1.8	2.0	1.8	1.2	1.5	2.0	2.0
H - Systemic hormones	1.5	1.1	1.3	1.6	1.6	1.4	0.9	1.4	2.1	1.4	1.4	1.5
S - Sense Organs	1.2	0.8	2.0	2.7	1.8	1.1	1.3	2.2	2.9	3.5	2.0	2.1
V - Various	0.5	1.1	0.4	0.5	1.7	0.7	0.7	0.4	0.7	0.4	0.9	0.8
P - Antiparasitic	0.0	0.1	0.1	0.1	0.2	0.2	0.2	0.1	0.1	0.1	0.1	0.1

Table 1.9.10 International comparison of the 4-year CAGR on total expenditure in 2023 by ATC 1st level

ATC 1 level	Italy	Austria	Belgium	France	Germany	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	EU10
P - Antiparasitic	19.6%	-10.6%	22.5%	2.7%	4.2%	13.2%	4.8%	33.3%	9.3%	10.0%	8.8%	7.7%
D - Dermatological	14.2%	17.7%	10.6%	9.0%	11.2%	10.8%	12.6%	16.5%	7.2%	10.8%	11.3%	12.0%
R - Respiratory	11.1%	11.5%	10.6%	8.6%	8.9%	14.5%	8.9%	8.0%	-0.4%	7.5%	8.8%	9.0%
L - Antineoplastic	10.7%	8.5%	7.7%	10.8%	5.2%	16.1%	8.5%	8.6%	3.4%	12.6%	9.2%	9.2%
S - Sense Organs	9.8%	16.6%	5.3%	4.4%	2.0%	12.9%	14.0%	18.9%	2.0%	8.8%	7.3%	7.2%
A - Gastrointestinal	6.8%	3.7%	5.6%	3.9%	4.9%	13.5%	5.4%	5.9%	5.3%	8.3%	6.5%	6.2%
M - Musculoskeletal	5.1%	4.5%	3.2%	4.0%	4.8%	11.6%	5.8%	6.7%	2.3%	4.9%	6.0%	5.3%
C - Cardiovascular	4.9%	3.5%	15.0%	8.9%	3.7%	5.3%	4.7%	2.4%	5.6%	4.2%	5.1%	5.2%
B - Haematological	4.7%	4.0%	5.8%	6.1%	4.1%	8.0%	5.0%	6.1%	2.2%	7.9%	5.3%	5.5%
N - SNC	4.5%	5.7%	2.5%	1.3%	0.4%	5.7%	5.6%	3.1%	-1.7%	3.8%	3.2%	2.5%
G - Genitourinary and sex hormones	3.5%	1.6%	2.2%	2.7%	0.6%	7.9%	2.4%	2.9%	-0.7%	6.9%	3.8%	3.3%
J - Antimicrobial	2.5%	3.2%	2.8%	4.8%	4.7%	8.2%	4.1%	3.2%	3.0%	5.8%	3.8%	4.3%
H - Systemic hormones	0.5%	-3.4%	1.3%	0.5%	0.6%	4.3%	-1.4%	1.4%	4.6%	1.9%	1.3%	1.0%
V - Various	-2.1%	4.5%	5.4%	2.1%	1.9%	17.1%	7.9%	6.8%	5.8%	6.5%	3.4%	2.9%

In terms of consumption, drugs of the cardiovascular system, gastrointestinal system and Central Nervous System absorb the largest share in Italy, 25.9%, 17.1% and 15.7% respectively. A similar percentage is observed in Italy for drugs of the gastrointestinal system compared to the 10 European countries analyzed, while a much higher percentage is found for drugs of the cardiovascular system and a much lower percentage is found in Italy for drugs of the Central Nervous System (Table 1.9.11). Increases (CAGR 2020-2023) in total consumption were recorded in Italy for pesticides (+10.8%), respiratory drugs (+5.3%), and antimicrobials (+4.9%). At the 10-country level, similarly, there are increases for pesticides (+6.7%), antimicrobials (+4.4%), genito-urinary drugs (+3.2%) and respiratory drugs (+3.1%) (Table 1.9.12).

Table 1.9.11 International comparison of the percentage distribution of total consumption in 2023 by ATC 1st level

ATC 1 level	Italy	Austria	Belgium	France	Germany	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	EU10
C - Cardiovascular	25.9	18.7	18.1	16.5	23.4	21.6	23.0	18.1	18.4	17.6	18.7	20.3
A - Gastrointestinal	17.1	14.2	15.4	18.0	14.1	22.8	15.2	15.2	18.0	18.0	16.9	17.0
N - SNC	15.7	16.5	23.1	24.2	15.4	15.0	24.1	27.9	26.7	22.7	17.0	20.5
R - Respiratory	13.9	27.8	21.6	16.7	19.4	17.9	12.7	16.1	17.4	19.8	21.8	17.9
B - Haematological	7.1	4.7	5.4	4.8	5.3	4.7	4.5	4.4	5.0	4.6	4.6	5.1
M - Musculoskeletal	6.2	7.1	4.5	4.9	5.7	6.9	7.7	6.1	3.7	3.1	5.6	5.3
H - Systemic hormones	3.9	3.2	2.4	2.8	4.0	2.6	2.3	2.8	3.1	2.9	2.6	3.2
G - Genitourinary and sex hormones	2.8	1.9	2.7	2.3	2.6	2.7	2.8	2.1	2.2	3.1	2.4	2.6
S - Sense Organs	2.3	1.2	2.2	4.3	2.4	1.7	1.9	2.3	2.2	1.8	2.7	2.5
D - Dermatological	2.1	2.3	1.8	2.1	4.1	1.6	2.9	2.0	1.1	3.3	4.0	2.7
J - Antimicrobial	2.0	1.2	1.8	2.0	1.1	1.8	1.6	1.9	1.1	2.0	2.0	1.7
L - Antineoplastic	0.8	0.6	0.8	0.6	0.6	0.4	0.7	0.7	0.8	0.8	0.7	0.6
V - Various	0.2	0.4	0.1	0.7	1.3	0.3	0.4	0.1	0.1	0.1	0.6	0.5
P - Antiparasitic	0.0	0.1	0.1	0.1	0.6	0.1	0.2	0.1	0.1	0.2	0.2	0.2

Table 1.9.12 International comparison of the 4-year CAGR on total consumption in 2023 by ATC 1st level

ATC 1 level	Italy	Austria	Belgium	France	Germany	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	EU10
P - Antiparasitic	10.8%	-8.4%	18.9%	1.3%	7.5%	3.2%	0.6%	26.9%	5.1%	-0.1%	7.4%	6.7%
R - Respiratory	5.3%	6.8%	4.7%	2.8%	2.5%	7.2%	4.2%	4.7%	1.5%	-0.3%	3.8%	3.1%
J - Antimicrobial	4.9%	6.0%	5.8%	2.2%	6.2%	4.8%	4.7%	5.4%	3.4%	4.3%	1.7%	4.4%
S - Sense Organs	3.0%	2.6%	4.0%	1.9%	0.9%	5.6%	3.8%	3.5%	2.7%	4.4%	4.5%	2.7%
M - Musculoskeletal	2.5%	-1.0%	-1.2%	-0.4%	-1.3%	2.5%	0.1%	1.4%	0.3%	1.0%	1.2%	0.5%
G - Genitourinary and sex hormones	2.1%	0.7%	1.3%	0.7%	1.1%	3.0%	2.1%	3.3%	2.1%	10.0%	3.0%	3.2%
L - Antineoplastic	1.7%	2.4%	1.7%	1.9%	2.3%	3.9%	1.3%	2.0%	1.0%	2.2%	-2.0%	2.1%
H - Systemic hormones	1.7%	-0.4%	-0.7%	1.1%	-1.1%	1.6%	2.0%	3.0%	4.2%	0.7%	2.0%	0.7%
C - Cardiovascular	1.0%	0.1%	0.5%	-0.1%	0.7%	1.4%	0.5%	0.9%	1.7%	1.8%	1.2%	0.9%
N - SNC	1.0%	1.5%	0.8%	-0.2%	0.9%	2.4%	1.5%	2.1%	1.4%	0.3%	0.9%	0.9%
B - Haematological	0.9%	0.4%	-1.8%	1.8%	0.2%	1.8%	-0.2%	1.2%	0.4%	1.1%	1.0%	0.9%
D - Dermatological	0.6%	-1.8%	-1.4%	-2.4%	-1.8%	-1.2%	-4.1%	0.1%	-0.1%	-0.6%	-0.5%	-1.2%
A - Gastrointestinal	-0.2%	-0.3%	-0.8%	-0.5%	-0.2%	1.9%	1.5%	1.3%	1.1%	1.4%	0.5%	0.5%
V - Various	-3.2%	-5.4%	-0.1%	4.6%	-8.5%	-6.8%	0.4%	-0.3%	2.8%	-4.3%	-5.4%	-4.9%

Large differences are found in the ranks of the 20 active substances with the highest expenditure in the local area (Table 1.9.13), where the highest similarity rate, calculated as the percentage of countries which include a given substance in their ranking, is found for paracetamol (56%), ibuprofen (44%) and atorvastatin (44%). For 8 active substances the similarity rate is 0%, indicating that in no country other than Italy are these medicines included in the top 20 active substances by expenditure. These include the combination amoxicillin/clavulanic acid, confirming that Italy has higher antibiotic consumption and spending than other countries. For the remaining 10 active ingredients, the similarity rate does not exceed 22%. The similarity rate per country, calculated as the number of active ingredients in common with Italy in the top 20 ranking, never exceeds 25%. Less variability is found if we analyse the first 30 active ingredients by local consumption (Table 1.9.14); indeed, for 4 active ingredients a similarity rate of 100% is found, indicating that the active ingredient is present in the ranking of the first 20 in all the countries analysed.

Table 1.9.13 International comparison of the first 20 active ingredients in Italy: ranking by local expenditure in 2023

Active substance	Italy	Austria	Belgium	Germany	France	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	Similarity score
paracetamol	1	154	6	203	6	38	12	8	11	28	11	56
ibuprofen	2	38	17	29	75	4	9	10	45	106	8	44
pantoprazole	3	53	8	58	95	29	31	30	475	395	24	11
diclofenac	4	41	25	44	77	7	25	55	97	78	17	11
colecalciferol	5	142	43	93	81	15	53	56	168	53	27	11
atorvastatin	6	63	24	111	41	18	10	2	73	1	6	44
amoxicillin/ clavulanic acid	7	77	71	84	91	37	24	66	471	290	30	0
bisoprolol	8	86	83	220	47	9	32	80	174	86	43	11
ketoprofen	9	960	460	1,854	212	34	385	594	489	560	163	0
esomeprazole	10	150	120	323	40	116	17	18	158	108	47	22
flurbiprofen	11	183	245	300	439	115	58	336	455	837	172	0
alprazolam	12	524	50	1,156	280	184	49	149	563	988	201	0
ezetimibe/rosuvastatin	13	71	18	267	141	128	13	27			84	22
omeprazole	14	363	29	219	113	36	39	14	46	10	35	22
beclomethasone/ formoterol	15	62	26	33	74	61		26	83	3	19	11
tadalafil	16	160	69	200	51	120	34	76	124	214	77	0
doconexent/ ethyl-eicosapent	17	884	830	1,083	892	861	697	248		402	361	0
lansoprazole	18	332	450	1,348	203	743	166	85	490	46	164	0
mesalazine	19	121	112	110	165	68	41	46	41	18	46	11
acetylcysteine	20	461	109	136	351	127	60	57	282	399	101	0
		0	20	0	5	25	25	25	5	20	25	

Table 1.9.14 International comparison of the first 20 active ingredients in Italy: ranking by local consumption in 2023

Active substance	Italy	Austria	Belgium	Germany	France	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	Similarity score
metformin	1	11	3	12	3	1	4	9	2	2	4	100
acetylsalicylic acid	2	6	5	4	4	3	10	7	15	19	5	100
levothyroxine sodium	3	4	7	3	5	6	7	5	12	9	7	100
bisoprolol	4	9	8	7	8	7	5	11	25	14	8	89
pantoprazole	5	5	4	8	17	15	6	37	111	138	13	67
atorvastatin	6	12	9	15	7	13	3	8	6	4	9	100
diclofenac	7	3	10	10	6	5	9	16	29	47	10	78
ibuprofen	8	10	6	2	10	11	2	3	7	24	6	89
paracetamol	9	16	1	26	1	23	1	1	1	3	2	78
ketoprofen	10	424	200	910	56	26	593	187	185	285	45	0
furosemide	11	39	120	137	16	62	13	25	32	37	31	22
ramipril	12	37	116	5	18	14	42	52	59	10	17	44
salbutamol	13	15	12	6	2	31	11	4	11	1	3	89
flurbiprofen	14	72	128	91	216	168	145	412	248	750	53	0
amlodipine	15	18	24	14	31	24	33	24	10	8	14	44
omeprazole	16	204	18	31	21	36	12	2	8	7	12	56
esomeprazole	17	57	35	90	12	35	15	42	43	95	27	22
naphazoline	18	59	748	1,047		873		1,465			11	0
olmesartan medoxomil	19	724	54	194	901	515	115	81		311	172	0
lansoprazole	20	189	276	576	67	516	85	95	266	12	47	11
		55	55	55	65	45	65	50	45	55	70	

With regard to spending in the hospital setting (Table 1.9.15), it can be seen that the top three molecules in Italy (pembrolizumab, daratumumab and nivolumab) are present in the rankings of the top 20 active ingredients by spending in all the countries analyzed. Apixaban and rivaroxaban, ranked sixth and eighth in hospital spending in Italy, are not in the top 20 in any other country. These differences may also be attributed to the different methods of medicine distribution, together with the different epidemiology of the disease in the various countries. As a matter of fact, since oral anticoagulant medicines in Italy are distributed directly and "on behalf", they fall within the hospital channel, whereas in other countries these medicines are considered in the local channel. Same consideration can be made for the antidiabetics semaglutide and dulaglutide, which rank 13th and 16th in Italy and are not in the top 20 in any other country.

Table 1.9.15 International comparison of the first 20 active ingredients in Italy: ranking by hospital expenditure in 2023

Active substance	Italy	Austria	Belgium	Germany	France	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	Similarity score
pembrolizumab	1	1	1	1	1	1	1	1	2	2	1	100
daratumumab	2	2	3	4	2	4	6	5	1	12	2	100
nivolumab	3	3	5	5	4	2	10	9	6	16	4	100
adalimumab	4	169	239	169	437	109	19	2	387	1	5	33
epoetin alfa	5	244	54	163	111	121	244	102	882	141	51	0
apixaban	6	147	211	99	84	275	538	384	126	150	61	0
ibrutinib	7	274	9	436	340	12	11	7	347	25	15	44
rivaroxaban	8	188	290	148	192	180	725	454	317	248	70	0
enzalutamide	9	222	12	272	305	5	14	17	357	8	13	56
sofosbuvir/velpatasvir	10	490	67	487	222	18	102	11	101	17	25	33
lenalidomide	11	630	22	607	26	129	300	56	520	9	19	11
immunoglobulin base	12	7	4	2	3	35	3	8	4	6	3	89
semaglutide	13	326	503	437	299	668		850	286	587	92	0
elexacaftor/ivacaftor/ tezacaftor	14	479	13	510	118	6	18	12		4	11	56
dupilumab	15	378	422	243	394	94	25	35	221	23	38	0
dulaglutide	16	496	526	424	412	712	1,275	1,009	655	724	104	0
ivacaftor	17	658	25	599	122	19	50	38	1,339	5	16	22
bictegravir/emtricitabine/ tenofovir alafenamide	18	593	139	462	107	1.229	7	4	255	28	18	22
osimertinib	19	289	19	529	152	22	9	15	230	30	28	33
edoxaban	20	221	280	277			696	497	502	284	112	0
		20	40	20	20	40	50	55	20	50	55	

Wide variability is found in the ranks of the active ingredients with the highest hospital consumption (Table 1.9.16): as many as 13 have a similarity rate of 0% and include rivaroxaban, dabigatran, clopidogrel, edoxaban, dapagliflozin, dapagliflozin/metformin, sacubitril/valsartan, empagliflozin, ticagrelor, metformin/sitagliptin, empaglifozin/metformin, olanzapine, and methadone. These differences may be attributable to the different ways of supplying these medicines, which are mainly supplied in direct distribution and on behalf in Italy, whereas in other countries they are supplied in a local context. As a matter of fact, analysing the first 20 active ingredients by overall expenditure and consumption, at local and hospital level (Table 1.9.17 and Table 1.9.18 respectively), the similarity rates are higher: the first 4 active ingredients by expenditure and by consumption in Italy present a similarity rate always higher than 75%.

Table 1.9.16 International comparison of the first 20 active ingredients in Italy: ranking by hospital consumption in 2023

Active substance	Italy	Austria	Belgium	Germany	France	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	Similarity score
apixaban	1	42	65	42	14	74	195	98	24	34	8	11
rivaroxaban	2	133	169	160	138	79	380	229	200	114	28	0
quetiapine	3	13	26	45	110	3	48	17	60	113	19	33
dabigatran etexilate	4	208	289	380	281	119	635	299	277	495	44	0
clopidogrel	5	110	116	129	150	125	221	155	116	74	31	0
edoxaban	6	153	176	240			415	291	314	143	50	0
dapagliflozin	7	164	219	154	204	208	218	323	157	163	61	0
lidocaine	8	7	3	17	5	8	12	76	2	79	7	78
dapagliflozin/metformin	9	351	1,319	650	1,040	886	1,106	811	1,073	1,710	121	0
sacubitril/valsartan	10	140	217	126	222	284	302	279	219	192	94	0
enoxaparin sodium	11	12	20	65	17	9	24	22	173	41	26	44
empagliflozin	12	170	227	128	371	144	391	315	184	382	81	0
ticagrelor	13	285	309	266	341	209	329	363	223	208	106	0
pantoprazole	14	5	7	6	8	1	19	53	129	295	13	67
metformin/sitagliptin	15	222	788	298	325	897		473	604	1,353	131	0
furosemide	16	18	66	53	10	4	18	14	14	40	17	67
empagliflozin/metformin	17	167	893	2,385	1,409	1,444		991	529	1,480	148	0
olanzapine	18	128	58	121	124	54	109	64	56	156	66	0
carbidopa/levodopa	19	271	5	150	30	23	43	5	176	48	30	22
methadone	20	1,032	589	543	118	62	167	54	58	135	83	0
		25	20	10	25	25	15	15	10	0	25	

Table 1.9.17 International comparison of the first 20 active ingredients in Italy: ranking by total expenditure in 2023

Active substance	Italy	Austria	Belgium	Germany	France	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	Similarity score
pembrolizumab	1	1	1	2	1	2	1	1	3	2	1	100
daratumumab	2	2	3	14	2	6	9	5	2	14	5	100
nivolumab	3	4	5	25	5	3	18	9	10	23	7	78
adalimumab	4	10	8	4	11	328	35	2	11	1	3	78
epoetin alfa	5	200	112	123	100	387	604	174	1,091	233	87	0
apixaban	6	8	10	1	4	5	4	15	1	8	2	100
ibrutinib	7	17	15	24	15	28	22	7	26	32	13	44
rivaroxaban	8	13	16	6	14	1	5	41	20	19	6	89
semaglutide	9	65	11	30	36	7	15	10	6	38	12	56
enzalutamide	10	14	20	10	13	11	27	24	16	10	10	78
sofosbuvir/velpatasvir	11	83	175	207	147	36	221	13	31	22	43	11
lenalidomide	12	215	31	198	64	418	730	89	624	11	41	11
dulaglutide	13	102	71	38	27	45	23	56	41	52	32	0
immunoglobulin base	14	9	4	3	3	105	3	8	4	7	4	89
paracetamol	15	130	14	205	7	60	26	22	19	55	19	33
elexacaftor/ivacaftor/ tezacaftor	16	11	21	15	8	14	34	14	912	4	11	67
dupilumab	17	6	66	11	24	319	43	49	30	30	21	22
ivacaftor	18	16	35	33	20	38	90	58	401	5	17	33
bictegravir/emtricitabine/ tenofovir alafenamide	19	56	28	67	38	1,762	10	4	138	36	24	22
osimertinib	20	30	27	68	23	55	14	18	28	41	28	22
		60	55	45	60	40	45	60	50	50	65	

Table 1.9.18 International comparison of the first 20 active ingredients in Italy: ranking by 2023 total consumption

Active substance	Italy	Austria	Belgium	Germany	France	Poland	Portugal	Spain	Sweden	United Kingdom	Europe	Similarity score
metformin	1	11	3	12	3	1	4	9	2	3	4	100
acetylsalicylic acid	2	6	5	4	4	3	11	7	15	19	5	100
levothyroxine sodium	3	4	7	3	5	6	8	5	13	9	7	100
bisoprolol	4	9	8	8	8	7	7	11	25	14	8	89
pantoprazole	5	5	4	7	15	15	6	35	115	148	13	67
atorvastatin	6	12	10	15	7	13	3	8	6	4	9	100
diclofenac	7	3	9	11	6	5	10	17	29	48	10	78
paracetamol	8	14	1	22	1	21	1	1	1	2	2	78
ibuprofen	9	10	6	2	10	11	2	3	8	21	6	89
furosemide	10	36	111	123	16	58	12	25	31	37	28	22
ketoprofen	11	412	187	968	54	26	627	198	185	302	45	0
salbutamol	12	16	12	6	2	31	5	4	11	1	3	89
ramipril	13	38	119	5	19	14	42	53	60	10	17	44
flurbiprofen	14	74	132	96	226	169	151	422	256	902	56	0
amlodipine	15	18	24	14	30	24	32	24	10	8	14	44
omeprazole	16	207	20	32	24	35	13	2	7	7	12	56
esomeprazole	17	57	36	94	12	36	14	43	43	99	29	22
naphazoline	18	58	833	1,103		905		2,078			11	0
lansoprazole	19	193	284	608	60	523	86	94	270	12	47	11
olmesartan medoxomil	20	746	55	209	967	521	118	83		336	180	0
		55	55	55	65	45	65	50	45	55	70	

Patent expired medicines and biosimilars

In Italy there is still a low incidence of expenditure for generic medicines compared to the other European countries, standing - with a percentage of 44.6% - third last in the ranking of the 10 countries. The average percentage of territorial spending on equivalent drugs in the countries analyzed is 51.0% (European average: 50.9%) and ranges between 36.5% in Belgium and 68.2% in Poland (Figure 1.9.8); while the percentage of consumption ranges between 52.9% in Belgium and 84.5% in Great Britain (Figure 1.9.9) with Italy ranking, likewise for spending, third to last with a 55.7% incidence of equivalent drugs.

The penetration of biosimilars in terms of expenditure and consumption was also investigated (Figures 1.9.10 and 1.9.11). Italy ranks first in the incidence of, respectively, expenditure (80.8%) and consumption (66.9%) of biosimilars, compared to European average of 64.7% for expenditure and 31.8% for consumption. Figure 1.9.19 illustrates the penetration of biosimilars in terms of consumption by single molecule. At European level, the highest percentage of biosimilar consumption is recorded for filgrastim, epoetin, rituximab, infliximab, bevacizumab and pegfilgrastim. The incidence of bevacizumab biosimilar consumption increased in all countries, reaching a European coverage of 89% (in 2021 it was 58%). Low biosimilar penetration rates are observed in all countries for insulins and low molecular weight heparin. Teriparatide, which had a low incidence (34%) of biosimilar consumption in Europe in 2021, increased to 64%.

Figure 1.9.8 International comparison of the percentage distribution of 2023 local pharmaceutical expenditure for patent-expired medicines

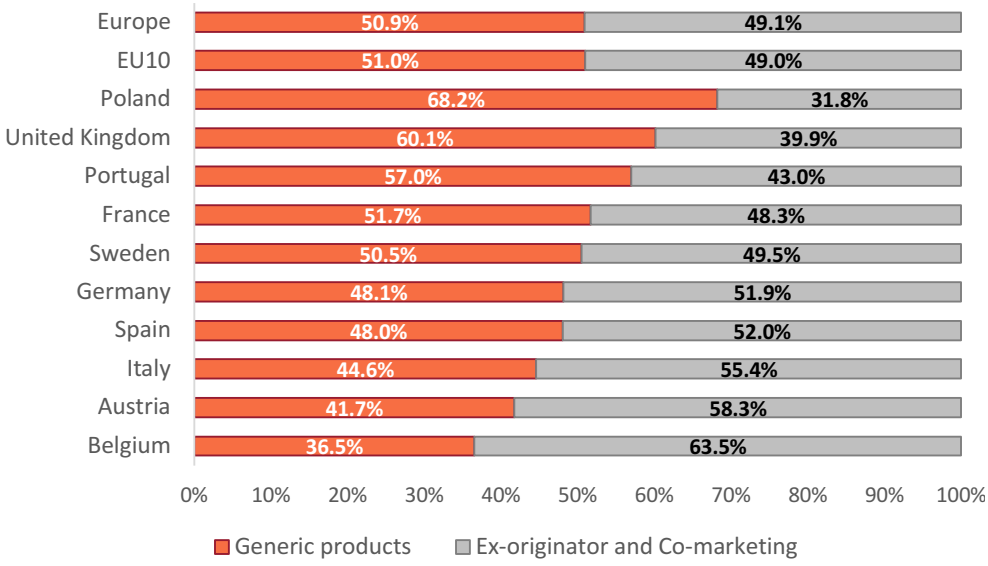


Figure 1.9.9 International comparison of the percentage distribution of 2023 local consumption for patent-expired medicines

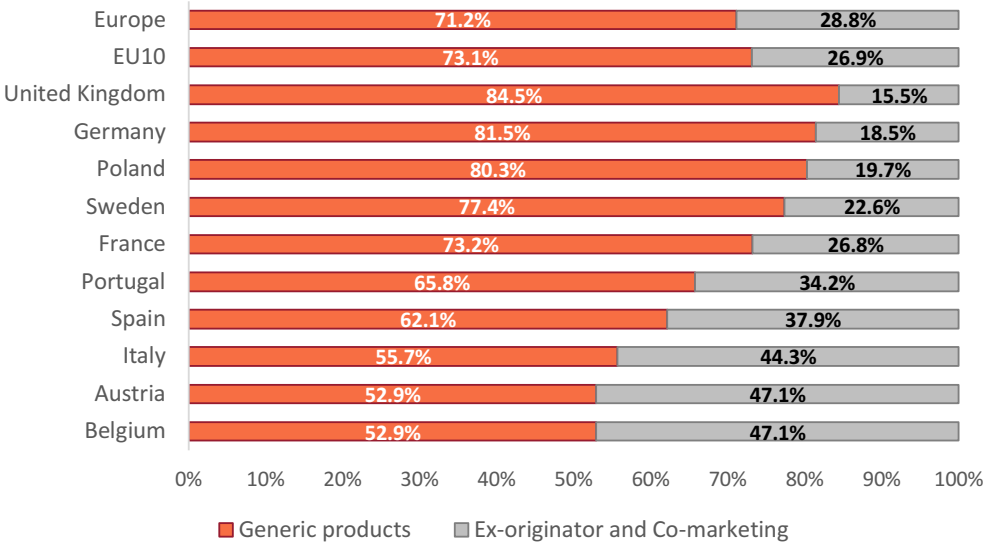


Figure 1.9.10 International comparison of the percentage distribution of 2023 expenditure on biosimilar medicines

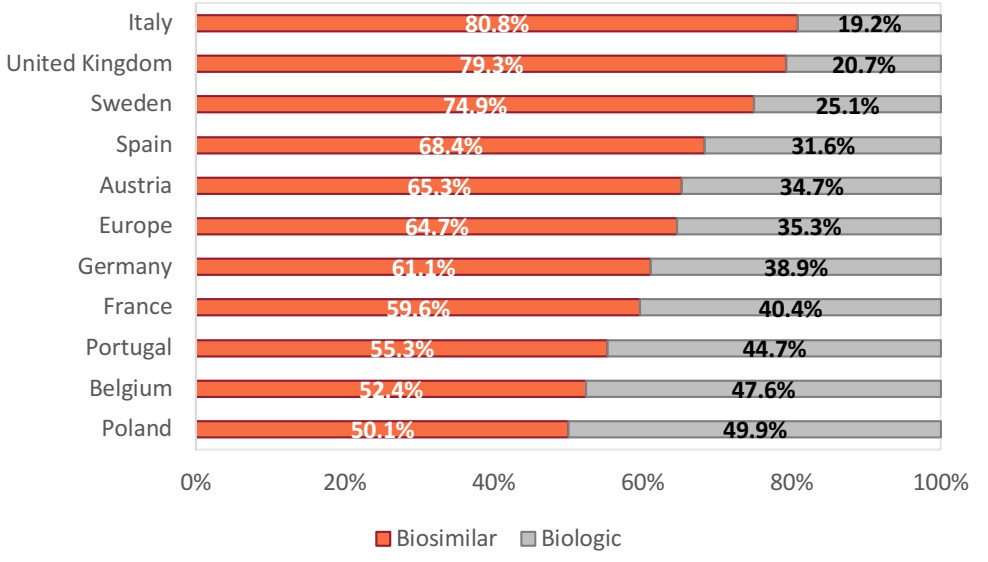


Figure 1.9.11 International comparison of the percentage distribution of 2023 biosimilar medicine consumption

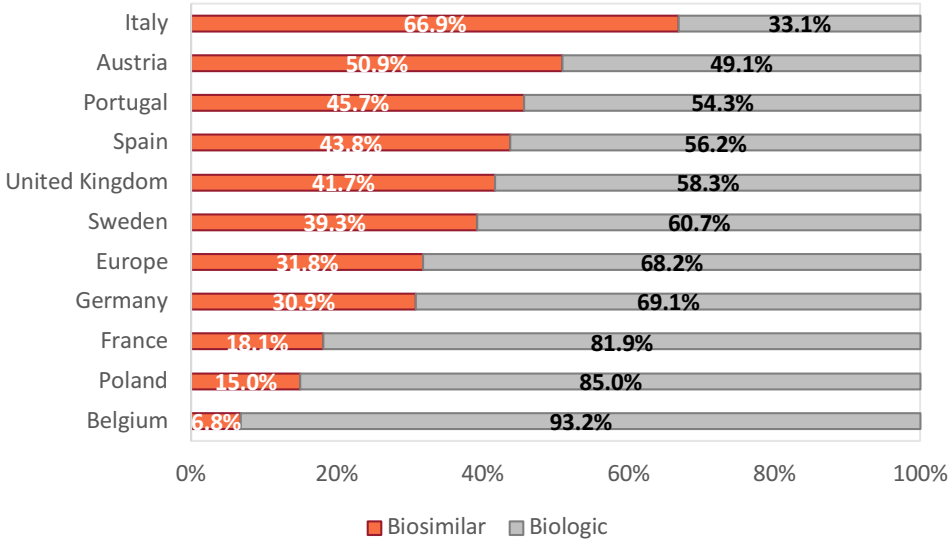


Figure 1.9.19 Percentage distribution of biosimilar consumption (Standard Units) by country and molecule

Molecule	Italy	Austria	Belgium	Germany	France	Poland	Portugal	Spain	Sweden	United Kingdom	Europe
adalimumab	87	30	36	78	55	100	78	74	92	90	70
bevacizumab	97	98	100	88	98	100	85	83	84	45	89
enoxaparina	82	62	4	41	8	0	56	54	0	71	40
epoetina	95	68	8	95	64		99	98	99	23	90
etanercept	83	28	24	81	55	92	58	59	88	86	65
filgrastim	97	100	72	86	97	100	100	97	97	100	96
follitropina	62	47	65	64	72	74	74	77	52	56	47
infliximab	97	95	95	84	82	100	94	87	95	97	86
insulina aspart	2			1	5	18			6	2	4
insulina glargine	17	28	4	21	35	30	24	26	39	17	19
insulina lispro	14	0		8		30			57	1	9
pegfilgrastim	86	53	70	62	86	100	100	88	99	94	81
rituximab	99	100	90	93	97	100	97	98	98	97	95
somatropina	25	39	44	37	39	99	62	14	32	29	35
teriparatide	84	81		48	50		26	62	76	96	64
trastuzumab	99	100	65	83	97	100	92	93	98	76	90

Table 1.9.20 shows, by means of the Herfindhal-Hirschman index (HHI), the concentration and market shares of competitors of individual patent-expired biological products by country. This index is commonly used to quantify the level of market competition and is defined as the sum of the squares of the market shares. The index takes values ranging between 0 and 1, where the maximum value corresponds to a situation of complete monopoly, while very low values are obtained in markets in which there is a large number of competing actors, each holding a small market share. Insulin lispro, insulin aspart, and insulin glargine have a high concentration index in most of the countries considered, as there are, in addition to the reference product, a small number of biosimilars with still minimal market shares. Somatropin is characterized by a high concentration index in several countries (average Europe: 0.5), given by the presence of only one biosimilar on the market, despite the patent having long expired.

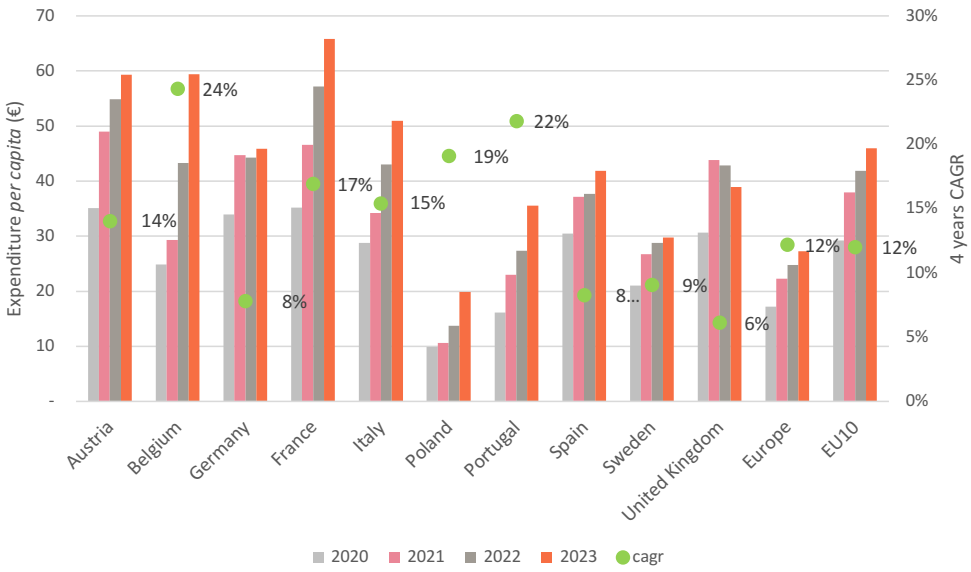
Table 1.9.20 Patent-expired biological medicines: Herfindhal-Hirschman Index (HHI) by country (year 2023)

Molecule	Italy	Austria	Belgium	Germany	France	Poland	Portugal	Spain	Sweden	United Kingdom	Europe
adalimumab	0.2	0.5	0.5	0.2	0.3	0.8	0.3	0.3	0.2	0.3	0.2
bevacizumab	0.2	0.3	0.5	0.2	0.3	0.4	0.3	0.2	0.3	0.4	0.2
enoxaparina	0.3	0.5	0.9	0.6	0.9	1.0	0.4	0.3	1.0	0.5	0.4
epoetina	0.5	0.4	0.7	0.2	0.4	1.0	0.6	0.9	1.0	0.7	0.3
etanercept	0.4	0.6	0.6	0.4	0.4	0.9	0.4	0.3	0.5	0.7	0.3
filgrastim	0.4	0.5	0.5	0.4	0.4	0.5	0.8	0.5	0.3	0.4	0.3
follitropina	0.5	0.5	0.4	0.4	0.4	0.4	0.4	0.4	0.7	0.5	0.3
infliximab	0.3	0.4	0.5	0.4	0.4	0.6	0.4	0.3	0.3	0.5	0.3
insulina aspart	1.0	1.0	1.0	1.0	0.9	0.8	1.0	1.0	0.9	1.0	0.8
insulina glargine	0.8	0.7	0.9	0.7	0.6	0.7	0.7	0.7	0.5	0.7	0.7
insulina lispro	0.8	1.0	1.0	0.9	1.0	0.6	1.0	1.0	0.5	1.0	0.9
pegfilgrastim	0.3	0.4	0.3	0.3	0.2	0.6	0.5	0.4	0.5	0.6	0.2
rituximab	0.6	0.5	0.5	0.4	0.4	0.6	0.4	0.5	0.6	0.5	0.4
somatropina	0.5	0.5	0.5	0.5	0.5	0.9	0.5	0.5	0.5	0.6	0.5
teriparatide	0.3	0.3	1.0	0.5	0.4	1.0	0.6	0.3	0.5	0.4	0.3
trastuzumab	0.3	0.3	0.3	0.3	0.4	0.4	0.2	0.3	0.3	0.2	0.2

Orphan medicines

Italy, with EUR 51.0 per capita, ranks 4th for orphan drug expenditure, after France (EUR 65.8), Belgium (EUR 59.4) and Austria (EUR 59.3) (Figure 1.9.12). All countries show an increasing trend in spending in the years 2022 and 2023, with the exception of Great Britain (-1%). In 2023, the expenditure per capita at the European level was EUR 27.2 with a variation compared to 2022 of +9.9%. The countries with the largest variations compared to 2022 were Poland (+45.3%), Belgium (+37.2%) and Portugal (+29.7%). The average annual change (CAGR) over the period 2020-2023 at European level was +12% and the countries with the highest variations were Belgium (+24%), Portugal (+22%) and Poland (+19%).

Figure 1.9.12 *Per capita* spending trend for orphan medicines in the period 2020-2023

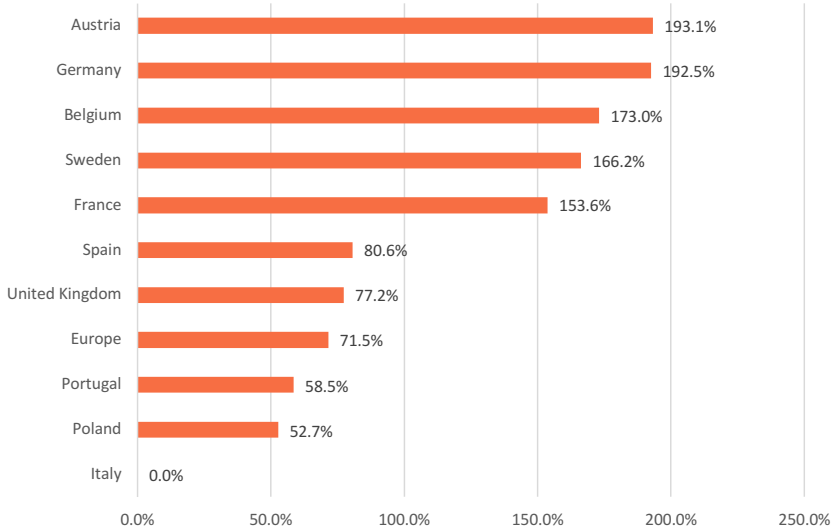


Comparison on European prices

Figures 1.9.13 and 1.9.14 show the comparison of the weighted average ex-factory price for 2023 consumption, relating separately to medicines dispensed by local pharmacies and medicines dispensed by hospitals. Figure 1.9.15 shows a comparison of prices in the overall market, including both local and hospital medicines. The analysis considered medicinal products that are identical or have a similar packaging to those marketed in Italy. The percentage of expenditure on products in common with the comparator country (Italy) was therefore calculated on the total expenditure recorded in the country concerned and on the total amount of expenditure recorded in Italy. The average price in this basket was calculated as the ratio between the expenditure and the dose units supplied in each country. This approach makes it possible to overcome the problem of the different ways of delivering drugs in the various countries. The Italian local/community distribution channel does not include medicines sup-

plied via direct and "on-behalf" distribution. Conversely, they are included in the hospital channel. For example, unlike other countries, the Italian local/community channel does not include new oral anticoagulants and more recently marketed antidiabetics (e.g. glyphozine), which are included in the hospital channel. The comparison should be made only between Italy (reference country) and the other countries considered, as the analysed basket changes each time based on the country selected. A further element to consider when interpreting the results is the lack of an impact evaluation of conditional reimbursement agreements, including confidential discounts, which may be applied differently in different countries, as well as the effect of tenders. An attempt was made to partially overcome this limitation by applying actual purchase prices for Italy and Germany, i.e. the countries for which they were available. Taking the local/community-delivered medicines into account, Figure 1.9.13 shows that all countries have higher average prices than Italy, ranging from the lowest difference of +52.7% with Poland, to the highest of +193.1% with Austria. On average in Europe prices are 71.5% higher than in Italy. The case is different when looking at hospital drugs for which Belgium, France, Portugal and Germany have lower prices than those charged in Italy, with differences ranging from -58.2 % in Germany to -13.4 % in Belgium. Italy has lower prices than Sweden (+623.8%), UK (+547.8%), Austria (+474.5%), Poland (+ +341.3%) and Spain (+10.8%) (Figure 1.9.14). Looking at the European average, as for the shared basket, hospital prices are 91.6% higher than in Italy. Applying purchase prices for Italy and Germany, the difference in prices between the two countries remains almost the same (Germany -49.4% compared to Italy), indicating that the effect of tenders or conditional reimbursability agreements in the basket considered is stronger in Italy. Considering the overall market, covering both medicines delivered at a local level and in hospital settings, Italy reports lower prices than Belgium (+85.9%), Germany (+77.9%), Austria (+33.2%), Sweden (+20.3%), Spain (+7.1%) and Great Britain (+4.2%), while the following counties have lower prices than Italy: France (-12.6%), Poland (-36.2%) and Portugal (-36.5%) (Figure 1.9.15). Considering the European average, both local/community and hospital prices are 61.8% higher than in Italy. Applying purchase prices, Germany shows prices that are 134.5% higher than Italy, a greater difference than that found using the base auction prices. This could be due to the effect of tenders for the purchase of medicines which are dispensed in Italy in direct distribution and "on behalf" while in Germany they are purchased and dispensed by local/territorial pharmacies. When interpreting the results, it is important to consider the corresponding medicines between Italy and other countries, in particular their coverage on the country's pharmaceutical expenditure. In the total market, the largest expenditure coverage is observed in Spain (68%) and the lowest in Germany (26%).

Figure 1.9.13 International comparison of medicine prices in 2023 (ex-factory prices): local assistance



	Italy	Poland	Portugal	Europe	United Kingdom	Spain	France	Sweden	Belgium	Germany	Austria
Coverage (%) of the country's expenditure	100%	22%	36%	24%	34%	39%	26%	15%	19%	5%	28%
Coverage (%) of Italy's expenditure	100%	17%	22%	100%	17%	29%	21%	12%	22%	25%	22%

(with tender prices):

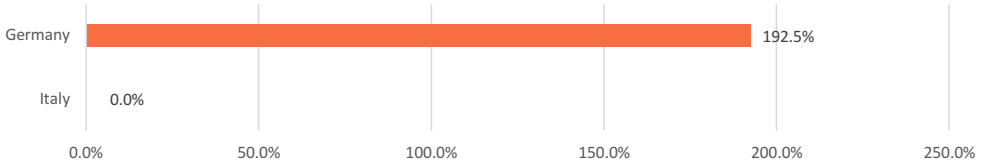
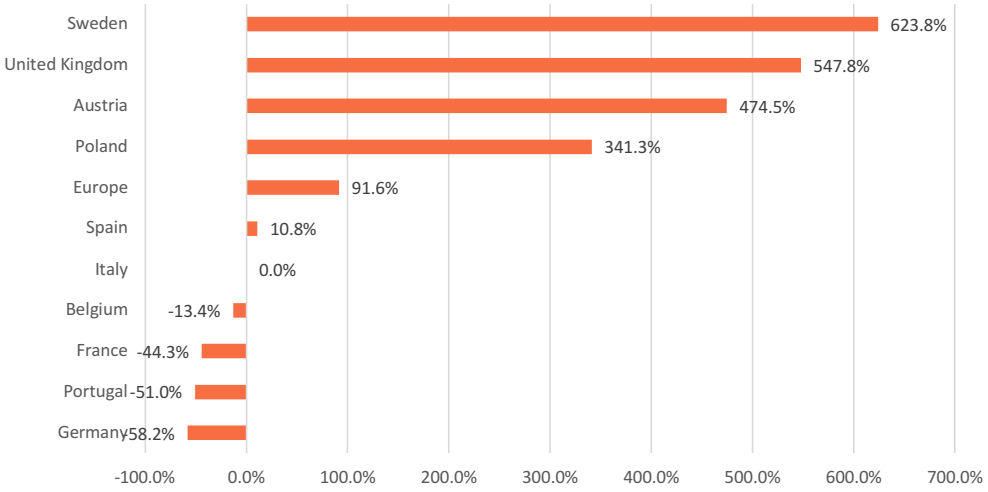


Figure 1.9.14 International comparison of medicine prices in 2023 (ex-factory prices): hospital care



	Germany	Portugal	France	Belgium	Italy	Spain	Europe	Poland	Austria	United Kingdom	Sweden
Coverage (%) of the country's expenditure	66%	86%	77%	90%	100%	86%	70%	51%	68%	37%	67%
Coverage (%) of Italy's expenditure	76%	63%	69%	68%	100%	71%	100%	35%	46%	46%	43%

(with tender prices):

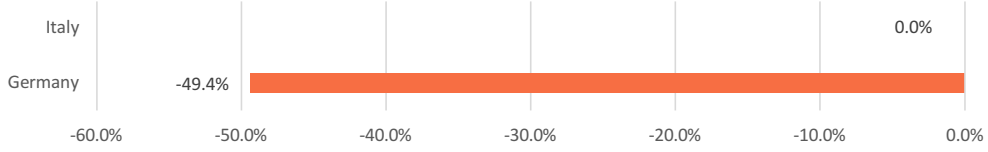
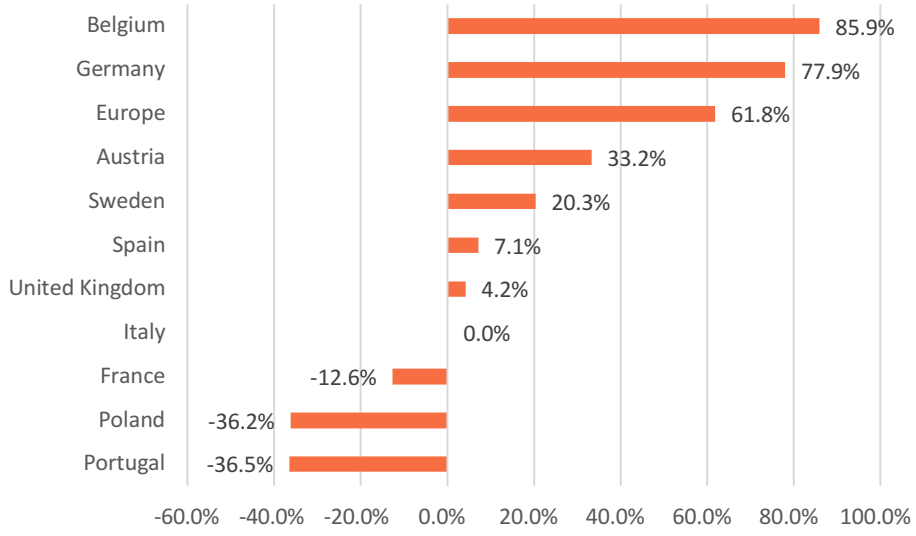
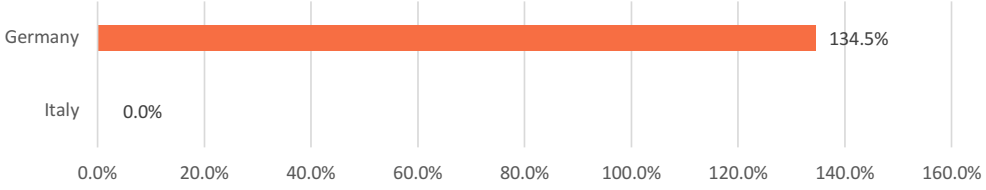


Figure 1.9.15 International comparison of medicine prices in 2023 (ex-factory prices): community and hospital assistance



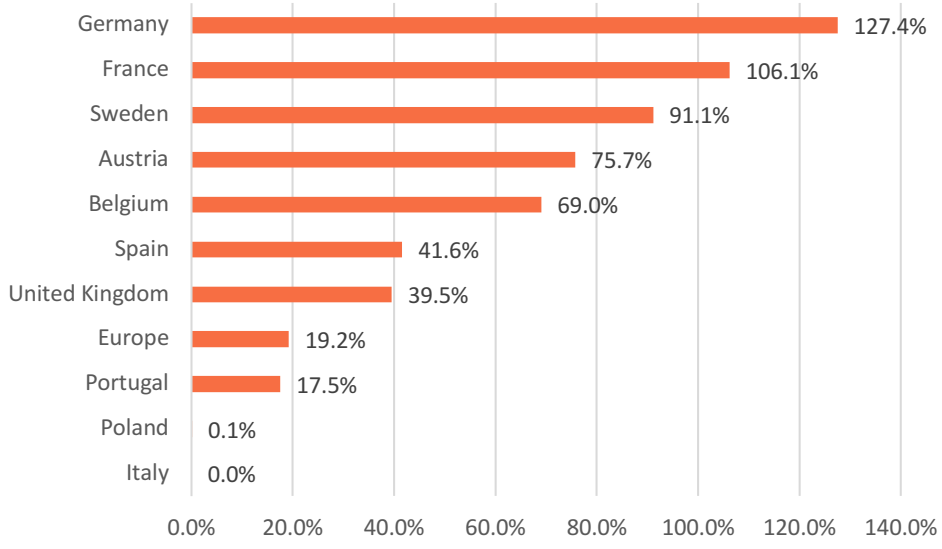
	Portugal	Poland	France	Italy	United Kingdom	Spain	Sweden	Austria	Europe	Germany	Belgium
Coverage (%) of the country's expenditure	60%	33%	52%	100%	38%	68%	35%	48%	47%	26%	60%
Coverage (%) of Italy's expenditure	57%	31%	62%	100%	39%	66%	35%	41%	100%	68%	61%

(with tender prices):



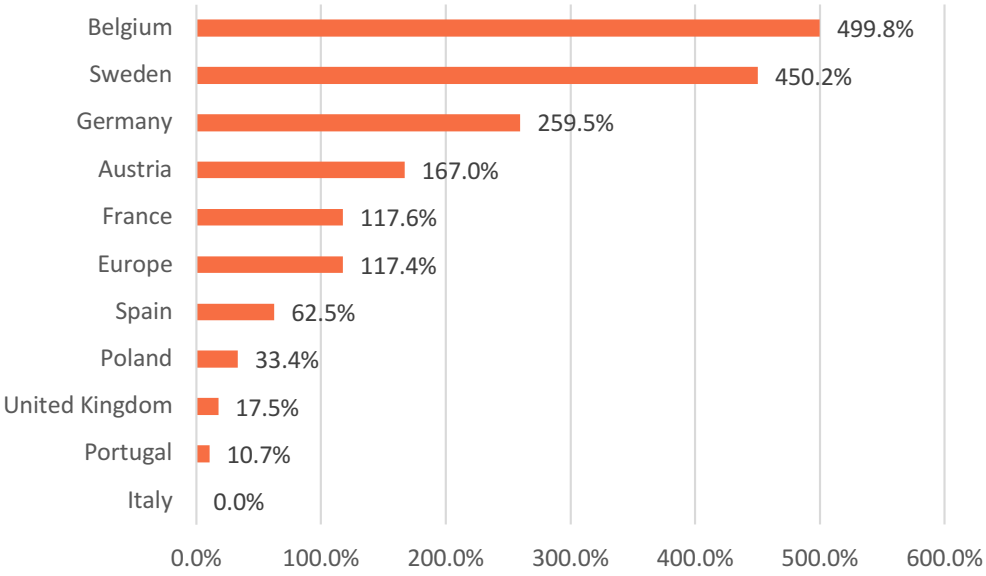
A price comparison was also conducted, distinguishing between medicines with competition (off-patent) and those without competition (on-patent). In the territorial area, Italy has lower prices than all the countries considered both in the market without competition (Figure 1.9.17), and with competition (Figure 1.9.16). In the hospital sector, in the market with competition, Italy has higher prices than Belgium (-29.1%), France (-45.3%), Germany (-52.0%) and Portugal (-61.0%) (Figure 1.9.18). As already emphasised, this analysis does not take into account the effect of tenders, which occur precisely in the market with competition in the hospital sector. Instead, in the market without competition, only Portugal show lower prices than Italy, respectively prices (-17.8%; Figure 1.9.19).

Figure 1.9.16 International comparison of medicine prices (ex-factory prices) WITH COMPETITION in 2023: local assistance



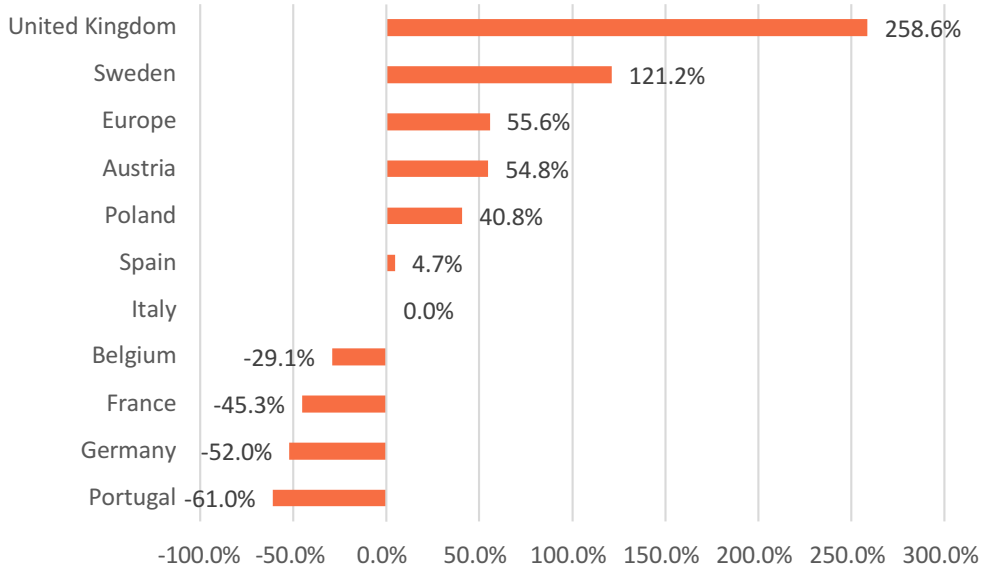
	Italy	Poland	Portugal	Europe	United Kingdom	Spain	Belgium	Austria	Sweden	France	Germany
Coverage (%) of the country's expenditure	100%	13%	23%	19%	16%	28%	16%	22%	13%	27%	6%
Coverage (%) of Italy's expenditure	100%	15%	18%	95%	13%	25%	19%	19%	8%	18%	21%

Figure 1.9.17 International comparison of medicine prices (ex-factory prices) WITHOUT COMPETITION in 2023: local assistance



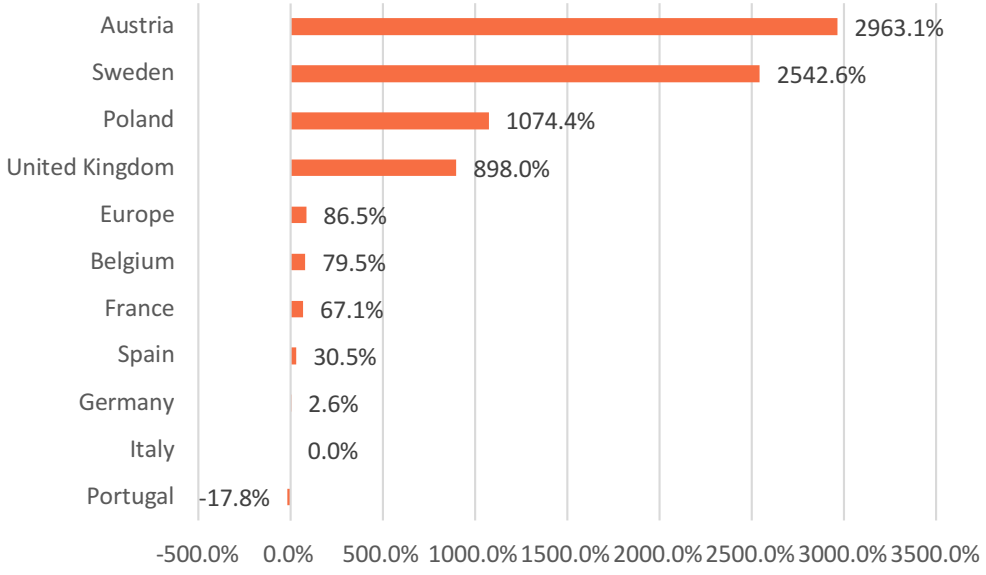
	Italy	Portugal	United Kingdom	Poland	Spain	Europe	France	Austria	Germany	Sweden	Belgium
Coverage (%) of the country's expenditure	98%	66%	79%	59%	67%	9%	24%	30%	4%	15%	23%
Coverage (%) of Italy's expenditure	98%	43%	55%	24%	57%	45%	43%	47%	44%	45%	47%

Figure 1.9.18 International comparison of medicine prices (ex-factory prices) WITH COMPETITION in 2023: hospital assistance



	Portugal	Germany	France	Belgium	Italy	Spain	Poland	Austria	Europe	Sweden	United Kingdom
Coverage (%) of the country's expenditure	65%	43%	54%	73%	100%	75%	37%	39%	49%	35%	24%
Coverage (%) of Italy's expenditure	47%	62%	51%	42%	100%	59%	28%	30%	92%	31%	35%

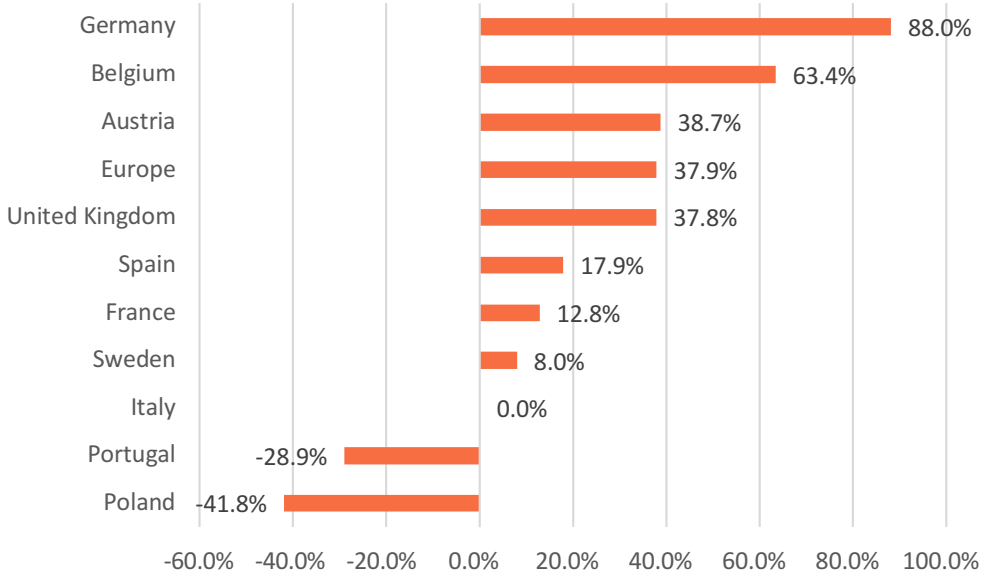
Figure 1.9.19 International comparison of medicine prices (ex-factory prices) WITHOUT COMPETITION in 2023: hospital assistance



	Portugal	Italy	Germany	Spain	France	Belgium	Europe	United Kingdom	Poland	Sweden	Austria
Coverage (%) of the country's expenditure	92%	100%	91%	90%	93%	95%	48%	45%	54%	93%	92%
Coverage (%) of Italy's expenditure	68%	100%	81%	76%	76%	79%	69%	50%	37%	46%	51%

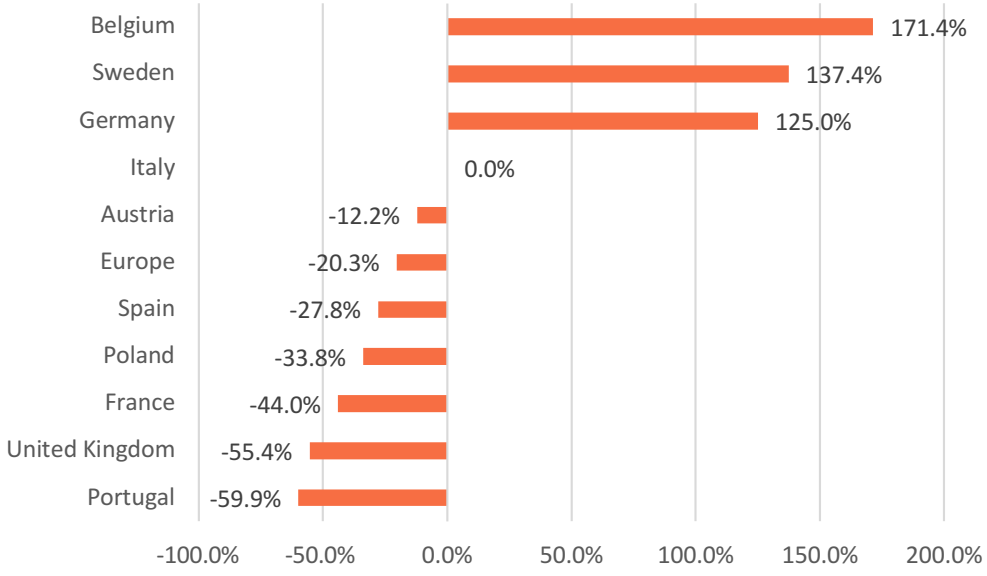
Figures 1.9.20 and 1.9.21 show price comparisons in the market with competition and in the market without competition, respectively, considering local and hospital care together. In the market with competition only PortugalIn the market with competition only Portugal (-28.9%) and Poland (-41.8%) have lower prices than Italy; in the market without competition, all the countries, with the exception of Belgium (+171.4%), Sweden (+137.4%) and Germany (+125.0%), have lower prices than Italy. Comparing prices at a local level and considering only medicines reimbursable in Italy, all the countries have prices higher than Italy with the widest difference for Germany (+920%) and the smallest for Poland (+17%) (Table 1.9.22).

Figure 1.9.20 International comparison of medicine prices (ex-factory prices) WITH COMPETITION in 2023: hospital and local assistance



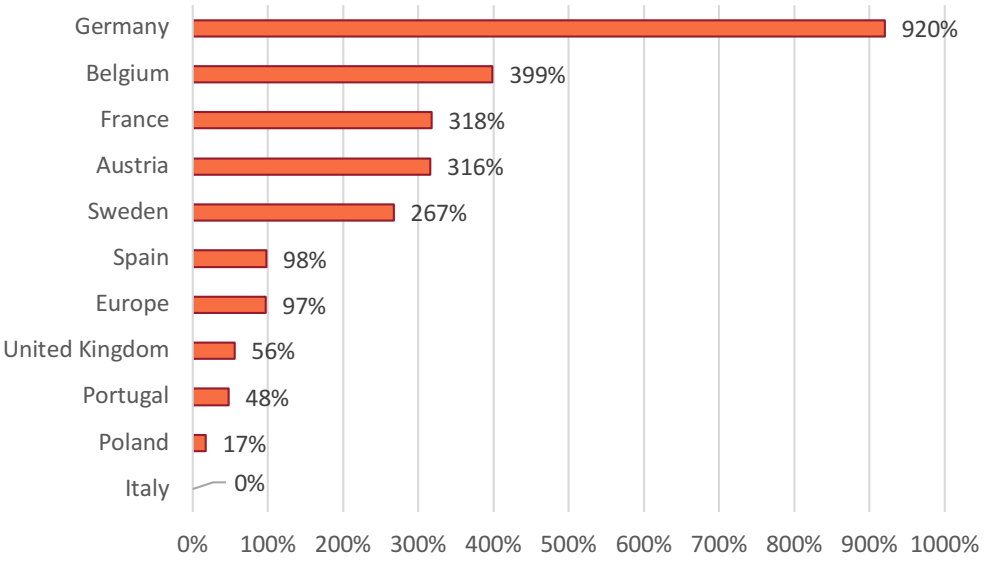
	Poland	Portugal	Italy	Sweden	France	Spain	United Kingdom	Europe	Austria	Belgium	Germany
Coverage (%) of the country's expenditure	17%	35%	100%	21%	37%	46%	21%	29%	31%	35%	17%
Coverage (%) of Italy's expenditure	22%	34%	100%	20%	36%	44%	24%	93%	26%	32%	45%

Figure 1.9.21 International comparison of medicine prices (ex-factory prices) WITHOUT COMPETITION in 2023: hospital and local assistance



	Portugal	United Kingdom	France	Poland	Spain	Europe	Austria	Italy	Germany	Sweden	Belgium
Coverage (%) of the country's expenditure	84%	53%	64%	57%	86%	30%	60%	100%	35%	47%	77%
Coverage (%) of Italy's expenditure	75%	51%	84%	37%	84%	65%	52%	100%	88%	48%	87%

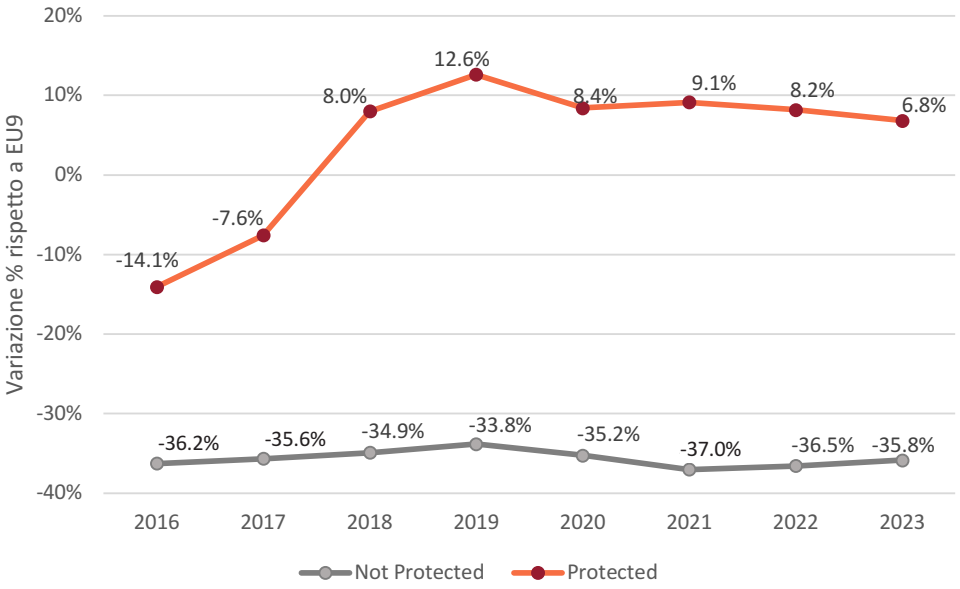
Figure 1.9.22 International comparison of reimbursable medicine prices in Italy in 2023 (ex-factory prices): local assistance



	Italy	Poland	Portugal	United Kingdom	Europe	Spain	Sweden	Austria	France	Belgium	Germany
Coverage (%) of the country's expenditure	40%	6%	11%	11%	10%	15%	6%	12%	11%	8%	3%
Coverage (%) of Italy's expenditure	40%	9%	10%	8%	40%	13%	5%	11%	8%	9%	10%

An analysis was conducted of the trends in the period 2016-2023 of prices in Italy compared to the other countries, separately in the patented medicines market and in the patent-expired medicines market (Figure 1.9.23). Information was collected relating to the 9 countries (EU 9) included in the analysis per single package on patent protection, expenditure and consumption. Only products showing the same patent coverage in the various countries that were marketed in Italy were included in the analysis. In order to compare the price in Italy with the average price of the countries considered, an annual comparison index was calculated between the average prices in Italy and the EU9 average prices for patented medicines and off-patent medicines. It can be noted that in Italy the price of patent-expired medicines is 36.2% lower than the EU9 average in 2016 and 35.8% than 2023, noting that the price difference of patent-expired drugs compared to the average of the 9 European countries has remained almost stable during the period under consideration. By contrast, if we consider the market of patented medicines, up to 2017, prices in Italy were below the EU9 average, while since 2018 prices in Italy have been slightly above the EU9 average. Over the last five years, the difference is gradually narrowing, from +12.6% in 2019 to +6.8% in 2023.

Figure 1.9.23 International comparison of the price of patent-expired and patent-covered medicines between 2016 and 2023 (ex-factory prices): community and hospital assistance



The same analysis was conducted including only those medicines that are classified in band H in Italy and it was observed that the price in Italy of patent-expired medicines is 31.5% lower than the EU9 average in 2016 and 15.4% lower in 2023, highlighting how the prices of patent-expired medicines have moved closer to the EU9 average over the period considered. By contrast, the price of patent-covered medicines in Italy was 41.5% lower than the EU9 average in 2016 and 42.6% lower in 2023, widening the gap with the EU9 average (Figure 1.9.24). For C-range medicines in hospital setting, Italy's prices are also below the EU9 average (Figure 1.9.25). For patent-expired medicines in the period 2016-2020, the difference in Italian prices compared to the EU9 average widened from -25.2% in 2016 to -30.9% in 2020. In the period 2021-2023, the price difference narrowed slightly. For patent-covered medicines, Italian prices in 2016-2018 were higher than the EU average while in 2019-2023 they were lower and, particularly in 2023, are 26.1% lower.

Figure 1.9.24 Sub-analysis class H medicines hospital assistance: international price comparison of patent-expired and patent-covered medicines between 2016 and 2023 (ex-factory prices)

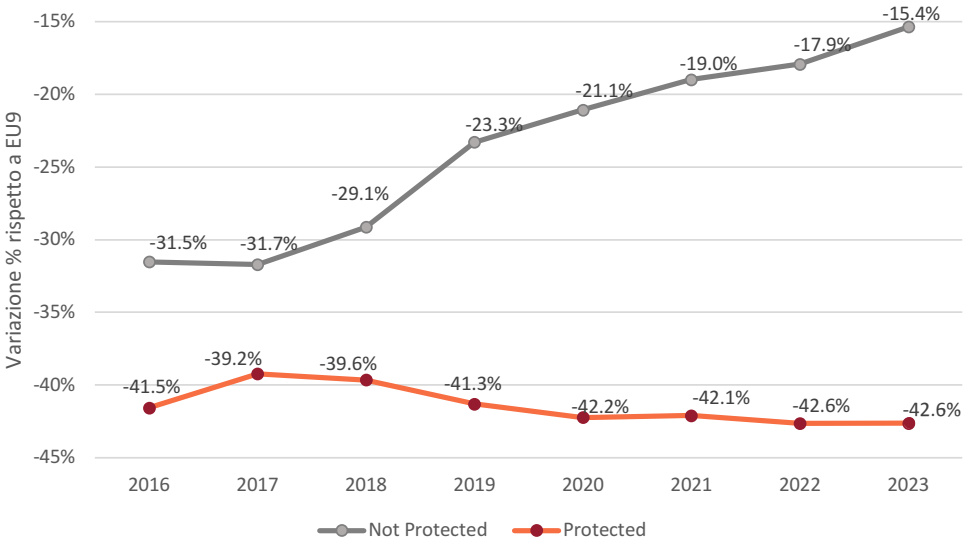
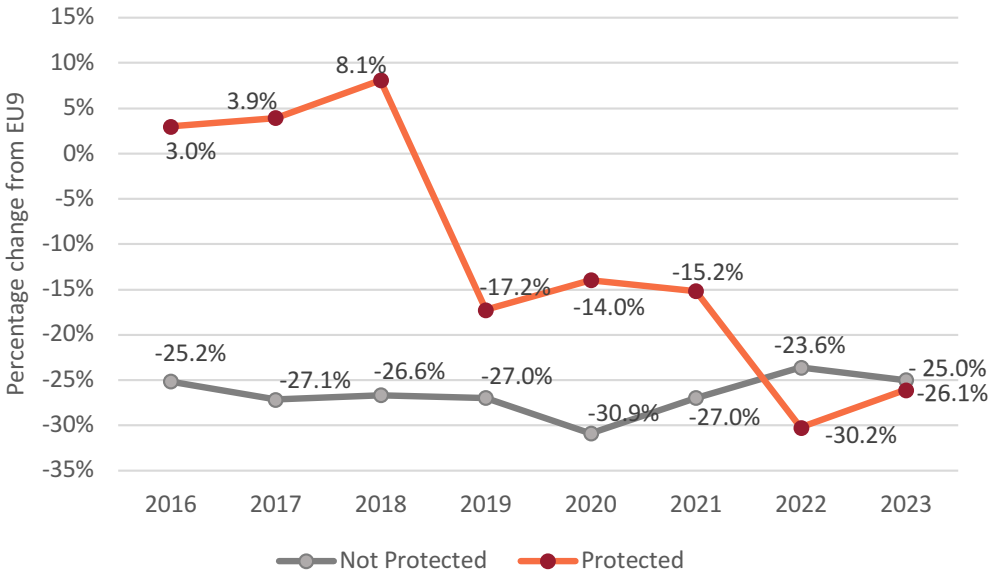


Figure 1.9.25 Sub-analysis class C medicines hospital assistance: international price comparison of patent-expired and patent-covered medicines between 2016 and 2023 (ex-factory prices)

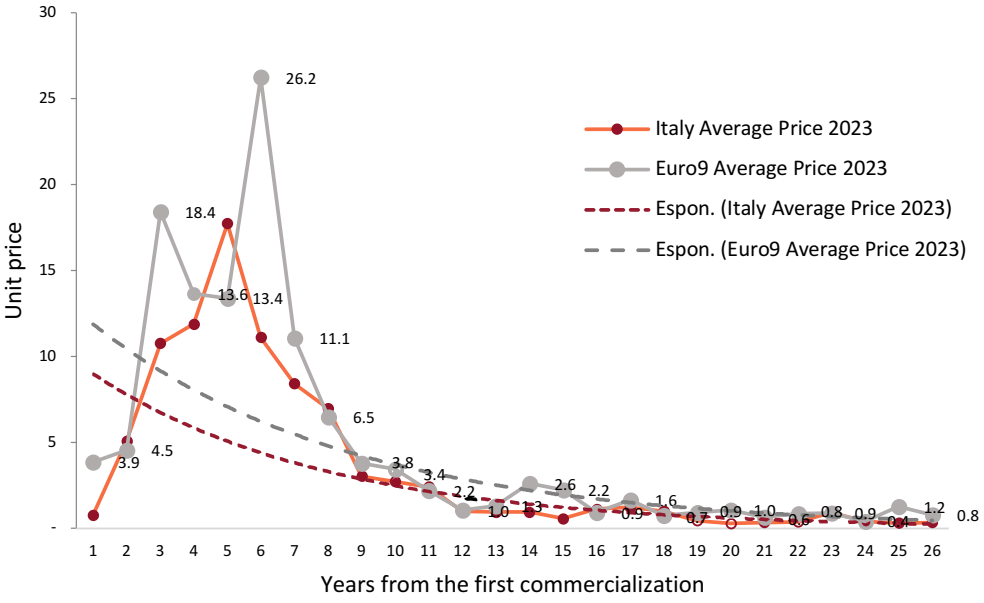


Finally, a comparison of prices was conducted in Italy compared to the EU9 average based on the launch date of the products. After pooling data from 9 countries (EU9) per product and package size, packages were classified according to the first marketing start date in Europe (10 countries). The analysis was carried out by launch year comparing the average price in Italy with the average European price by selecting the package sizes consumed in Italy and at least in another of the 9 European countries. For the comparison, the average was used over the eight years from 2016 to 2023. Should a product be marketed for a shorter period, the average price for the years on sale shall be applied. As years since the first market launch increase, both the average price in Italy and in the 9 countries considered decreases (Figure 1.9.26a). Based on a comparison index of average prices in Italy with average prices in the nine countries, it can be noted that the difference increases with years since first marketing (Figure 1.9.26b). Finally, a price comparison was conducted for certain categories of medicines with respect to the European average (Figures 1.9.27 and 1.9.28). As for drugs indicated for multiple sclerosis, there is a price variation in Italy compared to Europe of more than 100%, while for drugs for asthma and COPD, prices in Italy are 9% lower than the European average. For drugs indicated for diseases of impaired cellular metabolism function, there is a reduction in the difference from Europe, which in 2022 was 100% and in 2023 does not reach 50%, probably due to the recent price renegotiations that took place in Italy (Figure 1.9.27).

For drugs belonging to ATC L (antineoplastics and immunomodulators), the largest differences are found for antineoplastics belonging to the subgroups of monoclonal antibodies and antibody-drug conjugates ACM PD-1/PD-L1 inhibitors with a difference of +46% and interleukin inhibitors with a difference of -32% (Figure 1.9.28).

Figure 1.9.26 International comparison of the average price calculated over 8 years (2016-2023), for medicines with the same year of launch (ex-factory prices): local and hospital assistance

a) Comparison on unit price



b) price ratio in Italy vs Euro9

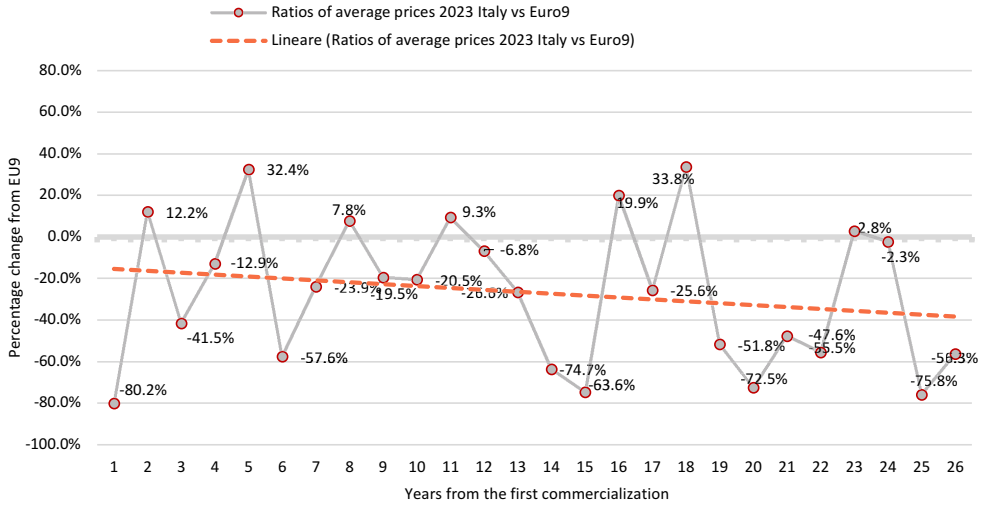


Figure 1.9.27 International price comparison by therapeutic category in 2023: local and hospital assistance

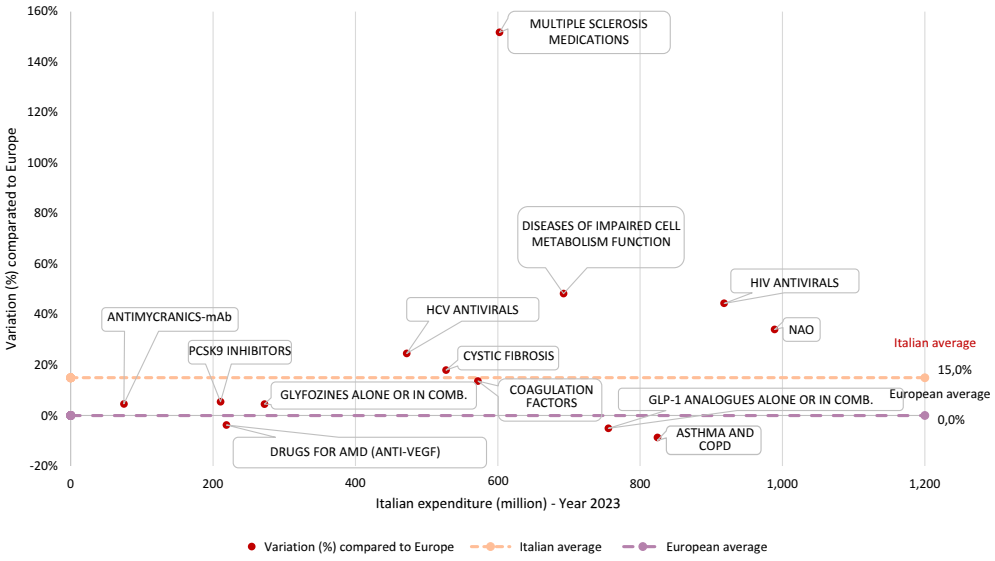
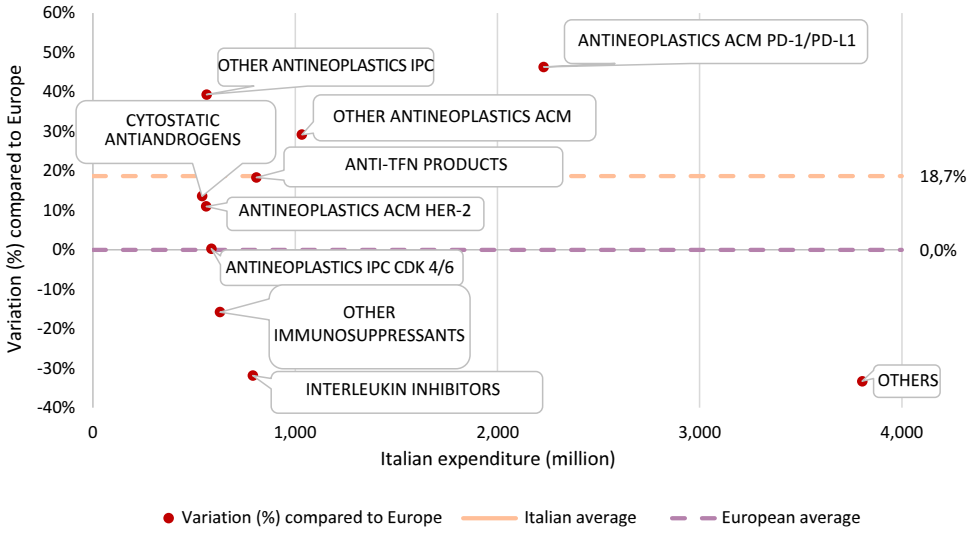


Figure 1.9.28 International price comparison for ATC 4th level under ATC L in 2023: local and hospital assistance



Section 2

Detailed analysis of expenditure and consumption of medicines

BACK TO CONTENTS

2.1 Patent-expired medicines and biosimilars

Patent-expired medicines under approved care regime

In 2023, patent-expired medicines accounted for 73.6% of expenditure and 86.7% of consumption in class A under approved care regime. The percentage share of generic medicines (unbranded), i.e. medicines based on patent-expired active ingredients, excluding those with patent coverage, accounted for 22.8% of expenditure and 31.2% of consumption (Figure 2.1.1 and Figure 2.1.2). This confirms the growing trend in both expenditure and consumption for these medicines, although it has been relatively moderate over the past three years (Figure 2.1.3 and 2.1.4).

At national level, per capita expenditure on patent-expired medicines amounted to 122.4 euro in 2023, up by 3.0% compared to 2022, and with an increase in the percentage incidence on total expenditure which went from 71.6% in 2022 to 73.6% in 2023. Taking into account the last two years, the percentage of expenditure on generic medicines has also increased slightly from 30.5% to 31.0% (difference in percentage points: +0.5%) (Table 2.1.1). The Regions in the South (75.7%) and in the Centre (74.8%) have the highest share of expenditure on patent-expired medicines, both in comparison with the Northern Regions (71.4%) and the Italian average (73.6%). As a matter of fact, the lowest value was recorded in the Province of Bolzano (87 euro), while the highest one in Campania (149.5 euro). An opposite trend is observed when considering the percentage of expenditure on generic medicines: the Northern Regions show higher values (39.5%) compared to the Central (28.7%) and Southern Regions (22.5%).

In 2023, 978.4 daily doses per 1000 inhabitants of patent-expired medicines were consumed, a slight decrease compared to the previous year (-0.5%), corresponding to 86.7% of total DDDs. The percentage of use of generic medicines increased slightly, reaching 35.9% in 2023 (difference in percentage points compared to 2022: +0.7%) (Table 2.1.2). The Northern Regions consume a greater percentage of generic medicines (45.4%) compared to the Central (34.1%) and Southern Regions (25.2%). As a matter of fact, the highest value was recorded in the Province of Trento (50.4%), while the lowest one in Basilicata (21.6%).

In the use of patent-expired medicines, the regional heterogeneity in terms of both expenditure and consumption is plain to see. The composition of expenditure on medicines under approved care regime (Figure 2.1.5) shows that the use of generic medicines is lower in Campania, Sicily and Basilicata (19-21%), whereas the highest values are recorded in the Province of Trento and Lombardy (44% and 43% respectively). In the northern Regions, the consumption of generic medicines is higher than the national average, with 45%. In the Centre and the South and Islands, the consumption of the ex-originator medicines prevails with 66% and 75% respectively. The Province of Trento shows an equal consumption between ex originator and generic medicines (50%). By contrast, Calabria, Basilicata and Campania are the Regions with the lowest share of consumption of generic medicines (22%) (Figure 2.1.6).

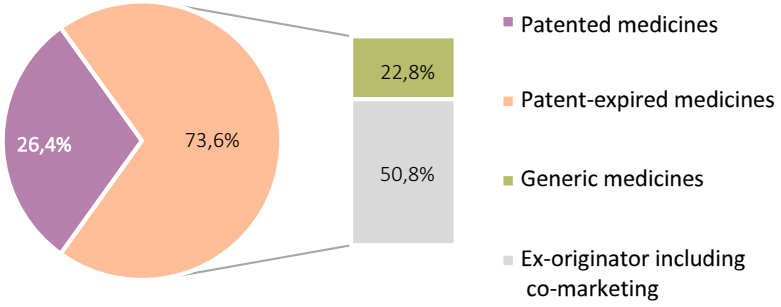
The three therapeutic categories with the highest incidence of expenditure for patent-expired medicines (Table 2.1.3) are represented by medicines active on the genito-urinary system (91.5%), cardiovascular medicines (91.4%), and anti-infectives for systemic use (89.4%). For the category of miscellaneous (V), oncology and immunosuppressants (L), medicines active on the genito-urinary system (G), cardiovascular medicines (C), medicines active on the central nervous system (N) and medicines active on the gastrointestinal tract and metabolism (A) the highest percentages of expenditure are recorded for generics, respectively equal to

58.6%, 30.5%, 28.3%, 27.7%, 27.0% and 26.2%.. When looking at consumption, medicines acting on the cardiovascular system (95.1%) and on the genitourinary system (93.8%) as well as antiinfectives for systemic use (92.6%) confirm the trend shown for expenditure. The category of systemic hormones, excluding sex hormones and insulins (H), on the other hand, has a higher incidence of consumption (82%) compared to that of expenditure (52.4%). Categories with the highest incidence of consumption of generic medicines are: ATC code N (39.3%), L (38.9%), C (37.2%), G (33.4%), V (33.2%) and A (31.7%).

As for expenditure on the top 20 active ingredients of patent-expired class A-NHS (private purchase), more than one third belong to cardiovascular medicines, followed by medicines acting on the gastrointestinal system and metabolism (Table 2.1.4). In 2023, atorvastatin is the most expensive active substance, with an absolute value of 274.4 million euro, down 0.6% compared to the previous year, and a percentage incidence of generics equal to 42.2%, followed by pantoprazole (265.5 million euro) and cholecalciferol (194.6 million euro). The active substances with the highest incidence of expenditure on generic medicines are lansoprazole (71.9%) and pantoprazole (57.3%). In contrast, the incidence of spending on generics for the combination ezetimibe/rosuvastatine (5.7%), olmesartan/amlodipine (16.3%), and amoxicillin/clavulanic acid (19.2%) is very low; the latter, together with the ezetimibe/rosuvastatine combination, shows the greatest increase in spending in 2023, +17% and +25% respectively, amounting to an expenditure of 178.7 and 106.8 million euro. However, cholecalciferol and ramipril show a reduction in expenditure of 16.5% and 8.0% respectively.

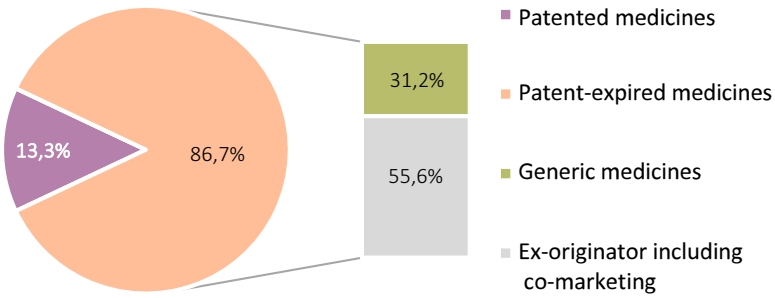
When considering consumption, cholecalciferol records the highest values (101.9 DDD/1000 inhabitants per day), followed by three active substances that refer to the cardiovascular system and three to the gastrointestinal system and metabolism, respectively: ramipril (60.7 DDD/1000 inhabitants per day), atorvastatin (50.6 DDD/1000 inhabitants per day) and amlodipine (28.4 DDD/1000 inhabitants per day) for the cardiovascular system; pantoprazole (29.4 DDD/1000 inhabitants per day), metformin (23.0 DDD/1000 inhabitants per day) and omeprazole (17.1 DDD/1000 inhabitants per day) for the gastrointestinal system and metabolism.

Figure 2.1.1 Expenditure on medicines supplied under approved care regime (class A-NHS) and broken down by patent coverage in 2023



Generic medicines are medicinal products containing active substances with expired patents, with the exception of those which have benefited from patent cover, pursuant to Article 1(bis) of Decree-Law No 87 of 27 May 2005, converted with amendments by Law No 149 of 26 July 2005.

Figure 2.1.2 Consumption of medicines supplied under approved care regime (class A-NHS) and broken down by patent coverage in 2023



Generic medicines are medicinal products containing active substances with expired patents, with the exception of those which have benefited from patent cover, pursuant to Article 1(bis) of Decree-Law No 87 of 27 May 2005, converted with amendments by Law No 149 of 26 July 2005.

Figure 2.1.3 Trends in the impact of expenditure on generic and patent-expired medicines on the total spending on medicines under approved care regime (class A-NHS): comparison 2011-2023

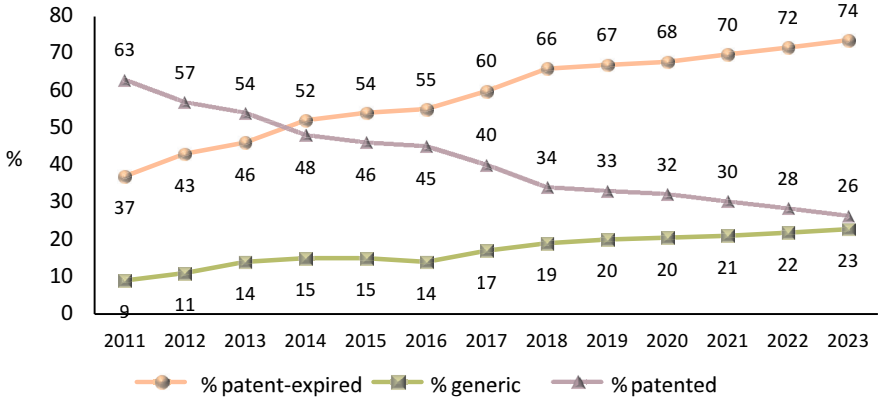


Table 2.1.1 Regional expenditure under approved care regime of patent-expired medicines* (class A-NHS): comparison 2023-2022

Region	*Per capita* expenditure (euro)		% on overall expenditure		% of expenditure on generics**	
	2022	2023	2022	2023	2022	2023
Piedmont	102.2	105.8	72.9	75.1	38.1	38.9
Valle d'Aosta	94.4	98.4	71.8	74.3	37.4	38.3
Lombardy	115.0	120.9	61.8	64.5	42.9	43.1
Province of Bolzano	82.8	87.0	71.8	74.8	36.5	36.9
Province of Trento	106.3	110.2	74.9	76.5	43.5	44.0
Veneto	98.8	101.9	74.4	76.3	35.7	35.9
Friuli VG	106.0	111.0	73.3	76.1	38.7	38.7
Liguria	107.7	111.0	74.0	76.1	34.8	35.1
Emilia R.	101.2	104.5	77.5	78.7	36.4	36.6
Tuscany	98.0	99.9	71.4	73.5	38.1	39.4
Umbria	117.5	115.8	75.8	77.8	28.1	28.8
Marche	118.8	124.3	74.5	75.8	25.9	26.2
Lazio	133.0	135.7	73.3	74.9	23.7	24.0
Abruzzo	136.0	140.2	73.8	76.5	27.4	27.6
Molise	125.6	130.2	75.1	76.8	24.1	24.5
Campania	147.7	149.5	74.7	76.2	18.8	18.9
Puglia	136.7	139.4	73.4	75.1	24.8	25.0
Basilicata	140.7	146.9	73.7	75.1	20.4	20.9
Calabria	139.7	144.2	74.4	76.3	19.1	19.4
Sicily	128.9	131.4	73.8	75.4	20.8	21.4
Sardinia	123.1	130.5	72.3	74.9	31.1	32.4
Italy	**118.8**	**122.4**	**71.6**	**73.6**	**30.5**	**31.0**
North	106.2	110.6	69.1	71.4	39.2	39.5
Centre	118.8	121.3	73.1	74.8	28.1	28.7
South and Islands	136.8	140.0	73.9	75.7	22.1	22.5

* transparency lists published by AIFA over the years 2022-2023 have been used
** calculated on the expenditure of patent-expired medicines

Figure 2.1.4 Trend in the incidence of consumption (doses) of patent-expired medicines and generic medicines on total consumption of medicines under approved care regime (class A-NHS): comparison 2011-2023

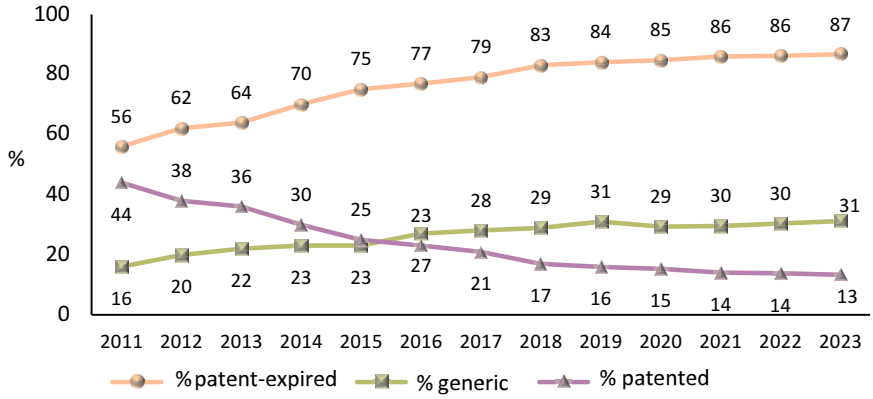


Table 2.1.2 Regional consumption under approved care regime of patent-expired medicines* (class A-NHS): comparison 2023-2022

Region	DDD/1000 inhabitants per day		% of total DDDs		% of expenditure on generics**	
	2022	2023	2022	2023	2022	2023
Piedmont	901.4	899.7	85.7	86.3	44.3	45.6
Valle d'Aosta	807.8	812.2	86.9	87.1	43.5	44.9
Lombardy	939.3	947.9	85.5	86.0	47.2	48.0
Province of Bolzano	712.5	730.5	84.4	84.8	41.7	42.4
Province of Trento	941.0	949.7	88.0	88.3	49.6	50.4
Veneto	846.0	850.2	84.2	85.2	41.5	42.2
Friuli VG	963.8	972.5	87.2	88.0	44.7	45.4
Liguria	863.5	851.4	86.2	86.5	40.3	41.2
Emilia R.	984.9	984.5	86.8	87.3	43.0	43.7
Tuscany	908.1	902.3	83.0	84.7	45.4	47.1
Umbria	1039.9	1004.5	87.6	88.1	32.5	34.1
Marche	981.4	993.1	87.1	87.3	29.8	30.3
Lazio	1036.5	1020.0	87.5	87.5	26.9	27.4
Abruzzo	1052.5	1040.4	86.6	87.1	29.6	29.9
Molise	1017.5	1021.6	87.0	87.2	25.9	26.3
Campania	1133.2	1106.4	87.6	87.8	21.9	21.9
Puglia	1088.5	1070.5	86.5	86.8	26.1	26.8
Basilicata	1118.0	1125.8	87.2	87.3	21.1	21.6
Calabria	1057.4	1050.4	86.8	87.3	21.4	21.8
Sicily	1043.1	1027.0	87.8	87.9	24.0	24.8
Sardinia	1001.4	1023.5	83.6	85.4	35.1	35.2
Italy	**983.3**	**978.4**	**86.2**	**86.7**	**35.2**	**35.9**
North	916.2	919.9	85.7	86.3	44.5	45.4
Centre	988.4	977.7	86.1	86.7	33.2	34.1
South and Islands	1076.5	1062.6	86.9	87.3	24.8	25.2

* transparency lists published by AIFA over the years 2022-2023 have been used
** calculated on the expenditure of patent-expired medicines

Figure 2.1.5 Composition by Region of 2023 expenditure on patent-expired medicines under approved care regime (class A-NHS)

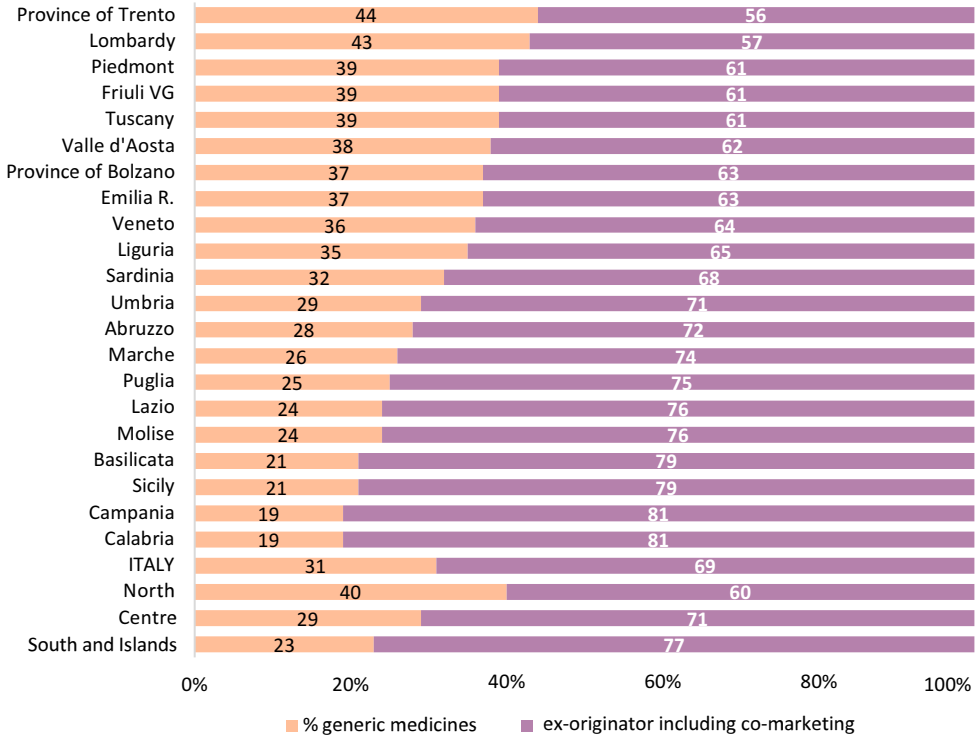


Figure 2.1.6 Composition by Region of 2023 consumption of patent-expired medicines under approved care regime (class A-NHS)

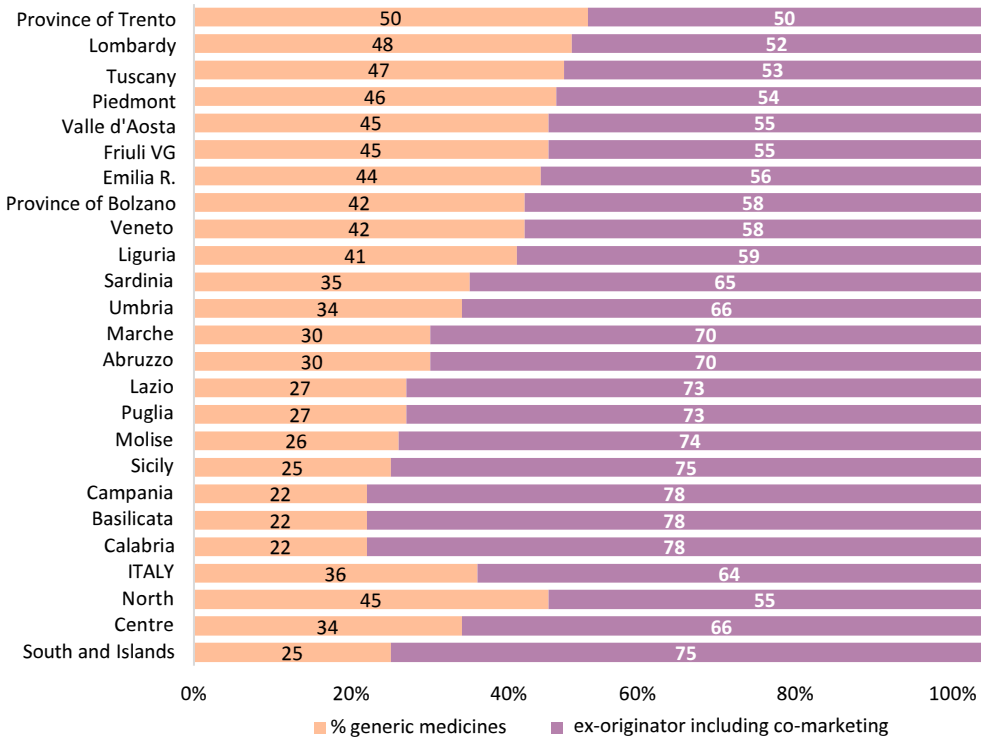


Table 2.1.3 Incidence of 2023 expenditure and consumption of patent-expired medicines under approved care regime (class A-NHS) by ATC 1st level

ATC 1st level	Expenditure under approved care regime		Consumption (DDDs) under approved care regime	
	% patent expired	% generic**	% patent expired	% generic**
A	66.8	26.2	86.9	31.7
B	50.0	14.4	69.0	17.5
C	91.4	27.7	95.1	37.2
D	34.5	5.9	31.7	3.3
G	91.5	28.3	93.8	33.4
H	52.4	5.9	82.0	5.4
J	89.4	22.6	92.6	25.8
L	85.7	30.5	87.3	38.9
M	80.1	19.1	83.3	27.9
N	68.7	27.0	79.2	39.3
P	78.6	2.9	91.0	4.5
R	37.0	4.0	58.0	12.4
S	47.9	6.6	55.2	10.6
V	62.5	58.6	34.8	33.2

* transparency lists published by AIFA over the year 2023 have been used
** calculated on overall expenditure and consumption of patent-expired medicines

Table 2.1.4 Expenditure and consumption of the top 20 highest expenditure patent-expired active substances* under approved care regime (class A-NHS): comparison 2023-2022

ATC	Active substance	Expenditure *(million)*	Inc. %^	Δ % 23-22	% generic**	DDD/1000 inhab. per day	Average cost DDD
C	atorvastatin	274.4	2.8	-0.6	42.2	50.6	0.25
A	pantoprazole	265.5	2.7	-0.3	57.3	29.4	0.42
A	cholecalciferol	194.6	2.0	-16.5	23.2	101.9	0.09
J	amoxicillin/ clavulanic acid	178.7	1.8	17.0	19.2	6.1	1.37
C	bisoprolol	171.4	1.7	3.0	33.9	13.2	0.60
C	omega-3	130.3	1.3	2.7	45.5	2.7	2.27
A	esomeprazole	129.9	1.3	-0.8	34.4	15.9	0.38
C	olmesartan	121.6	1.2	7.6	23.7	18.0	0.31
A	omeprazole	121.3	1.2	-4.9	41.9	17.1	0.33
A	lansoprazole	117.9	1.2	-8.0	71.9	12.5	0.44
C	ramipril	111.7	1.1	-2.8	41.8	60.7	0.09
C	ezetimibe/rosuvastatin	106.8	1.1	25.0	5.7	13.4	0.37
C	ezetimibe	106.7	1.1	7.2	47.3	6.8	0.73
A	metformin	98.9	1.0	1.0	28.7	23.0	0.20
N	levetiracetam	96.9	1.0	0.4	40.5	2.2	2.02
C	olmesartan/amlodipine	95.1	1.0	10.9	16.3	11.0	0.40
C	amlodipine	94.1	1.0	-0.4	37.8	28.4	0.15
C	nebivolol	93.6	1.0	1.9	24.4	17.2	0.25
C	rosuvastatin	93.1	0.9	6.3	37.1	16.8	0.26
L	letrozole	92.2	0.9	3.6	47.2	1.9	2.24
	Total of the top 20	**2694.7**	**27.2**	**1.2**	**37.0**	**448.7**	**0.28**
	Total	**7202.6**	**72.8**	**3.0**	**31.0**	**978.4**	**0.34**

* transparency lists published by AIFA over the years 2022-2023 have been used
^ calculated on overall expenditure under approved care regime
** calculated on overall expenditure of the active substance

Expenditure for citizen cost-sharing on the reference price of patent-expired medicines

In 2023, spending on citizen cost-sharing for the share exceeding the reference price of patent-expired medicines (hereafter cost-sharing) was 18 euro per capita (about 1.05 billion euro). This value represents 71.3% of the total citizen cost-sharing (including the ticket per prescription and/or packaging) and shows a reduction of 2.5% compared to the previous year (Table 2.1.5) and a CAGR decreasing by 0.7% starting from 2018.

The highest per capita expenditure for citizen cost-sharing is recorded in the South and Islands (23.5 euro), while the lowest is recorded in the North with 13.3 euro (Table and Figure 2.1.5), differing from the national average value, in terms of percentage points, by +5.5% and -4.7% respectively. Calabria, Lazio and Campania are the Regions with the highest expenditure values (26.2, 24.8 and 24.5 euro respectively), while the Province of Bolzano and Trento and Valle d'Aosta record the lowest values, equal to 11.9, 12.7 and 12.5 euro respectively.

An analysis of the correlation between expenditure on citizen cost-sharing and regional per capita income shows that Regions with the lowest income are those with the highest citizen cost-sharing. In particular, for Calabria, Sicily and Campania, which have a per capita income slightly above 10.000 euro, there is a higher citizen cost-sharing compared to the national average (>20 euro) (Figure 2.1.7). Among the top 20 therapeutic categories with the highest citizen cost-sharing on reference price, lipid-modifying substances not in combination (8.3%), beta-blockers (7.6%), angiotensin II antagonists alone (5.0%) and in combination (6.1%), and antidepressants (4.8%) account for a little more than one third of the total cost-sharing (Table 2.1.6).

Compared to 2022, the value of citizen cost-sharing expenditure increased for aerosol adrenergics (+58.9%), for other beta-lactam antibacterials (+6.8%), and for beta-lactam antibacterials, penicillins (+6.6%) (Table 2.1.6). This trend is determined, in the case of adrenergics for aerosols, by the entry of the formoterol/budesonide combination on the transparency list in November 2022, while for the antibacterial categories by the increase in consumption (+14.5% for other antibacterials and +15.2% for penicillins) compared to the previous year. For the latter categories, the same trend can also be found at the level of active ingredients, where an increase in expenditure for citizen cost-sharing can be observed for amoxicillin/clavulanic acid (+13.7%) and cefixime (+16.3%) (Table 2.1.7). On the contrary, there continued to be a reduction in expenditure for the citizen cost-sharing for peptic ulcer medicines (-21.3%), ACE inhibitors in combination (-14.6%) and vitamins A and D, including combinations (-17.2%), in this case mainly due to a reduction in the citizen cost-sharing for cholecalciferol (-23.2%) (Tables 2.1.6 and 2.1.7). For this active ingredient there was a decrease in consumption (-14.7%), which had an impact on the reduction in both expenditure and citizen cost-sharing.

Among the top 30 active ingredients with the greatest impact on the reference price, a little more than one third relate to the category of medicines acting on the cardiovascular system; in particular, bisoprolol, atorvastatin and ramipril cover 10% of total expenditure for citizen cost-sharing (Table 2.1.7). The top 30 active ingredients showing the greatest absolute change in citizen cost-sharing expenditure in 2023 were ranolazine, the combination formoterol/beclometasone and mesalazine. The change for ranolazine (9.3 million) and the formoterol/beclometasone combination (8.3 million) is due to their entry on the transpar-

ency list during 2023 (Table 2.1.8). For mesalazine, the increase in citizen cost-sharing could be due not only to the increase in consumption (+2.7%) but also to the probable price reduction of generic medicines. Among the top 30 active ingredients by difference between retail price and reference price, those with very high differences are distributed almost exclusively through the direct purchasing channel and have high costs, while most medicines with a small difference between retail price and reference price are mainly distributed under approved care regime (Table 2.1.9). In fact, considering the average difference between the retail price and the reference price and the share of expenditure in relation to the distribution channel (Table 2.1.10), it is noted that the majority of products with an average difference of less than 3 euro are supplied under approved care regime (69.3%), accounting for more than half (62.7%) of total citizen cost-sharing expenditure. Only 1.2% of products with a difference of more than 20 euro are distributed under approved care regime.

By taking into account the top 10 therapeutic categories (ATC 3rd level) with a higher share of spending on the reference price, it is observed that in the North generic medicines are more used than in the Centre and the South (Table 2.1.11), with the widest differences for the categories of beta-blockers (C07A), angiotensin II antagonists (C09C), ACE inhibitors in combination (C09B) and calcium channel blockers with predominantly vascular effect (C08C). Males tend to rely on generic medicines more than females. Overall, the analysis stratified by age shows a different use of generic medicines, depending on the categories considered; in fact, for beta-blockers (C07A), ACE inhibitors in combination (C09B), medicines used to treat benign prostatic hypertrophy (G04C) and antithrombotic medicines (B01A), it is possible to note a use of generic medicines that increases with age; on the contrary, for the other categories, the use of generic medicines decreases with age.

Table 2.1.5 Distribution of share on reference price by Region (Table and Figure) (year 2023)

Region	Weighted *per capita* expenditure	Δ % 23-22	CAGR (%) 2018-2023	Δ % national average
Piedmont	13.3	-4.8	-2.3	-26.1
Valle d'Aosta	12.5	-3.7	-1.4	-30.5
Lombardy	13.7	-2.4	-0.8	-23.6
Province of Bolzano	11.9	-1.8	-0.6	-34.0
Province of Trento	12.7	-2.8	-0.2	-29.4
Veneto	13.7	-3.0	-0.6	-23.5
Friuli VG	14.1	-2.4	-1.4	-21.3
Liguria	14.6	-3.6	-1.1	-18.6
Emilia R.	14.5	-2.5	0.2	-19.2
Tuscany	13.0	-5.9	-1.6	-27.5
Umbria	17.9	-6.2	-2.1	-0.2
Marche	18.8	-1.4	-1.0	4.8
Lazio	24.8	-2.2	-0.3	38.0
Abruzzo	21.0	-0.5	-0.0	17.2
Molise	21.7	-0.5	0.2	20.6
Campania	24.5	-2.5	-0.5	36.4
Puglia	21.5	-2.6	-0.8	19.5
Basilicata	24.0	-0.4	2.0	33.9
Calabria	26.2	2.6	1.6	45.7
Sicily	23.3	-2.3	-1.5	29.8
Sardinia	17.0	-2.0	-1.0	-5.5
Italy	**18.0**	**-2.5**	**-0.7**	**-**
North	13.3	-3.0	-0.9	-25.7
Centre	19.7	-3.2	-0.8	9.9
South and Islands	23.5	-1.7	-0.5	30.7

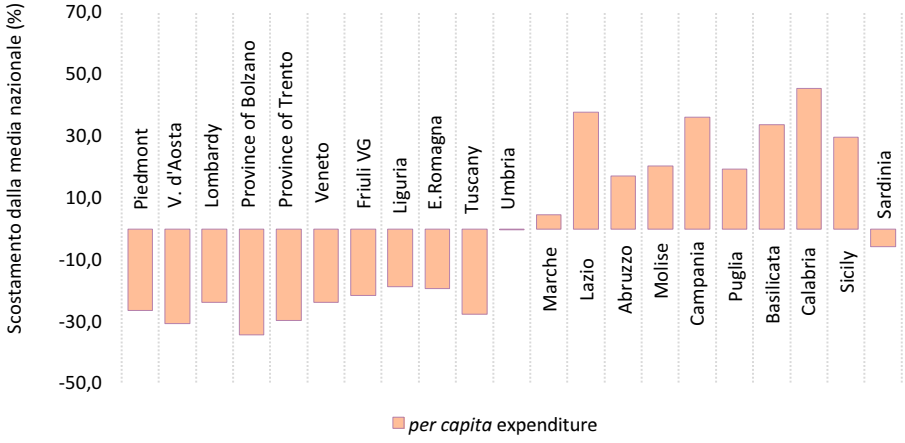


Figure 2.1.7 Correlation analysis between citizen cost-sharing expenditure and *per capita* income (year 2023)

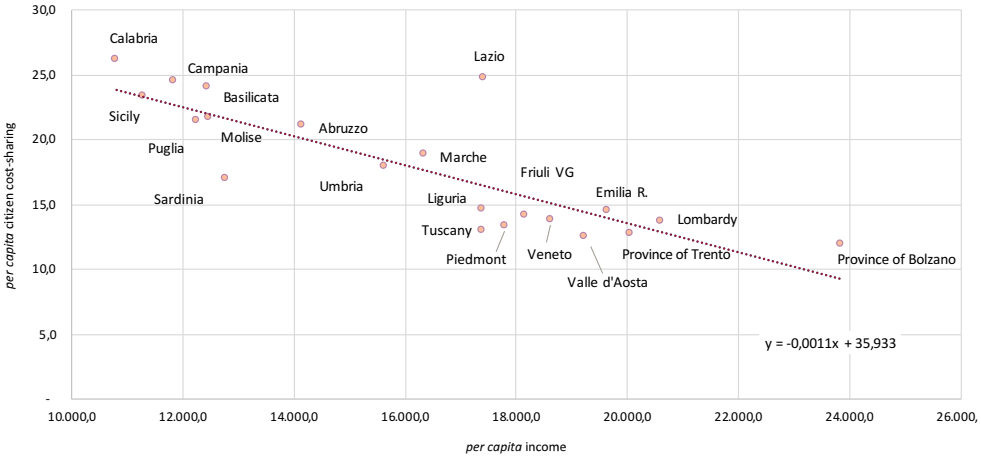


Table 2.1.6 Top 20 therapeutic categories with the largest share of expenditure on reference price (year 2023)

ATC 3rd level	Therapeutic category	DDD/1000 inhab. per day	Δ % 23-22	% generic	Total expenditure^	Δ % 23-22	Citizen cost-sharing	Δ % 23-22	%*	% cum.
C10A	Lipid modifying substances, not combined	94.6	0.5	48.71	743.54	1.3	87.4	-5.6	8.3	8.3
C07A	Beta blockers	45.8	1.0	41.48	333.23	1.3	80.4	0.4	7.6	15.9
C09D	Angiotensin II antagonists, in combination	43.4	2.4	22.82	339.67	-1.1	64.3	0.2	6.1	22.0
C09C	Angiotensin II antagonists	58.6	1.0	32.13	294.62	1.7	53.4	-0.8	5.0	27.0
N06A	Antidepressants	45.0	2.9	49.05	422.11	2.8	50.7	0.7	4.8	31.8
C09B	Angiotensin-converting enzyme (ACE) inhibitors, in combination	36.6	0.1	22.39	280.19	-0.4	50.6	-14.6	4.8	36.6
G04C	Medicines used in benign prostatic hypertrophy	41.0	3.3	35.95	272.65	2.1	46.8	-0.5	4.4	41.0
B01A	Antithrombotics	66.5	-0.3	20.89	325.13	-4.1	43.0	0.1	4.1	45.1
C09A	Angiotensin-converting enzyme inhibitors (ACE), not in combination	78.6	-2.2	54.07	201.94	-3.8	41.5	-6.2	3.9	49.0
C08C	Selective calcium channel blockers with predominantly vascular effect	49.3	-0.3	39.70	232.75	-3.0	32.4	-4.1	3.1	52.1
M01A	Non-steroidal anti-inflammatory and anti-rheumatic medicines	17.1	-5.6	18.42	144.19	-5.5	30.9	-7.6	2.9	55.0
A10B	Oral hypoglycemic agents	32.7	-4.3	37.43	321.60	-3.4	24.7	-5.1	2.3	57.3
S01E	Antiglaucoma and miotic preparations	21.4	2.4	10.75	219.46	2.8	24.6	-4.5	2.3	59.6
J01C	Beta-lactam antibacterials, penicillins	7.0	15.2	27.08	197.95	15.4	23.7	6.6	2.2	61.8
A11C	Vitamins A and D, including their combinations	119.1	-14.4	21.42	235.88	-14.9	23.5	-17.2	2.2	64.0
J01D	Other beta-lactam antibacterials	2.2	14.5	13.51	172.45	13.3	22.4	6.8	2.1	66.1
N03A	Anti-epileptics	9.5	-0.4	19.43	273.27	-4.1	19.1	1.9	1.8	67.9
A02B	Treatments for peptic ulcer	77.2	-3.2	52.56	663.91	-5.6	19.0	-21.3	1.8	69.7
R03A	Adrenergics for aerosol	18.9	2.1	1.83	584.65	-0.8	17.3	58.9	1.6	71.3
R03B	Other anti-asthmatics for aerosol	9.1	-4.0	4.18	237.21	-5.8	15.7	-1.0	1.5	72.8
	Top 20 therapeutic categories	**873.7**	**-2.3**	**34.72**	**6496.39**	**-1.2**	**771.4**	**-2.9**	**73.0**	**72.8**
	Total	**1128.1**	**-1.1**	**31.16**	**9782.02**	**0.0**	**1056.8**	**-2.5**	**100.0**	**100.0**

^gross expenditure including expenditure on citizen cost-sharing * calculated on overall citizen cost-sharing

Table 2.1.7 Top 30 substances with the largest share of expenditure on the reference price (year 2023)

ATC 5th level	Active ingredient	DDD/1000 inhab. per day	Δ % 23-22	% generic	Total expenditure^	Δ % 23-22	Citizen cost-sharing	Δ % 23-22	%*	% cum.	Average difference between retail price and reference price
C07AB07	bisoprolol	13.2	3.3	48.3	171.45	3.0	55.5	1.5	5.2	5.2	1.32
C10AA05	atorvastatin	50.6	-0.5	49.7	274.38	-0.6	38.1	-5.9	3.6	8.8	1.18
C09AA05	ramipril	60.7	-1.3	54.7	111.69	-2.8	24.5	-4.7	2.3	11.1	0.86
B01AC06	acetylsalicylic acid	46.0	0.8	21.7	70.69	0.4	24.3	0.1	2.3	13.4	0.74
J01CR02	amoxicillin/clavulanic acid	6.1	16.7	22.5	179.74	17.2	22.8	13.7	2.2	15.6	1.16
A11CC05	cholecalciferol	116.7	-14.7	21.4	198.01	-17.2	19.8	-23.2	1.9	17.5	0.79
C09CA08	olmesartan	18.0	7.7	28.4	121.61	7.6	19.4	5.6	1.8	19.3	1.41
C08CA01	amlodipine	28.3	1.4	48.4	94.07	-0.4	18.7	-5.5	1.8	21.1	0.92
C09DB02	olmesartan/amlodipine	11.0	11.3	19.8	95.07	10.9	16.6	10.2	1.6	22.7	1.97
C09DA08	olmesartan/hydrochlorothiazide	10.8	3.7	20.2	76.85	3.2	16.1	2.0	1.5	24.2	1.94
G04CA02	tamsulosin	11.6	3.6	41.8	68.85	2.2	15.2	0.2	1.4	25.6	1.30
A10BA02	metformin	23.0	-0.6	40.1	98.89	1.0	15.1	-3.8	1.4	27.0	0.54
B01AC04	clopidogrel	6.4	7.4	44.9	75.31	5.2	14.5	-2.5	1.4	28.4	2.94
A05AA02	ursodeoxycholic acid	2.8	5.3	38.1	56.31	5.2	14.5	6.1	1.4	29.8	2.20
C10AX06	omega-3	2.7	4.9	51.4	130.32	2.6	14.5	-6.6	1.4	31.2	1.28
C07AB12	nebivolol	17.2	2.2	28.3	93.57	1.9	13.0	1.4	1.2	32.4	0.98
C09BB04	perindopril/amlodipine	5.3	0.8	28.7	48.39	0.2	12.4	-0.6	1.2	33.6	3.25
N02BF02	pregabalin	2.7	9.7	40.6	87.19	8.5	11.6	2.8	1.1	34.7	1.30
J01DD08	cefixime	1.3	14.9	14.8	67.47	15.0	11.5	16.3	1.1	35.8	2.00
C10AA07	rosuvastatin	16.8	6.3	42.6	93.16	6.3	11.3	-1.6	1.1	36.9	0.93
G04CB02	dutasteride	8.5	1.3	34.1	60.90	-0.1	11.2	-3.4	1.1	38.0	1.95
H03AA01	levothyroxine	23.5	3.5	2.3	86.97	5.9	11.0	0.9	1.0	39.0	0.52

continued

Table 2.1.7 – *continued*

ATC 5th level	Active ingredient	DDD/1000 inhab. per day	Δ % 23-22	% generic	Total expenditure	Δ % 23-22	Citizen cost-sharing	Δ % 23-22	%*	% cum.	Average difference between retail price and reference price
C02CA04	doxazosin	7.5	-0.7	37.2	71.52	-1.3	11.0	-2.4	1.0	40.0	1.26
J01XX01	fosfomycin	0.4	0.3	40.0	37.41	-0.3	10.9	-1.1	1.0	41.0	2.69
N06AB10	escitalopram	7.7	0.7	40.4	56.94	-0.2	10.9	-3.0	1.0	42.0	2.20
C01BC04	flecainide	3.2	3.9	17.8	56.09	3.1	9.8	-0.4	0.9	42.9	1.79
N06AB05	paroxetine	7.9	-0.1	42.6	57.10	-2.8	9.7	6.4	0.9	43.8	1.60
A07EC02	mesalazine	5.5	2.7	11.6	127.14	1.2	9.6	97.1	0.9	44.7	2.66
G04CA04	silodosin	6.7	4.0	26.3	44.63	3.1	9.4	0.6	0.9	45.6	1.84
C01EB18	ranolazine	1.2	1,562.5	0.5	51.64	1419.1	9.3		0.9	46.5	6.78
	Total top 30	**523.2**	**-2.1**	**33.3**	**2,863.36**	**3.5**	**492.0**	**2.1**	**46.5**	**46.5**	**1.20**
	Total	**1,128.1**	**-1.1**	**31.2**	**9,782.02**	**0.0**	**1,056.8**	**-2.5**	**100.0**	**100.0**	**1.02**

^gross expenditure including expenditure on citizen cost-sharing

* calculated on overall citizen cost-sharing

Table 2.1.8 Top 30 active substances by change (2023-2022) in citizen cost-sharing for the share exceeding the reference price

ATC	Active ingredient	Citizen cost-sharing *(million)*	Δ % 23-22 *(million)*	Expenditure 2023^ *(million)*	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22	% consumption generic	Δ % 23-22
C01EB18	ranolazine	9.31	9.3	51.64	>100.0	1.2	>100	0.5	-
R03AK08	formoterol/beclomethasone	8.34	8.3	131.92	-11.6	4.1	2.2	1.1	-
A07EC02	mesalazine	9.61	4.7	127.14	1.2	5.5	2.7	11.6	29.8
J01CR02	amoxicillin/clavulanic acid	22.77	2.7	179.74	17.2	6.1	16.7	22.5	3.1
N02AX06	tapentadol	2.38	2.4	60.94	-1.4	0.6	4.2	-	-
J01DD08	cefixime	11.52	1.6	67.47	15.0	1.3	14.9	14.8	-7.1
N03AF01	carbamazepine	3.08	1.6	13.23	-5.5	1.1	-3.3	7.9	30.2
C09DB02	olmesartan/amlodipine	16.61	1.5	95.07	10.9	11.0	11.3	19.8	-3.2
N02AA55	naloxone/oxycodone	1.98	1.4	30.56	-17.7	0.4	-1.9	-	-
A07EA06	budesonide	1.32	1.3	6.35	-12.2	0.1	-4.0	18.7	-
A11CC06	calcifediol	1.08	1.1	13.12	-5.0	0.2	-4.6	-	-
C09CA08	olmesartan	19.39	1.0	121.61	7.6	18.0	7.7	28.4	6.5
A05AA02	ursodeoxycholic acid	14.46	0.8	56.31	5.2	2.8	5.3	38.1	-1.1
C07AB07	bisoprolol	55.49	0.8	171.45	3.0	13.2	3.3	48.3	2.7
N02AE01	buprenorphine	0.88	0.7	22.83	16.3	0.2	11.6	-	-
R03BA01	beclomethasone	9.27	0.7	38.51	1.3	1.7	0.3	0.9	-69.6
A10BH01	sitagliptin	0.73	0.6	8.13	>100.0	0.4	>100	39.0	46.1
S01ED51	timolol/bimatoprost	1.97	0.6	18.82	3.2	1.4	1.1	8.0	>100
N06AB05	paroxetine	9.65	0.6	57.10	-2.8	7.9	-0.1	42.6	2.1
N06AB06	sertraline	8.98	0.5	51.16	5.4	9.7	6.0	63.4	-0.2
B01AC30	clopidogrel/acetylsalicylic acid	3.30	0.5	13.21	19.3	1.0	20.1	29.8	3.9
H05BX01	cinacalcet	0.64	0.4	1.94	97.4	0.0	82.8	96.8	-0.3

continued

Table 2.1.8 – *continued*

ATC	Active ingredient	Citizen cost-sharing *(million)*	Δ % 23-22 *(million)*	Expenditure 2023^ *(million)*	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22	% consumption generic	Δ % 23-22
G04CA01	alfuzosin	6.59	0.3	56.97	5.4	10.3	5.4	31.2	-4.8
N02BF02	pregabalin	11.58	0.3	87.19	8.5	2.7	9.7	40.6	8.4
C09DA08	olmesartan/hydrochlorothiazide	16.10	0.3	76.85	3.2	10.8	3.7	20.2	6.4
R03BA02	budesonide	2.49	0.3	30.12	13.8	0.9	10.5	3.4	-8.9
G02CB03	cabergoline	0.66	0.2	9.60	-0.1	0.1	0.3	7.6	-3.5
H01CB03	lanreotide	0.28	0.2	1.44	>100.0	0.0	>100	-	-
J01DD13	cefpodoxime	0.96	0.2	9.51	28.2	0.1	25.4	3.2	-2.4
M05BB03	alendronic acid/cholecalciferol	4.45	0.2	23.48	-0.7	1.9	-1.6	10.2	-16.7
	Total top 30	**255.89**	**1,239.0**	**1,633.41**	**-87.2**	**114.7**	**-91.5**	**29.6**	**1.4**
	Total	**1,056.80**	**-26.9**	**9,782.02**	**-0.1**	**1128.1**	**-0.8**	**31.2**	**2.8**

^gross expenditure including expenditure on citizen cost-sharing

Table 2.1.9 Top 30 active ingredients by difference between retail price and reference price (2023)

ATC	Active ingredient	Difference between the retail price and the reference price	Total 2023 *(million)*	Δ % 23-22	%* expenditure under approved care regime	DDD/1000 inhab. per day	%** consumption under approved care regime	Citizen cost-sharing *(million)*	%	Δ% 23-22
A16AX04	nitisinone	957.24	0.02	-	2.5	<0.05	0.6	0.00	0.0	-
L01EA01	imatinib	838.09	0.06	66.6	0.4	<0.05	0.1	0.02	0.0	>100
B01AC11	iloprost	603.24	0.01	-62.5	0.2	<0.05	0.0	0.00	0.0	-
J02AC03	voriconazole	165.81	0.03	16.2	1.9	<0.05	0.2	0.01	0.0	-4.0
V03AC03	deferasirox	114.07	3.03	>100	10.5	<0.05	6.0	0.03	0.0	10.8
C02KX01	bosentan	44.54	0.07	-23.9	2.4	<0.05	0.3	0.03	0.0	-26.5
A10BD08	vildagliptin/metformin	35.00	0.33	316.0	7.6	<0.05	4.0	0.07	0.0	-
A07EA06	budesonide	30.66	6.35	-12.2	87.8	0.1	88.7	1.32	0.1	-
J05AF10	entecavir	28.19	0.77	49.5	7.9	<0.05	1.1	0.08	0.0	35.2
C01EB18	ranolazine	22.79	51.64	>100	92.0	1.2	87.5	9.31	0.9	-
L04AA06	mycophenolate	15.82	0.08	-47.0	0.4	<0.05	0.1	0.01	0.0	-38.4
N02AX06	tapentadol	14.87	60.94	-1.4	98.4	0.6	97.3	2.38	0.2	
H01CB03	lanreotide	12.81	1.44	>100	4.4	<0.05	1.3	0.28	0.0	>100
N06DA03	rivastigmine	8.80	3.49	-12.4	43.2	0.1	17.6	0.18	0.0	-39.1
R03AK08	formoterol/beclomethasone	5.62	131.92	-11.6	98.5	4.1	97.7	8.34	0.8	>100
A10BD07	sitagliptin/metformin	5.61	1.68	>100	9.0	0.1	5.6	0.16	0.0	-
N05AX13	paliperidone	2.92	2.43	-6.3	3.3	<0.05	4.1	0.13	0.0	-17.1
A07EC02	mesalazine	2.59	127.14	1.2	99.6	5.5	98.1	9.61	0.9	97.1
M03BX01	baclofen	1.99	5.14	-4.0	78.1	0.5	84.6	0.94	0.1	-18.3
J05AB01	acyclovir	1.56	14.92	3.5	94.2	0.2	90.5	0.21	0.0	-43.1

continued

Table 2.1.9 – *continued*

ATC	Active ingredient	Difference between the retail price and the reference price	Total 2023 *(million)*	Δ % 23-22	%* expenditure under approved care regime	DDD/1000 inhab. per day	%** consumption under approved care regime	Citizen cost-sharing *(million)*	%	Δ% 23-22
N02BF01	gabapentin	1.17	21.71	4.4	97.2	0.5	78.2	0.51	0.0	-18.5
A11CC06	calcifediol	1.09	13.12	-5.0	99.1	0.2	98.2	1.08	0.1	-
J05AB15	brivudine	0.81	8.23	5.2	99.3	<0.05	98.7	1.23	0.1	4.7
G02CB03	cabergoline	0.65	9.60	-0.1	99.7	0.1	96.5	0.66	0.1	57.4
R03AK06	salmeterol/fluticasone	0.61	45.55	-12.4	98.4	1.8	96.8	5.49	0.5	-9.6
H05BX02	paracalcitol	0.50	0.40	-24.4	12.9	<0.05	1.8	0.01	0.0	-93.3
C03DA01	spironolactone	0.26	4.47	-20.6	96.4	0.5	92.0	0.29	0.0	16.5
N06AB08	fluvoxamine	0.25	4.82	-1.9	98.9	0.5	96.6	0.87	0.1	-17.7
G02CB01	bromocriptine	0.22	0.14	-12.9	98.5	<0.05	97.3	0.02	0.0	-4.8
J05AB09	famciclovir	0.22	4.20	-3.3	99.3	<0.05	97.0	0.18	0.0	1.3
	Total top 30		**523.72**	**5.7**	**69.5**	**16.0**	**76.4**	**43.48**	**4.1**	**155.6**
	Total		**9782.02**	**0.0**	**37.5**	**1128.1**	**85.3**	**1056.8**	**100.0**	**-2.5**

* calculated on overall expenditure on the active substance including under approved care regime and direct purchases
** calculated on overall consuption of the active substance including under approved care regime and direct purchases

Table 2.1.10 Average difference between the retail price and the reference price and share of expenditure under approved care regime and in direct and "on behalf" distribution (year 2023)

Average difference between retail price and reference price (€)	% expenditure under approved care regime*	% expenditure in direct and "on behalf" distribution*	% citizen cost-sharing on total citizen cost-sharing
<1	11.2	3.1	7.2
≥1-<2	20.9	2.9	18.5
≥2-<3	37.2	2.4	37.0
≥3-<5	19.1	3.4	22.7
≥5-<10	9.3	2.9	10.4
≥10<20	1.2	2.5	1.7
≥20	1.2	82.8	2.5

* calculated on overall expenditure under approved care regime

** calculated on expenditure in direct and "on behalf" distribution

Table 2.1.11 Distribution by geographical area, gender and age of patients using generic medicines for the top 10 therapeutic categories (ATC 3rd level) with the largest share of expenditure on the reference price (year 2023)

	C10A	C07A	C09D	C09C	N06A	C09B	G04C	B01A	C09A	C08C
Geographical Area										
North	65.4	61.5	34.2	47.8	56.7	33.8	55.8	23.3	68.1	56.5
Centre	54.6	45.1	26.0	37.0	48.4	25.1	44.4	21.0	55.0	43.4
South and Islands	45.4	35.5	20.1	26.0	36.7	18.5	33.4	17.9	40.7	31.9
Gender										
Females	53.5	45.5	25.8	35.2	48.7	26.2	40.9	17.9	55.5	43.9
Males	58.1	52.9	28.2	39.0	49.4	26.7	45.3	23.7	58.2	48.6
Age group										
<50	58.2	46.2	28.8	40.3	51.6	24.3	39.0	8.4	59.5	51.4
50-60	59.0	48.0	29.7	39.6	51.6	26.3	41.8	21.3	59.9	50.7
60-70	57.6	48.6	28.7	38.2	50.7	27.2	45.2	24.3	58.1	48.4
70-80	54.2	48.0	25.5	35.3	47.9	26.1	45.8	22.2	55.2	44.4
>80	53.0	50.9	24.8	35.4	44.7	26.6	46.3	20.3	55.2	44.1
Total	**55.7**	**48.8**	**26.9**	**37.0**	**49.0**	**26.4**	**45.3**	**20.8**	**56.9**	**46.3**

C10A: Lipid modifying substances, not combined
C07A: Beta blockers
C09D: Angiotensin II antagonists, combined
C09C: Angiotensin II antagonists
N06A: Antidepressants
C09B: Angiotensin-converting enzyme (ACE) inhibitors, in combination
G04C: Medicines for benign prostatic hypertrophy
B01A: Antithrombotics
C09A: Angiotensin-converting enzyme (ACE) inhibitors, not in combination
C08C: Selective calcium channel blockers with predominantly vascular effect

Patent-expired biologic medicines

Analysing the level of competition in the biosimilars market (HHI) and the market shares per competitor (Figure 2.1.8), eculizumab, whose biosimilar entered the market in 2023, insulin aspart and insulin lispro are the active ingredients with the highest market concentration, presenting an HHI value of 0.97, 0.90 and 0.78, respectively, as the largest market share belongs to the ex-originator, which competes with only one type of biosimilar. The situation is reversed for somatropin (HHI=0.65), for which the largest market share is made of a single biosimilar on the market.

Follitropin alfa (HHI 0.43), teriparatide (HHI 0.55), and epoetin (HHI 0.56) have greater competitiveness; as a matter of fact, there are two other competitors in addition to the originator, although the originator still holds the largest market share. In the case of enoxaparin (HHI=0.44), filgrastim (HHI=0.39) and pegfilgrastim (HHI=0.30) the competitiveness is even greater; as a matter of fact, the ex-originator market represents a small share (very small in the case of filgrastim) compared with that of the 3 available biosimilars. Etanercept (HHI=0.40) and infliximab (HHI=0.32) have a low market concentration, although the largest share is held by one of the biosimilars. In the case of rituximab (HHI=0.43), the largest market share is held by one of the three biosimilars, with the ex-originator and the other two sharing the remaining share. For bevacizumab (HHI=0.18), two of the five available biosimilars account for about two-thirds of the market share, with the remaining share split between the other biosimilars and the ex-originator. Finally, trastuzumab and adalimumab have the lowest HHI value (0.22 and 0.25), an indication of high competition, where there are at least four competitors.

Analysing the trend in expenditure and consumption of patent-expired biological medicines for ATC 4th level (Table 2.1.12), it is noted that for follitropin and somatropin the greatest incidence of expenditure is represented by the therapeutic category of other biologicals, i.e. those medicines that do not fall either under the definition of reference product or biosimilar, reaching percentages oscillating between 45% and 70%, while consumption is around 40% (Figures 2.1.14 and 2.1.18).

In the case of anti-TNF-alpha therapies, although the highest incidence of expenditure is attributable to golimumab and certolizumab (other anti-TNF-alpha therapies, 37.2%), the highest percentage of consumption is attributable to adalimumab biosimilars (55.5%), which has been constantly increasing since 2018 (>100%) (Table 2.1.12).

Analysing the trend over the last decade it is observed a clear reduction in reference product expenditure for both adalimumab and etanercept (Figure 2.1.9). In the case of growth factors, it is possible to note that, although the category of other growth factors accounts for approximately a quarter of expenditure, overall expenditure is sharply decreasing (-54.6% between 2018 and 2023), compared to an increase in consumption, covered for over 80% by biosimilars of filgrastim and pegfilgrastim (42.73% and 42.71% respectively), both increasing compared to last year (Table 2.1.12 and Figure 2.1.13). For long-acting insulins, insulin glargine (ex-originator, biosimilar and other insulin glargine) accounts for more than 70% of the category's expenditure, while other long-acting insulins account for almost a third of expenditure and a quarter of consumption (Table 2.1.12 and Figure 2.1.16).

Rituximab, trastuzumab and infliximab, that are the only three molecules with two different formulations available, subcutaneous and intravenous, show a high incidence of both expenditure and consumption of the biosimilar (Table 2.1.12 and Figures 2.1.17, 2.1.20 and 2.1.21); moreover, for all three medicines a reduction in expenditure for the biosimilar can be observed against an increase in consumption. In contrast, intravenous ex-originators show the

largest contractions in both spending and consumption compared with the previous year.
In the case of low molecular weight heparins and epoetins, there is a higher incidence of both consumption and expenditure on biosimilars (Figures 2.1.11 and 2.1.12).
Bevacizumab has a high percentage incidence of the biosimilar both in terms of expenditure (95.8%) and consumption (98.9%), showing for 2023 a slight reduction in expenditure (-4.4%) against an increase in consumption (+18.1%) (Table 2.1.12 and Figure 2.1.10). Also for teriparatide, a similar trend is recorded, with an incidence of the biosimilar equal to 93% for expenditure and 93.4% for consumption, with significant increases (respectively +11.6% and +19%) compared to the previous year (Table 2.1.12 and Figure 2.1.19). Since September 2023, the biosimilar of eculizumab has been introduced to the market, accounting for approximately 1% of expenditure and 1.5% of consumption of the molecule in three months (Table 2.1.12 and Figure 2.1.22).
Analysing the regional variability in the consumption of patent-expired biologic medicines, compared to the national average (Figure 2.1.23), it can be observed that Lombardy, Province of Bolzano, Abruzzo, Molise, Calabria and Sardinia tend to consume greater quantities of former originators. Liguria, Marche, Tuscany, Emilia Romagna, Basilicata and Sicily are the Regions with a higher consumption of biosimilars than the national average.
Analysing the regional variability in terms of consumption of biosimilars and average DDD cost for patent-expired biologic medicines in direct purchases (Figure 2.1.24), it is evident that for Emilia Romagna, Tuscany, Veneto, Piedmont, Province of Trento, Liguria, Umbria, Marche, Basilicata and Sicily the higher consumption of biosimilars corresponds to a lower average DDD cost than the national average; while for Campania, despite the consumption of biosimilars is above the national average, a higher cost per day of therapy of patent-expired biologic medicines is recorded. The Friuli Venezia Giulia Region shows a consumption of biosimilars in line with the national average but at a higher average cost per DDD. Lombardy, Province of Bolzano, Lazio, Abruzzo, Molise and Calabria show the highest values of cost per day of therapy compared to a lower consumption of biosimilar. Finally, the Regions Valle d'Aosta, Puglia and Sardinia show consumption of biosimilar and average cost per day of therapy below the national average.

Figure 2.1.8 Patent-expired biologic medicines: Herfindahl-Hirschman Index (HHI) and market shares by competitor (year 2023)

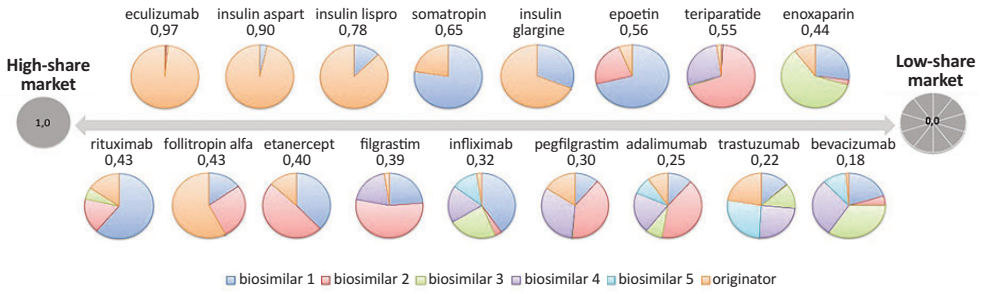


Table 2.1.12 Biosimilars, provision through public health facilities and NHS prescriptions (year 2023)

Group and subgroup	Per capita expenditure	Incidence %	Δ % 23-22	Δ % 23-18	DDD/1000 inhab. per day	Incidence %	Δ % 23-22	Δ % 23-18	Average cost	Δ % 23-22	Δ % 23-18
Anti-TNF-alpha	**3.93**	**100.00**	**-5.49**	**-57.58**	**1.38**	**100.00**	**7.76**	**58.04**	**7.77**	**-12.30**	**-73.16**
Biosimilar adalimumab	0.88	22.46	7.26	>100	0.77	55.49	15.28	>100	3.15	-6.96	-74.87
Biosimilar etanercept	0.74	18.86	6.88	-4.25	0.28	20.30	14.02	165.48	7.22	-6.27	-63.93
Originator adalimumab	0.47	12.09	-24.28	-89.98	0.08	6.00	-25.04	-79.87	15.65	1.01	-50.19
Originator etanercept	0.37	9.37	-28.58	-80.70	0.04	3.11	-23.32	-75.80	23.46	-6.86	-20.26
Other anti-TNF-alpha	1.46	37.22	-2.40	-18.83	0.21	15.11	2.06	22.35	19.15	-4.37	-33.65
Bevacizumab	**0.64**	**100.00**	**-12.00**	**-80.01**	**0.13**	**100.00**	**14.83**	**10.17**	**13.47**	**-23.37**	**-81.86**
Biosimilar	0.62	95.81	-4.41		0.13	98.98	18.14		13.03	-19.09	
Originator	0.03	4.19	-68.75	-99.16	<0.005	1.02	-69.06	-98.87	55.15	1.01	-25.70
Eculizumab	**2.01**	**100.00**	**0.21**	**81.79**	**0.01**	**100.00**	**2.74**	**33.76**	**710.85**	**-2.46**	**35.90**
Biosimilar eculizumab	0.02	0.87			<0.005	1.54			400.04		
Originator Eculizumab	2.00	99.13	-0.65	80.22	0.01	98.46	1.16	31.71	715.71	-1.79	36.83
Low molecular weight heparins	**2.30**	**100.00**	**1.13**	**17.72**	**6.79**	**100.00**	**3.20**	**1.33**	**0.93**	**-2.01**	**16.18**
Biosimilar	1.73	75.13	6.01	>100	5.50	80.97	7.93	>100	0.86	-1.78	73.08
Fondaparinux	0.21	9.33	-21.15	-10.39	0.37	5.47	-23.63	-18.09	1.58	3.25	9.41
Originator	0.18	7.99	5.55	-83.30	0.63	9.22	4.31	-84.48	0.80	1.19	7.60
Altre heparins	0.17	7.55	-12.32	-56.28	0.29	4.33	-26.15	-71.06	1.62	18.72	51.07
Epoetins	**2.47**	**100.00**	**-0.58**	**-25.28**	**4.02**	**100.00**	**4.54**	**21.53**	**1.68**	**-4.89**	**-38.51**
Biosimilar	1.33	53.81	4.81	11.71	3.36	83.43	7.54	64.17	1.08	-2.54	-31.95
Originator	0.21	8.65	-14.53	-69.05	0.21	5.25	-17.21	-59.93	2.77	3.24	-22.77
Other epoetins	0.93	37.54	-4.04	-34.95	0.46	11.32	-3.53	-38.36	5.57	-0.53	5.54

continued

Table 2.1.12 – *continued*

Group and subgroup	Per capita expenditure	Incidence %	Δ % 23-22	Δ % 23-18	DDD/1000 inhab. per day	Incidence %	Δ % 23-22	Δ % 23-18	Average cost	Δ % 23-22	Δ % 23-18
Growth factors	**0.35**	**100.00**	**-0.47**	**-54.88**	**0.12**	**100.00**	**7.93**	**35.48**	**7.98**	**-7.78**	**-66.69**
Biosimilar filgrastim	0.11	30.39	10.60	-18.73	0.05	42.73	4.65	26.49	5.67	5.68	-35.74
Biosimilar pegfilgrastim	0.07	18.84	-6.72		0.05	42.71	11.82		3.52	-16.57	
Originator filgrastim	0.03	8.88	38.34	-13.68	<0.005	1.06	40.32	-2.29	66.76	-1.41	-11.66
Originator pegfilgrastim	0.06	17.50	29.43	-85.44	0.01	7.76	28.90	-73.43	17.99	0.41	-45.21
Other growth factors	0.08	24.40	-25.76	-54.60	0.01	5.73	-16.24	-41.13	33.96	-11.36	-22.89
Follitropins	**1.04**	**100.00**	**17.66**	**10.88**	**0.10**	**100.00**	**-5.65**	**-19.00**	**28.00**	**24.70**	**1.04**
Biosimilar	0.11	10.99	40.04	91.15	0.02	22.95	43.03	149.19	13.41	-2.09	0.11
Originator	0.21	20.57	4.97	-39.82	0.03	30.95	7.97	-27.89	18.61	-2.78	0.21
Other follitropin	0.71	68.44	18.92	36.19	0.05	46.09	-24.77	-35.37	41.57	58.07	0.71
Infliximab	**0.56**	**100.00**	**7.40**	**-55.21**	**0.46**	**100.00**	**12.61**	**48.32**	**3.32**	**-4.62**	**0.56**
Biosimilar infliximab IV	0.37	66.09	-5.45	-47.42	0.39	85.01	6.17	71.83	2.58	-10.94	0.37
Biosimilar infliximab SC	0.15	26.09	>100		0.06	12.58	>100		6.89	-4.13	0.15
Originator infliximab IV	0.04	7.82	-39.90	-91.98	0.01	2.41	-39.96	-86.56	10.76	0.10	0.04
Fast acting insulins	**0.14**	**100.00**	**-15.20**	**-35.98**	**0.88**	**100.00**	**-1.96**	**1.09**	**0.43**	**-13.51**	**0.14**
Biosimilar insulin aspart	<0.005	1.26	>100		0.01	0.86	>100		0.62	-2.40	0.00
Biosimilar insulin lispro	0.01	9.77	-24.74	90.87	0.06	6.70	-27.61	28.40	0.62	3.97	0.01
Originator insulin aspart	0.05	33.09	-24.91	-44.71	0.21	23.42	-5.87	-16.80	0.60	-20.22	0.05
Originator insulin lispro	0.04	26.28	-13.45	-58.28	0.40	45.16	4.39	9.91	0.25	-17.09	0.04
Other fast acting insulins	0.04	29.60	-1.85	4.75	0.21	23.85	-2.09	-2.51	0.53	0.24	0.04
Long-acting insulins	**2.06**	**100.00**	**-8.61**	**-9.79**	**6.03**	**100.00**	**-2.57**	**5.06**	**0.94**	**-6.20**	**2.06**
Biosimilar	0.20	9.46	-4.49	-6.56	0.63	10.38	-4.89	-2.09	0.85	0.42	0.20
Originator	0.48	23.20	-18.44	-55.98	1.37	22.67	-18.00	-51.63	0.96	-0.53	0.48
Other insulin glargine	0.81	39.17	14.20	>100	2.55	42.24	14.17	>100	0.87	0.02	0.81
Other long-acting insulins	0.58	28.16	-23.39	-20.83	1.49	24.72	-8.74	1.00	1.07	-16.05	0.58

continued

Table 2.1.12 – *continued*

Group and subgroup	Per capita expenditure	Incidence %	Δ % 23-22	Δ % 23-18	DDD/1000 inhab. per day	Incidence %	Δ % 23-22	Δ % 23-18	Average cost	Δ % 23-22	Δ % 23-18
Rituximab	**0.63**	**100.00**	**-14.31**	**-70.78**	**0.48**	**100.00**	**8.44**	**-5.38**	**3.62**	**-20.98**	**0.63**
Biosimilar IV	0.43	68.07	-14.97	-40.84	0.40	84.37	13.54	>100	2.92	-25.12	0.43
Originator IV	0.01	2.24	-21.28	-98.29	<0.005	0.67	-33.29	-97.43	12.01	18.01	0.01
Originator SC	0.19	29.69	-12.13	-69.17	0.07	14.96	-11.49	-66.15	7.20	-0.73	0.19
Somatropin	**1.09**	**100.00**	**-5.63**	**-21.91**	**0.27**	**100.00**	**-2.72**	**2.05**	**11.08**	**-2.99**	**1.09**
Biosimilar	0.37	33.71	46.34	72.33	0.12	45.00	53.68	>100	8.30	-4.78	0.37
Originator	0.20	18.52	25.25	-18.80	0.03	12.98	25.89	-14.01	15.81	-0.51	0.20
Other somatropin	0.52	47.77	-29.90	-44.24	0.11	42.02	-33.51	-32.89	12.59	5.44	0.52
Teriparatide	**0.09**	**100.00**	**4.76**	**-59.83**	**0.04**	**100.00**	**16.82**	**-9.70**	**5.86**	**-10.33**	**-55.52**
Biosimilar	0.09	93.02	11.58		0.04	93.37	19.04		5.84	-6.26	
Originator	<0.005	2.67	-73.07	-98.93	<0.005	1.95	-61.06	-98.23	8.00	-30.84	-39.30
Other patent-expired teriparatide (synthesis)	<0.005	4.31	96.96		<0.005	4.68	117.81		5.40	-9.57	
Trastuzumab	**0.65**	**100.00**	**-20.29**	**-83.95**	**0.15**	**100.00**	**-8.40**	**-27.00**	**11.60**	**-12.98**	**-78.02**
Biosimilar IV	0.36	54.84	-22.32	>100	0.12	77.73	-5.67	>100	8.19	-17.65	-75.05
Originator IV	0.01	1.06	-58.36	-99.66	<0.005	0.27	-58.88	-99.43	44.89	1.26	-40.43
Originator SC	0.29	44.10	-15.70	-85.19	0.03	22.00	-15.73	-73.86	23.26	0.04	-43.36
Total	**17.96**	**100.00**	**-3.54**	**-44.13**	**20.87**	**100.00**	**1.97**	**8.86**	**2.36**	**-5.40**	**-48.68**
Biosimilar	7.56	42.12	4.06	73.48	11.99	57.44	8.22	>100	1.73	-3.84	-34.16
Originator	4.87	27.13	-10.69	-77.08	3.14	15.04	-10.61	-66.97	4.25	-0.09	-30.62
Other	5.52	30.75	-6.29	-15.41	5.74	27.52	-2.30	12.18	2.63	-4.08	-24.59

Figure 2.1.9 Incidence (%) of expenditure on biosimilar medicines compared to total expenditure for the therapeutic category (ATC 4th level): anti-TNF-alpha

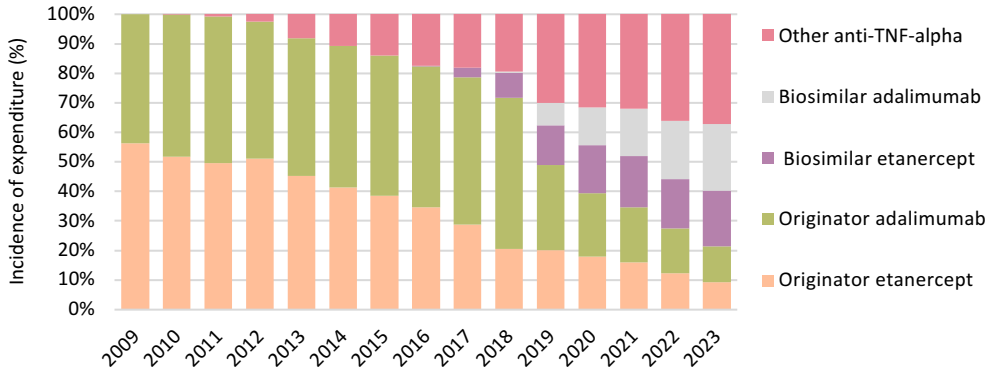


Figure 2.1.10 Incidence (%) of expenditure on biosimilar medicines compared to total expenditure for the therapeutic category: bevacizumab

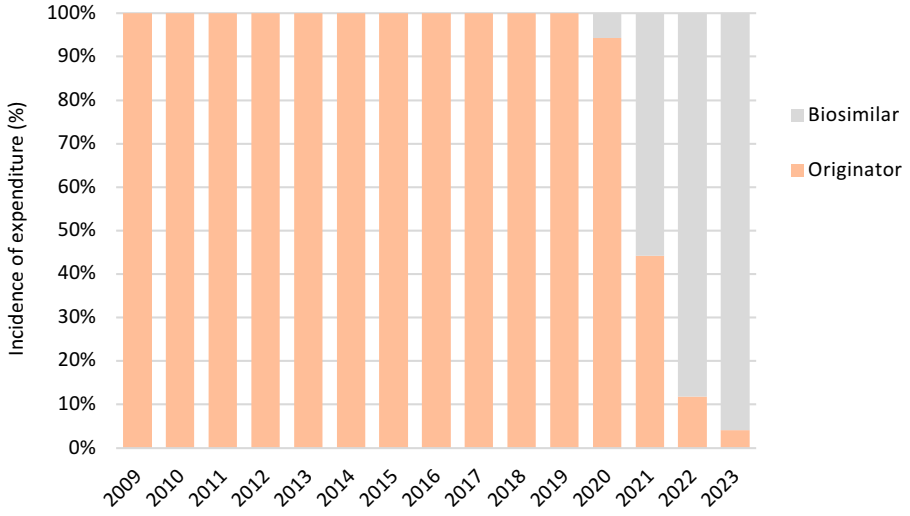


Figure 2.1.11 Incidence (%) of expenditure on biosimilar medicines compared to total expenditure for the therapeutic category (ATC 4th level): low molecular weight heparins

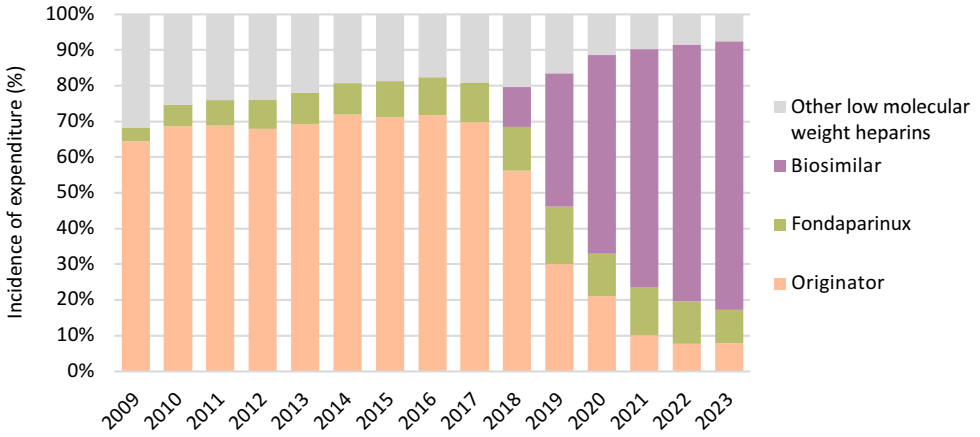


Figure 2.1.12 Incidence (%) of expenditure on biosimilar medicines compared to total expenditure for the therapeutic category (ATC 4th level): epoetin

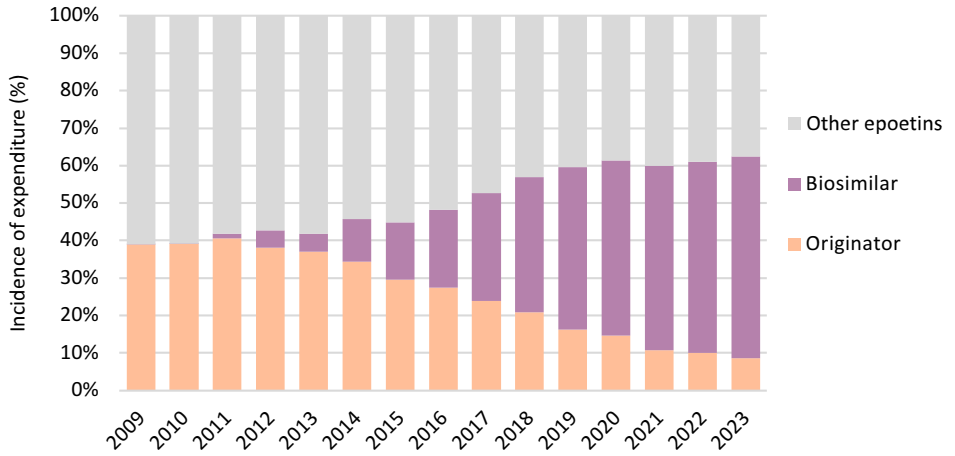


Figure 2.1.13 Incidence (%) of expenditure on biosimilar medicines compared to total expenditure for the therapeutic category (ATC 4th level): growth factors

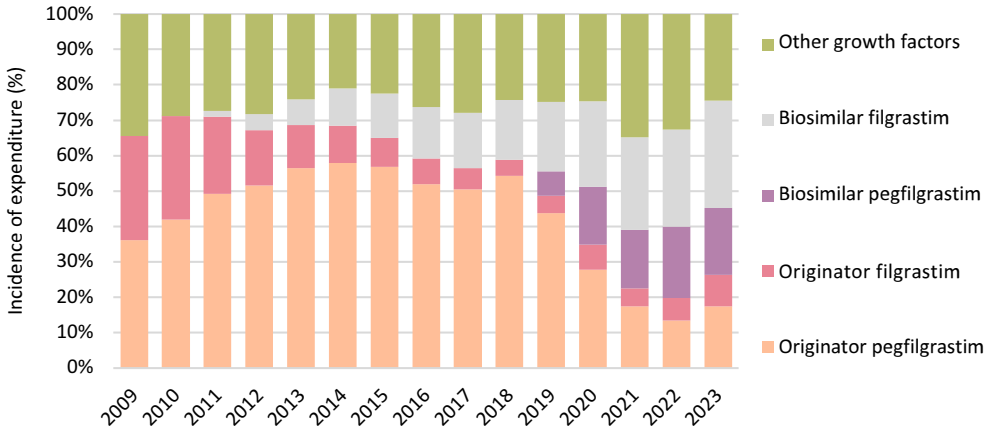


Figure 2.1.14 Incidence (%) of expenditure on biosimilar medicines compared to total expenditure for the therapeutic category (ATC 4th level): follitropin

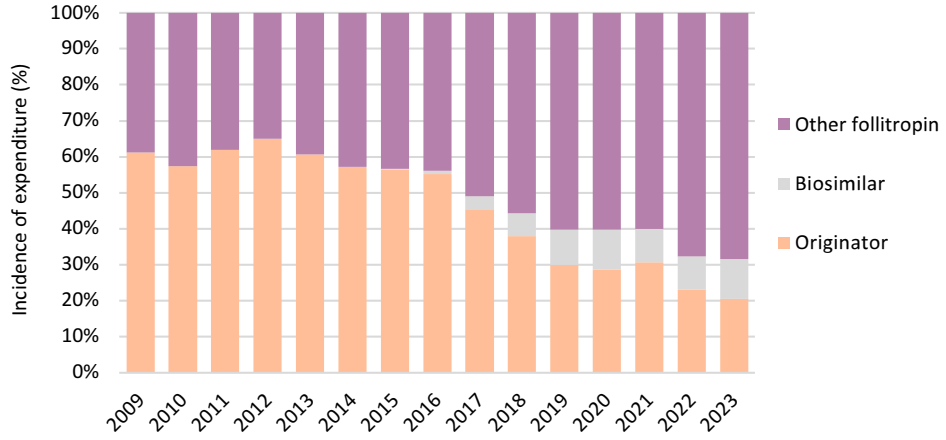


Figure 2.1.15 Incidence (%) of expenditure on biosimilar medicine compared to total expenditure for the therapeutic category (ATC 4th level): fast acting insulins

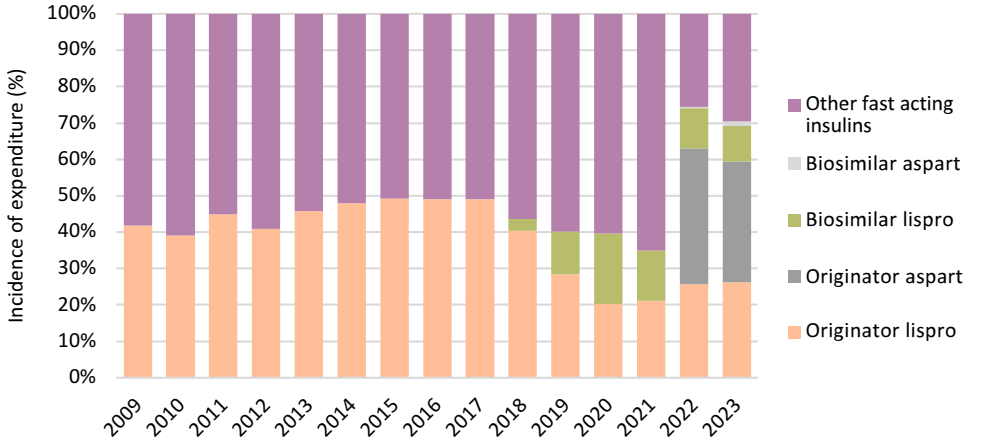


Figure 2.1.16 Incidence (%) of expenditure on biosimilar medicines compared to total expenditure for the therapeutic category (ATC 4th level): long-acting insulins

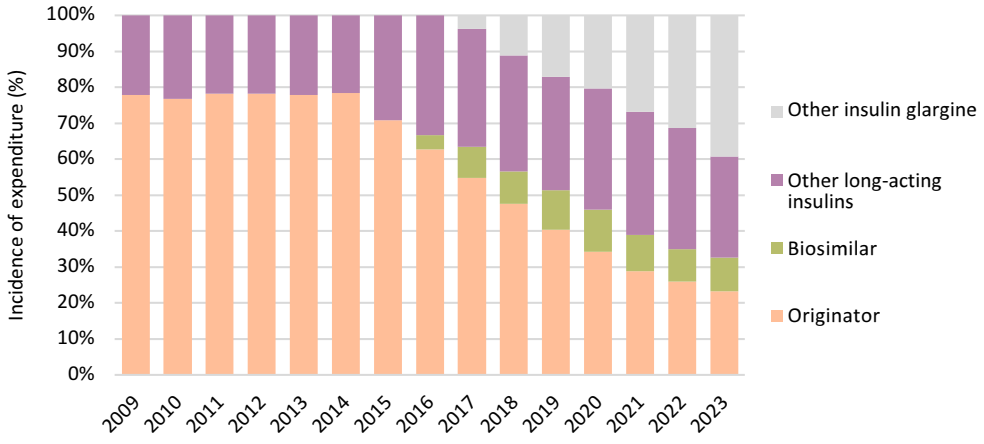


Figure 2.1.17 Incidence (%) of expenditure on biosimilar medicines compared to total expenditure for the therapeutic category: rituximab

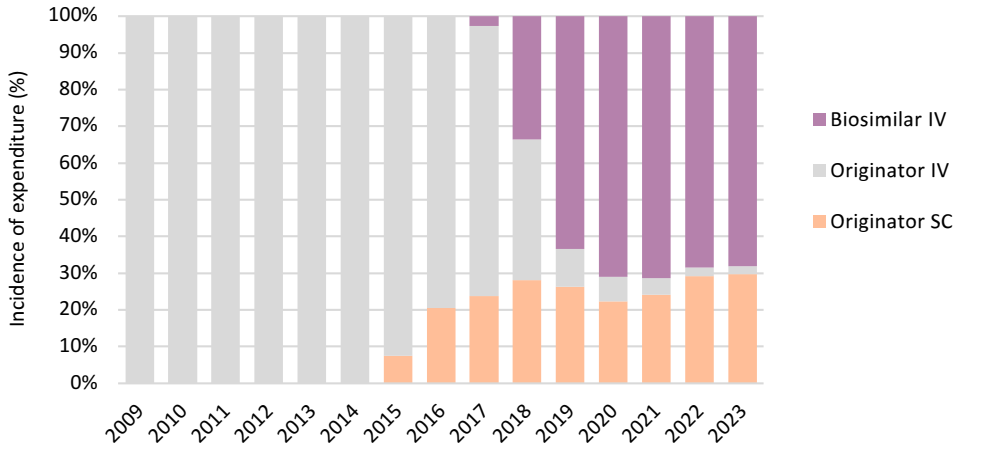


Figure 2.1.18 Incidence (%) of expenditure on biosimilar medicines compared to total expenditure for the therapeutic category: somatropin

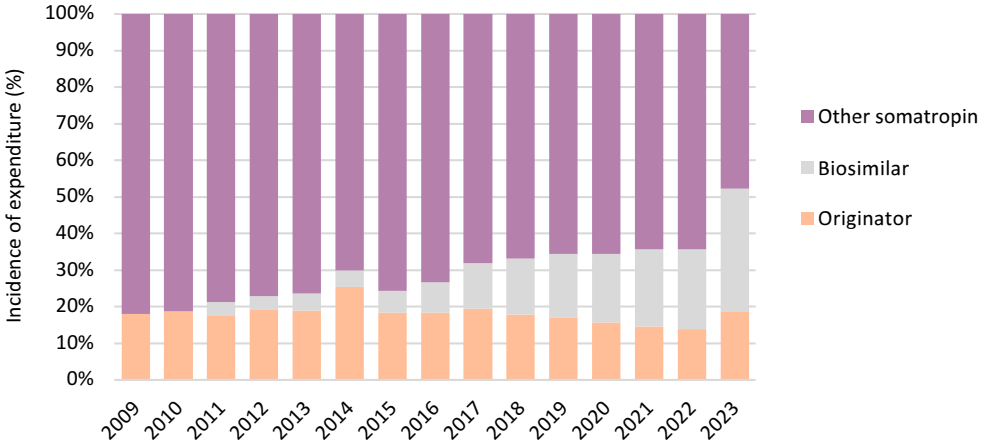


Figure 2.1.19 Incidence (%) of expenditure on biosimilar medicines compared to total expenditure for the therapeutic category: teriparatide

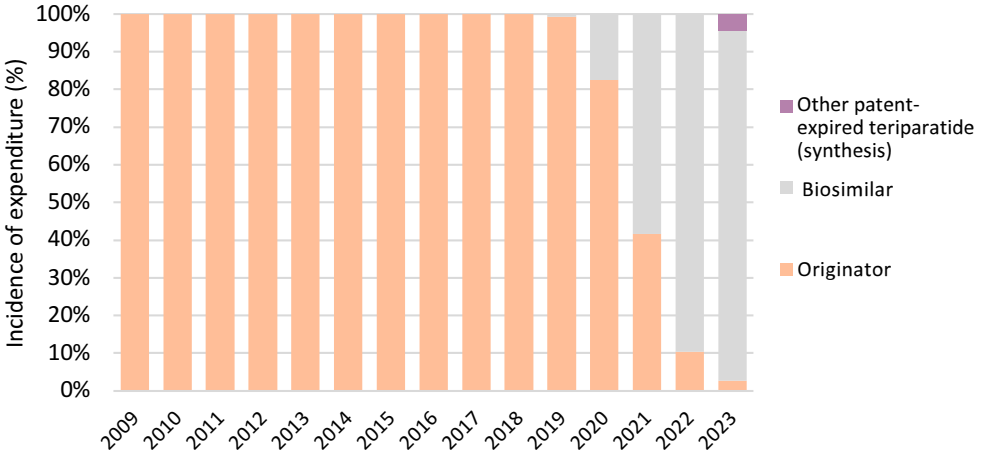


Figure 2.1.20 Incidence (%) of expenditure on biosimilar medicines compared to total expenditure for the therapeutic category: trastuzumab

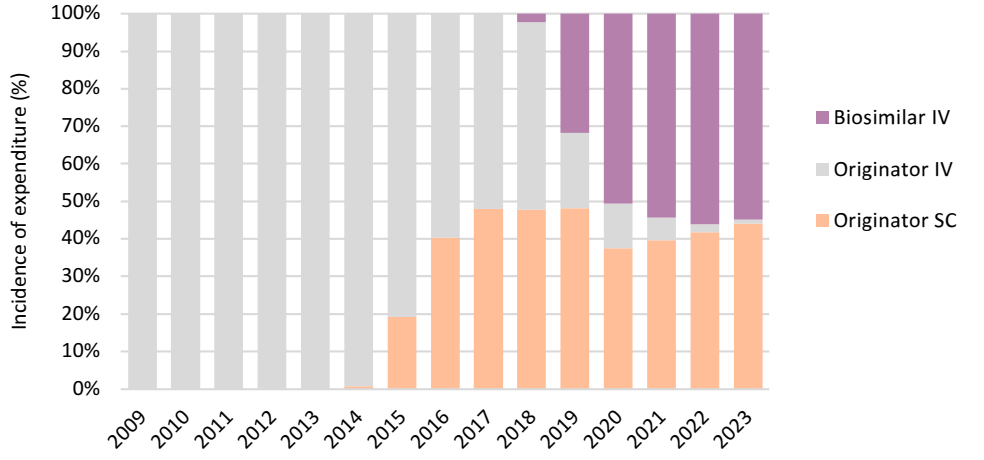


Figure 2.1.21 Incidence (%) of expenditure on biosimilar medicines compared to total expenditure for the therapeutic category: infliximab

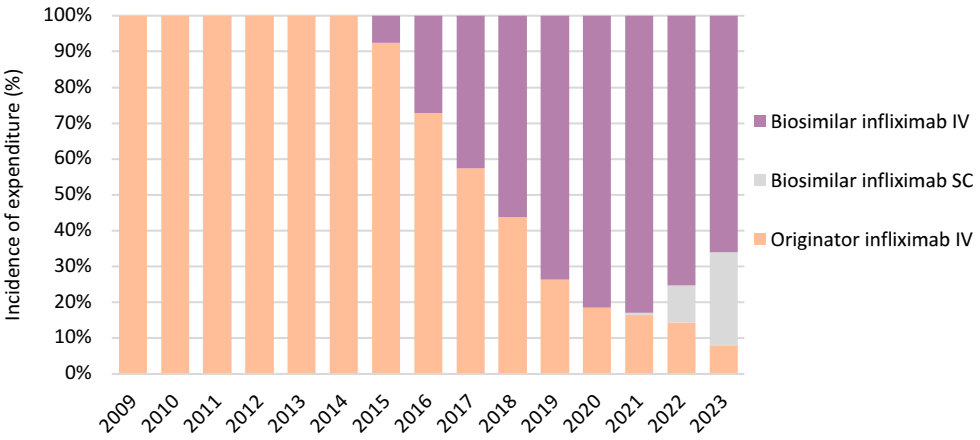


Figure 2.1.22 Incidence (%) of expenditure on biosimilar medicines compared to total expenditure for the therapeutic category: eculizumab

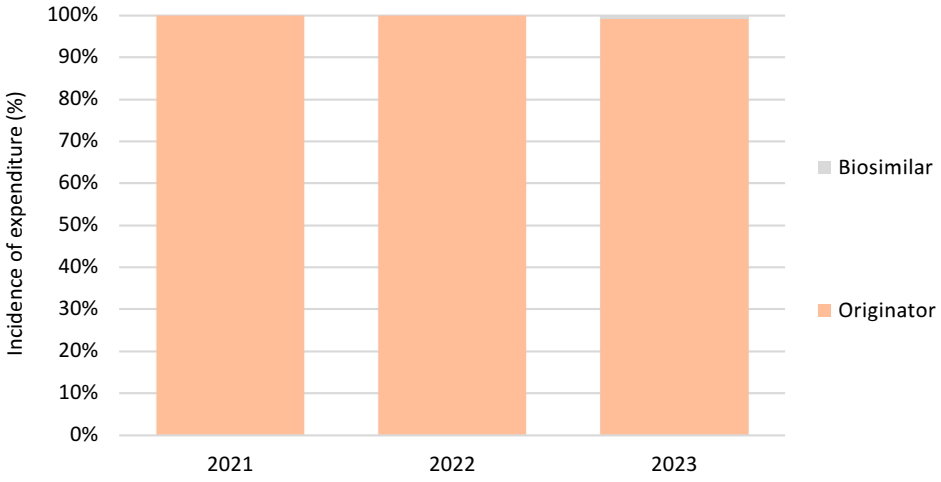


Figure 2.1.23 Consumption (DDD/1000 inhab. per day) of biosimilar vs originator medicines compared to the national average (year 2023)

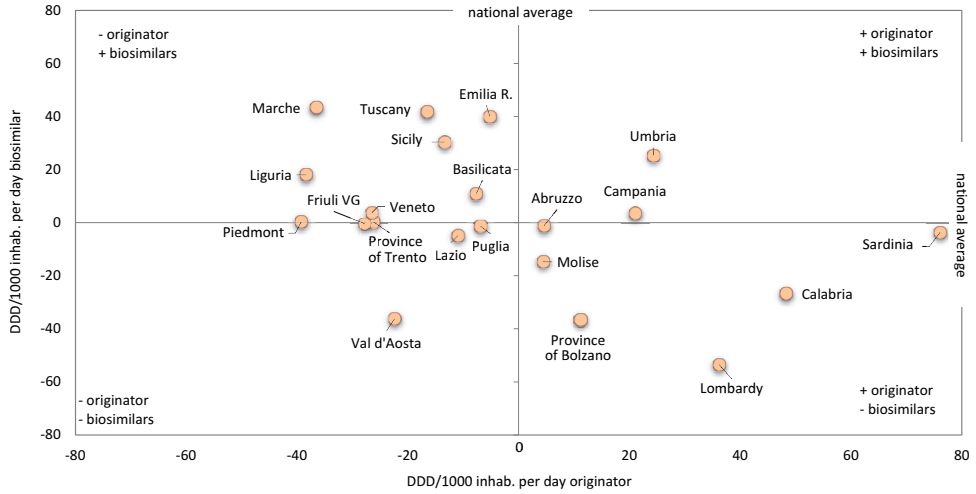
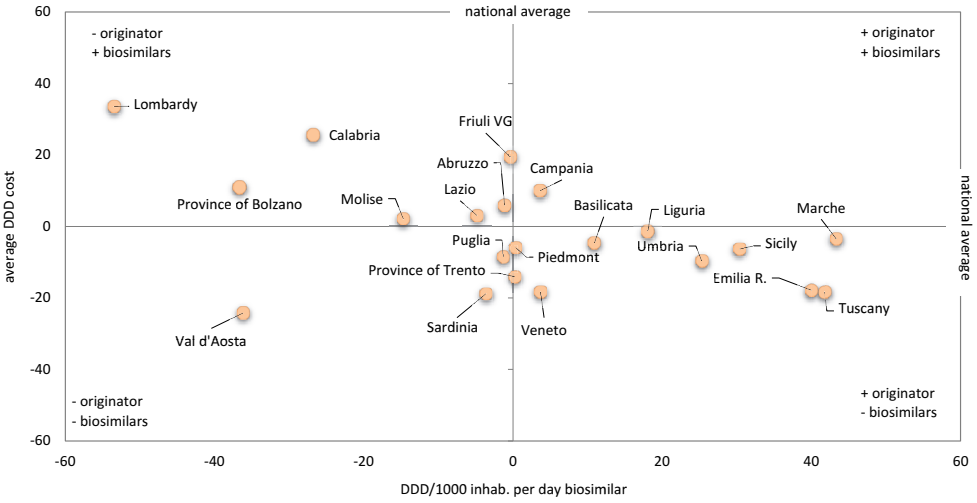


Figure 2.1.24 Regional variability in biosimilar medicines consumption and average DDD cost of patent-expired biologics in 2023 (% deviations from national average)



2.2 Class C medicines reimbursed by the NHS

Class C-NN medicines

Decree-Law no. 158 of 2012 (the so-called Balduzzi Decree) converted into Law 189/2012 (art. 12) establishes that medicines approved by the European Medicines Agency (EMA) and awaiting price negotiation in Italy, within 60 days of the publication in the Official Journal of the European Union of the Community Marketing Authorisation, are to be placed in class C-Non-Negotiated (so-called C-NN), so that they may be immediately available. Public health facilities can purchase the medicine by negotiating the price directly with the manufacturing companies, if they have decided to market the product. Law No. 118/2022 (Annual Law on the Market and Competition 2021) eliminated the possibility for the company concerned not to submit the application for the purpose of obtaining a different classification. In addition, for orphan medicines or other medicines of exceptional therapeutic and social importance, it is established that, in case of non-submission within thirty days of granting the MA, AIFA shall urge the company to submit the request for price and reimbursement within the next thirty days. Once this term has expired, information is given on the AIFA's institutional website and the lowest price is applied within the fourth level of the Anatomic Therapeutic Chemical classification system (ATC) to which the medicine belongs. Once classified as C-NN, these medicines can be immediately purchased by public health facilities at a price proposed by the company and not centrally negotiated. In addition, medicines purchased in C-NN, although constituting NHS expenditure, do not contribute to the determination of expenditure for the purposes of monitoring ceilings and potential overruns.

Table 2.2.1 describes the per capita expenditure and consumption (DDD/1000 inhabitants per day) with regional detail of class C-NN medicines reimbursed by the NHS and purchased directly by public health facilities in 2023. During the year, there were 229 MAs in the class C-NN, a decrease compared to the previous year (-28.7%); at the regional level, a greater number of MAs is observed in the Northern Regions (n=158) compared to the Central (n=111) and Southern Regions (n=128). Total expenditure on class C-NN medicines was approximately 47.5 million, down 63.1% from 2022, mainly due to a reduction in consumption. The Central Regions are those with the highest per capita expenditure (1.21 euro), compared to the Southern (0.73 euro) and the Northern (0.69 euro) ones, the latter registering the greatest reduction in expenditure compared to 2022 (-71.1%). In terms of consumption, a strong reduction is observed at national level (-66.8%), more marked in the Centre (-74.0%), followed by the South (-69.2%) and the North (-61.3%). There are no particular differences between the Regions, with values of DDD/1000 inhabitants per day ranging between 0.03 in Puglia and Sicily to 0.26 in Veneto. The clear regional variability is highlighted, however, by the average cost per day of therapy for these medicines, which goes from 81.4 euro in the Province of Bolzano (Δ% 23-22: >100%) to 4.0 euro in Molise (Δ% 23-22: -11.0%). Analysing the top 30 active ingredients by expenditure purchased directly by public health facilities (Table 2.2.2), they cover almost all of the expenditure for medicines in class C-NN (99.6%). In first place, with an expenditure equal to 38 million euro, is confirmed the active ingredient remdesivir, which covers about 80% of the total expenditure for class C-NN, although it left class C-NN during the year. Consequently, a strong reduction of approximately 68% is observed in both indicators for this molecule. In second place is the drug-conjugated antibody trastuzumab deruxtecan with an expenditure of 1.55 million euro; it is followed by glucarpidase, a recombinant bacterial enzyme indicated to reduce toxic plasma concentrations of methot-

rexate, which records an expenditure of 1.36 million euro and an average DDD cost of about 30 thousand euro, and the antibiotic cefazolin which records an expenditure of 1.22 million euro or 22.9% of the total expenditure for this molecule. With regard to consumption, cefazolin is the most widely used medicine in class C-NN in 2023, while memantine drops from first to third position, recording a clear reduction in both expenditure (-85.8%) and in consumption (-89.7%) (Table 2.2.3).

81.3% of the expenditure for medicines classified in class C-NN concerns medicines with a price lower than two euro, with considerable regional variability ranging from 3.6% in Calabria to 97.4% in Campania; while the price range between 101 and 500 euro involves 8.3% of expenditure, and only 0.3% concerns medicines with a price higher than 500 euro (Table 2.2.4). For some medicines, prices per package in class C-NN are recorded at 1 euro due to the agreements that some Regions make with pharmaceutical companies to acquire these medicines. This appears to be a corporate strategy to enter the market early and acquire market shares before the negotiation.

Table 2.2.1 Regional per capita expenditure and consumption 2023* of medicines purchased directly from public health facilities in class C-NN

Region	N MA	Δ % 23-22	Per capita expenditure	Δ % 23-22	Inc. %	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
Piedmont	62	-38.6	0.52	-76.0	4.9	0.12	-69.2	11.6	-22.1
Valle d'Aosta	11	-54.2	1.04	-75.7	0.3	0.06	-74.9	49.9	-3.2
Lombardy	110	-28.6	0.54	-74.9	11.2	0.04	-43.5	35.4	-55.6
Province of Bolzano	19	-42.4	1.07	-26.7	1.1	0.04	-86.3	81.4	>100
Province of Trento	16	-46.7	0.52	-60.7	0.6	0.05	-85.9	26.1	>100
Veneto	58	-31.8	0.56	-73.0	5.7	0.26	-9.5	6.0	-70.2
Friuli VG	35	-34.0	1.26	-54.2	3.3	0.05	-73.3	64.5	71.2
Liguria	38	-50.6	1.38	-67.0	4.7	0.06	-71.8	60.5	16.9
Emilia R.	60	-43.9	0.88	-69.0	8.3	0.07	-85.3	32.3	>100
Tuscany	57	-34.5	1.07	-65.3	8.6	0.08	-30.9	38.5	-49.8
Umbria	26	-27.8	1.22	-54.6	2.3	0.09	-73.9	38.8	74.0
Marche	37	-30.2	1.09	-49.1	3.5	0.10	-8.9	30.8	-44.2
Lazio	68	-45.6	1.34	-57.0	15.9	0.08	-84.3	46.9	>100
Abruzzo	45	-27.4	1.26	-54.8	3.4	0.06	-86.2	59.6	>100
Molise	9	-25.0	0.11	-77.9	0.1	0.07	-75.2	4.0	-11.0
Campania	54	-41.3	0.41	-64.9	4.5	0.07	28.1	16.5	-72.6
Puglia	50	-40.5	0.78	-53.9	6.4	0.03	-81.0	67.8	>100
Basilicata	17	-50.0	1.30	-39.5	1.5	0.14	-17.5	24.8	-26.7
Calabria	47	-23.0	0.73	-37.7	2.8	0.04	-74.0	47.8	>100
Sicily	63	-30.8	0.81	-26.9	8.0	0.03	-17.5	65.1	-11.5
Sardinia	28	-28.2	0.87	-52.5	3.0	0.23	-80.7	10.1	>100
Italy	**229**	**-28.7**	**0.81**	**-63.1**	**100.0**	**0.08**	**-66.8**	**26.1**	**10.5**
North	158	-32.8	0.69	-71.1	40.1	0.10	-61.3	18.9	-25.3
Centre	111	-35.1	1.21	-58.9	30.3	0.08	-74.0	41.2	58.1
South and Islands	128	-38.2	0.73	-49.6	29.7	0.07	-69.2	30.2	63.5

*Not including vaccines (ATC J07) and oxygen (V03AN01)

Table 2.2.2 Top 30 active ingredients by expenditure directly purchased by public health facilities in class C-NN: comparison 2023-2021*

ATC 5th level	Active ingredient	Rank 2023	Rank 2022	Rank 2021	Expenditure *(million)*	Δ % 23-22	% expenditure**	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
J05AB16	remdesivir	1	1	1	38.00	-68.0	41.6	<0.005	-68.0	379.5	0.0
L01FD04	trastuzumab deruxtecan	2	22		1.55	>100	4.3	0.01	>100	13.6	59.5
V03AF09	glucarpidase	3	6		1.36	66.7	84.9	<0.005	66.6	30,250.0	0.0
J01DB04	cefazolin	4		53	1.22		22.9	0.02		3.5	
V04CL	allergy tests	5	3	23	0.95	-33.1	59.9	<0.005	-34.1	61.6	1.4
V09AB03	iodine ioflupane (123I)	6	36	11	0.78	>100	6.8	<0.005	>100	765.0	-1.4
L01XX73	sotorasib	7			0.65		100.0	<0.005		277.1	
V03AB14	protamine	8	64		0.52	>100	100.0	<0.005	>100	5.1	>100
N05BA06	lorazepam	9	33		0.47	>100	79.5	0.01	>100	4.2	>100
V09GA04	technetium human albumin (99mTc)	10	35	37	0.27	>100	37.0	<0.005	>100	63.9	15.2
M05BA08	zoledronic acid	11	7	28	0.25	-61.3	5.3	<0.005	-61.3	176.2	-0.2
L04AX05	pirfenidone	12	28		0.22	>100	0.7	<0.005	>100	27.0	-15.4
V10XX05	lutetium vipivotde (177Lu)	13			0.22		100.0	<0.005		55,000.0	
B05DB	hypertonic solutions for peritoneal dialysis	14	15	50	0.15	-17.2	0.5	<0.005	-13.9	7.4	-4.0
R07AX01	nitric oxide	15	21	21	0.12	30.2	5.5	<0.005	-12.1	2,448.3	48.0
M01AE01	ibuprofen	16	31	76	0.12	81.2	5.4	0.02	96.4	0.3	-7.8
V09IX07	fluorocholine (18F)	17	153	4	0.09		2.0	<0.005		2,934.5	
J05AE08	atazanavir	18	24	40	0.08	-1.4	23.6	<0.005	-16.7	2.0	18.3
L02BX03	abiraterone	19	40		0.08	>100	0.4	<0.005	>100	3.2	0.0
V09XA01	iodine norcholesterol (131I)	20	37	86	0.06	>100	100.0	<0.005	63.6	1,198.6	23.3
L04AK02	teriflunomide	21			0.06		0.1	<0.005		80.8	

continued

Table 2.2.2 – *continued*

ATC 5th level	Active ingredient	Rank 2023	Rank 2022	Rank 2021	Expenditure *(million)*	Δ % 23-22	% expenditure**	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
V09IX14	gallium gozetotide (68Ga)	22			0.05		100.0	<0.005		52,800.0	
J01GB06	amikacin	23	17		0.03	-75.0	2.8	<0.005	-75.0	366.8	0.0
J05AP55	sofosbuvir/velpatasvir	24	44	94	0.03	87.4	0.1	<0.005	28.5	60.0	45.8
N06DX01	memantine	25	14	42	0.03	-85.8	1.2	0.01	-89.7	0.1	38.8
L04AC22	spesolimab	26			0.02		100.0	<0.005		21,230.0	
V09CA02	technetium succimer (99mTc)	27	32	78	0.02	-61.2	22.5	<0.005	-63.5	83.8	6.2
V09HB01	indium oxinate (111In)	28	47	79	0.02	44.3	100.0	<0.005	38.7	254.9	4.0
L01AC01	thiotepa	29			0.01		0.3	<0.005		475.6	
L01FX13	enfortumab vedotin	30	69		0.01	>100	0.3	<0.005	>100	0.4	-0.6
	Total top 30				**47.42**	**-61.3**	**13.0**	**0.07**	**-50.5**	**31.3**	**-21.9**
	Total				**47.50**	**-63.2**	**0.3**	**0.08**	**-66.8**	**26.4**	**10.9**

*Not including vaccines (ATC J07) and oxygen (V03AN01); **calculated on total molecule expenditure

Table 2.2.3 Top 30 active ingredients by expenditure directly purchased by public health facilities in class C-NN: comparison 2023-2021

ATC 5th level	Active ingredient	Rank 2023	Rank 2022	Rank 2021	Expenditure *(million)*	Δ % 23-22	% expenditure*	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
J01DB04	cefazolin	1		28	1.22		22.9	0.02		3.52	
M01AE01	ibuprofen	2	7	53	0.12	81.2	5.4	0.02	96.4	0.34	-7.8
N06DX01	memantine	3	1	4	0.03	-85.8	1.2	0.01	-89.7	0.11	38.8
L01EF03	abemaciclib	4	8		0.01	83.3	0.0	0.01	75.5	0.04	4.4
L01FD04	trastuzumab deruxtecan	5	30		1.55	>100	4.3	0.01	>100	13.61	59.5
N05BA06	lorazepam	6	21		0.47	>100	79.5	0.01	>100	4.16	126.1
V03AB14	protamine	7	48		0.52	>100	100.0	<0.005	>100	5.07	295.9
J05AB16	remdesivir	8	4	9	38.00	-68.0	41.6	<0.005	-68.0	379.50	0.0
J05AE08	atazanavir	9	16	20	0.08	-1.4	23.6	<0.005	-16.7	1.98	18.3
M02AA15	diclofenac	10	25	34	0.00	61.6	3.6	<0.005	65.6	0.07	-2.5
L01FX13	enfortumab vedotin	11	42		0.01	>100	0.3	<0.005	>100	0.41	-0.6
L02BX03	abiraterone	12	34		0.08	>100	0.4	<0.005	>100	3.16	0.0
B05DB	hypertonic solutions for peritoneal dialysis	13	24	37	0.15	-17.2	0.5	<0.005	-13.9	7.35	-4.0
L04AF03	upadacitinib	14	13		0.00	-78.9	0.0	<0.005	-68.5	0.01	-33.3
V04CL	allergy tests	15	23	40	0.95	-33.1	59.9	<0.005	-34.1	61.56	1.4
L01FX24	teclistamab	16			0.00		61.7	<0.005		0.08	
G03FA04	progesterone/estradiol	17	92		0.00	>100	100.0	<0.005	>100	0.40	-32.3
L04AX05	pirfenidone	18	47		0.22	>100	0.7	<0.005	>100	27.04	-15.4
N07BC02	methadone	19			0.00		0.0	<0.005		0.67	
V09GA04	technetium human albumin (99mTc)	20	64	68	0.27	>100	37.0	<0.005	>100	63.86	15.2
J05AE30	nirmatrelvir/ritonavir	21	122		0.00		81.8	<0.005		0.00	

continued

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Table 2.2.3 – *continued*

ATC 5th level	Active ingredient	Rank 2023	Rank 2022	Rank 2021	Expenditure *(million)*	Δ % 23-22	% expenditure*	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
G02BB01	etonogestrel/ethinylestradiol	22	6	5	0.00	-98.7	0.2	<0.005	-98.1	0.25	-28.6
B05BB01	electrolytes for intravenous solutions	23	45	12	0.01	35.1	0.0	<0.005	34.9	1.93	0.1
S01LA09	faricimab	24			0.00		0.9	<0.005		1.26	
J05AP57	glecaprevir/pibrentasvir	25			0.00		0.0	<0.005		0.16	
L01XX73	sotorasib	26			0.65		100.0	<0.005		277.09	
L01XX75	tebentafusp	27	59		0.00	>100	0.0	<0.005	>100	0.11	0.0
G03AD02	ulipristal	28	112	152	0.01	>100	42.8	<0.005	>100	6.25	-64.5
M05BA08	zoledronic acid	29	40	76	0.25	-61.3	5.3	<0.005	-61.3	176.20	-0.2
N05BA09	clobazam	30	39	98	0.01	-64.4	4.9	<0.005	-69.4	6.22	16.3
	Total top 30				**44.59**	**-63.3**	**9.9**	**0.08**	**-48.0**	**25.01**	**-29.5**
	Total				**47.50**	**-63.2**	**0.3**	**0.08**	**-66.8**	**26.44**	**10.9**

Table 2.2.4 Percentage distribution by Region of class C-NN expenditure by NHS price range* (year 2023)

Region	NHS price range (EUR)					
	<2	2-20	21-50	51-100	101-500	≥500
Piedmont	43.4	22.9	8.9	5.1	18.1	1.6
Valle d'Aosta	88.9	0.6	-	0.1	10.4	-
Lombardy	62.1	3.2	6.3	6.3	21.3	0.7
Province of Bolzano	14.7	1.3	6.2	4.9	72.7	0.2
Province of Trento	20.3	3.9	-	30.5	44.8	0.5
Veneto	60.8	31.2	3.1	1.0	3.9	0.1
Friuli VG	19.3	0.2	7.1	6.7	65.8	0.9
Liguria	17.0	5.5	12.4	1.8	63.0	0.2
Emilia R.	10.0	22.6	6.0	14.6	45.5	1.3
Tuscany	86.3	0.6	2.0	1.1	8.9	1.0
Umbria	94.2	0.0	0.4	-	5.3	0.1
Marche	93.9	0.1	1.4	0.5	3.9	0.3
Lazio	92.0	0.1	0.4	0.5	6.9	0.0
Abruzzo	28.1	2.2	4.8	5.6	57.1	2.2
Molise	30.2	50.8	-	6.3	-	12.7
Campania	97.4	-	0.6	0.3	1.7	0.0
Puglia	45.1	1.5	6.5	1.2	43.6	2.1
Basilicata	10.0	23.5	13.3	-	49.4	3.8
Calabria	3.6	86.5	0.2	0.4	9.2	0.2
Sicily	87.6	0.3	1.8	0.2	9.9	0.2
Sardinia	93.5	3.2	0.2	-	3.0	0.1
Italy	**81.3**	**7.2**	**1.7**	**1.1**	**8.3**	**0.3**
North	53.0	21.9	4.9	3.8	15.9	0.5
Centre	91.5	0.2	0.9	0.6	6.6	0.3
South and Islands	85.8	6.6	1.0	0.3	6.1	0.2

* Not including vaccines (ATC J07) and oxygen (V03AN01))

Class C medicines reimbursed by the NHS purchased directly from public health facilities

This section presents consumption and expenditure data on class C medicines purchased by public health facilities. It is important to monitor these medicines since, although constituting NHS expenditure, they do not contribute to the determination of expenditure for the purposes of monitoring pharmaceutical expenditure ceilings and potential overruns.

Regarding class C medicines dispensed directly by public health facilities, per capita expenditure was equal to 12.04 euro, with a 6.1% increase compared to the previous year. On the contrary, consumption, equal to 38.8 DDD/1000 inhabitants per day, is down by 6.9%; therefore, the trend in spending is attributable to the increase in the average DDD cost compared to the previous year which was 13.7% (Table 2.2.5). The Northern Regions show higher values of expenditure (12.43 euro) and of consumption (42.5 DDD/1000 inhabitants per day) than the Central (11.93 euro and 38.6 DDD/1000 inhabitants per day) and the Southern Regions (11.54 euro and 33.5 DDD/1000 inhabitants per day). The average DDD cost is fairly heterogeneous at the regional level, with the highest values found in the South (0.94 euro) compared to the North (0.80 euro) and the Centre (0.84 euro). The Northern Regions are those that record the greatest increases in the average cost with respect to 2022 (+18.3%), while in the Centre and in the South there is an increase of 8.6%. Analysing the regional variability, the per capita expenditure value turns out to be higher in the Marche (16.07 euro) and lower in Molise (7.83 euro). Analysing consumption, on the other hand, the Region Emilia Romagna, with a value of 68.0 days of therapy per 1000 inhabitants per year, records the highest value, and Abruzzo with 24.9 DDD/1000 inhabitants per year the lowest; the latter Region also has the highest DDD cost (1.57 euro).

With an expenditure equal to 79.9 million, water-soluble, nephrotropic, low osmolarity radiological contrast media represent the category with the highest expenditure for purchases made directly by class C public health facilities, up by 3.1% compared to 2022. With regard to consumption, solutions that influence electrolyte balance (ATC B05BB) are the most used category (6.8 DDD/1000 inhabitants per day) and with a low average DDD cost (0.46 euro), while fibrinogen (ATC B02BB) records the highest average DDD cost (2,013.67 euro) (Table 2.2.6).

Considering the top 30 active ingredients by class C expenditure purchased directly by public health structures (Table 2.2. 7), 12 belong to ATC 5th level, including the contrast medium iomeprole which, with a per capita expenditure of 0.53 euro, represents the fourth active ingredient by expenditure; 9 belong to the class of medicines active on blood and haemopoietic organs (ATC B) and are mainly infusion solutions or for dialysis; 6 are antimicrobials for systemic use, including amphotericin B which, with a per capita expenditure of 0.85 euro and an increase over the previous year of 3%, confirms itself as the second molecule by expenditure. There is a notable increase in expenditure and consumption, almost 90% over 2022, of andexanet alfa, a specific reversal agent for FXa inhibitors, which rises from rank 28 in 2022 to rank 14 in 2023, with an average DDD cost of over 3,500 euro. With regard to consumption (Table 2.2.8), this year too electrolytes are confirmed as the most used class C active ingredients purchased directly from public health facilities; followed by cyanocobalamin (3.8 DDD/1000 inhabitants per day) and paracetamol (2.4 DDD/1000 inhabitants per day). It is highlighted that the top 30 active ingredients with the highest consumption cover 17.0% of expenditure and 75.6% of the total DDD of medicines in class C purchased directly from public health facilities; therefore, other active ingredients, which represent less than a quarter of total consumption (24.6% of DDD), account for 83% of total expenditure on medicines in class C (Table 2.2.8).

Table 2.2.5 Regional per capita expenditure and consumption 2023 of medicines purchased directly from public health facilities* in class C

Region	Per capita expenditure	Δ % 23-22	Inc. %	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
Piedmont	12.27	9.0	7.7	39.3	-9.7	0.85	20.4
Valle d'Aosta	13.92	17.0	0.2	45.6	-13.0	0.83	34.2
Lombardy	10.39	7.5	14.4	26.8	-18.0	1.06	30.6
Province of Bolzano	12.21	4.9	0.9	40.9	-18.2	0.82	27.9
Province of Trento	10.11	0.0	0.8	43.2	-3.3	0.64	3.1
Veneto	15.38	1.7	10.6	57.6	-1.8	0.73	3.3
Friuli VG	13.44	26.9	2.4	39.9	-14.6	0.92	48.1
Liguria	12.57	13.9	2.9	32.9	-16.0	1.04	35.2
Emilia R.	13.79	-1.2	8.7	68.0	-10.6	0.55	10.1
Tuscany	13.17	4.8	7.1	44.5	2.2	0.81	2.3
Umbria	14.41	12.6	1.8	48.4	-5.3	0.81	18.6
Marche	16.07	1.3	3.5	60.5	-13.9	0.73	17.3
Lazio	9.58	4.4	7.6	27.2	-2.9	0.96	7.2
Abruzzo	14.34	9.1	2.6	24.9	-9.4	1.57	20.1
Molise	7.83	11.3	0.3	25.4	6.1	0.84	4.5
Campania	10.21	5.8	7.5	33.7	0.7	0.83	4.7
Puglia	11.88	3.3	6.5	33.6	-6.0	0.97	9.6
Basilicata	14.76	-0.3	1.1	33.0	-17.7	1.22	20.9
Calabria	11.95	7.3	3.0	29.6	-8.6	1.10	17.1
Sicily	11.41	14.0	7.5	32.2	10.5	0.97	2.9
Sardinia	12.34	7.7	2.9	49.0	-4.7	0.69	12.7
Italy	**12.04**	**6.1**	**100.0**	**38.8**	**-6.9**	**0.85**	**13.7**
North	12.43	5.8	48.5	42.5	-10.8	0.80	18.3
Centre	11.93	4.6	20.0	38.6	-3.9	0.84	8.6
South and Islands	11.54	7.5	31.5	33.5	-1.3	0.94	8.6

*Not including vaccines (ATC J07) and oxygen (V03AN01)

Table 2.2.6 Top 20 categories (ATC 4th level) by expenditure directly purchased by public health facilities* in class C: comparison 2023-2022

ATC 4th level	Category	Expenditure *(million)*	Δ % 23-22	% expenditure**	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
V08AB	Water-soluble, nephrotropic, low-osmolarityradiological contrast media	79.9	3.1	11.3	0.1	-0.5	58.11	3.8
B05BB	Solutions affecting the electrolyte balance	67.3	13.0	9.5	6.8	0.8	0.46	12.4
J02AA	Antibiotics	50.2	3.0	7.1	<0.05	4.3	101.55	-1.0
B05BA	Parenteral nutritional solutions	42.2	-4.3	6.0	0.6	-15.7	3.36	13.8
J06BA	Human normal immunoglobulin	33.6	23.8	4.7	<0.05	26.0	528.42	-1.5
B05DB	Hypertonic solutions	27.6	6.3	3.9	0.2	15.2	8.38	-7.6
V08CA	Paramagnetic contrast media	26.8	2.8	3.8	<0.05	4.7	48.25	-1.7
J01CR	Penicillin combinations, incl. beta-lactamase inhibitors	16.8	9.6	2.4	0.1	23.4	8.22	-11.0
B02BC	Local hemostatics	13.1	15.1	1.9	<0.05	10.1	334.93	4.7
V03AB	Antidotes	12.6	66.7	1.8	0.1	-9.3	6.54	84.3
B05DA	Isotonic solutions	11.8	5.1	1.7	0.1	-14.9	10.32	23.8
V09AB	Iodine-123I compounds	10.8	8.0	1.5	<0.05	9.0	811.40	-0.7
N01BB	Amides	10.4	3.6	1.5	2.1	-3.1	0.24	7.2
V09FX	Various thyroid diagnostic radiopharmaceuticals	10.1	39.3	1.4	<0.05	32.0	251.59	5.7
B02BB	Fibrinogen	9.9	-25.9	1.4	<0.05	-21.8	2,013.67	-5.0
B05ZB	Hemofiltrates	9.7	21.7	1.4	0.1	10.7	8.87	10.1
J01XB	Polymyxins	9.6	-6.2	1.4	<0.05	-10.2	38.53	4.6
V03AF	Detoxifying substances for cytostatic treatments	9.2	-22.7	1.3	0.1	-1.2	5.23	-21.6
N02BE	Anilides	8.5	31.8	1.2	2.4	-41.9	0.16	127.5
H02AB	Glycocorticoids	8.3	12.2	1.2	0.7	-16.7	0.58	34.9
	Total of the top 20	**469.2**	**6.7**	**66.2**	**13.2**	**-13.0**	**1.66**	**22.9**
	Total	**708.5**	**5.8**	**100.0**	**38.8**	**-6.9**	**0.85**	**13.7**

*Not including vaccines (ATC J07) and oxygen (V03AN01); **calculated on the total expenditure for medicines purchased directly from public health facilities in class C

Table 2.2.7 Top 30 active ingredients by expenditure directly purchased by public health facilities* in class C: comparison 2023-2022

ATC 5th level	Active ingredient	Rank 2022	Rank 2021	Per capita expenditure	Δ % 23-22	% expenditure**	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
B05BB01	electrolytes for intravenous solutions	1	1	1.09	13.1	9.0	26.65	0.6	0.45	12.7
J02AA01	amphotericin B	2	2	0.85	3.0	7.1	0.02	4.3	101.55	-1.0
B05BA10	parenteral nutrition solutions	3	3	0.59	-4.2	4.9	0.11	-37.3	14.96	53.1
V08AB10	iomeprol	4	4	0.53	-2.8	4.4	0.02	-4.3	76.83	1.8
B05DB	hypertonic solutions for peritoneal dialysis	5	5	0.47	6.3	3.9	0.15	15.2	8.38	-7.6
J06BA01	human normal immunoglobulin for extravascular administration	6	6	0.42	31.6	3.5	<0.005	41.1	593.89	-6.5
J01CR05	piperacillin/tazobactam	7	8	0.26	9.2	2.1	0.09	24.9	8.17	-12.4
V08AB09	iodinaxol	8	7	0.25	6.6	2.1	0.01	4.3	79.57	2.5
B02BC30	human fibrinogen/human thrombin	9	11	0.23	15.0	1.9	<0.005	10.2	334.35	4.6
V08CA09	gadobutrol	10	10	0.23	4.9	1.9	0.01	5.1	77.79	0.0
B05DA	isotonic solutions for peritoneal dialysis	11	12	0.20	5.1	1.7	0.05	-14.9	10.32	23.8
V09AB03	iodine ioflupane (123I)	12	15	0.18	8.0	1.5	<0.005	9.0	811.40	-0.7
V08AB05	iopromide	13	13	0.18	-2.3	1.5	0.01	-10.0	59.77	8.8
V03AB38	andexanet alfa	14	28	0.18	88.3	1.5	<0.005	88.9	3,515.33	-0.1
B02BB01	human fibrinogen	15	9	0.17	-25.9	1.4	<0.005	-21.8	2,013.67	-5.0
J01XB01	colistimetate	16	14	0.16	-6.2	1.4	0.01	-10.2	38.53	4.6
J06BA02	human normal immunoglobulin for intravascular administration	17	17	0.15	5.9	1.2	<0.005	4.5	402.81	1.6
N02BE01	paracetamol	18	24	0.14	31.7	1.2	2.41	-41.9	0.16	127.3
V09FX01	technetium pertechnetate (99mTc)	19	25	0.14	30.8	1.2	<0.005	36.5	372.16	-4.0
B05ZB	haemofiltration solution	20	23	0.14	25.9	1.2	0.04	14.7	9.81	10.0
A11BA	vitamin complex	21	18	0.13	-2.5	1.1	0.07	-13.5	5.08	12.9
V08AB11	iobitridol	22	19	0.13	6.7	1.1	0.01	-3.1	51.96	10.3
V08AB04	iopamidol	23	21	0.13	5.7	1.1	0.01	2.1	28.39	3.7
B01AX01	defibrotide	24	26	0.13	21.3	1.0	<0.005	21.4	4,099.74	0.1

continued

Table 2.2.7 - *continued*

ATC 5th level	Active ingredient	Rank 2022	Rank 2021	Per capita expenditure	Δ % 23-22	% expenditure**	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
B01AC11	iloprost	25	20	0.12	-2.7	1.0	0.01	13.5	58.13	-14.1
H02AB04	methylprednisolone	26	29	0.11	22.3	0.9	0.40	8.4	0.75	13.0
V03AF07	rasburicase	27	16	0.11	-28.9	0.9	<0.005	-33.0	892.39	6.3
V08AB02	ioexol	28	34	0.11	32.0	0.9	0.01	16.6	37.28	13.5
V04CX	indocyanine green	29	32	0.10	16.9	0.8	<0.005	17.7	162.57	-0.5
J01CA01	ampicillin	30	33	0.09	12.3	0.8	0.01	12.1	23.97	0.3
	Total top 30			**7.73**	**7.1**	**64.2**	**10.11**	**-14.5**	**2.09**	**25.5**
	Total			**12.04**	**5.8**	**100.0**	**38.80**	**-6.9**	**0.85**	**13.7**

*Not including vaccines (ATC J07) and oxygen (V03AN01)

**calculated on the total expenditure for medicines purchased directly from public health facilities in class C

Table 2.2.8 Top 30 active ingredients by expenditure directly purchased by public health facilities* in class C: comparison 2023-2022

ATC 5th level	Active ingredient	Rank 2022	Rank 2021	DDD/1000 inhab. per day	Δ % 23-22	% cum	Per capita expenditure	Δ % 23-22	% expenditure**	% cum	Average DDD cost	Δ % 23-22
B05BB01	electrolytes for intravenous solutions	1	1	6.7	0.6	17.0	1.09	13.13	9.0	9.0	0.45	12.7
B03BA01	cyanocobalamin	2	3	3.8	0.8	26.9	0.00	0.00	0.0	9.0	0.00	-0.6
N02BE01	paracetamol	3	2	2.4	-41.9	33.2	0.14	31.71	1.2	10.2	0.16	127.3
C03CA01	furosemide	4	4	2.4	-0.2	39.3	0.04	8.35	0.3	10.5	0.04	8.8
V07AB	sodium chloride	5	5	2.0	11.9	44.5	0.06	15.23	0.5	11.0	0.08	3.2
N01BB02	lidocaine	6	6	1.5	-0.5	48.3	0.09	0.34	0.7	11.8	0.16	1.1
D08AC52	chlorhexidine/ethyl alcohol	7	7	1.0	2.5	50.8	0.02	2.63	0.2	11.9	0.06	0.3
G02BA03	levonorgestrel	8	8	1.0	17.9	53.3	0.02	13.09	0.2	12.1	0.05	-3.9
N05BA06	lorazepam	9	10	0.8	5.7	55.3	0.00	-4.62	0.0	12.1	0.01	-9.6
D06BA01	silver sulfadiazine	10	12	0.7	0.3	57.0	0.06	-1.13	0.5	12.6	0.24	-1.2

continued

Table 2.2.8 – *continued*

ATC 5th level	Active ingredient	Rank 2022	Rank 2021	DDD/1000 inhab. per day	Δ % 23-22	% cum	Per capita expenditure	Δ % 23-22	% expenditure**	% cum	Average DDD cost	Δ % 23-22
D08AG02	povidone iodine	11	9	0.6	-17.4	58.6	0.05	15.64	0.4	13.0	0.21	40.3
D08AJ01	benzalkonium chloride/ethyl alcohol	12	11	0.6	-20.7	60.1	0.01	-14.63	0.1	13.1	0.05	7.9
N05BA01	diazepam	13	15	0.4	0.3	61.2	0.03	-7.83	0.2	13.3	0.17	-7.9
B05BA03	glucose	14	13	0.4	-4.0	62.3	0.07	0.26	0.6	13.9	0.42	4.7
N05BA	delorazepam	15	18	0.4	4.5	63.4	0.03	12.22	0.2	14.1	0.18	7.7
H02AB04	methylprednisolone	16	19	0.4	8.4	64.4	0.11	22.28	0.9	15.0	0.75	13.0
D06AX07	gentamicin	17	16	0.4	-7.0	65.4	0.00	-8.39	0.0	15.0	0.02	-1.3
A11DA01	thiamine	18	21	0.4	4.6	66.4	0.01	2.82	0.1	15.1	0.04	-1.5
A11GA01	ascorbic acid	19	14	0.4	-16.0	67.4	0.00	-16.91	0.0	15.1	0.02	-0.9
N05BA12	alprazolam	20	20	0.4	3.8	68.3	0.00	38.59	0.0	15.1	0.02	33.8
V07AB	water solvent/diluent	21	23	0.4	8.0	69.3	0.05	17.80	0.4	15.5	0.36	9.3
S01FA56	tropicamide/phenylephrine	22	17	0.4	-12.5	70.2	0.05	6.52	0.4	15.9	0.37	22.0
C01CA03	noradrenaline	23	29	0.3	13.6	70.9	0.02	4.30	0.2	16.1	0.20	-8.0
D06BA51	silver sulfadiazine/hyaluronic acid	24	26	0.3	3.4	71.7	0.01	3.55	0.1	16.2	0.13	0.3
B05XA01	potassium chloride	25	25	0.3	-1.1	72.4	0.01	15.18	0.1	16.3	0.12	16.7
B05XA03	sodium chloride	26	28	0.3	0.1	73.1	0.01	21.13	0.1	16.4	0.11	21.4
A06AG01	sodium phosphate	27	31	0.3	7.8	73.8	0.05	11.95	0.5	16.8	0.56	4.1
N05CF02	zolpidem	28	36	0.2	16.2	74.4	0.00	16.30	0.0	16.9	0.03	0.3
D07CC01	gentamicin/betamethasone	29	34	0.2	3.0	75.0	0.00	0.51	0.0	16.9	0.05	-2.2
B05XA05	magnesium sulfate	30	33	0.2	0.1	75.6	0.01	25.10	0.1	17.0	0.08	25.2
	Total top 30			**29.4**	**-4.8**	**75.6**	**2.05**	**12.18**	**17.0**	**17.0**	**0.19**	**18.2**
	Total			**38.9**	**-6.9**	**100.0**	**12.04**	**5.82**	**100.0**	**100.0**	**0.85**	**13.7**

*Not including vaccines (ATC J07) and oxygen (V03AN01)

**calculated on the total expenditure for medicines purchased directly from public health facilities in class C

2.3 Direct and "on behalf" distribution

This section was developed by analysing data from regional flows of direct distribution (DD) and distribution in name and on behalf (DPC), which may have a variable degree of completeness, despite a specific LEA fulfilment for the necessary reconciliation with other current information flows.

In 2023, per capita expenditure for medicines dispensed through alternative delivery methods, i.e. direct distribution (DD) and "on behalf" distribution (DPC) of class A, H and C, was equal to 173.85 euro (10.2 billion euro), an increase of 6.9% compared to the previous year.

At the national level, DD expenditure has a percentage incidence of 75.6%, equal to a per capita value of 131.49 euro (7.7 billion euro), while DPC expenditure is 24.4%, equal to a per capita value of 42.36 euro (2.5 billion euro; Table 2.3.1, Figure 2.3.1 and Figure 2.3.5).

As far as DD is concerned, expenditure is predominantly represented by class H medicines (5.0 billion euro; about 65%), while consumption of class A medicines accounts for 63% (Figure 2.3.1 and 2.3.2).

In the years between 2019 and 2023, an increasing trend was recorded in the expenditure on class H medicines (+31%), which went from a value of 3.8 billion euro to approximately 5 billion, and on class C medicines (+25%), which increased from 80 to 100 million euro. Consumption in the various reimbursement classes, however, remained almost stable (Figure 2.3.2).

The increase in expenditure on class H medicines could have been determined by an increase in the average DDD cost of medicines belonging to this reimbursement class, which occurred in the years 2020 and 2021, and then stabilised in recent years (Figure 2.3.5).

DPC expenditure, on the other hand, shows a constant increase over time, going from a value of 1.9 billion euro in 2019 to 2.5 billion in 2023 (+28.7%; Figure 2.3.3). This trend would seem to be attributable to an increase in consumption equalt to 51%; (Figure 2.3.4).

At the regional level, there is a wide variability, linked to the organisational differences in the regional health services and the related medicine distribution methods (Table 2.3.1 and Figure).

In particular, the overall per capita expenditure in the two delivery channels records a higher value in the Southern Regions (190.25 euro) compared to that of the Central (176.28 euro) and the Northern Regions (161.34 euro), although very different trends are evident for the two different dispensing methods. In fact, a greater recourse to DPC in the Centre (29.4%) and to DD in the North (78.1%) is observed. Most of the Regions, approximately 12, show an incidence of expenditure on direct distribution higher than the national average of 75.6% and among these the highest values are observed in Sardinia (99.2%), Valle d'Aosta (85.8%), Emilia Romagna (84.3%) and Umbria (79.4%). The lowest values, on the other hand, are recorded in the Province of Trento (62.6%) and in Lazio (63.8%). Analysing the expenditure values of the DD, however, Sardinia (200.72 euro), Umbria (167.73 euro) and Emilia Romagna (156.23 euro) show the highest per capita expenditure values, while the Province of Trento (81.20 euro), Valle d'Aosta (90.19 euro) and the Province of Bolzano (99.14 euro) show the lowest. As regards DPC, however, Molise (64.42 euro), Lazio (60.92 euro) and Campania (58.10 euro) recorded the highest per capita expenditure. It should be noted that, for the second consecutive year, Sardinia and Valle d'Aosta show data that are not consistent with the national value and with the regional historical series. Excluding these two Regions, the

lowest expenditure values are recorded in Emilia Romagna (29.01 euro) and in the Province of Bolzano (32.13 euro).

At the national level, class H medicines represent the main share of expenditure in direct distribution (64.7%), followed by class A medicines (34.0%), while class C medicines represent a residual share (1.3%) (Table 2.3.2). The highest share of expenditure on class H medicines is observed in the Central Regions (67.9%), while the Northern and the Southern Regions show lower values, 62.8% and 65.3% respectively. Considering the per capita expenditure for medicines dispensed in DD, the highest values are recorded in Sardinia for class H medicines (137.64 euro), in Emilia Romagna for class A medicines (62.08 euro) and in Veneto for class C medicines (3.94 euro). The lowest values, on the other hand, are observed in the Province of Trento for class A medicines (23.10 euro), Molise for class C (0.63 euro) and Valle d'Aosta for class H medicines (52.52 euro).

Almost exclusively class A medicines are dispensed in DPC, which record a per capita expenditure equal to 42.34 euro at a national level (Table 2.3.3); the Central and Southern Regions are above this value, with a per capita expenditure equal to 51.71 and 46.54 euro respectively, while in the Northern Regions the expenditure is lower, equal to 35.38 euro per capita.

Analysing the regional variability for quantity and average DDD cost of medicines dispensed in direct and "on behalf" distribution (Figure 2.3.6), Emilia Romagna remains the Region with the highest consumption of lower-cost medicines, although the Province of Trento has a lower cost per day of therapy, but with significantly lower consumption; Sardinia and Lombardy consume smaller quantities at higher costs. An analysis of the NHS transfer prices of the packages dispensed through the DPC shows that 41.4% of the packages fall in the price range between 30 and 49 euro, 18.6% have a price lower than 5 euro, 17.1% have a price between 50 and 149 euro, 14.1% between 10 and 29 euro, while a smaller share of 6.2% falls within the price range of 5-9 euro and a residual share of 2.5% has a cost higher than 150 euro (Table 2.3.4). A wide regional variability is observed: in Sicily, a third of the packages dispensed through the DPC have a price for the NHS of less than 5 euro or between 30 and 49 euro, in Molise only a quarter of the packages dispensed have a price between 30 and 49 euro or less than 5 euro or between 50 and 149 euro, while in Lombardy and in the Province of Bolzano, approximately 60% of the packages dispensed have a price between 30 and 49 euro.

If the price to the public is considered, the largest share (52.7%) of packages dispensed in DPC concerns medicines with a price between 50 and 149 euro, while approximately 3% relates to medicines with a price up to 9 euro (Table 2.3.5). Overall, there is less regional variability compared to the analyses in which the price of transfer to the NHS was considered.

As regards the cost of the service (Table 2.3.6), at a national level the average value was 7.17 euro, while at a geographical area level it can be seen that the Central and Southern Regions present higher values (7.58 and 7.37 euro respectively), slightly increasing compared to the previous year (national value 7.05 euro, North 6.69 euro, Centre 7.65 euro, South and Islands 7.04 euro). The highest average cost was recorded in Abruzzo (12.69 euro) and Basilicata (11.62 euro), more than double that of Emilia Romagna and Liguria (4.15 and 5.49 euro respectively; Table 2.3.6). Abruzzo and Basilicata show a cost of the service higher than the NHS transfer price for medicines costing less than 9 euro. Analysing the retail price of medicines, this trend is even more evident, deviating significantly from the national average values and all other regional ones (Table 2.3.7). Overall, in Italy the cost of the DPC service on the NHS price has an average impact of 17.6% (Table 2.3.8). As expected, the incidence of the

cost of the service on the purchase price decreases as the price range increases, being independent of the price of the medicines. In the case of the NHS price, the incidence goes from 367.8% in the price range up to 5 euro to 2.4% in the range above 150 euro. Considering, on the other hand, the retail price, the incidence goes from an incidence of 186.8% in medicines with a price up to 5 euro to 2.6% in the last price range (Table 2.3.9).

Considering the categories with the highest expenditure provided in direct distribution (Table 2.3.10), antineoplastic and immunomodulatory medicines confirm the highest value, equal to 66.56 euro, up 2.3% compared to the previous year. This increase appears to be linked to the growth in consumption (+9.8%), which stands at 6.9 DDD/1000 inhabitants per day. In fact, there is a reduction in the average DDD cost of 6.8%, with a value of 26.57 euro.

Interleukin inhibitors represent 15.6% of expenditure and 16.8% of consumption for this category, followed by other protein kinase inhibitors (7.0% of expenditure) and Bruton's tyrosine kinase inhibitors (6.4%).

The category with the highest consumption is represented by inhibitors of tumor necrosis factor alpha (TNF-alpha) with an absolute value of 1.4 DDD/1000 inhabitants per day and an incidence on consumption of the category equal to 20.8%. The highest average cost is recorded for PARP inhibitors (137.23 euro) and for ALK kinase inhibitors (135.93 euro), although both are decreasing compared to 2022, respectively by 2.6% and 7.4%.

The second category for expenditure is represented by general antimicrobials for systemic use, which have a value of 14.27 euro per capita, an increase of 3.1% compared to 2022. Associations for the treatment of HIV and antivirals for HCV represent approximately 70% of the expenditure of the category. The category of normal human immunoglobulin, on the other hand, increased by 5.2% compared to the previous year, with an expenditure of 1.27 euro per capita and an average DDD cost of 252.44 euro, the highest in the category. Medicines active on blood and hematopoietic organs are the third category in terms of expenditure (12.31 euro per capita), up 5.7% compared to the previous year. For these medicines, there was an increase in the average DDD cost of 8% and a reduction in consumption of 2.1%. Coagulation factors represent almost half of the expenditure for the entire category (5.35 euro, 43.4%) and show the highest average DDD cost (350.15 euro) after medicines used in hereditary angioedema with a value of 644.45 euro. Heparin is the category with the highest consumption, in this supply channel, with a value of 1.4 DDD/1000 inhabitants per day, equal to 21.1% of the total.

Considering, instead, the categories with the highest expenditure supplied in DPC (Table 2.3.11), medicines active on the blood and haematopoietic organs are the category with the highest expenditure (14.98 euro per capita), up 3.6% compared to the previous year. This increase is correlated to an increase in consumption (+3.4%), with the average DDD cost being substantially stable (+0.2%), which is equal to 1.44 euro. Direct factor Xa inhibitors represent more than half of the expenditure (59.4%) and consumption (51.0%). Coagulation factors are the category with the highest average DDD cost equal to 544.10 euro. Medicines active on the gastrointestinal system represent the second category for expenditure with a value of 14.48 euro per capita, up 16% and with consumption (26.8 DDD) increased by 17.0% compared to 2022. The subgroup with the highest expenditure for this category is represented by GLP-1 analogues, which represent 41% of expenditure and 24% of consumption, in addition to having the highest average DDD cost (2.53 euro). They are followed by slow-acting injectable insulins and analogues, with a reduction in both expenditure (2.75 euro, -1.6%) and consumption (5.9 DDD, -0.8%).

Among the top 30 active ingredients for expenditure dispensed in DD (Table 2.3.12), 19 belong to ATC L and ibrutinib is by far the most expensive in category L (192 million euro), although down compared to the previous year (-3.4%). The combination elexacaftor/tezacaftor/ivacaftor and the single active ingredient ivacaftor, both indicated for the treatment of patients with cystic fibrosis, are the active ingredients with the highest expenditure, with a value of 261.7 and 204.9 million euro, an increase compared to the previous year of 37.4% and 20.6%, respectively. Tafamidis, indicated for the treatment of hereditary wild-type transretinal amyloidosis in adult patients with cardiomyopathy, and risdiplam, indicated for the treatment of 5q spinal muscular atrophy in patients diagnosed with SMA type 1/2/3 or with one to four copies of SMN2, show the greatest variation in expenditure (>100% and +97.5%, respectively). Overall, the top 30 active ingredients by expenditure distributed in DD represent 44.1% of total expenditure.

With regard to consumption, among the active ingredients supplied in direct distribution with the highest use (Table 2.3.13), cholecalciferol is in first place with a value of 2.1 DDD per 1000 inhabitants per day and an expenditure of 400 thousand euro, followed by cyanocobalamin and furosemide, with values of 1.5 DDD/1000 inhabitants per day. The top 30 active ingredients with the highest consumption account for a total of 8.5% of the total expenditure.

Among the top 30 active ingredients supplied in direct distribution with the highest average cost per DDD (Table 2.3.14), eight belong to ATC L, five are medicines active on the blood and haematopoietic organs and for the treatment of rare metabolic diseases (ATC A).

At the top of the list, there are five gene therapy medicines, in order CAR-T tisangenlecleucel (489 thousand euro) and brexucabtagene autoleucel (317 thousand euro), voretigene neparvovec for the treatment of hereditary retinal dystrophy in adult and paediatric patients with 297 thousand euro for DDD, onasemnogene abeparvovec indicated in the treatment of patients with spinal muscular atrophy (SMA) with approximately 270 thousand euro for DDD and another CAR-T, namely axicabtagene ciloleucel with 239 thousand euro. For the latter and for two other gene therapies, tisagenlecleucel and onasemnogene abeparvovec, there was an increase in the average DDD cost due to the change in the accounting methods for the expenditure of these medicines that were subject to conditional reimbursement agreements, Payment at result, which provided for the distribution and attribution of fractions of the cost of the treatment over time following verification of the maintenance of therapeutic success. Subsequently, the change provided for the revision of the contractual agreements and the accounting of the entire cost of the infusion treatment. Next in line is catridecacog (recombinant coagulation factor XIII) with a cost of 15.5 thousand euro per DDD, and in seventh place is an antitumor radiopharmaceutical, lutetium oxodotreotide (177Lu) with an average cost per DDD of 14.3 thousand euro. The top 30 active ingredients by average cost, however, represent only 1.9% of the total expenditure.

Among the active ingredients supplied in direct distribution that have shown the greatest change in expenditure compared to 2022 (Table 2.3.15), almost half belong to ATC L. However, inclisiran comes first with an expenditure of 13.1 million euro and an average cost per day of therapy of 8.82 euro, marking a high increase (>100%) both in terms of expenditure and consumption, having been reclassified in October 2022. In second place is vosotiride with an expenditure of 18.2 million euro and an average cost of 310.70 euro, an innovative non-oncological medicine indicated in patients aged 4 months and older, whose epiphyses are not closed, following genetic analysis. For most of the active ingredients considered, the

increase in expenditure is related to an increase in consumption, furthermore the top 30 represent 17.7% of the total expenditure.

The top 30 active ingredients with the highest increase in consumption in the direct distribution channel represent 7.9% of total DDDs and among these the following molecules recorded increases greater than 100%: inclisiran, atezolizumab, avelumab, pembrolizumab, bromazepam, tafamidis and dapagliflozin (Table 2.3.16).

Among the top 30 active ingredients with the highest reduction in expenditure in the direct distribution channel, which together constitute 13.3% of total expenditure, there are lenalidomide (-81.9%), abiraterone (-72.3%) and deferasirox (-57.3%) (Table 2.3.17). The three molecules also show a reduction in the average DDD cost, respectively of 84.3%, 71.4% and 56.9%, probably attributable to the entry of generics into the market during 2022. Hydroxocobalamin (-68.2%), baricitinib (-27.6%) and raltegravir (-27.0%) are the molecules that show the greatest reduction in consumption in DD (Table 2.3.18).

In the case of DPC, however, the new oral anticoagulants (NOACs) are confirmed in the first two places for expenditure also in 2023: apixaban with 198.4 million euro, an increase of 9.3% compared to last year, and rivaroxaban with 185.3 million euro, an increase of 3.6% (Table 2.3.19), both due to an increase in consumption, respectively of 11.5% and 4.0%. The GLP-1 analogues semaglutide follow with 165.7 million and an increase in expenditure of 86.9%, and dulaglutide with 162.7 million and an increase of 8.8%. For both of these active ingredients, the increase in expenditure is exclusively attributable to an increase in consumption (respectively +93.9% and +18.6%). Overall, the top 30 active ingredients constitute 78.3% of the total expenditure of the DPC.

With regard to consumption, among the active ingredients supplied in DPC with the greatest use (Table 2.3.20), apixaban is in first place with a value of 5.42 DDD/1000 inhabitants per day, followed by rivaroxaban (5.41 DDD) and clopidogrel (4.6 DDD). Of particular interest is the increase in consumption in this delivery channel for semaglutide (+93.9%) and dapagliflozin (+84.5%) and that the top 30 active ingredients constitute 83.5% of consumption and 69% of total expenditure in DPC.

Of the top 30 active ingredients supplied in DPC with the highest average cost for DDD (Table 2.3.21), almost two thirds are medicines active on the blood and hematopoietic organs; the activated human antihemophilic prothrombin complex, with an average DDD cost of more than 7 thousand euro, is the medicine with the highest cost in this delivery channel. In 2023, the greatest increase in DPC expenditure was recorded for the follitropin alfa/lutropin alfa combination (+96.8%), correlated with an increase in the average DDD cost of 15.3% and consumption (+71.1%), for semaglutide (+86.9%), correlated with a strong increase in consumption (+93.9%; Table 2.3.22). Of the top 30 active ingredients for increased consumption, a third are antidiabetics, with variations ranging between +93.9% for semaglutide and +18.6% for dulaglutide (Table 2.3.23).

On the contrary, the sitagliptin/metformin combination (-37.5%), lanreotide (-31.2%) and liraglutide (-29.2%) showed a reduction in expenditure. For the three molecules, the contraction is correlated to a reduction in the average DDD cost, while consumption is increasing only for lanreotide (+5.2%) (Table 2.3.24). Finally, considering the medicines with the greatest reduction in consumption (Table 2.3.25), the highest values are highlighted for ranolazine (-91.6%), followed by vildagliptin (-34.9%) and fondaparinux (-26.3%). For ranolazine, the reduction in consumption is due to the change in the supply channel, in particular the transition to supply under the approved care regime.

Figure 2.3.1 Annual trend (2019-2023) in expenditure on medicines supplied in direct distribution (DD) by reimbursement class

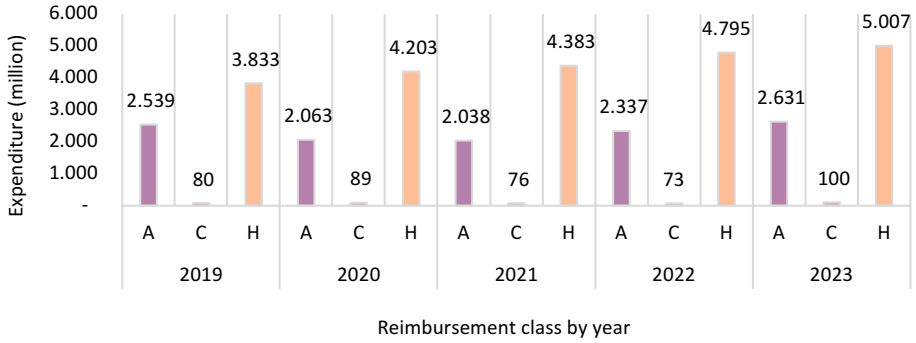


Figure 2.3.2 Annual trend (2019-2023) in consumption (DDD/1000 inhabitants per day) on medicines supplied in direct distribution (DD) by reimbursement class

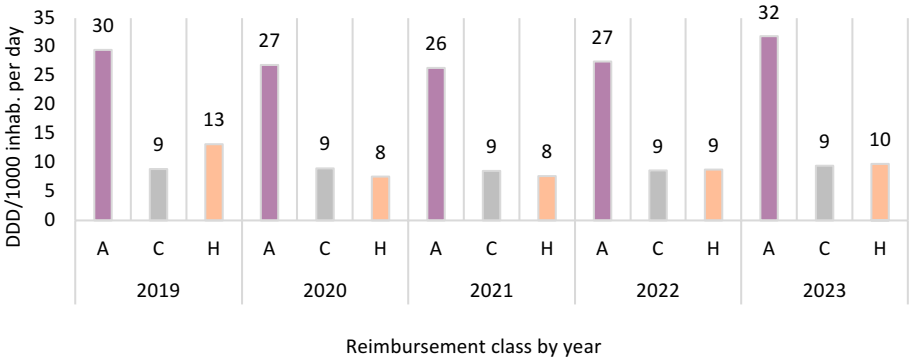


Figure 2.3.3 Annual trend (2019-2023) in expenditure on medicines supplied in "on behalf" distribution (DPC)

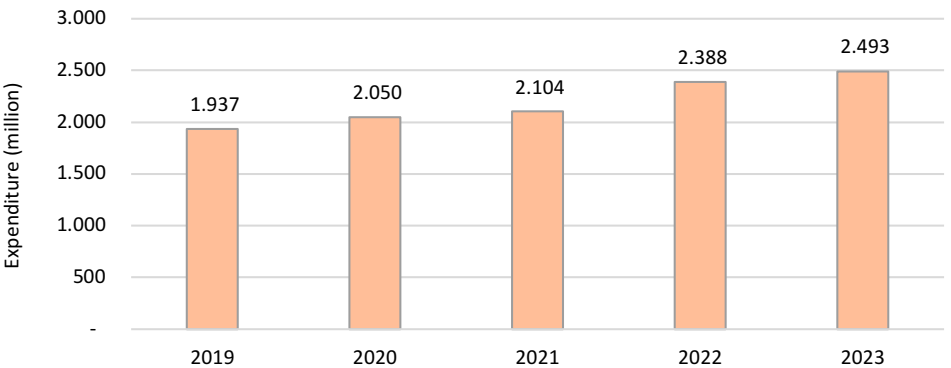


Figure 2.3.4 Annual trend (2019-2023) in consumption (DDD/1000 inhabitants per day) on medicines supplied in direct and "on behalf" distribution

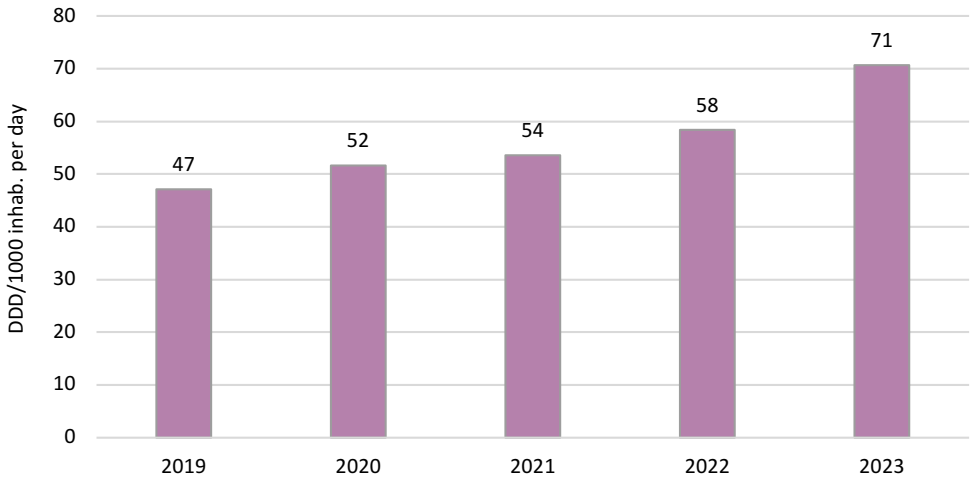


Figure 2.3.5 Annual trend (2019-2023) in average DDD cost of medicines supplied in direct (by reimbursement class) and "on behalf" distribution

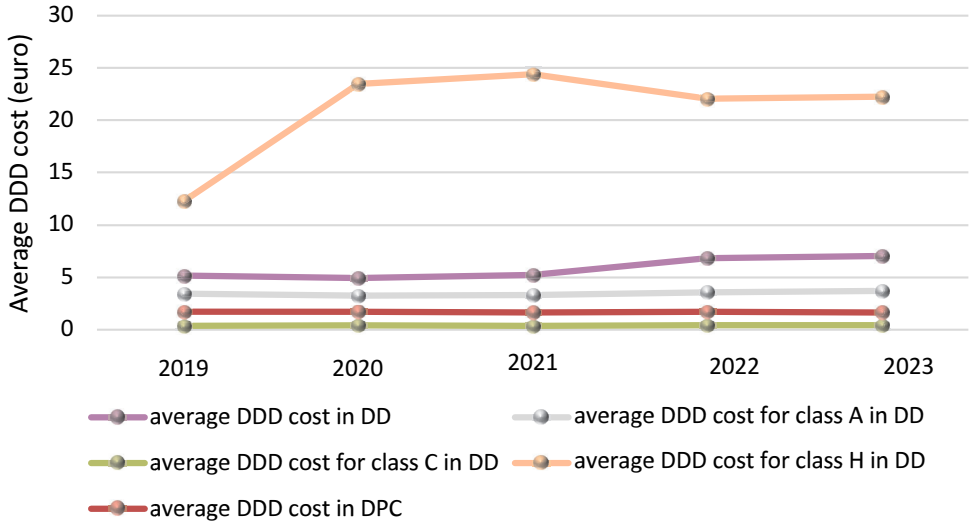


Table 2.3.1 Composition of regional expenditure 2023 for medicines supplied in direct distribution (DD*) and "on behalf" distribution (DPC*) (Table and Figure)

Region	Per capita expenditure			Δ % 23-22	Inc. % DD	Inc. % DPC
	DD	DPC	Total			
Piedmont	125.52	38.75	164.27	9.7	76.4	23.6
Valle d'Aosta	90.19	14.94	105.13	12.7	85.8	14.2
Lombardy	116.15	32.56	148.71	9.1	78.1	21.9
Province of Bolzano	99.14	32.13	131.27	-10.3	75.5	24.5
Province of Trento	81.20	48.58	129.77	39.6	62.6	37.4
Veneto	123.31	39.58	162.89	5.5	75.7	24.3
Friuli VG	131.24	44.96	176.20	9.6	74.5	25.5
Liguria	132.38	39.23	171.60	7.8	77.1	22.9
Emilia R.	156.23	29.01	185.23	6.9	84.3	15.7
Tuscany	129.60	41.71	171.31	8.5	75.7	24.4
Umbria	167.73	43.40	211.13	6.0	79.4	20.6
Marche	150.00	47.89	197.89	6.8	75.8	24.2
Lazio	107.35	60.92	168.27	8.2	63.8	36.2
Abruzzo	151.84	57.19	209.03	12.0	72.6	27.4
Molise	131.27	64.42	195.69	5.7	67.1	32.9
Campania	139.60	58.10	197.70	0.4	70.6	29.4
Puglia	140.36	49.66	190.02	0.4	73.9	26.1
Basilicata	148.33	39.97	188.30	6.1	78.8	21.2
Calabria	135.87	53.80	189.67	2.3	71.6	28.4
Sicily	131.88	40.80	172.68	7.0	76.4	23.6
Sardinia	200.72	1.70	202.42	24.5	99.2	0.8
Italy	**131.49**	**42.36**	**173.85**	**6.9**	**75.6**	**24.4**
North	125.94	35.39	161.34	8.1	78.1	21.9
Centre	124.50	51.78	176.28	7.8	70.6	29.4
South and Islands	143.71	46.54	190.25	4.9	75.5	24.5

Note: consolidated data as of 23 April 2024, relating to medicines with MA; * expenditure is net of oxygen
Sardinia and Valle d'Aosta show data on the DPC that are not consistent with the national value and with the regional historical series

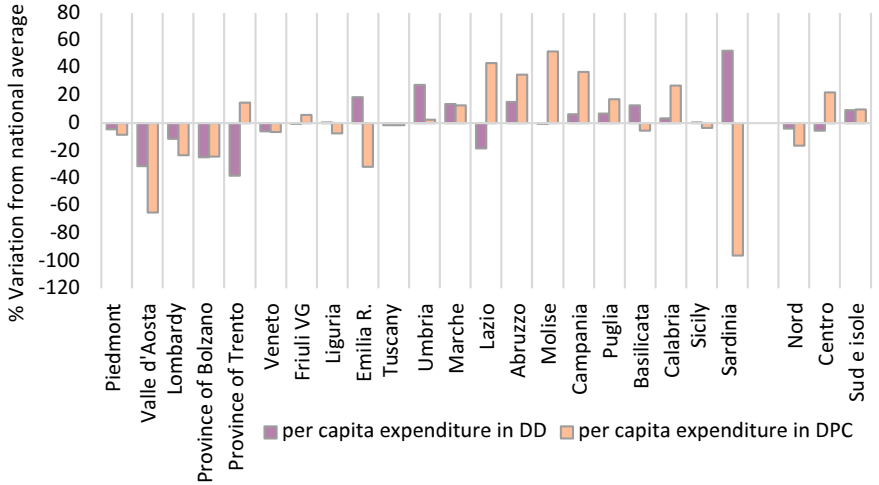


Table 2.3.2 Composition by reimbursement class of regional expenditure 2023 for medicines supplied in direct distribution (DD)*

Region	Per capita expenditure				Inc. % A	Inc. % C	Inc. % H
	Class A	Class C	Class H	Total			
Piedmont	44.03	2.13	79.36	125.52	35.1	1.7	63.2
Valle d'Aosta	35.89	1.77	52.52	90.19	39.8	2.0	58.2
Lombardy	37.92	0.92	77.31	116.15	32.6	0.8	66.6
Province of Bolzano	39.17	1.83	58.14	99.14	39.5	1.8	58.6
Province of Trento	23.10	2.44	55.66	81.20	28.4	3.0	68.5
Veneto	46.17	3.94	73.19	123.31	37.4	3.2	59.4
Friuli VG	39.93	2.17	89.14	131.24	30.4	1.7	67.9
Liguria	48.62	1.09	82.66	132.38	36.7	0.8	62.4
Emilia R.	62.08	2.90	91.24	156.23	39.7	1.9	58.4
Tuscany	45.46	1.60	82.54	129.60	35.1	1.2	63.7
Umbria	43.24	2.22	122.27	167.73	25.8	1.3	72.9
Marche	48.54	0.68	100.78	150.00	32.4	0.5	67.2
Lazio	30.89	0.84	75.62	107.35	28.8	0.8	70.4
Abruzzo	52.75	1.88	97.21	151.84	34.7	1.2	64.0
Molise	41.24	0.63	89.39	131.27	31.4	0.5	68.1
Campania	44.19	1.35	94.06	139.60	31.7	1.0	67.4
Puglia	49.98	1.65	88.73	140.36	35.6	1.2	63.2
Basilicata	56.50	2.16	89.68	148.33	38.1	1.5	60.5
Calabria	42.72	1.22	91.93	135.87	31.4	0.9	67.7
Sicily	47.78	1.32	82.78	131.88	36.2	1.0	62.8
Sardinia	60.58	2.50	137.64	200.72	30.2	1.2	68.6
Italy	**44.71**	**1.72**	**85.06**	**131.49**	**34.0**	**1.3**	**64.7**
North	44.71	2.08	79.15	125.94	35.5	1.7	62.8
Centre	38.75	1.17	84.58	124.50	31.1	0.9	67.9
South and Islands	48.35	1.54	93.82	143.71	33.6	1.1	65.3

Note: consolidated data as of 23 April 2024, relating to medicines with MA * expenditure is net of oxygen
Sardinia and Valle d'Aosta show data on the DPC that are not consistent with the national value and with the regional historical series

Table 2.3.3 Composition by reimbursement class of regional expenditure 2023 for medicines supplied in direct "on behalf" distribution (DPC)*

Region	Per capita expenditure				Inc. % A	Inc. % C	Inc. % H
	Class A	Class C	Class H	Total			
Piedmont	38.74	0.01	-	38.75	100.0	0.0	0.0
Valle d'Aosta	14.94	<0.005	-	14.94	100.0	0.0	0.0
Lombardy	32.55	-	0.01	32.56	100.0	-	0.0
Province of Bolzano	32.13	-	-	32.13	100.0	-	0.0
Province of Trento	48.44	0.05	0.08	48.58	99.7	0.1	0.3
Veneto	39.57	0.01	<0.005	39.58	100.0	0.0	0.0
Friuli VG	44.96	-	-	44.96	100.0	-	0.0
Liguria	39.23	<0.005	<0.005	39.23	100.0	0.0	0.0
Emilia R.	28.99	0.01	<0.005	29.00	100.0	0.0	0.0
Tuscany	41.71	-	-	41.71	100.0	-	0.0
Umbria	43.39	0.01	-	43.40	100.0	0.0	0.0
Marche	47.89	-	-	47.89	100.0	-	0.0
Lazio	60.78	0.08	<0.005	60.86	99.9	0.1	0.1
Abruzzo	57.18	<0.005	-	57.19	100.0	0.0	0.0
Molise	64.31	0.02	0.09	64.42	99.8	0.0	0.2
Campania	58.10	<0.005	<0.005	58.10	100.0	0.0	0.0
Puglia	49.66	-	-	49.66	100.0	-	0.0
Basilicata	39.97	-	-	39.97	100.0	-	0.0
Calabria	53.79	<0.005	-	53.79	100.0	0.0	0.0
Sicily	40.80	-	-	40.80	100.0	-	0.0
Sardinia	1.70	<0.005	-	1.70	99.9	0.1	0.1
Italy	**42.34**	**0.01**	**<0.005**	**42.35**	**100.0**	**0.0**	**0.0**
North	35.38	0.01	<0.005	35.39	100.0	0.0	0.0
Centre	51.71	0.04	<0.005	51.75	99.9	0.1	0.1
South and Islands	46.54	0.00	<0.005	46.54	100.0	0.0	0.0

Sardinia and Valle d'Aosta show data that are not consistent with the national value and with the regional historical series

Note: consolidated data as of 23 April 2024, relating to medicines with MA
* expenditure is net of oxygen

Figure 2.3.6 Regional variability by quantity and average DDD cost of medicines supplied in direct distribution (DD) and "on behalf" distribution (DPC) in 2023

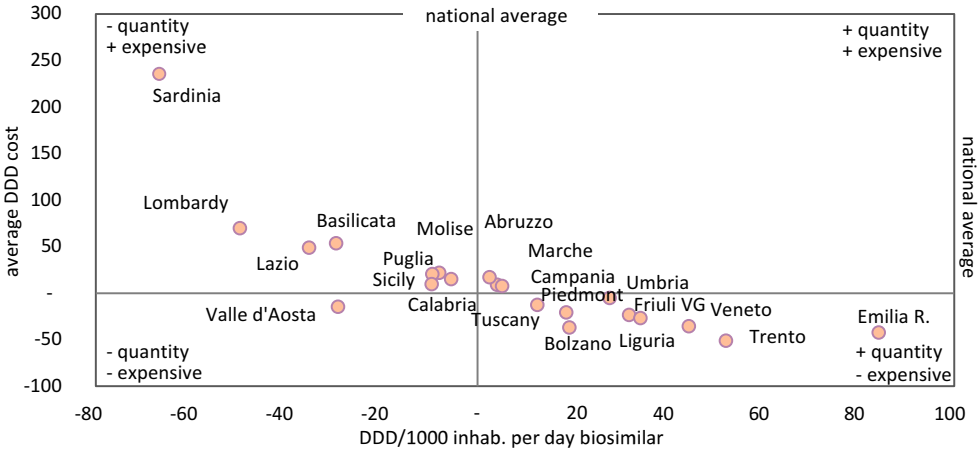


Table 2.3.4 Distribution (%) of the number of packages by NHS price range of medicines supplied in "on behalf" distribution (DPC) in 2023

Region	Total packages	Price range (€)					
		<5	5-9	10-29	30-49	50-149	≥150
Piedmont	3,361,938	24.6	5.2	12.8	38.9	16.2	2.3
Valle d'Aosta	10,715	28.3	3.6	15.7	37.7	13.3	1.3
Lombardy	5,584,848	2.3	0.6	10.9	61.9	19.3	5.1
Province of Bolzano	272,519	6.3	1.9	13.8	60.0	16.1	1.9
Province of Trento	529,677	10.2	5.0	26.0	39.7	16.4	2.9
Veneto	5,203,290	16.7	6.7	12.3	46.2	16.5	1.7
Friuli VG	1,334,869	18.6	1.9	11.0	48.6	17.4	2.4
Liguria	2,238,069	26.0	6.8	18.8	33.9	13.2	1.3
Emilia R.	5,024,877	29.8	5.6	17.7	37.1	9.3	0.4
Tuscany	4,889,240	19.6	6.3	23.7	35.8	13.4	1.3
Umbria	1,237,412	26.3	2.9	18.9	37.3	13.4	1.3
Marche	2,379,604	15.8	16.9	19.9	33.0	12.6	1.9
Lazio	4,454,940	16.5	4.8	5.5	45.0	22.7	5.5
Abruzzo	1,515,644	8.9	3.5	21.0	40.9	22.6	3.1
Molise	440,764	24.5	4.9	13.2	24.5	29.9	3.0
Campania	7,419,935	19.3	12.5	11.9	35.8	18.0	2.5
Puglia	4,076,079	9.2	2.5	14.7	48.1	22.9	2.6
Basilicata	227,792	3.6	1.7	24.3	45.5	22.4	2.6
Calabria	2,275,080	12.4	6.7	16.3	42.1	19.7	2.9
Sicily	5,771,281	33.0	6.4	9.4	32.4	17.1	1.7
Sardinia	76,152	18.8	5.1	14.1	45.0	14.5	2.5
Italy	**58,324,725**	**18.6**	**6.2**	**14.1**	**41.4**	**17.1**	**2.5**
North	23,560,802	17.9	4.4	14.0	45.9	15.3	2.4
Centre	12,961,196	18.5	7.4	16.3	38.6	16.4	2.9
South and Islands	21,802,727	19.5	7.5	13.0	38.1	19.5	2.4

Note: consolidated data as of 23 April 2024, relating to medicines with MA

Table 2.3.5 Distribution (%) of the number of packages by price range to the public of medicines supplied in "on behalf" distribution (DPC) in 2023

Region	Total packages	Price range (€)					
		<5	5-9	10-29	30-49	50-149	≥150
Piedmont	3,361,938	0.3	5.2	21.2	7.5	50.7	15.1
Valle d'Aosta	10,715	0.0	6.0	21.2	15.3	48.5	9.0
Lombardy	5,584,848			2.5	0.7	77.2	19.7
Province of Bolzano	272,519		0.0	7.2	5.3	74.8	12.7
Province of Trento	529,677	0.0	2.2	21.0	11.6	49.4	15.8
Veneto	5,203,290	0.1	0.3	19.6	8.9	58.0	13.2
Friuli VG	1,334,869		6.9	10.5	4.6	61.4	16.7
Liguria	2,238,069	0.0	6.4	33.6	7.8	42.3	9.8
Emilia R.	5,024,877	0.0	3.9	22.2	18.7	47.6	7.5
Tuscany	4,889,240	0.0	0.7	27.2	14.0	47.4	10.7
Umbria	1,237,412	0.2	7.4	30.0	9.7	40.7	12.0
Marche	2,379,604	0.0	3.7	29.3	15.6	40.0	11.4
Lazio	4,454,940	0.7	6.3	10.8	7.7	52.1	22.3
Abruzzo	1,515,644	0.0	1.5	11.4	9.5	58.6	18.9
Molise	440,764	0.5	4.6	24.5	10.5	48.9	11.1
Campania	7,419,935	0.0	0.4	28.1	6.2	48.1	17.2
Puglia	4,076,079	0.0	0.3	3.0	10.6	61.2	24.9
Basilicata	227,792		1.1	2.7	13.5	64.8	18.0
Calabria	2,275,080	0.0	3.6	12.2	8.6	52.8	22.9
Sicily	5,771,281	0.0	7.1	27.0	6.8	42.3	16.9
Sardinia	76,152	1.0	0.0	16.0	11.2	57.9	13.8
Italy	**58,324,725**	**0.1**	**2.9**	**19.3**	**9.0**	**52.7**	**16.0**
North	23,560,802	0.1	2.7	17.0	8.5	58.0	13.7
Centre	12,961,196	0.3	3.8	22.2	11.7	47.0	14.9
South and Islands	21,802,727	0.0	2.7	19.9	7.8	50.4	19.1

Note: consolidated data as of 23 April 2024, relating to medicines with MA

Table 2.3.6 Cost (euro) of the service per package, broken down by Region and by NHS price range of medicines supplied in "on behalf" distribution (DPC) (year 2023)

Region	Price range (€)						Cost of the service	
	<5	5-9	10-29	30-49	50-149	≥150	average	per capita
Piedmont	6.46	6.50	6.54	6.50	6.46	6.41	6.48	4.93
Valle d'Aosta	7.37	7.32	7.39	7.40	7.38	7.42	7.39	0.63
Lombardy	9.24	7.95	9.33	9.34	9.25	9.02	9.29	5.27
Province of Bolzano	8.08	8.10	8.08	8.09	8.07	8.08	8.08	4.46
Province of Trento	5.66	5.64	5.66	5.66	5.66	5.65	5.66	5.64
Veneto	6.95	6.89	6.95	7.00	7.00	7.00	6.98	7.46
Friuli VG	7.06	8.18	8.20	8.24	8.22	8.21	8.01	8.51
Liguria	5.48	5.49	5.47	5.50	5.50	5.49	5.49	7.51
Emilia R.	4.15	4.31	4.16	4.14	4.11	4.21	4.15	4.67
Tuscany	5.84	6.07	6.06	6.07	6.08	6.06	6.02	7.75
Umbria	6.64	6.64	6.63	6.63	6.64	6.60	6.63	9.20
Marche	5.79	5.74	5.67	5.83	5.21	5.83	5.70	8.88
Lazio	7.43	9.09	8.83	11.19	11.76	12.77	10.56	8.32
Abruzzo	15.10	12.65	12.49	12.66	12.30	10.40	12.69	14.84
Molise	7.59	7.52	7.39	7.55	7.57	7.33	7.54	11.03
Campania	7.56	7.54	7.55	7.60	7.59	7.53	7.57	10.80
Puglia	6.85	6.86	6.86	6.86	6.86	6.85	6.85	7.23
Basilicata	13.02	11.93	12.55	11.07	11.56	10.96	11.62	4.87
Calabria	8.05	8.12	8.08	7.91	7.61	8.05	7.91	9.96
Sicily	5.68	5.68	5.67	5.68	5.66	5.64	5.67	7.03
Sardinia	7.05	7.14	7.27	7.65	7.56	7.38	7.44	0.34
Italy	**6.35**	**6.74**	**6.86**	**7.46**	**7.59**	**8.34**	**7.17**	**7.10**
North	5.72	5.97	6.41	7.15	7.15	7.81	6.75	5.76
Centre	6.43	6.63	6.36	8.14	8.70	10.52	7.58	8.28
South and Islands	6.94	7.31	7.76	7.45	7.41	7.39	7.37	8.31

Note: consolidated data as of 23 April 2024, relating to medicines with MA

Table 2.3.7 Cost (euro) of the service per package, broken down by Region and by price range to the public of medicines supplied in "on behalf" distribution (DPC) (year 2023)

Region	Price range (€)						Cost of the service	
	<5	5-9	10-29	30-49	50-149	≥150	average	per capita
Piedmont	6.44	6.45	6.51	6.51	6.49	6.44	6.48	4.93
Valle d'Aosta	7.63	7.40	7.37	7.37	7.39	7.40	7.39	0.63
Lombardy	-	-	9.32	9.30	9.33	9.12	9.29	5.27
Province of Bolzano	-	8.08	8.07	8.08	8.09	8.07	8.08	4.46
Province of Trento	5.64	5.66	5.66	5.66	5.66	5.65	5.66	5.64
Veneto	0.09	4.06	6.97	6.99	7.00	7.00	6.98	7.46
Friuli VG	-	6.15	7.51	8.19	8.23	8.21	8.01	8.51
Liguria	4.93	5.47	5.48	5.49	5.50	5.50	5.49	7.51
Emilia R.	4.28	4.18	4.16	4.20	4.14	4.09	4.15	4.67
Tuscany	6.10	6.05	5.90	6.06	6.07	6.08	6.02	7.75
Umbria	6.66	6.65	6.63	6.61	6.64	6.64	6.63	9.20
Marche	5.94	5.81	5.73	5.73	5.75	5.38	5.70	8.88
Lazio	9.31	7.11	8.26	7.36	11.29	12.10	10.56	8.32
Abruzzo	17.13	22.98	12.53	12.50	12.69	12.06	12.69	14.84
Molise	7.59	7.74	7.53	7.55	7.55	7.38	7.54	11.03
Campania	7.32	7.81	7.54	7.55	7.60	7.57	7.57	10.80
Puglia	6.73	6.84	6.86	6.86	6.86	6.86	6.85	7.23
Basilicata	-	16.06	13.43	12.78	11.27	11.48	11.62	4.87
Calabria	8.04	8.13	8.09	8.09	8.10	7.30	7.91	9.96
Sicily	5.58	5.68	5.69	5.67	5.68	5.66	5.67	7.03
Sardinia	8.14	6.95	6.95	6.95	7.64	7.51	7.44	0.34
Italy	**7.57**	**6.31**	**6.48**	**6.41**	**7.45**	**7.64**	**7.17**	**7.10**
North	4.37	5.41	5.90	5.54	7.13	7.25	6.75	5.76
Centre	9.10	6.72	6.35	6.32	8.05	9.12	7.58	8.28
South and Islands	7.56	6.95	7.10	7.52	7.52	7.26	7.37	8.31

Note: consolidated data as of 23 April 2024, relating to medicines with MA

Table 2.3.8 Incidence (%) of the cost of the DPC service on the NHS price by price range in 2023

Region	Cost of the service	Price range (€)						Incidence of the cost of the service on purchase cost
		<5	5-9	10-29	30-49	50-149	≥150	
Piedmont	21,801,640	478.6	102.6	31.0	17.4	9.0	2.0	17.6
Valle d'Aosta	79,134	559.3	95.4	36.7	19.5	10.5	2.5	23.5
Lombardy	51,890,140	217.7	100.4	37.9	24.3	12.3	2.8	16.2
Province of Bolzano	2,202,985	368.7	113.7	38.4	21.4	10.7	3.1	18.9
Province of Trento	2,996,502	285.6	80.9	33.7	15.1	7.4	1.3	12.8
Veneto	36,320,170	456.8	104.5	33.8	18.6	9.6	2.7	18.8
Friuli VG	10,691,561	578.2	124.2	36.7	21.7	11.1	2.4	18.9
Liguria	12,290,611	355.2	83.9	35.0	14.7	7.7	2.5	19.1
Emilia R.	20,873,101	259.2	55.5	20.9	11.1	5.9	1.7	16.1
Tuscany	29,449,978	289.9	86.4	37.2	16.3	8.7	2.4	19.7
Umbria	8,207,988	477.1	93.5	37.7	17.7	9.2	2.2	21.2
Marche	13,558,952	247.1	77.4	31.8	15.4	6.8	2.2	17.6
Lazio	47,036,726	360.9	122.6	46.7	26.1	14.0	2.6	15.7
Abruzzo	19,229,830	477.7	154.1	60.5	32.6	15.7	3.1	26.0
Molise	3,322,643	507.9	115.8	36.9	19.9	10.3	2.4	17.1
Campania	56,198,021	434.9	97.7	35.8	20.5	10.3	1.8	18.6
Puglia	27,941,279	269.5	94.1	32.9	18.5	9.0	2.2	14.6
Basilicata	2,647,646	429.0	167.0	62.2	29.9	16.2	4.0	25.7
Calabria	18,004,232	369.6	113.0	40.2	21.0	10.8	2.1	17.6
Sicily	32,749,623	416.3	82.0	25.2	15.3	7.7	1.8	17.2
Sardinia	566,571	373.6	91.1	36.0	20.8	10.2	3.1	20.2
Italy	**418,059,332**	**367.8**	**92.9**	**34.6**	**19.6**	**10.2**	**2.4**	**17.6**
North	159,145,843	359.7	86.3	31.3	18.9	9.8	2.5	17.2
Centre	98,253,644	322.3	91.1	37.2	20.5	11.2	2.5	17.4
South and Islands	160,659,845	405.1	97.9	36.8	20.0	10.0	2.1	18.0

Table 2.3.9 Incidence (%) of the cost of the DPC service on the price to the public by price range in 2023

Region	Cost of the service	Price range (€)					
		<5	5-9	10-29	30-49	50-149	≥150
Piedmont	21,801,640	156.3	70.3	35.5	16.4	7.5	2.3
Valle d'Aosta	79,134	204.0	82.3	44.2	18.1	7.8	2.8
Lombardy	51,890,140			31.6	21.6	10.2	2.7
Province of Bolzano	2,202,985		109.9	31.6	20.4	9.4	3.4
Province of Trento	2,996,502	130.2	61.5	24.5	13.0	6.6	1.8
Veneto	36,320,170	2.7	55.5	38.5	18.2	7.8	2.8
Friuli VG	10,691,561		68.3	53.7	20.6	9.3	3.0
Liguria	12,290,611	403.8	59.3	28.7	12.8	6.2	2.4
Emilia R.	20,873,101	107.4	44.5	22.9	10.7	4.7	1.8
Tuscany	29,449,978	261.0	87.6	25.7	15.3	6.9	2.4
Umbria	8,207,988	173.0	74.0	35.7	14.7	7.2	2.6
Marche	13,558,952	207.6	63.8	31.0	13.9	6.3	2.1
Lazio	47,036,726	223.9	76.5	37.2	18.9	12.3	3.4
Abruzzo	19,229,830	492.0	306.1	53.2	31.4	14.4	4.0
Molise	3,322,643	189.1	84.1	42.4	19.6	8.5	2.3
Campania	56,198,021	436.4	98.9	38.9	20.1	8.8	2.3
Puglia	27,941,279	137.0	87.8	28.9	17.8	7.9	2.5
Basilicata	2,647,646		205.3	54.7	30.5	13.2	4.2
Calabria	18,004,232	610.1	87.6	36.3	19.9	9.5	2.6
Sicily	32,749,623	910.6	63.8	33.5	14.9	6.5	2.0
Sardinia	566,571	185.9	94.4	37.2	17.8	8.7	2.8
Italy	**418,059,332**	**186.8**	**70.0**	**33.3**	**16.2**	**8.4**	**2.6**
North	159,145,843	113.0	58.9	31.4	13.9	8.0	2.5
Centre	98,253,644	220.2	74.4	29.9	15.7	8.9	3.0
South and Islands	160,659,845	182.6	78.8	37.5	19.5	8.7	2.5

Table 2.3.10 Expenditure and consumption 2023 for medicines dispensed in direct distribution (DD) by ATC 1st level

(any ATC 1st level category includes the therapeutic subgroups in decreasing order of expenditure, up to tthe cumulative expenditure value of 90%)

ATC 1st level (ATC 4th level)	Per capita expenditure	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
Italy	**131.49**	**100.0**	**7.6**	**51.1**	**100.0**	**4.8**	**7.04**	**2.7**
Antineoplastic and immunomodulating agents	**66.56**	**100.0**	**2.3**	**6.9**	**100.0**	**9.8**	**26.57**	**-6.8**
Interleukin inhibitors	10.40	15.6	17.4	1.2	16.8	21.3	24.78	-3.2
Other kinase protein inhibitors	4.68	7.0	11.6	0.1	1.9	17.8	100.68	-5.2
Bruton tyrosine kinase (BTK) inhibitors	4.27	6.4	16.1	0.1	1.5	23.9	116.39	-6.3
Cyclin-dependent kinase inhibitors (CDK)	4.16	6.3	14.4	0.2	2.6	18.5	63.80	-3.4
Tumor necrosis factor alpha inhibitors (TNF-alpha)	4.14	6.2	-5.8	1.4	20.8	10.4	7.95	-14.7
Other immunosuppressants	4.13	6.2	-41.1	0.5	8.0	-1.7	20.70	-40.1
Antiandrogens	3.65	5.5	41.7	0.2	2.5	47.8	59.02	-4.1
Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors	2.94	4.4	3.0	0.1	1.0	9.2	122.65	-5.7
BCR-ABL tyrosine kinase inhibitors	2.60	3.9	-14.2	0.2	2.3	-0.5	46.13	-13.7
Janus-associated kinase (JAK) inhibitors	2.31	3.5	15.1	0.1	0.9	16.4	108.60	-1.2
Selective immunosuppressants	2.31	3.5	-4.5	0.5	6.9	11.2	13.31	-14.0
Sphingosine 1-phosphate (S1P) receptor modulators	2.28	3.4	-3.8	0.2	2.2	10.4	40.87	-12.8
Poly(ADP-ribose) polymerase (PARP) inhibitors	2.07	3.1	14.8	<0.05	0.6	17.9	137.23	-2.6
Monoclonal antibodies	1.88	2.8	41.8	0.1	1.7	13.7	43.89	24.7
Janus-associated kinase (JAK) inhibitors	1.59	2.4	17.2	0.2	3.3	4.2	19.13	12.4
Serine-threonine kinase B-RAF (BRAF) inhibitors	1.52	2.3	5.2	<0.05	0.5	4.5	114.75	0.7
Anaplastic lymphoma kinase inhibitors (ALK)	1.44	2.2	4.4	<0.05	0.4	12.7	135.93	-7.4
Other antineoplastics	1.30	2.0	31.6	0.1	0.8	19.9	65.56	9.7
Dihydroorotate dehydrogenase (DHODH) inhibitors	1.05	1.6	17.4	0.1	1.8	15.6	23.12	1.6
Interferons	0.91	1.4	-12.6	0.2	2.6	-16.9	14.33	5.2
PD-1/PDL-1 inhibitors	0.88	1.3	-15.6	0.4	5.6	>100	6.25	-85.4
General antimicrobials for systemic use	**14.27**	**100.0**	**3.1**	**3.0**	**100.0**	**1.0**	**13.12**	**2.1**
Antivirals for treatment of HIV infections, combinations	8.51	59.6	1.5	1.5	48.9	3.0	16.00	-1.5
Antivirals for treatment of HCV infections	1.32	9.3	-2.9	<0.05	1.4	0.4	88.46	-3.2
Human normal immunoglobulin	1.27	8.9	5.2	<0.05	0.5	13.9	252.44	-7.7

continued

Table 2.3.10 – *continued*

ATC 1st level (ATC 4th level)	Per capita expenditure	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
Integrase inhibitors	1.17	8.2	-1.0	0.3	9.0	-8.4	11.92	8.0
Other antivirals	0.50	3.5	99.4	<0.05	0.4	50.1	107.96	32.9
Triazole derivatives	0.26	1.8	8.6	<0.05	1.2	13.4	20.38	-4.2
Blood and blood forming organs	**12.31**	**100.0**	**5.7**	**6.8**	**100.0**	**-2.1**	**4.99**	**8.0**
Blood coagulation factors	5.35	43.4	-0.8	<0.05	0.6	-1.3	350.15	0.5
Other hemostatics for systemic use	3.25	26.4	14.4	0.1	1.6	9.0	83.85	4.9
Platelet aggregation inhibitors, excl. heparin	0.85	6.9	-6.9	1.3	19.2	1.0	1.79	-7.8
Other antianemic preparations	0.75	6.1	34.3	0.7	10.9	1.5	2.79	32.3
Medicines used in hereditary angioedema	0.66	5.3	23.4	<0.05	0.0	43.2	644.45	-13.8
Heparins	0.46	3.7	1.4	1.4	21.1	0.8	0.87	0.6
Respiratory system	**10.42**	**100.0**	**21.6**	**0.9**	**100.0**	**10.1**	**30.47**	**10.5**
Other preparations for the respiratory system	8.12	78.0	22.1	0.1	7.2	19.9	328.58	1.8
Other systemic medicines for obstructive airway disorders	2.00	19.2	24.1	0.2	21.9	29.5	26.70	-4.2
Mucolytics	0.19	1.8	-3.7	0.1	10.7	13.1	5.17	-14.9
Central nervous system	**6.76**	**100.0**	**27.0**	**10.0**	**100.0**	**2.6**	**1.85**	**23.8**
Other medicines for the nervous system	2.80	41.4	77.7	0.2	1.7	45.6	44.41	22.1
Other antipsychotics	1.45	21.4	-2.3	0.9	9.1	6.7	4.35	-8.4
Calcitonin gene-related peptide antagonists	0.54	8.0	21.0	0.3	2.8	22.4	5.26	-1.2
DOPA and derivatives	0.51	7.6	4.0	0.2	1.7	3.8	8.51	0.3
Other antiepileptics	0.36	5.3	56.3	0.3	2.7	15.3	3.63	35.6
Medicines used in opioid addiction	0.33	4.8	-18.1	1.5	15.3	-9.5	0.58	-9.6
Gastrointestinal system and metabolism	**6.55**	**100.0**	**11.4**	**7.6**	**100.0**	**5.5**	**2.35**	**5.6**
Enzymes	3.16	48.2	3.9	<0.05	0.1	15.2	907.38	-9.8
Various products for gastrointestinal system and metabolism	1.62	24.7	13.3	<0.05	0.5	13.1	110.98	0.2
Bile acids and derivatives	0.44	6.7	18.8	0.1	1.5	9.6	10.27	8.4
GLP-1 (glucagon-like peptide-1) receptor analogues	0.18	2.7	6.4	0.2	2.4	8.8	2.66	-2.2
SGLT2 cotransporter inhibitors (sodium-glucose type 2)	0.15	2.3	89.6	0.3	4.0	89.8	1.33	-0.1
Amino acids and derivatives	0.14	2.1	18.8	0.1	0.7	66.5	7.19	-28.7
Enzyme preparations	0.12	1.9	84.3	0.2	2.5	1.3	1.77	81.9
Other medicines for biliary therapy	0.12	1.8	>100	<0.05	0.0	>100	1,095.04	37.0

continued

Table 2.3.10 – *continued*

ATC 1st level (ATC 4th level)	Per capita expenditure	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
Cardiovascular system	**5.51**	**100.0**	**29.7**	**8.0**	**100.0**	**10.7**	**1.88**	**17.1**
Other lipid modifying agents	3.39	61.6	48.7	1.1	14.0	65.9	8.25	-10.4
Antihypertensives for pulmonary arterial hypertension	1.34	24.4	8.7	0.1	1.2	1.7	39.81	6.9
Angiotensin II receptor blockers (ARBs), other combinations	0.41	7.4	8.6	0.3	3.7	18.6	3.75	-8.5
Dermatological medicines	**3.48**	**100.0**	**36.1**	**2.8**	**100.0**	**5.8**	**3.42**	**28.6**
Substances for dermatitis, excluding corticosteroids	3.37	96.8	37.2	0.3	11.4	31.1	28.95	4.6
Musculo-skeletal system	**2.83**	**100.0**	**63.7**	**2.1**	**100.0**	**0.6**	**3.74**	**62.8**
Other medicines for musculoskeletal system disorders	1.76	62.2	50.9	<0.05	0.5	70.2	515.25	-11.3
Other medicines acting on bone structure and mineralisation	1.02	36.0	99.0	1.5	71.5	-1.6	1.89	102.3
Systemic hormonal preparations, excluding sex hormones and insulins	**1.50**	**100.0**	**-2.3**	**1.3**	**100.0**	**4.3**	**3.07**	**-6.3**
Somatostatin and analogues	0.44	29.1	-3.9	0.1	4.2	2.9	21.38	-6.6
Somatropin and somatropin agonists	0.32	21.6	-12.8	0.1	6.7	-3.9	9.91	-9.3
Other hormones of the anterior pituitary lobe and analogues	0.30	19.8	-3.3	<0.05	0.9	0.1	66.75	-3.3
Other antiparathyroid substances	0.18	11.9	4.7	0.1	7.0	6.0	5.25	-1.2
Glycocorticoids	0.16	10.7	5.6	0.8	58.3	2.3	0.56	3.3
Various	**0.72**	**100.0**	**-30.0**	**0.6**	**100.0**	**16.5**	**3.15**	**-39.9**
Iron chelating agents	0.35	49.4	-51.7	<0.05	6.3	-1.0	24.68	-51.2
Medicines for treatment of hyper-kalemia and hyperphosphatemia	0.20	28.1	80.0	0.1	19.3	28.8	4.58	39.7
Sensory organs	**0.32**	**100.0**	**-35.6**	**0.2**	**100.0**	**-26.6**	**4.19**	**-12.3**
Antineovascularisation substances	0.19	59.3	-44.8	<0.05	3.2	-58.7	78.39	33.6
Genito-urinary system and sex hormones	**0.24**	**100.0**	**12.1**	**0.9**	**100.0**	**15.8**	**0.75**	**-3.2**
Gonadotropins	0.14	56.1	12.5	<0.05	2.1	-0.6	20.42	13.2

Note: consolidated data as of 23 April 2024, relating to medicines with MA

Table 2.3.11 Expenditure and consumption 2023 for medicines dispensed in "on behalf" distribution (DPC) by ATC 1st level
(any ATC 1st level category includes the therapeutic subgroups in decreasing order of expenditure, up to tthe cumulative expenditure value of 90%)

ATC 1st level and subgroups (ATC 4th level)	Per capita expenditure	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
Italy	**42.36**	**100.0**	**4.6**	**70.7**	**100.0**	**7.6**	**1.64**	**-2.7**
Blood and blood forming organs	**14.98**	**100.0**	**3.6**	**28.4**	**100.0**	**3.4**	**1.44**	**0.2**
Direct Xa factor inhibitors	8.89	59.4	9.8	14.5	51.0	11.2	1.68	-1.2
Other antianemic preparations	1.49	9.9	-3.3	2.1	7.4	6.3	1.93	-9.0
Direct thrombin inhibitors	1.31	8.7	-8.2	2.2	7.6	-5.3	1.66	-3.0
Blood coagulation factors	1.13	7.6	-3.2	<0.05	0.0	-16.1	544.10	15.4
Platelet aggregation inhibitors, excl. heparin	1.02	6.8	-7.2	6.8	24.1	-6.5	0.41	-0.7
Gastrointestinal system and metabolism	**14.48**	**100.0**	**16.0**	**26.8**	**100.0**	**17.0**	**1.48**	**-0.8**
GLP-1 (glucagon-like peptide-1) receptor analogues	5.94	41.0	31.4	6.4	24.0	33.9	2.53	-1.9
Insulins and injectable analogues, long-acting	2.75	19.0	-1.6	5.9	22.0	-0.8	1.28	-0.8
SGLT2 cotransporter inhibitors (sodium-glucose type 2)	2.51	17.3	63.5	5.2	19.3	67.3	1.33	-2.3
Oral hypoglycemic agents, in combination	2.26	15.6	2.1	5.8	21.8	8.6	1.06	-6.0
Antineoplastic and immunomodulating agents	**4.58**	**100.0**	**-0.2**	**2.9**	**100.0**	**2.9**	**4.34**	**-3.0**
Gonadotropin-releasing hormone analogues	1.84	40.2	3.2	1.1	38.0	6.2	4.60	-2.8
Calcineurin inhibitors	0.58	12.8	1.5	0.2	8.5	5.1	6.52	-3.4
Mammalian target of rapamycin (mTOR) kinase inhibitors	0.49	10.7	8.1	0.1	4.0	7.7	11.55	0.4
Selective immunosuppressants	0.46	10.0	18.5	0.1	3.7	14.0	11.88	4.0
Interferons	0.37	8.1	-18.0	0.1	2.9	-17.7	12.06	-0.3
Colony stimulating factors	0.23	5.1	-7.7	0.1	2.2	8.7	10.03	-15.1
Dihydroorotate dehydrogenase (DHODH) inhibitors	0.18	4.0	6.4	0.1	5.2	8.0	3.36	-1.5
Systemic hormonal preparations, excluding sex hormones and insulins	**1.78**	**100.0**	**-14.4**	**0.4**	**100.0**	**-0.7**	**10.94**	**-13.9**
Somatostatin and analogues	0.87	49.0	-17.1	0.2	35.6	3.1	15.05	-19.6
Somatropin and somatropin agonists	0.75	42.2	-3.3	0.2	37.7	-2.2	12.25	-1.1
Cardiovascular system	**1.57**	**100.0**	**-33.8**	**2.0**	**100.0**	**-26.8**	**2.17**	**-9.6**
Angiotensin II receptor blockers (ARBs), other combinations	1.34	85.5	29.5	1.0	49.3	46.1	3.76	-11.4

continued

Table 2.3.11 - *continued*

ATC 1st level and subgroups (ATC 4th level)	Per capita expenditure	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
Central nervous system	**1.21**	**100.0**	**1.1**	**6.2**	**100.0**	**3.6**	**0.54**	**-2.4**
Other antiepileptics	0.34	28.0	2.9	0.7	10.7	14.9	1.40	-10.4
Diazepines, oxazepines, thiazepines and oxepins	0.24	19.7	-5.1	2.1	33.9	-3.4	0.31	-1.8
Other dopaminergic substances	0.16	13.0	15.2	0.1	1.9	17.0	3.66	-1.5
Other antipsychotics	0.14	11.7	5.2	1.3	20.7	8.6	0.30	-3.2
Indole derivatives	0.10	8.4	13.9	0.1	2.1	16.7	2.15	-2.4
Musculo-skeletal system	**1.14**	**100.0**	**19.8**	**3.1**	**100.0**	**19.1**	**1.02**	**0.6**
Other medicines acting on bone structure and mineralisation	1.14	100.0	19.8	3.1	100.0	19.1	1.02	0.6
Respiratory system	**0.93**	**100.0**	**19.3**	**0.1**	**100.0**	**-3.0**	**25.67**	**23.1**
Other systemic medicines for obstructive airway disorders	0.93	100.0	21.0	0.1	99.4	23.8	25.80	-2.3
Genito-urinary system and sex hormones	**0.89**	**100.0**	**6.0**	**0.3**	**100.0**	**3.5**	**7.61**	**2.4**
Gonadotropins	0.84	93.8	8.5	0.1	24.5	-16.4	29.11	29.8
Various	**0.37**	**100.0**	**-17.2**	**0.2**	**100.0**	**16.8**	**5.80**	**-29.1**
Iron chelating agents	0.19	50.1	-39.3	<0.05	6.5	0.1	44.78	-39.4
Medicines for treatment of hyper-kalemia and hyperphosphatemia	0.15	41.5	32.7	0.1	71.5	16.7	3.37	13.7
General antimicrobials for systemic use	**0.26**	**100.0**	**1.6**	**0.3**	**100.0**	**4.6**	**2.42**	**-3.0**
Dermatological medicines	**0.17**	**100.0**	**258.1**	**0.1**	**100.0**	**38.8**	**8.11**	**158.0**
Substances for dermatitis, excluding corticosteroids	0.16	91.1	>100	<0.05	32.4	>100	22.81	60.0

Note: consolidated data as of 23 April 2024, relating to medicines with MA

Table 2.3.12 Top 30 active ingredients in descending order of expenditure 2023 for medicines dispensed by direct distribution (DD)

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	% cum*
R	elexacaftor/tezacaftor/ ivacaftor	A	261.7	37.4	282.87	4.6	0.0	31.7	100.0	0.0	3.4
R	ivacaftor	A	204.9	20.6	410.70	0.7	0.0	20.0	100.0	0.0	6.0
L	ibrutinib	H	192.0	-3.4	112.31	-9.1	0.1	6.6	100.0	0.0	8.5
D	dupilumab	H	190.5	32.1	28.35	1.1	0.3	30.9	95.4	4.6	11.0
L	osimertinib	H	168.7	3.9	131.01	-8.9	0.1	14.3	100.0	0.0	13.2
J	emtricitabine/tenofovir alafenamide/ bictegravir	H	150.9	18.8	19.94	1.5	0.4	17.3	100.0	0.0	15.1
L	enzalutamide	H	146.1	21.0	67.86	-8.8	0.1	33.0	100.0	0.0	17.0
L	ustekinumab	H	131.5	14.6	15.11	-4.4	0.4	20.2	100.0	0.0	18.7
L	ruxolitinib	H	129.7	10.6	110.55	0.2	0.1	10.6	100.0	0.0	20.4
L	secukinumab	H	121.9	4.9	29.17	-0.7	0.2	5.9	100.0	0.0	21.9
N	tafamidis	H	119.2	>100	63.48	-5.6	0.1	>100	100.0	0.0	23.5
L	dimethyl fumarate	A	118.5	-14.3	25.46	-10.6	0.2	-3.9	93.5	6.5	25.0
L	nintedanib	H	115.6	26.3	85.56	-3.5	0.1	31.2	100.0	0.0	26.5
J	dolutegravir/ lamivudine	H	112.7	22.2	16.65	-8.2	0.3	33.4	100.0	0.0	28.0
B	emicizumab	A	101.0	13.6	710.57	-2.2	0.0	16.4	95.6	4.4	29.3
L	ribociclib	H	95.9	21.8	64.66	-0.6	0.1	22.8	100.0	0.0	30.5
C	evolocumab	A	91.9	33.5	11.16	-8.2	0.4	45.7	100.0	0.0	31.7
L	fingolimod	A	90.6	-23.7	45.42	-10.7	0.1	-14.4	99.1	0.9	32.9
L	palbociclib	H	85.6	-9.4	65.84	-0.2	0.1	-9.0	100.0	0.0	34.0
C	alirocumab	A	81.7	45.3	7.15	-9.7	0.5	61.3	100.0	0.0	35.0
L	ixekizumab	H	79.7	14.3	29.84	0.1	0.1	14.3	100.0	0.0	36.1
L	adalimumab	H	78.8	-9.9	4.69	-21.0	0.8	14.3	100.0	0.0	37.1
L	olaparib	H	72.4	15.2	130.32	-1.9	0.0	17.7	100.0	0.0	38.0
L	venetoclax	H	72.4	32.5	156.90	-1.3	0.0	34.5	100.0	0.0	39.0
J	human normal immunoglobulin for extravascular administration	H	71.0	5.6	268.12	-8.8	0.0	16.1	100.0	0.0	39.9
M	risdiplam	H	67.9	97.5	400.89	1.4	0.0	95.1	100.0	0.0	40.7
L	etanercept	H	65.3	-12.5	9.56	-15.2	0.3	3.5	100.0	0.0	41.6
L	dabrafenib	H	64.5	-4.4	104.95	-1.7	0.0	-2.5	100.0	0.0	42.4
L	alectinib	H	63.6	3.8	145.58	-9.1	0.0	14.4	100.0	0.0	43.2
L	abemaciclib	H	63.5	53.4	60.09	-11.9	0.0	74.6	100.0	0.0	44.1
	Total top 30		**3,409.9**	**14.8**	**32.78**	**-5.6**	**4.8**	**21.3**	**99.3**	**0.7**	**44.1**
	Total		**7,738.2**	**7.4**	**7.04**	**2.7**	**51.1**	**4.8**	**75.6**	**24.4**	**100.0**

Note: consolidated data as of 23 April 2024, relating to medicines with MA
* Calculated on overall expenditure

Table 2.3.13 Top 30 active ingredients in descending order of consumption 2023 for medicines dispensed by direct distribution (DD)

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	% cum*
A	cholecalciferol	A	0.4	6.3	0.01	-0.6	2.1	7.2	99.4	0.6	0.0
B	cyanocobalamin	A	0.2	6.3	0.01	-2.2	1.5	8.9	99.9	0.1	0.0
C	furosemide	A	0.5	5.7	0.02	2.6	1.5	3.2	99.8	0.2	0.0
M	denosumab	A	19.0	8.2	0.61	11.5	1.5	-2.7	22.3	77.7	0.3
B	enoxaparin	A	24.1	1.4	0.84	-0.8	1.3	2.5	34.3	65.7	0.6
N	methadone	H	11.9	-26.4	0.43	-15.8	1.3	-12.4	100.0	0.0	0.7
C	atorvastatin	A	0.0	52.1	0.00	50.6	1.0	1.2	95.8	4.2	0.7
C	ramipril	A	0.2	>100	0.01	>100	1.0	2.1	99.8	0.2	0.7
B	acetylsalicylic acid	A	0.3	-7.1	0.01	-9.5	0.9	2.9	99.9	0.1	0.7
L	adalimumab	H	78.8	-9.9	4.69	-21.0	0.8	14.3	100.0	0.0	1.8
A	pantoprazole	A	0.5	55.5	0.04	42.9	0.6	9.1	99.4	0.6	1.8
C	amlodipine	A	0.1	>100	0.00	>100	0.6	9.9	99.2	0.8	1.8
A	lansoprazole	A	1.1	3.4	0.08	13.7	0.6	-8.9	99.5	0.5	1.8
B	epoetin alfa	A	12.7	1.0	1.06	-4.2	0.6	5.7	23.6	76.4	1.9
N	diazepam	C	0.5	13.9	0.04	17.0	0.6	-2.4	99.9	0.1	1.9
C	alirocumab	A	81.7	45.3	7.15	-9.7	0.5	61.3	100.0	0.0	3.0
B	electrolytes for intravenous solutions	C	3.1	-4.1	0.27	3.4	0.5	-7.1	100.0	0.0	3.0
N	lorazepam	C	0.1	>100	0.01	>100	0.5	5.8	99.1	0.9	3.0
A	lactulose	C	0.8	22.2	0.08	8.9	0.5	12.4	99.9	0.1	3.1
N	sertraline	A	0.0	-66.0	0.00	-67.6	0.5	5.4	98.2	1.8	3.1
L	ustekinumab	H	131.5	14.6	15.11	-4.4	0.4	20.2	100.0	0.0	4.8
N	paliperidone	H	39.1	-15.4	4.60	-22.6	0.4	9.5	97.1	2.9	5.3
A	omeprazole	A	0.4	5.1	0.04	-10.2	0.4	17.3	99.5	0.5	5.3
C	evolocumab	A	91.9	33.5	11.16	-8.2	0.4	45.7	100.0	0.0	6.4
D	chlorhexidine/ethyl alcohol	C	0.0	6.0	0.01	-14.2	0.4	23.8	100.0	0.0	6.4
J	emtricitabine/ tenofovir alafenamide/ bictegravir	H	150.9	18.8	19.94	1.5	0.4	17.3	100.0	0.0	8.4
D	sodium hypochlorite	C	0.3	-0.4	0.04	3.5	0.3	-3.6	100.0	0.0	8.4
N	quetiapine	A	2.4	24.1	0.33	22.3	0.3	1.7	28.1	71.9	8.4
N	olanzapine	H	2.2	5.8	0.31	6.4	0.3	-0.3	52.0	48.0	8.5
L	mycophenolate	A	13.4	7.7	1.95	-6.5	0.3	15.5	64.6	35.4	8.6
	Total top 30		**654.8**	**12.4**	**1.41**	**7.4**	**21.5**	**4.3**	**80.1**	**19.9**	**8.6**
	Total		**7,738.2**	**7.4**	**7.04**	**2.7**	**51.1**	**4.8**	**75.6**	**24.4**	**100.0**

Note: consolidated data as of 23 April 2024, relating to medicines with MA
* Calculated on overall expenditure

Table 2.3.14 Top 30 active ingredients by average DDD cost 2023 for medicines dispensed by direct distribution (DD)

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	% cum*
L	tisagenlecleucel^	H	2.0	-74.1	488,805.43	>100	<0.05	-93.1	100.0	0.0	0.0
L	brexucabtagene autoleucel	H	7.0	29.4	316,800.00	0.0	<0.05	29.7	100.0	0.0	0.1
S	voretigene neparvovec	H	1.5	25.0	297,000.00	0.0	<0.05	25.3	100.0	0.0	0.1
M	onasemnogene abeparvovec^	H	7.1	1.5	269,541.21	>100	<0.05	-97.1	100.0	0.0	0.2
L	axicabtagene ciloleucel^	H	5.0	-21.3	238,557.01	91.2	<0.05	-58.7	100.0	0.0	0.3
B	catridecacog (coagulation factor XIII, recombinant)	H	0.8	0.0	15,524.20	0.0	<0.05	0.2	100.0	0.0	0.3
V	lutetium oxodotreotide (177Lu)	H	0.4	-83.3	14,325.39	-3.5	<0.05	-82.7	100.0	0.0	0.3
L	gemtuzumab ozogamicin	H	0.0	60.0	12,403.06	>100	<0.05	-38.3	100.0	0.5	0.3
B	prothrombin complex	A	3.1	11.1	8,502.02	0.5	<0.05	10.8	89.2	10.8	0.3
C	volanesorsen	H	3.8	84.1	8,352.91	2.0	<0.05	80.9	100.0	0.0	0.4
L	alemtuzumab	H	0.1	-31.3	5,686.59	0.0	<0.05	-31.1	100.0	0.0	0.4
B	coagulation factor XIII	H	0.1	22.5	5,489.13	0.0	<0.05	22.8	100.0	0.0	0.4
B	activated heptacog alfa (recombinant DNA coagulation factor VII)	H	5.1	-29.6	3,950.06	-2.6	<0.05	-27.6	100.0	0.0	0.5
L	citarabine/daunorubicine	H	0.3	-7.3	3,817.23	0.0	<0.05	-7.1	100.0	0.0	0.5
L	plerixafor	H	0.2	-6.2	3,610.81	-1.1	<0.05	-4.9	100.0	0.0	0.5
B	caplacizumab	H	15.4	9.4	3,450.37	1.7	<0.05	7.9	100.0	0.0	0.7
V	radium dichloride (223Ra)	H	0.1	-51.1	3,242.05	0.0	<0.05	-51.0	100.0	0.0	0.7
A	elosulfase alpha	H	10.4	-1.6	2,849.13	-4.5	<0.05	3.2	100.0	0.0	0.8
L	pertuzumab/trastuzumab	H	0.3	>100	2,724.86	1.4	<0.05	>100	100.0	0.0	0.8
A	galsulfase	H	3.3	1.4	2,639.72	-4.7	<0.05	6.6	100.0	0.0	0.9
J	adjuvanted recombinant varicella zoster virus vaccine	C	0.5	-61.5	2,569.34	90.1	<0.05	-79.7	100.0	0.0	0.9
A	asphotase alpha	C	2.5	69.4	2,473.15	-1.9	<0.05	73.0	100.0	0.0	0.9
A	idursulfase	H	19.2	-14.0	2,352.80	-16.9	<0.05	3.7	100.0	0.0	1.1
M	ataluren	H	21.2	5.9	1,740.17	1.2	<0.05	4.8	100.0	0.0	1.4
A	agalsidase alfa	H	33.3	-2.4	1,639.68	-2.6	<0.05	0.4	100.0	0.0	1.8

continued

Table 2.3.14 – *continued*

ATC	Active ingredient	Class	Expenditure (EUR million)	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	% cum*
L	blinatumomab	H	0.1	32.3	1,638.65	-0.7	<0.05	33.6	100.0	0.0	1.8
L	pegcetacoplan	H	1.7	-	1,630.66	-	<0.05	-	100.0	0.0	1.9
B	human fibrinogen	C	0.5	3.5	1,617.45	-9.8	<0.05	15.0	100.0	0.0	1.9
A	laronidase	H	4.5	-13.2	1,333.99	-7.0	<0.05	-6.5	100.0	0.0	1.9
J	bezlotoxumab	H	0.0	-71.1	1,311.62	1.2	<0.05	-71.4	100.0	0.0	1.9
	Total top 30		**149.6**	**-4.6**	**2,551.51**	**-6.8**	**<0,05**	**2.1**	**99.8**	**0.2**	**1.9**
	Total		**7,738.2**	**7.4**	**7.04**	**2.7**	**51.1**	**4.8**	**75.6**	**24.4**	**100.0**

Note: consolidated data as of 23 April 2024, relating to medicines with MA; *calculated on total expenditure; ^ the changes recorded in the average DDD cost in 2023 compared to 2022 are due to the change in the accounting methods for the expenditure of medicines that were subject to conditional reimbursement agreements, Payment at result, which provided for the distribution and attribution of fractions of the cost of treatment over time following verification of the maintenance of therapeutic success. Subsequently, the change provided for the revision of the contractual agreements and the accounting of the entire cost of the infusion treatment.

Table 2.3.15 Top 30 active ingredients of medicines dispensed in direct distribution (DD) by expenditure increase 2023-2022

ATC	Active ingredient	Class	Expenditure (EUR million)	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	% cum*
C	inclisiran	A	13.1	> 100	8.82	-0.3	0.07	>100	100.0	0.0	0.2
M	vosoritide	H	18.2	>100	310.70	16.6	<0.005	>100	100.0	0.0	0.4
L	ofatumumab	H	32.4	>100	1,254.63	0.5	<0.005	>100	100.0	0.0	0.8
L	ozanimod	A	17.2	>100	40.11	-0.5	0.02	>100	99.6	0.4	1.0
L	acalabrutinib	H	51.9	>100	134.05	2.2	0.02	>100	100.0	0.0	1.7
L	apalutamide	H	60.8	>100	59.18	-6.9	0.05	>100	100.0	0.0	2.5
B	luspatercept	A	24.1	>100	107.64	0.2	0.01	>100	100.0	0.0	2.8
N	tafamidis	H	119.2	>100	63.48	-5.6	0.09	>100	100.0	0.0	4.4
M	risdiplam	H	67.9	97.5	400.89	1.4	0.01	95.1	100.0	0.0	5.2
L	upadacitinib	H	28.9	69.4	19.40	-6.4	0.07	81.4	100.0	0.0	5.6
L	filgotinib	H	13.2	65.9	20.03	1.3	0.03	64.2	100.0	0.0	5.8
M	burosumab	H	19.6	58.3	152.58	-18.8	0.01	95.4	100.0	0.0	6.0
L	abemaciclib	H	63.5	53.4	60.09	-11.9	0.05	74.6	100.0	0.0	6.8

continued

Table 2.3.15 – *continued*

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	% cum*
L	daratumumab	H	49.3	52.2	82.71	-11.5	0.03	-37.0	100.0	0.0	7.5
L	siponimod	A	22.7	48.8	30.52	-0.1	0.03	49.3	99.7	0.3	7.8
N	fremanezumab	A	10.1	48.4	7.23	-4.7	0.06	56.1	100.0	0.0	7.9
L	encorafenib	H	22.8	47.7	158.19	-2.8	0.01	52.3	100.0	0.0	8.2
L	tildrakizumab	H	21.6	45.5	23.58	-4.8	0.04	53.1	100.0	0.0	8.5
C	alirocumab	A	81.7	45.3	7.15	-9.7	0.53	61.3	100.0	0.0	9.5
L	infliximab	H	13.1	43.9	4.99	19.6	0.12	20.6	100.0	0.0	9.7
N	cannabidiol	A	10.6	43.1	48.40	0.0	0.01	43.4	100.0	0.0	9.8
J	tenofovir disoproxil/ lamivudine/doravirine	H	17.1	41.6	14.43	-0.1	0.06	42.0	100.0	0.0	10.1
L	guselkumab	H	56.2	40.6	24.61	-4.7	0.11	47.8	100.0	0.0	10.8
B	lanadelumab	A	26.8	40.1	565.89	-1.4	<0.005	42.4	100.0	0.0	11.1
N	patisiran	H	31.4	39.5	514.01	0.6	<0.005	38.9	100.0	0.0	11.5
L	risankizumab	H	51.1	38.0	27.40	-3.3	0.09	43.0	100.0	0.0	12.2
R	elexacaftor/tezacaftor/ ivacaftor	A	261.7	37.4	282.87	4.6	0.04	31.7	100.0	0.0	15.6
B	pegylated turoctocog alfa	A	28.2	35.6	263.26	0.8	<0.005	34.8	81.8	18.2	15.9
R	mepolizumab	A	47.2	35.3	27.20	-9.6	0.08	50.1	74.4	25.6	16.6
C	evolocumab	A	91.9	33.5	11.16	-8.2	0.38	45.7	100.0	0.0	17.7
	Total top 30		**1,373.2**	**62.8**	**31.54**	**3.1**	**1.64**	**61.0**	**98.4**	**1.6**	**17.7**
	Total		**7,738.2**	**7.4**	**7.04**	**2.7**	**51.15**	**4.8**	**75.6**	**24.4**	**100.0**

Selected among the active ingredients with an expenditure of at least 10 million euro

Note: consolidated data as of 23 April 2024, relating to medicines with MA

* Calculated on overall expenditure

Table 2.3.16 Top 30 active ingredients of medicines dispensed in direct distribution (DD) by consumption increase 2023-2022

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	% cum*
C	inclisiran	A	13.1	>100	8.82	-0.3	0.07	>100	100.0	0.0	0.2
L	atezolizumab	H	6.0	>100	1.40	-98.5	0.20	>100	100.0	0.0	0.2
L	avelumab	H	5.8	>100	3.93	-81.9	0.07	>100	100.0	0.0	0.3
L	pembrolizumab	H	28.5	-26.3	12.55	-77.2	0.11	>100	100.0	0.0	0.7
N	bromazepam	C	0.3	>100	0.19	>100	0.07	>100	99.9	0.1	0.7
N	tafamidis	H	119.2	>100	63.48	-5.6	0.09	>100	100.0	0.0	2.2
A	dapagliflozin	A	5.3	87.0	1.20	-9.4	0.21	>100	6.4	93.6	2.3
A	empagliflozin	A	3.0	>100	1.68	26.4	0.08	99.8	5.2	94.8	2.3
L	upadacitinib	H	28.9	69.4	19.40	-6.4	0.07	81.4	100.0	0.0	2.7
C	alirocumab	A	81.7	45.3	7.15	-9.7	0.53	61.3	100.0	0.0	3.8
N	fremanezumab	A	10.1	48.4	7.23	-4.7	0.06	56.1	100.0	0.0	3.9
J	emtricitabine/tenofovir disoproxil	H	0.8	4.0	0.53	-31.0	0.07	51.1	100.0	0.0	3.9
R	mepolizumab	A	47.2	35.3	27.20	-9.6	0.08	50.1	74.4	25.6	4.5
N	galcanezumab	A	12.2	27.3	5.79	-14.9	0.10	49.9	100.0	0.0	4.7
L	guselkumab	H	56.2	40.6	24.61	-4.7	0.11	47.8	100.0	0.0	5.4
A	semaglutide	A	6.0	33.3	3.31	-9.1	0.08	47.0	3.5	96.5	5.5
C	evolocumab	A	91.9	33.5	11.16	-8.2	0.38	45.7	100.0	0.0	6.7
L	risankizumab	H	51.1	38.0	27.40	-3.3	0.09	43.0	100.0	0.0	7.3
J	tenofovir disoproxil/ lamivudine/doravirine	H	17.1	41.6	14.43	-0.1	0.06	42.0	100.0	0.0	7.5
C	ezetimibe	A	0.1	14.8	0.10	-14.9	0.07	35.2	99.2	0.8	7.6
J	dolutegravir/lamivudine	H	112.7	22.2	16.65	-8.2	0.32	33.4	100.0	0.0	9.0
L	enzalutamide	H	146.1	21.0	67.86	-8.8	0.10	33.0	100.0	0.0	10.9
L	nintedanib	H	115.6	26.3	85.56	-3.5	0.06	31.2	100.0	0.0	12.4
D	dupilumab	H	190.5	32.1	28.35	1.1	0.31	30.9	95.4	4.6	14.9
C	rosuvastatin	A	0.1	31.2	0.04	5.9	0.07	24.2	99.1	0.9	14.9
D	chlorhexidine/ethyl alcohol	C	0.0	6.0	0.01	-14.2	0.35	23.8	100.0	0.0	14.9

continued

Table 2.3.16 – *continued*

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	% cum*
M	ibuprofen	A	0.2	14.5	0.14	-6.9	0.08	23.3	99.9	0.1	14.9
R	benralizumab	A	31.2	23.0	28.85	0.3	0.05	22.9	67.7	32.3	15.3
L	ribociclib	H	95.9	21.8	64.66	-0.6	0.07	22.8	100.0	0.0	16.5
N	promazine	C	1.4	6.2	1.09	-13.3	0.06	22.8	99.9	0.1	16.5
	Total top 30		**1,278.0**	**34.7**	**14.71**	**-16.2**	**4.03**	**60.3**	**79.0**	**21.0**	**16.5**
	Total		**7,738.2**	**7.4**	**7.04**	**2.7**	**51.15**	**4.8**	**75.6**	**24.4**	**100.0**

Selected among the active substances having DDD/1000 inhab. per day ≥0.05
Note: consolidated data as of 23 April 2024, relating to medicines with MA
* Calculated on overall expenditure

Table 2.3.17 Top 30 active ingredients of medicines dispensed in direct distribution (DD) by expenditure reduction 2023-2022

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	% cum*
L	lenalidomide	H	29.3	-81.9	7.97	-84.3	0.17	15.6	100.0	0.0	0.4
L	abiraterone	H	25.8	-72.3	19.09	-71.4	0.06	-3.1	100.0	0.0	0.7
V	deferasirox	A	16.3	-57.3	36.05	-56.9	0.02	-0.6	61.4	38.6	0.9
L	imatinib	A	13.7	-41.0	7.27	-39.7	0.09	-1.9	77.9	22.1	1.1
L	pirfenidone	H	31.5	-40.4	13.08	-24.3	0.11	-21.1	100.0	0.0	1.5
L	everolimus	H	13.5	-38.7	44.60	-40.8	0.01	3.7	96.9	3.1	1.7
L	dasatinib	H	37.3	-27.2	70.76	-29.0	0.02	2.8	100.0	0.0	2.2
N	methadone	H	11.9	-26.4	0.43	-15.8	1.30	-12.4	100.0	0.0	2.3
L	pembrolizumab	H	28.5	-26.3	12.55	-77.2	0.11	223.9	100.0	0.0	2.7
J	dolutegravir/abacavir/ lamivudine	H	33.9	-26.3	19.77	-1.8	0.08	-24.7	100.0	0.0	3.1
B	moroctocog alfa	A	16.5	-24.5	329.97	-0.1	<0.005	-24.2	82.7	17.3	3.3

continued

Table 2.3.17 – *continued*

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	% cum*
B	octocog alfa	A	35.0	-23.8	322.81	-0.5	0.01	-23.2	70.9	29.1	3.8
L	fingolimod	A	90.6	-23.7	45.42	-10.7	0.09	-14.4	99.1	0.9	5.0
J	emtricitabine/ tenofovir alafenamide	H	18.9	-20.4	10.07	-0.4	0.09	-20.0	100.0	0.0	5.2
J	raltegravir	H	18.4	-20.4	7.82	9.2	0.11	-27.0	100.0	0.0	5.4
J	emtricitabine/rilpivirine/ tenofovir alafenamide	H	61.6	-19.6	17.34	-5.6	0.17	-14.6	100.0	0.0	6.2
L	interferon beta 1a	A	32.3	-18.1	11.05	1.5	0.14	-19.1	67.3	32.7	6.7
B	treprostinil	H	27.1	-17.0	416.46	-18.1	<0.005	1.7	100.0	0.0	7.0
L	interferon beta 1a pegylated	A	13.2	-16.6	27.19	-7.6	0.02	-9.4	74.0	26.0	7.2
N	paliperidone	H	39.1	-15.4	4.60	-22.6	0.40	9.5	97.1	2.9	7.7
L	dimethyl fumarate	A	118.5	-14.3	25.46	-10.6	0.22	-3.9	93.5	6.5	9.2
H	somatropin	A	18.7	-14.0	9.77	-10.1	0.09	-4.1	29.7	70.3	9.5
A	idursulfase	H	19.2	-14.0	2,352.80	-16.9	<0.005	3.7	100.0		9.7
L	tacrolimus	A	11.6	-13.8	4.80	-1.2	0.11	-12.6	25.7	74.3	9.9
L	abatacept	H	54.9	-13.5	39.08	-19.9	0.07	8.2	100.0	0.0	10.6
J	darunavir/cobicistat	H	18.0	-12.9	11.43	-0.9	0.07	-11.9	100.0	0.0	10.8
L	etanercept	H	65.3	-12.5	9.56	-15.2	0.32	3.5	100.0	0.0	11.6
L	baricitinib	H	32.8	-10.8	20.36	23.5	0.07	-27.6	100.0	0.0	12.1
L	natalizumab	H	17.0	-10.0	48.56	-4.6	0.02	-5.5	100.0	0.0	12.3
L	adalimumab	H	78.8	-9.9	4.69	-21.0	0.78	14.3	100.0	0.0	13.3
	Total top 30		**1,029.1**	**-30.7**	**10.10**	**-27.5**	**4.73**	**-4.7**	**88.0**	**12.0**	**13.3**
	Total		**7,738.2**	**7.4**	**7.04**	**2.7**	**51.15**	**4.8**	**75.6**	**24.4**	**100.0**

Selected among the active ingredients with an expenditure of at least 10 million euro
Note: consolidated data as of 23 April 2024, relating to medicines with MA
* Calculated on overall expenditure

Table 2.3.18 Top 30 active ingredients of medicines dispensed in direct distribution (DD) by consumption reduction 2023-2022

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	% cum*
B	hydroxocobalamin	A	0.1	-40.6	0.02	87.3	0.13	-68.2	99.7	0.3	0.0
L	baricitinib	H	32.8	-10.8	20.36	23.5	0.07	-27.6	100.0	0.0	0.4
J	raltegravir	H	18.4	-20.4	7.82	9.2	0.11	-27.0	100.0	0.0	0.7
J	dolutegravir/abacavir/ lamivudine	H	33.9	-26.3	19.77	-1.8	0.08	-24.7	100.0	0.0	1.1
L	pirfenidone	H	31.5	-40.4	13.08	-24.3	0.11	-21.1	100.0	0.0	1.5
J	emtricitabine/ tenofovir alafenamide	H	18.9	-20.4	10.07	-0.4	0.09	-20.0	100.0	0.0	1.8
D	benzalkonium chloride/ethyl alcohol	C	0.0	4.4	0.03	30.1	0.07	-19.6	100.0	0.0	1.8
L	interferon beta 1a	A	32.3	-18.1	11.05	1.5	0.14	-19.1	67.3	32.7	2.2
B	nadroparin	A	1.5	-8.8	1.22	13.0	0.06	-19.1	43.7	56.3	2.2
B	warfarin	A	0.1	25.3	0.08	51.3	0.06	-17.0	100.0	0.0	2.2
L	glatiramer	A	6.9	-25.2	6.28	-10.9	0.05	-15.9	80.5	19.5	2.3
B	glucose	C	0.4	-12.4	0.30	3.3	0.06	-15.0	100.0	0.0	2.3
J	emtricitabine/rilpivirine/ tenofovir alafenamide	H	61.6	-19.6	17.34	-5.6	0.17	-14.6	100.0	0.0	3.1
L	fingolimod	A	90.6	-23.7	45.42	-10.7	0.09	-14.4	99.1	0.9	4.3
D	chlorhexidine	C	0.0	5.1	0.00	22.7	0.25	-14.1	100.0		4.3
B	epoetin zeta	A	2.8	-17.2	1.05	-3.5	0.13	-14.0	20.3	79.7	4.3
J	emtricitabine/ tenofovir alafenamide/ darunavir/cobicistat	H	42.1	-7.8	20.02	6.6	0.10	-13.3	100.0	0.0	4.8
L	tacrolimus	A	11.6	-13.8	4.80	-1.2	0.11	-12.6	25.7	74.3	5.0
N	methadone	H	11.9	-26.4	0.43	-15.8	1.30	-12.4	100.0	0.0	5.1
J	darunavir/cobicistat	H	18.0	-12.9	11.43	-0.9	0.07	-11.9	100.0	0.0	5.4
J	lamivudine	A	0.4	-11.7	0.33	-1.8	0.06	-9.9	59.6	40.4	5.4
A	insulin glargine	A	3.2	-10.3	0.88	-0.3	0.17	-9.8	4.0	96.0	5.4
C	enalapril	A	0.0	-14.4	0.01	-5.5	0.07	-9.3	99.8	0.2	5.4
L	palbociclib	H	85.6	-9.4	65.84	-0.2	0.06	-9.0	100.0	0.0	6.5

continued

Table 2.3.18 – *continued*

ATC	Active ingredient	Class	Expenditure (EUR million)	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	% cum*
L	tofacitinib	H	18.9	2.6	16.51	12.9	0.05	-9.0	100.0	0.0	6.8
A	dulaglutide	A	3.8	-14.3	2.06	-5.7	0.09	-8.9	2.3	97.7	6.8
A	lansoprazole	A	1.1	3.4	0.08	13.7	0.61	-8.9	99.5	0.5	6.8
C	ezetimibe/simvastatin	A	0.3	>100	0.24	>100	0.06	-8.2	100.0	0.0	6.8
J	dolutegravir	H	43.4	-5.9	15.41	1.7	0.13	-7.3	100.0	0.0	7.4
B	electrolytes for intravenous solutions	C	3.1	-4.1	0.27	3.4	0.52	-7.1	100.0	0.0	7.4
	Total top 30		**575.1**	**-17.8**	**5.29**	**-1.2**	**5.05**	**-17.1**	**65.4**	**34.6**	**7.4**
	Total		**7,738.2**	**7.4**	**7.04**	**2.7**	**51.15**	**4.8**	**75.6**	**24.4**	**100.0**

Selected among the active substances having DDD/1000 inhab. per day ≥0.05
Note: consolidated data as of 23 April 2024, relating to medicines with MA
* Calculated on overall expenditure

Table 2.3.19 Top 30 active ingredients in descending order of expenditure 2023 for medicines dispensed in "on behalf" distribution (DPC)

ATC	Active ingredient	Class	Expenditure (EUR million)	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	Inc. cum %*
B	apixaban	A	198.4	9.3	1.70	-1.8	5.42	11.5	3.0	97.0	8.0
B	rivaroxaban	A	185.3	3.6	1.59	-0.2	5.41	4.0	3.1	96.9	15.4
A	semaglutide	A	165.7	86.9	3.19	-3.4	2.42	93.9	3.5	96.5	22.0
A	dulaglutide	A	162.7	8.8	2.11	-8.0	3.58	18.6	2.3	97.7	28.6
B	edoxaban	A	139.4	19.0	1.77	-2.9	3.67	22.9	2.8	97.2	34.2
C	valsartan/sacubitril	A	78.8	29.2	3.76	-11.4	0.98	46.1	23.3	76.7	37.3
A	dapagliflozin	A	78.4	75.5	1.24	-4.7	2.95	84.5	6.4	93.6	40.5
B	dabigatran	A	76.9	-8.4	1.66	-3.0	2.15	-5.3	1.9	98.1	43.5
A	insulin glargine	A	76.3	-5.3	0.92	-1.9	3.86	-3.2	4.0	96.0	46.6
M	denosumab	A	66.1	17.5	1.00	-1.0	3.07	19.0	22.3	77.7	49.3
A	empagliflozin	A	54.8	64.6	1.49	4.0	1.72	58.6	5.2	94.8	51.5
L	triptorelin	A	54.3	5.3	2.74	-0.6	0.92	6.1	7.4	92.6	53.6

continued

Table 2.3.19 – *continued*

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	Inc. cum %*
L	leuprorelin	A	53.3	0.8	14.96	-5.6	0.17	7.0	8.9	91.1	55.8
B	ticagrelor	A	48.5	-3.5	2.32	-3.4	0.97	0.1	3.9	96.1	57.7
A	insulin degludec/li-raglutide	A	47.5	20.5	3.63	-9.0	0.61	32.6	2.8	97.2	59.6
B	enoxaparin	A	46.2	-1.0	0.88	-3.3	2.45	2.6	34.3	65.7	61.5
H	somatropin	A	44.2	-3.6	12.25	-1.1	0.17	-2.2	29.7	70.3	63.2
B	epoetin alfa	A	41.2	-0.6	1.35	-12.2	1.42	13.4	23.6	76.4	64.9
A	dapagliflozin/met-formin	A	35.0	17.3	1.23	-5.3	1.33	24.1	1.2	98.8	66.3
A	linagliptin	A	34.6	6.3	1.16	-3.3	1.39	10.2	2.7	97.3	67.7
L	tacrolimus	A	33.5	1.4	6.63	-3.8	0.24	5.7	25.7	74.3	69.0
B	darbepoetin alfa	A	33.0	-4.2	6.12	-2.5	0.25	-1.6	11.1	88.9	70.4
A	insulin degludec	A	30.0	-19.3	1.15	-15.8	1.22	-3.9	2.6	97.4	71.6
L	everolimus	A	26.9	8.5	11.56	0.6	0.11	8.1	23.3	76.7	72.6
H	octreotide	A	26.8	1.0	19.06	0.6	0.07	0.7	28.8	71.2	73.7
A	empagliflozin/met-formin	A	26.2	28.2	1.20	-0.4	1.02	29.1	1.5	98.5	74.8
H	lanreotide	A	23.5	-31.2	11.80	-34.4	0.09	5.2	22.0	78.0	75.7
R	omalizumab	A	23.5	7.6	26.35	-2.6	0.04	10.7	62.6	37.4	76.7
A	linagliptin/empagli-flozin	A	21.4	66.9	1.44	-0.1	0.69	67.4	2.3	97.7	77.5
L	apremilast	A	19.6	27.5	23.58	1.0	0.04	26.6	51.8	48.2	78.3
	Total top 30		**1,951.9**	**13.1**	**1.66**	**-14.4**	**48.27**	**16.4**	**88.4**	**11.6**	**78.3**
	Total		**2,492.9**	**4.4**	**1.64**	**-2.7**	**70.66**	**7.6**	**24.4**	**75.6**	**100.0**

Note: consolidated data as of 23 April 2024, relating to medicines with MA
* Calculated on overall expenditure

Table 2.3.20 Top 30 active ingredients in descending order of consumption 2023 for medicines dispensed in "on behalf" distribution (DPC)

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	Inc. cum %*
B	apixaban	A	198.4	9.3	1.70	-1.8	5.42	11.5	3.0	97.0	8.0
B	rivaroxaban	A	185.3	3.6	1.59	-0.2	5.41	4.0	3.1	96.9	15.4
B	clopidogrel	A	4.7	-13.5	0.05	-7.8	4.62	-6.0	4.3	95.7	15.6
A	insulin glargine	A	76.3	-5.3	0.92	-1.9	3.86	-3.2	4.0	96.0	18.6
B	edoxaban	A	139.4	19.0	1.77	-2.9	3.67	22.9	2.8	97.2	24.2
A	dulaglutide	A	162.7	8.8	2.11	-8.0	3.58	18.6	2.3	97.7	30.8
M	denosumab	A	66.1	17.5	1.00	-1.0	3.07	19.0	22.3	77.7	33.4
A	dapagliflozin	A	78.4	75.5	1.24	-4.7	2.95	84.5	6.4	93.6	36.6
B	enoxaparin	A	46.2	-1.0	0.88	-3.3	2.45	2.6	34.3	65.7	38.4
A	semaglutide	A	165.7	86.9	3.19	-3.4	2.42	93.9	3.5	96.5	45.1
B	dabigatran	A	76.9	-8.4	1.66	-3.0	2.15	-5.3	1.9	98.1	48.1
A	empagliflozin	A	54.8	64.6	1.49	4.0	1.72	58.6	5.2	94.8	50.3
B	epoetin alfa	A	41.2	-0.6	1.35	-12.2	1.42	13.4	23.6	76.4	52.0
A	linagliptin	A	34.6	6.3	1.16	-3.3	1.39	10.2	2.7	97.3	53.4
A	dapagliflozin/metformin	A	35.0	17.3	1.23	-5.3	1.33	24.1	1.2	98.8	54.8
A	insulin degludec	A	30.0	-19.3	1.15	-15.8	1.22	-3.9	2.6	97.4	56.0
B	clopidogrel/acetylsalicylic acid	A	6.1	-19.5	0.25	-8.3	1.14	-12.0	0.8	99.2	56.2
A	sitagliptin/metformin	A	18.0	-37.5	0.75	-27.9	1.11	-13.1	1.4	98.6	56.9
N	olanzapine	A	2.1	12.5	0.09	16.3	1.02	-3.1	52.0	48.0	57.0
A	empagliflozin/metformin	A	26.2	28.2	1.20	-0.4	1.02	29.1	1.5	98.5	58.1
C	valsartan/sacubitril	A	78.8	29.2	3.76	-11.4	0.98	46.1	23.3	76.7	61.2
B	ticagrelor	A	48.5	-3.5	2.32	-3.4	0.97	0.1	3.9	96.1	63.2
A	sitagliptin	A	7.5	-76.1	0.36	-68.0	0.97	-25.2	5.0	95.0	63.5
L	triptorelin	A	54.3	5.3	2.74	-0.6	0.92	6.1	7.4	92.6	65.7
N	quetiapine	A	6.0	-4.8	0.31	-0.2	0.91	-4.4	28.1	71.9	65.9
C	ivabradine	A	2.3	-12.6	0.14	-7.0	0.77	-5.8	4.8	95.2	66.0
N	memantine	A	2.0	-10.8	0.13	-23.0	0.73	16.2	6.2	93.8	66.1
A	linagliptin/empagliflozin	A	21.4	66.9	1.44	-0.1	0.69	67.4	2.3	97.7	66.9

continued

Table 2.3.20 – *continued*

ATC	Active ingredient	Class	Expenditure (EUR million)	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	Inc. cum %*
N	aripiprazole	A	3.4	0.4	0.25	-9.4	0.64	11.1	91.7	8.3	67.1
A	insulin degludec/liraglutide	A	47.5	20.5	3.63	-9.0	0.61	32.6	2.8	97.2	69.0
	Total top 30		**1,719.5**	**12.62**	**1.35**	**1.2**	**58.98**	**10.9**	**9.1**	**90.9**	**69.0**
	Total		**2,492.9**	**4.39**	**1.64**	**-2.7**	**70.66**	**7.6**	**24.4**	**75.6**	**100.0**

Note: consolidated data as of 23 April 2024, relating to medicines with MA
* Calculated on overall expenditure

Table 2.3.21 Top 30 active ingredients by average DDD cost 2023 for medicines dispensed in "on behalf" distribution (DPC)

ATC	Active ingredient	Class	Expenditure (EUR million)	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	Inc. cum %*
B	prothrombin complex	A	0.4	>100	7,277.83	-57.5	<0.005	28.8	89.2	10.8	0.0
B	C1-inhibitor, plasma-derived	A	3.8	-6.0	2,055.36	-6.1	<0.005	0.0	71.5	28.5	0.2
B	nonacog beta pegol	A	0.3	0.0	1,337.32	0.0	<0.005	0.0	94.0	6.0	0.2
B	albutrepenonacog alpha	A	6.1	7.5	1,326.93	1.8	<0.005	0.1	87.8	12.2	0.4
B	eftrenonacog alpha	A	1.4	-6.9	1,098.28	10.3	<0.005	-0.2	91.9	8.1	0.5
B	emicizumab	A	4.7	>100	1,064.82	-20.1	<0.005	17.5	95.6	4.4	0.7
B	nonacog alfa	A	1.7	-14.9	637.85	20.9	<0.005	-0.3	82.6	17.4	0.7
B	freeze-dried human blood coagulation factor VII	A	1.1	-7.5	591.09	17.9	<0.005	-21.3	56.3	43.7	0.8
B	damoctocog alfa pegol	A	7.5	35.2	568.10	9.4	<0.005	23.8	82.9	17.1	1.1
B	efmorocotog alfa	A	9.3	-8.0	551.72	10.3	<0.005	-16.4	84.1	15.9	1.5
B	rurioctocog alfa pegol	A	6.3	23.1	532.40	11.1	<0.005	11.1	70.5	29.5	1.7
B	octocog alfa	A	14.4	-25.2	515.90	15.4	<0.005	-35.0	70.9	29.1	2.3
B	lonoctogoc alfa	A	3.9	-1.6	510.93	6.0	<0.005	-7.0	80.6	19.4	2.4
B	turoctocog alfa	A	0.7	-49.8	510.22	26.0	<0.005	-60.0	91.3	8.7	2.5
G	corifollitropin alfa	A	1.1	9.3	493.09	0.2	<0.005	9.3	12.7	87.3	2.5

continued

Table 2.3.21 – *continued*

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	Inc. cum %*
B	moroctocog alfa	A	3.5	-21.0	487.99	7.4	<0.005	-26.3	82,7	17.3	2.6
B	pegylated turoctocog alfa	A	6.2	27.5	445.04	15.7	<0.005	10.5	81,8	18.2	2.9
B	simoctocog alfa	A	0.4	20.3	417.84	-6.7	<0.005	29.3	95,9	4.1	2.9
B	factor VIII/von Willebrand's factor	A	3.5	-1.6	395.67	23.4	<0.005	-20.1	77,6	22.4	3.1
G	follitropin alfa/lutropin alfa	A	17.9	96.8	365.96	15.3	<0.005	71.1	14,0	86.0	3.8
B	Iloprost	A	0.2	-60.5	193.22	0.0	<0.005	-60.4	79,7	20.3	3.8
J	human immunoglobulin antihepatitis B	A	5.0	-7.6	148.55	-1.3	<0.005	-6.2	34,3	65.7	4.0
J	tedizolid	A	0.0	42.9	120.02	-9.1	<0.005	57.5	91,7	8.3	4.0
H	pasireotide	A	1.0	-24.4	91.07	9.0	<0.005	-30.5	89,0	11.0	4.0
L	lenograstim	A	0.5	-50.3	88.61	-0.9	<0.005	-49.7	24,5	75.5	4.0
C	macitentan	A	1.5	-7.9	87.71	0.0	<0.005	-7.7	97,4	2.6	4.1
G	follitropin beta	A	1.8	37.4	81.61	1.1	<0.005	36.2	10,9	89.1	4.2
L	bexarotene	A	0.1	-30.8	78.63	0.0	<0.005	-30.6	93,7	6.3	4.2
J	isavuconazolo	A	0.9	-0.2	76.34	-0.3	<0.005	0.3	91,9	8.1	4.2
L	everolimus	A	0.4	1.2	75.54	-0.9	<0.005	2.3	96,9	3.1	4.2
	Total top 30		**105.5**	**9.9**	**367.68**	**12.8**	**0.01**	**-2.9**	**82,9**	**17.1**	**4.2**
	Total		**2,492.9**	**4.4**	**1.64**	**-2.7**	**70.66**	**7.6**	**24,4**	**75.6**	**100.0**

Note: consolidated data as of 23 April 2024, relating to medicines with MA

* Calculated on overall expenditure

Table 2.3.22 Top 30 active ingredients of medicines dispensed in "on behalf" distribution (DPC) by expenditure increase 2023-2022

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	Inc. cum %*
G	follitropin alfa/lutropin alfa	A	17.9	96.8	365.96	15.3	<0.005	71.1	14.0	86.0	0.7
A	semaglutide	A	165.7	86.9	3.19	-3.4	2.42	93.9	3.5	96.5	7.4
A	dapagliflozin	A	78.4	75.5	1.24	-4.7	2.95	84.5	6.4	93.6	10.5
A	linagliptin/empagliflozin	A	21.4	66.9	1.44	-0.1	0.69	67.4	2.3	97.7	11.4
A	empagliflozin	A	54.8	64.6	1.49	4.0	1.72	58.6	5.2	94.8	13.6
R	benralizumab	A	14.9	35.1	29.03	0.0	0.02	35.4	67.7	32.3	14.2
R	mepolizumab	A	16.2	31.7	26.09	-14.0	0.03	53.5	74.4	25.6	14.8
C	valsartan/sacubitril	A	78.8	29.2	3.76	-11.4	0.98	46.1	23.3	76.7	18.0
A	empagliflozin/metformin	A	26.2	28.2	1.20	-0.4	1.02	29.1	1.5	98.5	19.0
L	apremilast	A	19.6	27.5	23.58	1.0	0.04	26.6	51.8	48.2	19.8
A	insulin degludec/liraglutide	A	47.5	20.5	3.63	-9.0	0.61	32.6	2.8	97.2	21.7
B	edoxaban	A	139.4	19.0	1.77	-2.9	3.67	22.9	2.8	97.2	27.3
M	denosumab	A	66.1	17.5	1.00	-1.0	3.07	19.0	22.3	77.7	30.0
A	dapagliflozin/metformin	A	35.0	17.3	1.23	-5.3	1.33	24.1	1.2	98.8	31.4
B	apixaban	A	198.4	9.3	1.70	-1.8	5.42	11.5	3.0	97.0	39.3
A	dulaglutide	A	162.7	8.8	2.11	-8.0	3.58	18.6	2.3	97.7	45.9
L	everolimus	A	26.9	8.5	11.56	0.6	0.11	8.1	23.3	76.7	46.9
L	teriflunomide	A	10.3	7.7	25.56	-3.5	0.02	11.9	85.7	14.3	47.3
R	omalizumab	A	23.5	7.6	26.35	-2.6	0.04	10.7	62.6	37.4	48.3
A	linagliptin	A	34.6	6.3	1.16	-3.3	1.39	10.2	2.7	97.3	49.7
L	triptorelin	A	54.3	5.3	2.74	-0.6	0.92	6.1	7.4	92.6	51.9
B	rivaroxaban	A	185.3	3.6	1.59	-0.2	5.41	4.0	3.1	96.9	59.3
L	tacrolimus	A	33.5	1.4	6.63	-3.8	0.24	5.7	25.7	74.3	60.6
H	octreotide	A	26.8	1.0	19.06	0.6	0.07	0.7	28.8	71.2	61.7
L	leuprorelin	A	53.3	0.8	14.96	-5.6	0.17	7.0	8.9	91.1	63.8
B	epoetin alfa	A	41.2	-0.6	1.35	-12.2	1.42	13.4	23.6	76.4	65.5

continued

Table 2.3.22 – *continued*

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	Inc. cum %*
B	enoxaparin	A	46.2	-1.0	0.88	-3.3	2.45	2.6	34.3	65.7	67.3
G	follitropin alfa from recombinant DNA	A	15.4	-3.2	17.56	-9.3	0.04	7.0	13.4	86.6	68.0
B	ticagrelor	A	48.5	-3.5	2.32	-3.4	0.97	0.1	3.9	96.1	69.9
H	somatropin	A	44.2	-3.6	12.25	-1.1	0.17	-2.2	29.7	70.3	71.7
	Total top 30		**1,787.0**	**18.0**	**2.03**	**-3.0**	**40.83**	**21.3**	**17.7**	**82.3**	**71.7**
	Total		**2,492.9**	**4.4**	**1.64**	**-2.7**	**70.66**	**7.6**	**24.4**	**75.6**	**100.0**

Selected among the active ingredients with an expenditure of at least 10 million euro
Note: consolidated data as of 23 April 2024, relating to medicines with MA
* Calculated on overall expenditure

Table 2.3.23 Top 30 active ingredients of medicines dispensed in "on behalf" distribution (DPC) by consumption increase 2023-2022

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	Inc. cum %*
A	semaglutide	A	165.7	86.9	3.19	-3.4	2.42	93.9	3.5	96.5	6.6
A	dapagliflozin	A	78.4	75.5	1.24	-4.7	2.95	84.5	6.4	93.6	9.8
A	linagliptin/empagliflozin	A	21.4	66.9	1.44	-0.1	0.69	67.4	2.3	97.7	10.6
A	empagliflozin	A	54.8	64.6	1.49	4.0	1.72	58.6	5.2	94.8	12.8
A	empagliflozin/metformin	A	1.5	46.9	1.13	0.2	0.06	46.9	2.3	97.7	12.9
C	valsartan/sacubitril	A	78.8	29.2	3.76	-11.4	0.98	46.1	23.3	76.7	16.1
A	insulin degludec/liraglutide	A	47.5	20.5	3.63	-9.0	0.61	32.6	2.8	97.2	18.0
A	insulin glargine/lixisenatide	A	5.5	29.8	3.54	0.2	0.07	29.8	1.0	99.0	18.2
A	empagliflozin/metformin	A	26.2	28.2	1.20	-0.4	1.02	29.1	1.5	98.5	19.2
A	ertugliflozin	A	5.2	20.0	1.41	-5.3	0.17	27.0	2.7	97.3	19.5
A	dapagliflozin/metformin	A	35.0	17.3	1.23	-5.3	1.33	24.1	1.2	98.8	20.9
B	edoxaban	A	139.4	19.0	1.77	-2.9	3.67	22.9	2.8	97.2	26.5
A	canagliflozin	A	9.3	13.0	1.37	-5.4	0.32	19.7	3.0	97.0	26.8

continued

Table 2.3.23 – *continued*

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	Inc. cum %*
M	denosumab	A	66.1	17.5	1.00	-1.0	3.07	19.0	22.3	77.7	29.5
N	brivaracetam	A	4.2	15.9	2.28	-2.1	0.09	18.7	14.1	85.9	29.6
A	dulaglutide	A	162.7	8.8	2.11	-8.0	3.58	18.6	2.3	97.7	36.2
N	opicapone	A	8.7	16.9	3.61	-1.2	0.11	18.6	10.5	89.5	36.5
N	levetiracetam	A	4.9	14.2	0.80	-3.4	0.28	18.5	24.5	75.5	36.7
N	lurasidone	A	6.0	14.6	2.15	-2.5	0.13	17.8	13.2	86.8	37.0
L	letrozole	A	1.1	94.9	0.23	67.0	0.21	17.0	13.4	86.6	37.0
N	memantine	A	2.0	-10.8	0.13	-23.0	0.73	16.2	6.2	93.8	37.1
G	tadalafil	A	0.6	-47.9	0.17	-54.8	0.15	15.3	54.4	45.6	37.1
A	rifaximin	A	6.7	14.6	2.83	0.3	0.11	14.5	35.0	65.0	37.4
N	lacosamide	A	1.8	-58.2	1.23	-63.2	0.07	14.0	30.7	69.3	37.4
B	epoetin alfa	A	41.2	-0.6	1.35	-12.2	1.42	13.4	23.6	76.4	39.1
G	testosterone	A	1.4	-12.5	0.99	-22.1	0.07	12.7	63.8	36.2	39.1
B	apixaban	A	198.4	9.3	1.70	-1.8	5.42	11.5	3.0	97.0	47.1
N	perampanel	A	6.4	11.0	4.79	0.0	0.06	11.3	6.9	93.1	47.4
N	aripiprazole	A	3.4	0.4	0.25	-9.4	0.64	11.1	91.7	8.3	47.5
L	anastrozole	A	0.6	>100	0.20	163.7	0.15	10.2	8.4	91.6	47.5
	Total top 30		**1,184.7**	**26.1**	**1.71**	**-2.3**	**32.20**	**28.7**	**10.4**	**89.6**	**47.5**
	Total		**2,492.9**	**4.4**	**1.64**	**-2.7**	**70.66**	**7.6**	**75.6**	**24.4**	**100.0**

Selected among the active substances having DDD/1000 inhab. per day ≥0.05
Note: consolidated data as of 23 April 2024, relating to medicines with MA

Table 2.3.24 Active ingredients of medicines dispensed in "on behalf" distribution (DPC) by expenditure reduction 2023-2022

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	Inc. cum %*
A	sitagliptin/metformin	A	18.0	-37.5	0.75	-27.9	1.11	-13.1	98.6	1.4	0.7
H	lanreotide	A	23.5	-31.2	11.80	-34.4	0.09	5.2	78.0	22.0	1.7
A	liraglutide	A	10.6	-29.2	2.16	-8.8	0.23	-22.2	98.0	2.0	2.1
A	exenatide	A	10.3	-21.8	2.41	-5.6	0.20	-16.9	96.3	3.7	2.5
L	interferon beta 1a	A	15.7	-20.3	10.23	-1.2	0.07	-19.1	32.7	67.3	3.1
A	insulin degludec	A	30.0	-19.3	1.15	-15.8	1.22	-3.9	97.4	2.6	4.3
B	dabigatran	A	76.9	-8.4	1.66	-3.0	2.15	-5.3	98.1	1.9	7.4
B	epoetin zeta	A	11.1	-8.0	1.24	-0.5	0.42	-7.4	79.7	20.3	7.9
A	insulin glargine	A	76.3	-5.3	0.92	-1.9	3.86	-3.2	96.0	4.0	10.9
B	darbepoetin alfa	A	33.0	-4.2	6.12	-2.5	0.25	-1.6	88.9	11.1	12.2
H	somatropin	A	44.2	-3.6	12.25	-1.1	0.17	-2.2	70.3	29.7	14.0
B	ticagrelor	A	48.5	-3.5	2.32	-3.4	0.97	0.1	96.1	3.9	16.0
B	enoxaparin	A	46.2	-1.0	0.88	-3.3	2.45	2.6	65.7	34.3	17.8
B	epoetin alfa	A	41.2	-0.6	1.35	-12.2	1.42	13.4	76.4	23.6	19.5
	Total top 30		**485.3**	**-10.6**	**1.55**	**-8.0**	**14.56**	**-3.1**	**81.6**	**18.4**	**19.5**
	Total		**2,492.9**	**4.4**	**1.64**	**-2.7**	**70.66**	**7.6**	**75.6**	**24.4**	**100.0**

Selected among the active ingredients with an expenditure of at least 10 million euro
Note: consolidated data as of 23 April 2024, relating to medicines with MA
* Calculated on overall expenditure

Table 2.3.25 Top 30 active ingredients of medicines dispensed in "on behalf" distribution (DPC) by consumption reduction 2023-2022

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	Inc. cum %*
C	ranolazine	A	3.1	-95.6	1.49	-47.2	0.10	-91.6	32.2	67.8	0.1
A	vildagliptin	A	1.0	-66.7	0.54	-48.7	0.09	-34.9	4.1	95.9	0.2
B	fondaparinux	A	8.2	-25.9	1.60	0.7	0.24	-26.3	14.7	85.3	0.5
A	sitagliptin	A	7.5	-76.1	0.36	-68.0	0.97	-25.2	5.0	95.0	0.8
A	insulin detemir	A	2.9	-25.2	1.20	0.0	0.11	-25.0	4.5	95.5	0.9
B	nadroparin	A	2.0	-21.0	1.42	1.9	0.06	-22.3	43.7	56.3	1.0
A	liraglutide	A	10.6	-29.2	2.16	-8.8	0.23	-22.2	2.0	98.0	1.4
B	prasugrel	A	0.8	-42.3	0.37	-25.9	0.10	-21.9	6.3	93.7	1.4
A	vildagliptin/metformin	A	4.3	-52.6	0.63	-40.2	0.32	-20.5	1.9	98.1	1.6
A	alogliptin/metformin	A	3.6	-21.7	1.03	-3.0	0.16	-19.1	1.3	98.7	1.8
L	interferon beta 1a	A	15.7	-20.3	10.23	-1.2	0.07	-19.1	67.3	32.7	2.4
A	exenatide	A	10.3	-21.8	2.41	-5.6	0.20	-16.9	3.7	96.3	2.8
A	alogliptin	A	3.2	-17.9	1.17	-2.6	0.13	-15.6	1.5	98.5	2.9
A	sitagliptin/metformin	A	18.0	-37.5	0.75	-27.9	1.11	-13.1	1.4	98.6	3.7
B	clopidogrel/acetylsalicylic acid	A	6.1	-19.5	0.25	-8.3	1.14	-12.0	0.8	99.2	3.9
L	bicalutamide	A	1.3	9.8	0.17	24.7	0.37	-11.8	2.9	97.1	4.0
A	pioglitazone/metformin	A	2.6	-13.3	0.35	-5.5	0.34	-8.0	1.1	98.9	4.1
A	linagliptin/metformin	A	6.1	-10.9	1.15	-3.2	0.25	-7.7	0.5	99.5	4.3
A	alogliptin/pioglitazone	A	2.9	-10.0	1.04	-2.6	0.13	-7.4	1.1	98.9	4.4
B	epoetin zeta	A	11.1	-8.0	1.24	-0.5	0.42	-7.4	20.3	79.7	4.9
B	clopidogrel	A	4.7	-13.5	0.05	-7.8	4.62	-6.0	4.3	95.7	5.1
A	dapagliflozin/saxagliptin	A	3.1	-5.3	1.42	0.9	0.10	-6.0	1.9	98.1	5.2
C	ivabradine	A	2.3	-12.6	0.14	-7.0	0.77	-5.8	4.8	95.2	5.3
B	dabigatran	A	76.9	-8.4	1.66	-3.0	2.15	-5.3	1.9	98.1	8.4
N	quetiapine	A	6.0	-4.8	0.31	-0.2	0.91	-4.4	28.1	71.9	8.6
A	insulin degludec	A	30.0	-19.3	1.15	-15.8	1.22	-3.9	2.6	97.4	9.8

continued

Table 2.3.25 – *continued*

ATC	Active ingredient	Class	Expenditure *(EUR million)*	Δ % 23-22	Average DDD cost	Δ % 23-22	DDD/ 1000 inhab. per day	Δ % 23-22	% in DD	% in DPC	Inc. cum %*
N	gabapentin	A	0.3	-11.3	0.18	-7.5	0.08	-3.8	40.6	59.4	9.8
A	insulin glargine	A	76.3	-5.3	0.92	-1.9	3.86	-3.2	4.0	96.0	12.9
N	olanzapine	A	2.1	12.5	0.09	16.3	1.02	-3.1	52.0	48.0	13.0
L	degarelix	A	4.2	-6.2	3.45	-3.3	0.06	-2.8	3.0	97.0	13.1
	Total top 30		**327.1**	**-31.5**	**0.71**	**-21.5**	**21.25**	**-13.0**	**13.8**	**86.2**	**13.1**
	Total		**2,492.9**	**4.4**	**1.64**	**-2.7**	**70.66**	**7.6**	**75.6**	**24.4**	**100.0**

Selected among the active substances having DDD/1000 inhab. per day ≥0.05
Note: consolidated data as of 23 April 2024, relating to medicines with MA
* Calculated on overall expenditure

2.4 Inpatient and ambulatory care

In 2023, the total per capita expenditure for medicines dispensed in the context of inpatient and ambulatory care amounted to 204.80 euro (12.05 billion euro), with an increase of 8.5% compared to 2022. The analysis of the composition by reimbursement class highlights how the expenditure for class H medicines is predominant with a per capita value of 155.61 euro, equal to 75.9%, while for class A medicines there is a per capita expenditure of 25.71 euro, equal to 12.6% and for class C medicines a per capita expenditure of 23.48 euro equal to 11.5% (Table 2.4.1). Over the period 2016-2023, an increasing trend in expenditure has been recorded for all reimbursement classes in particular for class H medicines which from 5.5 billion euro in 2016 reached 9.2 billion euro in 2023, with a variation of 67.3% (Figure 2.4.1). Also for the average DDD cost, an increasing trend was observed going from 3.1 euro in 2016 to 4.9 euro in 2023. The highest average cost per DDD was recorded for class H medicines with a value equal to 23.6 euro, an increase of 6.8% compared to 2022 (Figure 2.4.2). The Southern Regions, overall, recorded the highest expenditure (215.08 euro), up 8.6% compared to 2022, in the face of lower consumption than the national average (108.38 DDD per 1000 inhabitants per day compared to 114.46 DDD per 1000 inhabitants per day of the national average) (Table 2.4.2). The Northern and Central Regions had a per capita expenditure of 200.23 and 198.69 euro respectively. For class A medicines, Sardinia had the highest per capita expenditure value (58.92 euro) and Tuscany (15.93 euro) the lowest. For class C medicines, Veneto had the highest expenditure value, equal to 29.53 euro and Lazio the lowest (20.53 euro). For class H medicines, Campania has the highest expenditure value (182.31 euro) and Valle d'Aosta (116.73 euro) the lowest. Overall, there is an increase in the average cost per DDD in the three geographical areas: North +5.8%, Centre +4.5% and South +4.2% compared to 2022, recording a national value of 4.90 euro (+5.1% compared to 2022).

The analysis of consumption by reimbursement class (Table 2.4.2) records an overall increase of 3.3% at national level, mainly in the Southern Regions (+4.3%), followed by the Central Regions (+3.0%), and those of the North (+2.8%), with a greater incidence of class A medicines compared to the previous year (difference in percentage points: +3.0).

Analysing the expenditure and consumption of medicines dispensed in hospital and ambulatory care (Table 2.4.3), in first place are confirmed antineoplastic and immunomodulatory medicines, which record an increase in consumption (+14.0%) with a consequent increase in per capita expenditure of 8.1% compared to 2022 (109.27 euro) and an average DDD cost of 30.3 euro, which records a reduction of 5.2% compared to last year. PD-1/PDL-1 inhibitors are confirmed as the subgroup with the highest per capita expenditure (14.96 euro), representing 13.7% of expenditure and 4.7% of consumption for the entire category. General antimicrobials for systemic use are the second category with the highest expenditure, with a per capita value of 32.93 euro, up compared to the previous year (+4.8%), with consumption standing at 5.3 DDD/1000 inhabitants per day and up 4.6%, while the average DDD cost remains stable (+0.2%). Also in 2023, antivirals for the treatment of HIV infections are confirmed as the medicines with the highest per capita expenditure (8.66 euro, stable compared to last year -0.5%), showing a slight increase in consumption (+2.1%) against a reduction in the average DDD cost (-2.6%) compared to the previous year. Medicines active on the blood and haematopoietic organs represent the third category for per capita expenditure (17.32 euro), up 8.6% compared to the previous year. Within this category, direct Xa factor inhibitors are the medicines with the highest expenditure (2.75 euro per capita and 15.9% of the category's expenditure), recording an increase of 26.1% of the category's ex-

penditure, accompanied by an increase in both consumption of 21.2% and in the average cost per day of therapy of 4.1%.

An analysis of the top 30 active ingredients with the highest expenditure shows that they account for 35.9% of the total expenditure for medicines dispensed in the context of inpatient and ambulatory care, with a value of about 4.3 billion euro (Table 2.4.4). Similarly to the previous year, pembrolizumab is the top expenditure active ingredient dispensed in the context of inpatient and ambulatory care, with 456.5 million euro, associated with a relative increase in consumption (+8.2%) and a slight reduction in the average cost per day of therapy (-4.9%), followed by daratumumab (456.3 million euro) and nivolumab (222.4 million euro); both active ingredients showed a reduction in average cost per day of therapy of 11.5% and 6.5% respectively. It should be noted that the increase in expenditure for these antineoplastic agents is related to higher consumption due to the authorisation of new therapeutic indications both in monotherapy and in combination with other medicines. Among the top 30 active ingredients with the highest expenditure, tafamidis is observed to have an expenditure increase of 84.4%, accompanied by a consumption growth of 95.3%. Tafamidis, indicated for the treatment of wild type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM), was granted reimbursability in 2021. In contrast, there was a 23% reduction in expenditure on the active ingredient remdesivir, accompanied by a reduction in consumption (-17.9%) and a reduction in the average cost per day of therapy (-5.9%). These effects can be attributed to the endemicisation of SARS-CoV-2 infection and to medicine price negotiations.

Analysing the active ingredients with the highest consumption dispensed in inpatient and ambulatory care (Table 2.4.5), in first place were electrolytes for intravenous solutions (6.7 DDD/1000 inhabitants per day; up by 0.5%), followed by cyanocobalamin (4.8 DDD/1000 inhabitants per day; up by 0.7%), and furosemide (3.3 DDD/1000 inhabitants per day; up by 0.3%), all with expenditure values that were either up or stable compared to last year (+12.5%, -0.4% and +4.2% respectively).

From the analysis of the active ingredients with the highest average cost per day of therapy, in the context of inpatient and ambulatory care (Table 2.4.6), CAR-Ts are at the top of the list: brexucabtagene autoleucel (autologous CD3+ cells transduced anti-CD19), indicated for the treatment of adult patients with mantle cell lymphoma and for the treatment of adult patients with acute lymphoblastic leukaemia, whose average cost per day of therapy is 300,960 euro (it should be noted that in most cases therapy is in a single administration), up 11.9% over last year, and axicabtagene ciloleucel, indicated for the treatment of adult patients with diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma, with an average DDD cost of 298,047 euro. This is followed by voretigene neparvovec, indicated for the treatment of adult and paediatric patients with vision loss due to hereditary retinal dystrophy, with an average cost per day of therapy of 297,000 euro, unchanged from last year. Altogether, the top 30 active ingredients with the highest average DDD cost account for 1.9% of the total expenditure on medicines dispensed in inpatient and ambulatory care (229.6 million) (Table 2.4.6).

Comparing expenditure in 2023 with the previous year, it can be seen that trastuzumab deruxtecan, a drug-conjugated monoclonal antibody indicated for the treatment of adult patients with HER2-positive unresectable or metastatic breast cancer, and vosoritide, indicated for the treatment of achondroplasia in patients aged 2 years and older, are the top two active ingredients with the highest increase in expenditure (>100%) (Table 2.4.7).

Analysing the top 30 active ingredients with the greatest increase in consumption compared with the previous year, which together represent 10.6% of the total expenditure made in the context of inpatient and ambulatory care (Table 2.4. 8), in first place there is atenolol with an increase in consumption greater than 100% which is accompanied by a reduction in expenditure of 10.9% due to a strong reduction in the average DDD cost (-63.1%), followed by the hypoglycaemic medicine semaglutide, a GLP-1 receptor agonist which records an increase greater than 100% which is associated with a variation in expenditure of +89.1%; entecavir, with an increase of >100% in consumption and expenditure; fulvestrant which shows an increase in consumption of 93.4%; and tetravalent influenza vaccine which shows an increase in consumption of over 90%.

Moving on to the analysis of the top 30 active ingredients by reduction in expenditure (Table 2.4.9), lenalidomide, an anti-cancer agent authorised for the treatment of multiple myeloma, myelodysplastic syndromes and certain types of lymphomas, recorded a reduction in expenditure of 80.4% compared to 2022, due to a marked reduction in the average DDD cost (-81.1%); followed by another antineoplastic agent, abiraterone, an androgen antagonist used in the treatment of prostate cancer which shows a reduction in expenditure of 77.1%; associated in this case too, with a marked reduction in the average DDD cost (-77.9%). For both of these medicines, the reduction in average DDD cost is attributable to the expiry of the patent during 2022 and the marketing of generic medicines.

In terms of consumption, the active ingredients registering a strong reduction in inpatient and ambulatory care (Table 2.4.10) are paracetamol (-42%), parenteral nutrition solutions (-37.4%), the tetravalent influenza vaccine (-31.2%), adrenalin (-29.8%) and mepivacaine (-26.9%).

Table 2.4.1 Composition by reimbursement class of regional expenditure 2023 for medicines dispensed in the context of inpatient and ambulatory care

Region	Per capita expenditure				Δ % 23-22	Average DDD cost	Δ % 23-22	Inc. % A	Inc. % C	Inc. % H
	Class A	Class C	Class H	Total						
Piedmont	20.84	22.91	150.59	194.33	7.4	4.17	7.8	10.7	11.8	77.5
Valle d'Aosta	36.44	22.81	116.73	175.99	14.9	3.03	14.6	20.7	13.0	66.3
Lombardy	29.14	21.88	139.84	190.85	11.4	5.56	5.8	15.3	11.5	73.2
Province of Bolzano	38.54	28.31	158.83	225.68	15.7	4.23	7.6	17.1	12.5	70.4
Province of Trento	34.85	26.54	121.61	182.99	2.1	3.92	12.3	19.0	14.5	66.5
Veneto	17.91	29.53	142.91	190.35	3.8	3.95	-1.9	9.4	15.5	75.1
Friuli VG	29.03	27.03	176.39	232.46	15.6	5.00	22.4	12.5	11.6	75.9
Liguria	25.86	24.83	172.12	222.81	11.4	5.08	8.7	11.6	11.1	77.3
Emilia R.	20.88	25.57	173.63	220.07	7.2	3.78	4.3	9.5	11.6	78.9
Tuscany	15.93	22.58	160.67	199.18	10.4	4.80	5.6	8.0	11.3	80.7
Umbria	31.11	24.36	170.57	226.03	8.2	4.15	-4.1	13.8	10.8	75.4
Marche	19.51	25.50	174.93	219.94	3.2	4.71	11.8	8.9	11.6	79.5
Lazio	20.25	20.53	147.52	188.3	7.1	5.63	2.9	10.8	10.9	78.3
Abruzzo	24.31	24.87	173.20	222.38	8.4	7.38	23.7	10.9	11.2	77.9
Molise	24.33	21.52	151.77	197.62	3.0	6.39	9.4	12.3	10.9	76.8
Campania	26.74	21.10	182.31	230.15	10.8	6.15	-1.2	11.6	9.2	79.2
Puglia	24.88	23.25	156.86	204.99	4.2	5.93	2.8	12.1	11.3	76.6
Basilicata	34.95	24.03	152.35	211.33	6.7	5.03	6.5	16.5	11.4	72.1
Calabria	39.1	24.00	161.40	224.50	5.4	6.29	21.0	17.4	10.7	71.9
Sicily	29.85	23.10	139.97	192.92	12.6	4.69	-2.2	15.5	12.0	72.5
Sardinia	58.92	22.03	161.18	242.13	7.8	3.68	8.9	24.3	9.1	66.6
Italy	**25.71**	**23.48**	**155.61**	**204.80**	**8.5**	**4.90**	**5.1**	**12.6**	**11.5**	**75.9**
North	24.61	24.6	151.02	200.23	8.8	4.51	5.8	12.3	12.3	75.4
Centre	19.59	22.11	156.99	198.69	7.6	5.05	4.5	9.9	11.1	79.0
South and Islands	31.06	22.71	161.32	215.08	8.6	5.44	4.2	14.4	10.6	75.0

Note: consolidated data as of 23 April 2024, relating to medicines with MA

Table 2.4.1 Annual trend by reimbursement class of expenditure for medicines dispensed in the context of inpatient and ambulatory care in the period 2016-2023

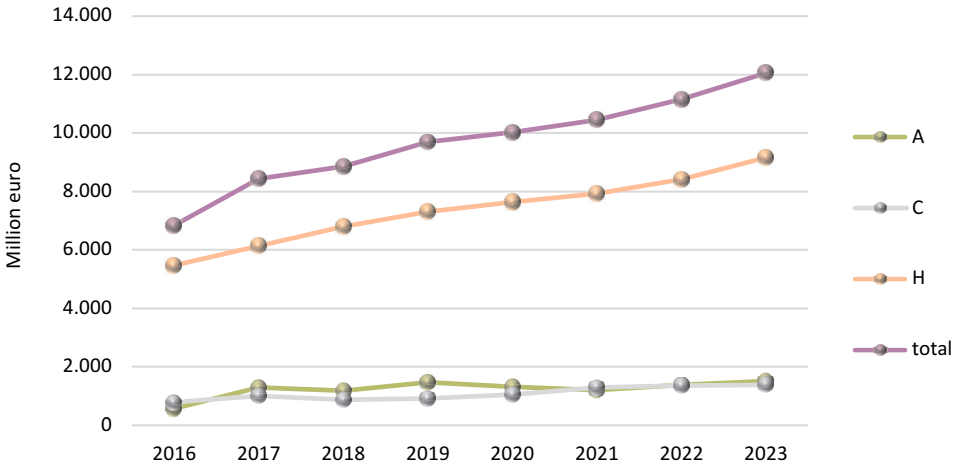


Table 2.4.2 Annual trend by reimbursement class of the average DDD cost for medicines dispensed in the context of inpatient and ambulatory care in the period 2016-2023

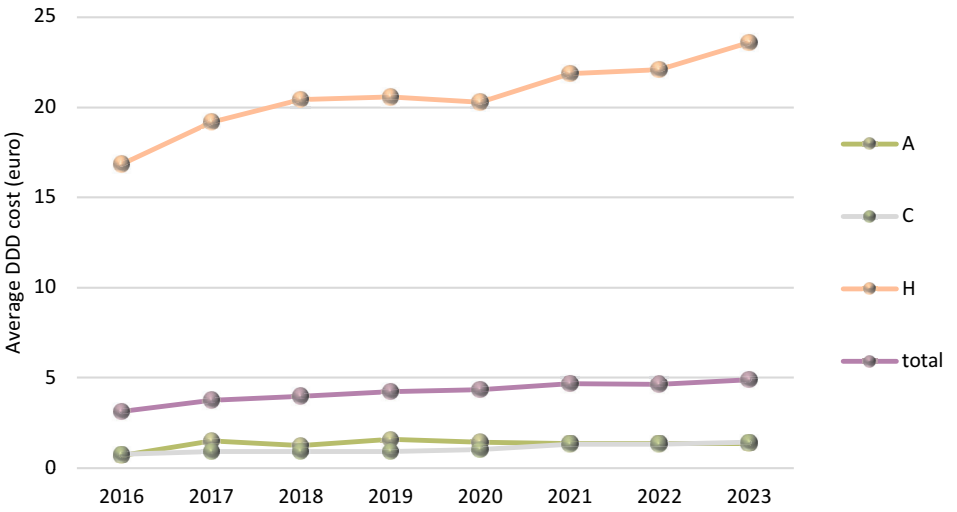


Table 2.4.2 Composition by reimbursement class of consumption 2023 for medicines dispensed in the context of inpatient and ambulatory care

Region	DDD/1000 inhabitants per day				Δ % 23-22	Inc. % A	Inc. % C	Inc. % H
	Class A	Class C	Class H	Total				
Piedmont	62.47	45.78	19.39	127.64	-0.4	48.9	35.9	15.2
Valle d'Aosta	89.14	52.48	17.58	159.20	0.2	56.0	33.0	11.0
Lombardy	47.54	30.52	16.01	94.07	5.3	50.5	32.4	17.1
Province of Bolzano	79.90	47.85	18.35	146.10	7.5	54.7	32.8	12.5
Province of Trento	61.70	50.41	15.86	127.97	-9.1	48.2	39.4	12.4
Veneto	45.57	68.97	17.54	132.08	5.8	34.5	52.2	13.3
Friuli VG	61.51	46.66	19.19	127.36	-5.6	48.3	36.6	15.1
Liguria	63.13	37.72	19.24	120.09	2.5	52.6	31.4	16.0
Emilia R.	60.20	77.43	21.71	159.34	2.8	37.8	48.6	13.6
Tuscany	43.14	49.52	21.07	113.72	4.6	37.9	43.5	18.6
Umbria	70.12	59.37	19.73	149.23	12.8	47.0	39.8	13.2
Marche	40.44	67.17	20.23	127.84	-7.7	31.6	52.5	15.9
Lazio	43.78	31.55	16.32	91.65	4.1	47.8	34.4	17.8
Abruzzo	34.94	28.84	18.83	82.61	-12.3	42.3	34.9	22.8
Molise	39.54	28.45	16.73	84.73	-5.8	46.7	33.6	19.7
Campania	44.58	39.71	18.21	102.50	12.2	43.5	38.7	17.8
Puglia	36.52	39.57	18.67	94.76	1.3	38.5	41.8	19.7
Basilicata	54.1	42.47	18.47	115.05	0.2	47.0	36.9	16.1
Calabria	47.04	34.98	15.84	97.86	-12.9	48.1	35.7	16.2
Sicily	61.34	34.81	16.54	112.69	15.1	54.4	30.9	14.7
Sardinia	108.10	54.70	17.62	180.42	-1.0	59.9	30.3	9.8
Italy	**51.73**	**44.67**	**18.07**	**114.46**	**3.3**	**45.2**	**39.0**	**15.8**
North	54.23	49.27	18.12	121.62	2.8	44.6	40.5	14.9
Centre	45.13	43.97	18.60	107.70	3.0	41.9	40.8	17.3
South and Islands	52.21	38.52	17.65	108.38	4.3	48.2	35.5	16.3

Table 2.4.3 Expenditure and consumption 2023 for medicines dispensed in the context of inpatient and ambulatory care by ATC 1st level

(any ATC category includes the therapeutic subgroups in decreasing order of expenditure, up to the value of 0.1 euro of per capita expenditure)

ATC 1st level and subgroups (ATC 4th level)	Per capita expenditure	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
Italy	**204.80**	**100.00**	**8.52**	**114.5**	**100.0**	**3.3**	**4.9**	**5.1**
Antineoplastic and immunomodulating agents	**109.27**	**100.00**	**8.06**	**9.9**	**100.0**	**14.0**	**30.3**	**-5.2**
PD-1/PDL-1 inhibitors (prot. cell death cell death prog. 1/lig 1)	14.96	13.70	12.92	0.5	4.7	26.3	89.1	-10.6
Interleukin inhibitors	11.50	10.59	17.43	1.3	13.2	19.8	24.3	-2.0
CD38 inhibitors (clusters of differentiation 38)	8.21	7.52	18.98	0.3	2.7	33.1	85.7	-10.6
Monoclonal antibodies	6.90	6.32	17.80	0.4	4.5	14.0	42.6	3.4
Other kinase protein inhibitors	4.75	4.35	14.57	0.1	1.3	17.4	105.0	-2.5
HER2 inhibitors (human epidermal growth factor receptor 2)	4.68	4.29	-1.01	0.2	2.5	-4.6	51.9	3.8
Bruton tyrosine kinase (BTK) inhibitors	4.52	4.14	18.94	0.1	1.0	20.8	122.7	-1.5
Tumor necrosis factor alpha inhibitors (TNF-alpha)	4.49	4.11	-4.08	1.8	18.7	9.0	6.7	-12.0
Cyclin-dependent kinase inhibitors (CDK)	4.36	3.99	14.44	0.2	1.9	19.9	62.7	-4.5
Antiandrogens	3.72	3.41	44.18	0.4	3.6	34.3	29.0	7.4
Other monoclonal antibodies and antibody-drug conjugates	3.37	3.08	31.52	<0.05	0.4	65.9	269.6	-20.7
Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors	3.01	2.76	2.42	0.1	0.7	7.0	121.8	-4.3
Complement inhibitors	2.97	2.72	29.53	<0.05	0.1	40.3	656.8	-7.7
Janus-associated kinase (JAK) inhibitors	2.49	2.28	16.98	0.1	0.6	17.8	109.3	-0.7
BCR-ABL tyrosine kinase inhibitors	2.41	2.20	-13.26	0.1	1.1	15.3	61.1	-24.8
Other immunosuppressants	2.34	2.14	-50.96	0.3	2.7	5.8	24.2	-53.6
Poly (ADP-RIBOSE) polymerase (PARP) inhibitors	2.15	1.97	13.82	<0.05	0.4	14.0	135.1	-0.2
Antineoplastic cell and gene therapy	1.88	1.72	53.36	<0.05	-	17.6	282,218.7	30.4
Other antineoplastics	1.87	1.71	22.43	<0.05	0.5	36.3	114.8	-10.1
Janus-associated kinase (JAK) inhibitors	1.70	1.55	17.15	0.2	2.2	22.9	21.0	-4.7
Serine-threonine kinase B-RAF (BRAF) inhibitors	1.59	1.46	5.94	<0.05	0.4	4.7	113.5	1.2
Anaplastic lymphoma kinase inhibitors (ALK)	1.49	1.36	3.13	<0.05	0.3	10.9	131.6	-7.0
Selective immunosuppressants	1.46	1.34	-11.62	0.2	2.0	5.6	19.9	-16.3
VEGF/VEGFR (vascular endothelial growth factor) inhibitors	1.12	1.03	-12.22	0.1	1.4	13.7	22.5	-22.8
EGFR (human epidermal growth factor receptor) inhibitors	1.05	0.96	-0.57	<0.05	0.3	3.9	91.7	-4.3

continued

Table 2.4.3 – *continued*

ATC 1st level and subgroups (ATC 4th level)	Per capita expendi-ture	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
General antimicrobials for systemic use	**32.93**	**100.00**	**4.77**	**5.3**	**100.0**	**4.6**	**16.9**	**0.2**
Antivirals for treatment of HIV infections, combinations	8.66	26.29	-0.51	1.5	27.2	2.1	16.3	-2.6
Influenza vaccines	2.56	7.77	-3.23	0.6	11.7	-3.8	11.2	0.6
Varicella Zoster vaccines	2.34	7.12	46.69	0.0	0.5	6.0	224.9	38.4
Human normal immunoglobulin	2.30	6.97	18.20	0.0	0.3	6.0	457.5	11.6
Meningococcal vaccines	1.84	5.58	5.28	0.1	2.0	4.0	46.9	1.2
Human papillomavirus vaccines	1.64	4.98	13.51	0.1	1.2	13.4	69.4	0.1
Nucleosides and nucleotides excl. reverse transcriptase inhibitors	1.62	4.92	-22.03	0.1	1.0	-5.2	81.9	-17.7
Pneumococcal vaccines	1.51	4.59	16.87	0.1	1.8	11.4	44.1	4.9
Integrase inhibitors	1.27	3.86	3.13	0.3	4.9	2.8	13.3	0.3
Antibiotics	0.85	2.59	3.13	<0.05	0.4	3.2	101.6	-0.1
Bacterial and viral vaccines in combination	0.84	2.54	-1.10	0.1	2.0	2.6	21.7	-3.6
Other cephalosporins and penems	0.80	2.42	7.40	<0.05	0.2	7.2	220.8	0.2
Measles vaccines	0.68	2.05	6.03	<0.05	0.8	0.1	42.9	5.9
Penicillin combinations, incl. beta-lactamase inhibitors	0.60	1.81	-4.03	0.4	8.1	6.6	3.8	-9.9
Third generation cephalosporins	0.53	1.62	1.74	0.3	5.4	8.3	5.1	-6.1
Carbapenems	0.48	1.46	11.82	0.1	1.2	-9.6	21.1	23.7
Other antibacterials	0.46	1.41	-3.77	0.1	2.2	-4.8	10.9	1.1
Other antivirals	0.37	1.12	40.23	<0.05	0.2	18.8	108.9	18.1
Antiviral monoclonal antibodies	0.32	0.97	14.80	<0.05	0.0	11.8	845.3	2.7
Blood and blood forming organs	**17.32**	**100.00**	**8.58**	**27.8**	**100.0**	**1.3**	**1.7**	**7.2**
Direct Xa factor inhibitors	2.75	15.87	26.14	4.6	16.5	21.2	1.6	4.1
Blood coagulation factors	2.40	13.83	-5.31	<0.05	0.1	3.7	327.0	-8.7
Other hemostatics for systemic use	2.03	11.73	14.89	0.1	0.3	13.9	60.5	0.9
Other antianemic preparations	1.35	7.8	8.68	1.7	6.2	5.5	2.2	3.0
Heparins	1.15	6.66	8.05	3.2	11.6	9.4	1.0	-1.2
Solutions affecting the electrolyte balance	1.15	6.66	12.56	6.9	24.7	0.7	0.5	11.8
Platelet aggregation inhibitors, excl. heparin	1.15	6.65	-7.15	3.0	10.7	-11.7	1.1	5.1
Iron, parenteral preparations	0.74	4.27	94.38	0.1	0.3	96.9	22.3	-1.3
Other antithrombotics	0.73	4.20	-2.07	0.2	0.7	11.3	10.7	-12.0
Parenteral nutrition solutions	0.72	4.15	-4.30	0.6	2.1	-16.0	3.3	14.0
Local hemostatics	0.51	2.94	15.12	<0.05	0.0	11.5	260.8	3.3
Hypertonic solutions	0.47	2.73	6.34	0.2	0.6	15.0	8.4	-7.5
Protease inhibitors	0.32	1.86	11.40	<0.05	0.0	-0.0	90.5	11.4
Direct thrombin inhibitors	0.29	1.68	4.49	0.7	2.5	3.1	1.2	1.3

continued

Table 2.4.3 – *continued*

ATC 1st level and subgroups (ATC 4th level)	Per capita expenditure	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
Gastrointestinal system and metabolism	**12.83**	**100.00**	**11.95**	**18.2**	**100.0**	**11.9**	**1.9**	**0.0**
Enzymes	5.78	45.06	2.93	<0.05	0.1	14.6	922.1	-10.2
GLP-1 (glucagon-like peptide-1) receptor analogues	1.68	13.06	37.92	2.0	10.8	36.0	2.3	1.4
Sodium-glucose type 2 (SGLT2) cotransporter inhibitors	0.87	6.82	64.26	2.1	11.5	68.8	1.1	-2.7
Insulins and injectable analogues, long-acting	0.85	6.66	8.44	2.1	11.7	10.7	1.1	-2.1
Various products for gastrointestinal system and metabolism	0.84	6.51	25.09	<0.05	0.0	8.4	281.8	15.4
Oral hypoglycemic agents, in combination	0.67	5.2	0.09	2.2	12.0	18.8	0.8	-15.8
Bile acids and derivatives	0.43	3.37	21.29	0.1	0.4	-1.1	16.9	22.6
Proton pump inhibitors	0.23	1.8	-5.14	2.5	13.5	2.5	0.3	-7.4
Dipeptil Peptidase 4 Inhibitors (DPP-4)	0.19	1.47	-40.18	0.9	4.9	-5.5	0.6	-36.7
serotonin antagonists (5HT3)	0.19	1.45	4.63	0.1	0.4	-5.2	7.6	10.3
Central nervous system	**9.18**	**100.00**	**15.19**	**17.8**	**100.0**	**-8.8**	**1.4**	**26.2**
Other medicines for the nervous system	3.20	34.9	61.95	0.1	0.8	66.5	63.0	-2.7
Other antipsychotics	2.68	29.18	-9.59	1.9	10.4	2.2	4.0	-11.5
DOPA and derivatives	0.52	5.71	3.05	0.1	0.7	-4.6	11.8	8.0
Medicines used in opioid addiction	0.41	4.52	6.49	2.3	12.8	-6.5	0.5	13.9
Other antiepileptics	0.33	3.56	15.05	0.3	1.9	29.5	2.7	-11.2
Halogenated hydrocarbons	0.20	2.15	-1.99	<0.05	0.1	0.6	52.4	-2.6
Diazepines, oxazepines, thiazepines and oxepins	0.20	2.15	-2.50	1.6	8.9	-4.1	0.3	1.7
Amides	0.18	1.94	2.28	2.1	11.6	-3.7	0.2	6.2
Other general anesthetics	0.18	1.93	19.46	0.2	1.4	2.4	2.0	16.7
Anilides	0.15	1.59	32.19	2.4	13.5	-42.0	0.2	>100
Other antidepressants	0.12	1.32	>100	0.3	1.7	10.8	1.1	>100
Various	**5.46**	**100.00**	**1.93**	**3.2**	**100.0**	**11.5**	**4.7**	**-8.5**
Water-soluble, nephrotropic, low osmotic radiological contrast media	1.36	24.91	2.63	0.1	2.0	-2.0	58.2	4.8
Antidotes	1.18	21.58	0.29	0.1	4.7	-5.9	21.6	6.5
Other diagnostic radiopharmaceuticals for cancer detection	0.53	9.72	12.07	<0.05	0.1	7.7	557.6	4.0
Paramagnetic contrast media	0.46	8.36	2.49	<0.05	0.8	2.6	48.3	-0.1
Detoxifying substances for cytostatic treatments	0.27	4.97	-10.69	0.2	7.1	2.2	3.3	-12.7
Various therapeutic radiopharmaceuticals	0.23	4.3	-17.43	<0.05	-	-7.4	9,375.2	-10.9
Iodine-123I compounds	0.20	3.6	15.58	<0.05	0.0	16.9	808.1	-1.2
Medicines for treatment of hyperkalemia and hyperphosphatemia	0.18	3.35	71.08	0.1	4.3	34.0	3.7	27.7
Various thyroid diagnostic radiopharmaceuticals	0.17	3.15	39.54	<0.05	0.1	32.0	251.7	5.7
Iron chelating agents	0.16	2.96	-39.40	<0.05	0.5	-7.8	25.9	-34.3
Other diagnostics	0.13	2.37	16.77	<0.05	0.2	4.0	48.7	12.3
Solvents and thinners, including cleaning solutions	0.11	1.97	-3.75	2.4	76.1	13.3	0.1	-15.0

continued

Table 2.4.3 – *continued*

ATC 1st level and subgroups (ATC 4th level)	Per capita expenditure	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
Musculo-skeletal system	**4.72**	**100.00**	**33.74**	**3.1**	**100.0**	**14.4**	**4.2**	**16.9**
Other medicines for musculoskeletal system disorders	2.86	60.61	23.92	<0.05	1.4	10.7	189.7	12.0
Other medicines acting on bone structure and mineralisation	1.27	26.90	83.80	1.6	51.1	25.9	2.2	46.0
Other muscle relaxants with peripheral action	0.30	6.34	20.56	<0.05	0.2	16.6	128.5	3.4
Sensory organs	**3.00**	**100.00**	**-7.55**	**1.8**	**100.0**	**-4.2**	**4.7**	**-3.5**
Antineovascularisation substances	2.15	71.82	-11.97	0.1	5.3	-12.0	62.9	0.0
Corticosteroids, not in combination	0.53	17.84	14.09	0.3	16.6	8.3	5.0	5.3
Other ophthalmological medicines	0.15	5.06	-13.38	0.1	4.6	2.7	5.2	-15.7
Dermatological medicines	**2.88**	**100.00**	**29.25**	**8.5**	**100.0**	**-1.1**	**0.9**	**30.7**
Substances for dermatitis, excluding corticosteroids	2.41	83.70	33.71	0.2	2.7	27.5	28.9	4.9
Biguanides and amidines	0.14	4.86	26.00	1.3	15.0	3.6	0.3	21.6
Respiratory system	**2.48**	**100.00**	**19.78**	**1.7**	**100.0**	**10.0**	**4.0**	**8.9**
Other preparations for the respiratory system	1.52	61.12	27.47	<0.05	0.6	30.0	379.9	-1.9
Other systemic medicines for obstructive airway disorders	0.66	26.41	15.89	0.1	4.4	23.3	24.2	-6.0
Cardiovascular system	**2.22**	**100.00**	**9.94**	**10.8**	**100.0**	**6.7**	**0.6**	**3.0**
Other lipid modifying agents	0.65	29.33	93.53	0.3	2.8	74.2	5.9	11.1
Angiotensin II receptor blockers (ARBs), other combinations	0.47	21.28	41.35	0.4	3.7	68.1	3.2	-15.9
Antihypertensives for pulmonary arterial hypertension	0.28	12.65	3.10	<0.05	0.3	28.4	23.6	-19.7
Adrenergics and dopaminergics	0.16	7.10	16.24	0.8	7.8	-16.8	0.5	39.7
Other cardiac preparations	0.12	5.27	-70.54	0.4	4.1	-43.2	0.7	-48.2
Vasopressin antagonists	0.11	5.10	6.87	<0.05	0.1	32.0	25.4	-19.0
Systemic hormonal preparations, excluding sex hormones and insulins	**1.72**	**100.00**	**2.75**	**3.8**	**100.0**	**-2.0**	**1.2**	**4.9**
Somatostatin and analogues	0.45	25.87	-3.20	0.1	2.0	14.2	16.3	-15.2
Glycocorticoids	0.39	22.75	6.36	3.2	82.6	-3.0	0.3	9.6
Other antiparathyroid substances	0.36	20.60	5.43	0.2	6.4	7.6	4.0	-2.1
Somatropin and somatropin agonists	0.32	18.74	2.60	0.1	1.9	-2.5	12.2	5.2
Genito-urinary system and sex hormones	**0.75**	**100.00**	**18.54**	**2.5**	**100.0**	**14.2**	**0.8**	**3.8**
Gonadotropins	0.42	55.53	28.28	<0.05	1.9	9.7	23.5	16.9
Prostaglandins	0.11	14.47	4.46	<0.05	1.7	-11.5	7.2	18.1

Note: consolidated data as of 23 April 2024, relating to medicines with MA

Table 2.4.4 Top 30 active ingredients in descending order of expenditure 2023 for medicines dispensed in the context of inpatient and ambulatory care

ATC 1st level	Active ingredient	Expenditure *(EUR million)*	Δ % 23-22	Inc. %*	% cum.	DDD/1000 inhabitants per day	Δ % 23-22	Average DDD cost	Δ % 23-22
L	pembrolizumab	456.50	2.7	3.8	3.8	0.2	8.2	87.70	-4.9
L	daratumumab	456.30	16.8	3.8	7.6	0.3	32.3	83.49	-11.5
L	nivolumab	222.40	14.2	1.8	9.4	0.1	22.4	109.12	-6.5
L	ibrutinib	199.80	-1.1	1.7	11.1	0.1	2.8	119.24	-3.5
L	osimertinib	173.00	3.3	1.4	12.5	0.1	11.5	130.70	-7.1
L	ocrelizumab	157.90	19.3	1.3	13.8	0.2	21.0	44.72	-1.2
J	emtricitabine/tenofovir alafenamide/bictegravir	157.70	17.1	1.3	15.1	0.4	17.4	19.96	0.0
L	ustekinumab	153.30	13.6	1.3	16.4	0.5	16.3	14.11	-2.1
L	enzalutamide	148.20	24.8	1.2	17.6	0.1	31.9	65.62	-5.2
L	ruxolitinib	139.20	12.4	1.2	18.8	0.1	12.0	111.23	0.6
L	pertuzumab	136.40	-11.8	1.1	19.9	0.1	-11.6	105.55	0.0
D	dupilumab	132.80	25.9	1.1	21.0	0.2	26.6	27.84	-0.3
L	secukinumab	125.00	4.6	1.0	22.0	0.2	6.4	28.95	-1.4
J	adjuvanted recombinant varicella zoster virus vaccine	123.40	66.1	1.0	23.0	<0.05	40.9	321.38	18.2
N	tafamidis	123.20	84.4	1.0	24.0	0.1	95.3	61.21	-5.4
L	nintedanib	120.60	28.5	1.0	25.0	0.1	30.0	91.01	-0.9
L	eculizumab	118.50	0.0	1.0	26.0	<0.05	2.7	710.85	-2.5
J	dolutegravirlamivudine	116.40	20.2	1.0	27.0	0.3	20.5	16.60	0.0
L	natalizumab	106.30	-4.7	0.9	27.9	0.1	4.3	45.83	-8.4
L	ribociclib	100.90	21.6	0.8	28.7	0.1	22.1	67.98	-0.2
J	human papillomavirus vaccine (human types 6, 11, 16, 18, 31, 33, 45, 52, 58)	96.50	13.3	0.8	29.5	0.1	13.4	69.37	0.1
J	remdesivir	91.30	-23.0	0.8	30.3	0.0	-17.9	356.96	-5.9
L	palbociclib	89.50	-8.0	0.7	31.0	0.1	-9.6	67.13	2.1
L	vedolizumab	86.00	8.8	0.7	31.7	0.1	11.7	30.18	-2.4
J	Meningococcal group B (MenB) vaccine	85.60	8.2	0.7	32.4	0.1	7.1	62.66	1.2
S	aflibercept	83.30	-4.6	0.7	33.1	<0.05	17.7	400.79	-18.7
L	ixekizumab	83.00	14.2	0.7	33.8	0.1	14.4	30.31	0.1
A	agalsidase alfa	82.80	-1.0	0.7	34.5	<0.05	9.8	960.53	-9.6
J	tetravalent influenza vaccine (surface antigen, inactivated, adjuvanted)	82.10	4.5	0.7	35.2	0.3	3.8	15.00	0.9
L	adalimumab	79.90	-6.6	0.7	35.9	0.9	9.6	4.37	-14.6
	Total top 30	**4,327.50**	**10.0**	**35.9**		**4.7**	**14.6**	**43.02**	**-3.9**
	Total	**12,052.70**	**8.3**	**100.0**		**114.5**	**3.3**	**4.90**	**5.1**

Note: consolidated data as of 23 April 2024, relating to medicines with MA
* calculated on the total expenditure

Table 2.4.5 Top 30 active ingredients in descending order of consumption 2023 for medicines dispensed in the context of inpatient and ambulatory care

ATC 1st level	Active ingredient	DDD/1000 inhabitants per day	Δ % 23-22	Expenditure *(EUR million)*	Δ % 23-22	Inc. %*	% cum.	Average DDD cost	Δ % 23-22
B	electrolytes for intravenous solutions	6.7	0.5	64.4	12.5	0.5	0.5	0.40	-0.1
B	cyanocobalamin	4.8	0.7	0.4	-0.4	0.0	0.5	<0.005	-100.0
C	furosemide	3.3	0.3	2.7	4.2	0.0	0.5	<0.005	-100.0
B	enoxaparin	2.7	12.9	49.6	11.5	0.4	0.9	0.80	-6.5
D	sodium hypochlorite	2.7	4.9	2.4	7.5	0.0	0.9	<0.005	-100.0
N	paracetamol	2.4	-42.0	8.6	31.8	0.1	1.0	0.20	175.5
V	sodium chloride	2.1	14.1	3.5	17.2	0.0	1.0	0.10	29.0
N	methadone	2.0	-9.0	14.5	-8.4	0.1	1.1	0.30	-10.3
B	apixaban	1.8	33.0	65.5	36.8	0.5	1.6	1.70	5.5
B	rivaroxaban	1.6	2.1	52.9	8.0	0.4	2.0	1.60	8.2
M	denosumab	1.6	25.2	30.2	31.9	0.3	2.3	0.90	4.9
A	insulin glargine	1.5	15.6	27.9	16.4	0.2	2.5	0.90	5.5
N	lidocaine	1.5	-0.1	5.2	0.4	0.0	2.5	0.20	25.5
B	clopidogrel	1.5	-20.3	1.9	-13.7	0.0	2.5	0.10	86.0
A	cholecalciferol	1.4	2.4	0.2	2.1	0.0	2.5	<0.005	-100.0
A	pantoprazole	1.2	6.9	8.3	8.1	0.1	2.6	0.30	-2.8
A	dapagliflozin	1.2	73.1	28.4	62.8	0.2	2.8	1.10	-7.4
B	edoxaban	1.2	36.2	43.4	36.8	0.4	3.2	1.70	-0.7
B	epoetin alfa	1.1	7.0	29.1	6.1	0.2	3.4	1.20	-0.5
H	methylprednisolone	1.0	-0.8	9.3	10.5	0.1	3.5	0.40	3.1
C	atenolol	1.0	141.6	0.0	-10.9	0.0	3.5	<0.005	-100.0
D	chlorhexidine/ ethyl alcohol	1.0	2.5	1.2	2.6	0.0	3.5	0.10	78.0
A	dulaglutide	1.0	11.2	39.4	8.2	0.3	3.8	1.90	-3.5
G	levonorgestrel	1.0	17.9	1.1	13.1	0.0	3.8	0.10	81.4
H	dexamethasone	0.9	9.4	1.4	5.3	0.0	3.8	0.10	30.7
A	semaglutide	0.9	103.9	52.8	89.1	0.4	4.2	2.80	-8.3
L	adalimumab	0.9	9.6	79.9	-6.6	0.7	4.9	4.40	-13.9
C	ramipril	0.8	9.1	0.2	6.2	0.0	4.9	<0.005	-100.0
N	olanzapine	0.8	-9.4	5.4	-1.4	0.0	4.9	0.30	4.1
D	povidone iodine	0.8	-11.7	4.1	11.3	0.0	4.9	0.20	4.9
	Total top 30	**52.1**	**3.5**	**633.9**	**17.6**	**5.3**		**0.60**	**20.6**
	Total	**114.5**	**3.3**	**12,052.7**	**8.3**	**100**		**4.90**	**5.1**

Note: consolidated data as of 23 April 2024, relating to medicines with MA
* calculated on the total expenditure

Table 2.4.6 Top 30 active ingredients by average DDD cost 2023 for medicines dispensed in the context of inpatient and ambulatory care

ATC 1st level	Active ingredient	DDD/1000 inhabitants per day	Δ % 23-22	Average DDD cost	Δ % 23-22	Expenditure *(EUR million)*	Δ % 23-22	Inc. %*	% cum.
L	brexucabtagene autoleucel	<0.005	51.3	300,960.00	11.9	24.1	68.9	0.2	0.2
L	axicabtagene ciloleucel^	<0.005	27.7	298,047.14	70.2	59.6	>100	0.5	0.7
S	voretigene neparvovec	<0.005	-15.2	297,000.00	0.0	6.5	-15.4	0.1	0.8
M	onasemnogene abeparvovec^	<0.005	-28.4	279,074.82	55.4	8.4	11.0	0.1	0.9
L	tisagenlecleucel	<0.005	-9.4	240,935.71	-2.0	27.2	-11.4	0.2	1.1
V	germanium chloride/ gallium chloride (68Ge/68Ga)	<0.005	3.8	98,413.67	13.5	2.9	17.6	0.0	1.1
S	ex vivo expanded autologous human corneal epithelial cells containing stem cells	<0.005	-49.9	94,310.54	0.0	0.1	-50.0	0.0	1.1
V	lutetium vipivotde (177Lu)	<0.005	-	55,000.00	-	0.2	-	0.0	1.1
V	gallium gozetotide (68Ga)	<0.005	-	52,800.00	-	0.1	-	0.0	1.1
B	susoctocog alpha (recombinant porcine factor VIII)	<0.005	-36.1	35,447.70	1.0	3.5	-35.6	0.0	1.1
V	glucarpidase	<0.005	>100	29,150.00	-3.6	1.6	96.3	0.0	1.1
L	spesolimab	<0.005	-	21,230.00	-	0.0	-	0.0	1.1
B	catridecacog (coagulation factor XIII, recombinant)	<0.005	15.8	15,524.20	0.0	3.2	15.6	0.0	1.1
V	lutetium oxodotreotide (177Lu)	<0.005	6.2	12,858.52	-22.7	11.8	-18.1	0.1	1.2
L	gemtuzumab ozogamicin	<0.005	25.8	12,403.06	0.0	4.8	25.5	0.0	1.2
B	X factor	<0.005	-	10,838.24	-	0.2	-	0.0	1.2
B	prothrombin complex	<0.005	29.0	8,593.15	3.9	6.5	33.7	0.1	1.3
C	volanesorsen	<0.005	46.5	8,190.19	0.0	4.3	46.2	0.0	1.3
V	gallium edotreotide (68 Ga)	<0.005	-24.4	7,670.35	-31.4	0.7	-48.3	0.0	1.3
L	tasonermin	<0.005	-57.0	6,413.00	0.0	0.0	-57.1	0.0	1.3
C	landiolol	<0.005	96.0	5,567.41	-0.3	1.7	95.0	0.0	1.3
L	alemtuzumab	<0.005	-24.6	5,518.02	4.50	2.8	-21.4	0.0	1.3
B	coagulation factor XIII	<0.005	21.0	5,487.96	-0.10	0.7	20.6	0.0	1.3
V	yttrium chloride (90Y)	<0.005	-18.0	4,669.76	4.30	0.1	-14.7	0.0	1.3
V	iobenguano (131I)	<0.005	76.7	4,117.49	98.4	0.3	>100	0.0	1.3
B	defibrotide	<0.005	21.4	4,099.74	0.1	7.4	21.3	0.1	1.4
B	activated heptacog alfa (recombinant DNA coagulation factor VII)	<0.005	-28.0	3,854.57	-5.0	18.4	-31.8	0.2	1.6
L	citarabine/daunorubicine	<0.005	40.0	3,817.23	0.2	12.5	40.0	0.1	1.7
L	plerixafor	<0.005	22.0	3,585.23	-0.7	9.4	20.8	0.1	1.8
V	andexanet alfa	<0.005	63.6	3,515.33	-0.1	10.6	63.0	0.1	1.9
	Total top 30	**<0.005**	**8.5**	**11,438.87**	**12.6**	**229.6**	**21.9**	**1.9**	
	Total	**114.46**	**3.3**	**4.90**	**5.1**	**12,052.70**	**8.3**	**100**	

Note: Consolidated data as of 23 April 2024, relating to medicines with MA; *calculated on total expenditure; ^changes in average DDD cost in 2023 compared to 2022 are due to changes in the methods of accounting for the expenditure on medicines that were subject to conditional reimbursement agreements, Payment at result, which provided for the allocation as well as the attribution of fractions of the cost of the treatment over time following verification of continued therapeutic success. Subsequently, the change provided for the revision of the contractual agreements and the accounting of the entire cost of the infusion treatment.

Table 2.4.7 Top 30 active ingredients of medicines dispensed in the context of inpatient and ambulatory care by expenditure increase 2023-2022

ATC 1st level	Active ingredient	Expenditure *(EUR million)*	Δ % 23-22	Inc. %*	% cum.	DDD/1000 inhabitants per day	Δ % 23-22	Average DDD cost	Δ % 23-22
L	trastuzumab deruxtecan	36.0	>100	0.3	0.3	0.01	>100	120.4	>100
M	vosoritide	21.7	>100	0.2	0.5	<0.005	>100	455.8	-1.5
L	pertuzumab/trastuzumab	37.9	>100	0.3	0.8	<0.005	>100	2,767.9	45.9
J	15-valent pneumococcal vaccine	25.0	>100	0.2	1.0	0.03	>100	45.8	-
L	dostarlimab	10.7	>100	0.1	1.1	0.03	>100	14.4	-0.1
J	cabotegravir	12.5	>100	0.1	1.2	0.05	>100	11.8	0.7
L	ofatumumab	37.0	>100	0.3	1.5	<0.005	>100	1,240.4	1.1
L	sacituzumab govitecan	27.7	>100	0.2	1.7	<0.005	>100	351.7	-
L	ravulizumab	53.3	>100	0.4	2.1	<0.005	>100	548.3	-9.7
L	acalabrutinib	57.5	>100	0.5	2.6	0.02	>100	137.3	1.7
L	axicabtagene ciloleucel^	59.6	>100	0.5	3.1	<0.005	27.7	298,047.1	70.2
L	apalutamide	61.6	>100	0.5	3.6	0.05	>100	56.1	-9.7
B	carboxymaltose iron	43.0	92.3	0.4	4.0	0.09	96.8	22.1	-2.1
A	semaglutide	52.8	89.1	0.4	4.4	0.87	>100	2.8	-7.0
N	tafamidis	123.2	84.4	1.0	5.4	0.09	95.3	61.2	-5.4
L	avelumab	35.8	76.5	0.3	5.7	0.02	66.9	110.8	6.0
A	empagliflozin	17.8	76.2	0.1	5.8	0.72	68.6	1.2	4.7
M	risdiplam	72.7	71.5	0.6	6.4	0.01	65.6	397.3	3.8
L	brexucabtagene autoleucel	24.1	68.9	0.2	6.6	<0.005	51.3	300,960.0	11.9
L	upadacitinib	32.4	68.7	0.3	6.9	0.08	70.0	19.6	-0.6
J	adjuvanted recombinant varicella zoster vaccine	123.4	66.1	1.0	7.9	0.02	40.9	321.4	18.2
L	isatuximab	27.2	63.5	0.2	8.1	0.01	64.9	152.5	-0.7
V	andexanet alfa	10.6	63.0	0.1	8.2	<0.005	63.6	3,515.3	-0.1
A	dapagliflozin	28.4	62.8	0.2	8.4	1.18	73.1	1.1	-5.7
C	alirocumab	11.5	51.5	0.1	8.5	0.07	57.6	7.1	-3.7
L	durvalumab	36.0	51.1	0.3	8.8	0.01	67.6	144.0	-9.6
L	filgotinib	14.9	50.5	0.1	8.9	0.03	50.2	21.0	0.4
L	abemaciclib	66.5	48.6	0.6	9.5	0.06	76.1	52.1	-15.4
L	tildrakizumab	23.5	47.5	0.2	9.7	0.05	58.8	23.0	-6.9
R	elexacaftor/tezacaftor/ivacaftor	45.6	46.4	0.4	10.1	0.01	50.7	316.1	-2.6
	Total top 30	**1,229.80**	**111.00**	**10.2**		**3.51**	**86.2**	**16.3**	**13.6**
	Total	**12,052.70**	**8.3**	**100**		**114.5**	**3.3**	**4.9**	**5.1**

Note: consolidated data as of 23 April 2024, relating to medicines with MA Selected among active ingredients with an expenditure of at least 10 million euro; * calculated on total expenditure; ^ The changes in the average DDD cost in 2023 compared to 2022 are due to the change in the methods of accounting for the expenditure on medicines that were subject to conditional reimbursement agreements, payment at result, which provided for the allocation and for the attribution of fractions of the cost of treatment over time following the verification of the maintenance of therapeutic success. Subsequently, the change provided for the revision of the contractual agreements and the accounting of the entire cost of the infusion treatment.

Table 2.4.8 Top 30 active ingredients of medicines dispensed in the context of inpatient and ambulatory care by consumption increase 2023-2022

ATC 1st level	Active ingredient	DDD/1000 inhabitants per day	Δ % 23-22	Average DDD cost	Δ % 23-22	Expenditure *(EUR million)*	Δ % 23-22	Inc. %*	% cum.
C	atenolol	0.98	>100	<0.005	-63.1	<0.005	-10.9	-	-
A	semaglutide	0.87	>100	2.84	-7	52.80	89.1	0.40	0.4
J	entecavir	0.23	>100	0.82	5.7	4.00	>100	-	0.4
L	fulvestrant	0.25	93.40	1.48	-45.6	7.90	4.9	0.10	0.5
J	tetravalent influenza vaccine (surface antigen, inactivated)	0.13	91.80	4.74	-34.1	12.90	26.1	0.10	0.6
A	linagliptin/empagliflozin	0.22	81.80	1.21	-2.9	5.80	76.2	-	0.6
A	dapagliflozin	1.18	73.10	1.12	-5.7	28.40	62.8	0.20	0.8
A	empagliflozin	0.72	68.60	1.16	4.7	17.80	76.2	0.10	0.9
C	valsartan/sacubitril	0.40	68.10	3.21	-15.9	27.80	41	0.20	1.1
A	pioglitazone	0.16	67.60	0.31	62.3	1.10	>100	-	1.1
A	canagliflozin	0.14	62.80	1.23	-3.6	3.80	56.6	-	1.1
C	doxazosin	0.15	49.70	<0.005	6.1	-	58.5	-	1.1
L	mitomycin	0.16	46.00	1.05	-28.9	3.60	3.6	-	1.1
L	guselkumab	0.11	43.60	24.39	0	58.20	43.3	0.50	1.6
C	rosuvastatin	0.10	36.60	0.05	25.3	0.10	70.7	-	1.6
B	edoxaban	1.17	36.20	1.72	0.7	43.40	36.8	0.40	2
R	ipratropium	0.23	34.20	0.12	2.4	0.60	37.1	-	2
B	apixaban	1.84	33.00	1.66	3.1	65.50	36.8	0.50	2.5
A	vildagliptin/metformin	0.16	32.50	0.50	-45.5	1.70	-27.9	-	2.5
L	daratumumab	0.25	32.30	83.49	-11.5	456.30	16.8	3.80	6.3
L	enzalutamide	0.11	31.90	65.62	-5.2	148.20	24.8	1.20	7.5
R	cetirizine	0.15	29.20	0.03	29.3	0.10	66.6	-	7.5
A	empagliflozin/metformin	0.33	27.90	0.92	-7.4	6.60	18.2	0.10	7.6
D	dupilumab	0.22	26.60	27.84	-0.3	132.80	25.9	1.10	8.7
M	denosumab	1.55	25.20	0.91	5.6	30.20	31.9	0.30	9
G	ethonogestrel	0.20	24.60	0.09	1.6	0.40	26.2	-	9
N	donepezil	0.28	24.50	0.06	47.5	0.40	83.2	-	9
A	insulin degludec/liraglutide	0.16	22.60	3.31	-1.7	11.70	20.3	0.10	9.1
R	acetylcysteine	0.22	22.50	0.18	-2.7	0.90	19	-	9.1
L	ocrelizumab	0.16	21.00	44.72	-1.2	157.90	19.3	1.30	10.4
	Total top 30	**12.84**	**49.60**	**4.64**	**-15.4**	**1,280.90**	**26.3**	**10.60**	
	Total	**114.5**	**3.30**	**4.90**	**5.1**	**12,052.70**	**8.3**	**100.00**	

Note: consolidated data as of 23 April 2024, relating to medicines with MA
* calculated on the total expenditure
Selected among the active substances having DDD/1000 inhab. per day = 0.1

Table 2.4.9 Top 30 active ingredients of medicines dispensed in the context of inpatient and ambulatory care by expenditure reduction 2023-2022

ATC 1st level	Active ingredient	Expenditure *(EUR million)*	Δ % 23-22	Inc. %*	% cum.	DDD/1000 inhabitants per day	Δ % 23-22	Average DDD cost	Δ % 23-22
L	lenalidomide	28.0	-80.4	0.2	0.2	0.15	3.7	8.65	-81.1
L	abiraterone	20.3	-77.1	0.2	0.4	0.06	3.7	15.63	-77.9
L	pirfenidone	30.2	-45.5	0.3	0.7	0.04	-0.5	35.05	-45.1
L	everolimus	10.6	-44.1	0.1	0.8	0.01	-3.5	38.25	-42.0
J	13-valent pneumococcal vaccine	25.8	-38.7	0.2	1.0	0.02	-38.7	48.84	0.3
L	dimethyl fumarate	12.3	-35.9	0.1	1.1	0.03	8.6	18.13	-40.9
L	dasatinib	34.2	-34.6	0.3	1.4	0.03	2.3	60.33	-35.9
S	ranibizumab	30.9	-34.2	0.3	1.7	0.08	-15.1	17.39	-22.4
B	activated heptacog alfa (recombinant DNA coagulation factor VII)	18.4	-31.8	0.2	1.9	<0.005	-28.0	3854.57	-5.0
J	varicella zoster vaccine, live attenuated	11.0	-28.6	0.1	2.0	0.01	-28.5	96.20	0.0
J	dolutegravir/abacavir/ lamivudine	33.7	-28.3	0.3	2.3	0.07	-28.1	21.48	0.0
J	raltegravir	18.3	-23.7	0.2	2.5	0.09	-24.0	9.69	0.6
L	abatacept	53.7	-23.6	0.4	2.9	0.07	9.2	34.64	-29.9
N	paliperidone	70.8	-23.6	0.6	3.5	0.78	4.4	4.23	-26.7
J	inactivated, split virus tetravalent influenza vaccine	44.8	-23.2	0.4	3.9	0.22	-31.2	9.51	11.7
J	emtricitabine/rilpivirine/ tenofovir alafenamide	60.2	-23.0	0.5	4.4	0.16	-16.6	17.96	-7.5
J	remdesivir	91.3	-23.0	0.8	5.2	0.01	-17.9	356.96	-5.9
B	octocog alfa	13.3	-22.9	0.1	5.3	0.00	-15.7	250.54	-8.4
J	emtricitabine/ tenofovir alafenamide	18.7	-22.6	0.2	5.5	0.08	-22.4	11.29	0.0
L	trastuzumab	38.3	-20.4	0.3	5.8	0.15	-8.4	11.61	-13.0
V	lutetium oxodotreotide (177Lu)	11.8	-18.1	0.1	5.9	<0.005	6.2	12858.52	-22.7
B	treprostinil	27.4	-17.1	0.2	6.1	<0.005	0.7	400.27	-17.5
L	decitabine	12.0	-16.4	0.1	6.2	<0.005	-16.5	585.19	0.3
J	darunavir/cobicistat	17.5	-15.6	0.1	6.3	0.07	-15.4	12.25	0.0
A	idursulfase	24.7	-14.8	0.2	6.5	<0.005	4.2	2264.25	-18
L	trastuzumab emtansine	65.0	-14.8	0.5	7.0	0.02	-14.6	152.8	0.0
L	rituximab	37.5	-14.3	0.3	7.3	0.48	8.4	3.64	-20.8
L	axitinib	22.6	-12.9	0.2	7.5	0.01	-9.3	97.17	-3.8
L	ramucirumab	28.1	-12.6	0.2	7.7	0.01	-6.8	231.9	-6.0
L	bevacizumab	37.9	-12.3	0.3	8.0	0.13	14.8	13.47	-23.5
	Total top 30	**949.1**	**-33.2**	**7.9**		**2.8**	**-5.8**	**15.87**	**-28.9**
	Total	**12,052.7**	**8.3**	**100**		**114.5**	**3.3**	**4.90**	**5.1**

Note: consolidated data as of 23 April 2024, relating to medicines with MA; * calculated on the total expenditure
Selected among the active ingredients with an expenditure of at least 10 million euro

Table 2.4.10 Top 30 active ingredients of medicines dispensed in the context of inpatient and ambulatory care by consumption reduction 2023-2022

ATC 1st level	Active ingredient	DDD/1000 inhabitants per day	Δ % 23-22	Average DDD cost	Δ % 23-22	Expenditure *(EUR million)*	Δ % 23-22	Inc. %*	% cum.
N	paracetamol	2.41	-42.0	0.17	127.6	8.60	31.8	0.1	0.1
B	parenteral nutrition solutions	0.11	-37.4	14.97	53.0	34.80	-4.4	0.3	0.4
J	tetravalent influenza vaccine (split virus, inactivated)	0.22	-31.2	9.51	11.7	44.80	-23.2	0.4	0.8
C	adrenaline	0.44	-29.8	0.36	62.7	3.40	14.0	0.0	0.8
N	mepivacaine	0.19	-26.9	0.18	58.4	0.80	15.6	0.0	0.8
N	sertraline	0.21	-25.3	<0.005	-58.1	0.00	-68.7	0.0	0.8
D	benzalkonium chloride/ ethyl alcohol	0.57	-20.7	0.05	7.9	0.60	-14.6	0.0	0.8
B	clopidogrel	1.49	-20.3	0.06	8.5	1.90	-13.7	0.0	0.8
H	prednisone	0.44	-20.0	0.06	26.4	0.60	0.9	0.0	0.8
A	sitagliptin	0.37	-17.1	0.21	-76.4	1.70	-80.5	0.0	0.8
C	ivabradine	0.30	-16.8	0.11	34.3	0.70	11.5	0.0	0.8
N	rivastigmine	0.12	-16.8	0.58	-15.3	1.60	-29.8	0.0	0.8
J	emtricitabine/rilpivirine/ tenofovir alafenamide	0.16	-16.6	17.96	-7.5	60.20	-23.0	0.5	1.3
H	hydrocortisone	0.46	-15.9	1.06	22.1	10.50	2.4	0.1	1.4
A	ascorbic acid	0.38	-15.6	0.02	0.2	0.20	-15.7	0.0	1.4
S	tropicamide/phenylephrine	0.36	-12.5	0.37	22.0	2.80	6.5	0.0	1.4
D	povidone iodine	0.79	-11.7	0.24	26.3	4.10	11.3	0.0	1.4
C	amiodarone	0.10	-10.1	0.21	-1.9	0.50	-12.0	0.0	1.4
B	calcium chloride	0.13	-9.7	0.14	63.1	0.40	46.9	0.0	1.4
N	olanzapine	0.80	-9.4	0.31	9.1	5.40	-1.4	0.0	1.4
N	methadone	2.00	-9.0	0.34	0.8	14.50	-8.4	0.1	1.5
L	fluorouracil	0.28	-8.7	0.24	8.8	1.50	-0.9	0.0	1.5
L	trastuzumab	0.15	-8.4	11.61	-13.0	38.30	-20.4	0.3	1.8
S	tropicamide	0.22	-7.4	0.18	7.8	0.90	-0.4	0.0	1.8
J	dolutegravir	0.12	-7.3	16.42	0.0	44.10	-7.5	0.4	2.2
C	nitroglycerin	0.12	-7.3	0.40	-5.6	1.10	-12.7	0.0	2.2
D	gentamicin	0.39	-7.0	0.02	-1.7	0.20	-8.8	0.0	2.2
N	ropivacaine	0.20	-6.9	0.21	10.5	0.90	2.7	0.0	2.2
B	acetylsalicylic acid	0.56	-6.6	0.02	1.0	0.20	-5.8	0.0	2.2
A	insulin degludec	0.40	-6.0	0.95	-17.2	8.10	-22.3	0.1	2.3
	Total top 30	**14.51**	**-21.1**	**0.94**	**6.9**	**293.00**	**-15.8**	**2.4**	
	Total	**114.50**	**3.3**	**4.90**	**5.1**	**12,052.70**	**8.3**	**100.0**	

Note: consolidated data as of 23 April 2024, relating to medicines with MA
* calculated on the total expenditure
Selected among the active substances having DDD/1000 inhab. per day = 0.1

2.5 Reimbursement of "extra tariff" medicines

The voluntary transmission of expenditure and consumption values for medicines purchased by a facility not directly managed by the NHS and subsequently reimbursed by the same as "extra tariff", in the last six years, has shown a constant increase, with the only exception of 2020 when it is possible to note a decrease for the most Regions (Figure 2.5.1). In the last year, only Campania and Molise showed a reduction in expenditure.

In 2023, the Regions that transmitted data are: Lombardy, Lazio, Veneto, Liguria, Molise and Campania (Table 2.5.1). Overall, this year's reimbursement for these medicines amounts to more than 660.6 million euro, with a per capita expenditure up on the previous year's figure (+18.0%). Lombardy and Lazio recorded the highest amounts of expenditure, reporting a per capita value of 42.82 euro and 33.20 euro, up 20.1% and 15.7% compared to 2022. The highest values of consumption were recorded in Lombardy (27.69 DDD/1000 inhabitants per day), Lazio (4.58 DDD/1000 inhabitants per day) and Liguria (4.29 DDD/1000 inhabitants per day), while Lombardy (>100%) and Veneto (+20.9%) recorded the largest increases and Campania (-13.7%) and Molise (-11.2%) the largest reductions.

Antineoplastic and immunomodulatory medicines (ATC L) represent the most expensive and consumed category, with values of 17.11 euro per capita and 9.33 DDD/1000 inhabitants per day respectively (Table 2.5.2). For this ATC there is an increase in expenditure (+20.7%) and a large variation in consumption (>100%) compared with the previous year. Antibacterial medicines for systemic use (ATC J) are the second highest expenditure and consumption category, reporting a per capita expenditure of 2.75 euro and 0.43 DDD/1000 inhabitants per day. From the analysis by ATC 1st level it is possible to observe a greater variation, in terms of both expenditure (+70.6%) and consumption (>100%), for the miscellaneous category (ATC V) which records a per capita expenditure of 0.24 euro and a consumption of 0.22 DDD/1000 inhabitants per day.

The trends highlighted by ATC 1st level would seem to be confirmed by the analysis of the top 30 active ingredients (Table 2.5.3), in which as many as 24 molecules belong to the group of antineoplastics and immunomodulators (ATC L) and in which pembrolizumab and ustekinumab represent the molecules with the highest per capita expenditure values, respectively 0.73 and 0.71 euro. The medicine with the highest cost per DDD turns out to be axicabtagene ciloleucel (242.990 euro), for the first time present in this information flow, followed by eculizumab (715.89 euro) and nusinersen (397.09 euro). Overall, a reduction in the average DDD cost can be seen.

Figure 2.5.1 Annual trend of expenditure for extra DRG medicines: years 2018-2023

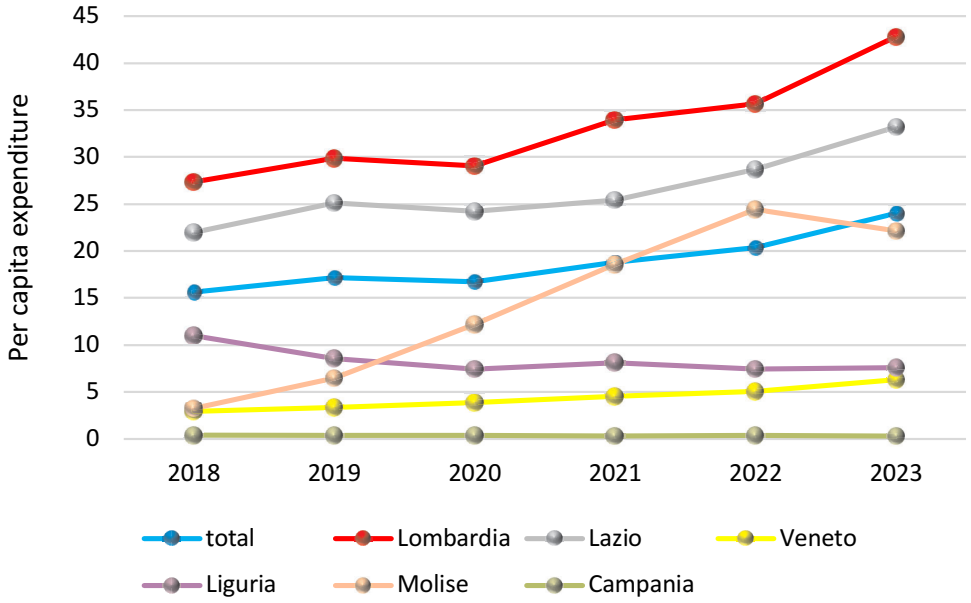


Table 2.5.1 Breakdown of expenditure and consumption for extra DRG medicines by Region: comparison 2023-2022

Region	Total expenditure	Per capita expenditure	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22
Lombardy	421,463,576	42.82	20.1	27.69	>100
Lazio	187,590,198	33.20	15.7	4.58	16.8
Veneto	30,742,977	6.31	24.3	0.94	20.9
Liguria	12,392,126	7.57	1.5	4.29	2.0
Molise	6,677,297	22.16	-9.3	1.11	-11.2
Campania	1,700,259	0.33	-15.4	0.09	-13.7
Total	**660,566,432**	**24.02**	**18.0**	**11.30**	**118.3**

Note: data updated to 10 May 2024, DDD consumption was calculated only for medicines with MA

Table 2.5.2 Breakdown of expenditure and consumption for extra DRG medicines by ATC 1st level: comparison 2023-2022

ATC 1st level	Per capita expenditure	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22
A	0.56	8.4	0.15	-1.4
B	0.50	8.5	0.21	2.8
C	0.54	32.6	0.20	35.5
D	0.32	22.2	0.03	7.8
G	0.02	2.3	0.03	25.5
H	0.11	14.0	0.05	13.1
J	2.75	10.8	0.43	17.3
L	17.11	20.7	9.33	>100
M	0.65	36.4	0.44	17.8
N	0.19	24.9	0.09	8.5
P	0.00	20.7	0.00	62.6
R	0.27	15.2	0.03	20.7
S	0.68	-5.4	0.09	3.6
V	0.24	70.6	0.22	>100
Total	**24.02**	**18.0**	**11.30**	**118.3**

Table 2.5.3 Top 30 active ingredients by expenditure on extra DRG medicines: comparison 2023-2022

ATC 1st level	Active ingredient	Per capita expenditure	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
L	pembrolizumab	0.73	36.0	0.04	>100	46.19	-50.4
L	ustekinumab	0.71	23.2	0.15	25.8	13.14	-2.1
L	ocrelizumab	0.67	14.0	0.04	16.6	46.38	-2.2
L	enzalutamide	0.64	47.5	0.03	62.0	67.07	-9.0
L	pertuzumab	0.55	3.9	0.42	>100	3.61	-92.5
J	emtricitabine, tenofovir alafenamide and bictegravir	0.49	9.5	0.07	9.5	19.95	0.0
L	vedolizumab	0.45	9.1	0.04	9.1	30.54	-0.1
L	osimertinib	0.42	>100	0.01	>100	100.96	4.0
J	lamivudine/dolutegravir	0.40	13.8	0.07	13.8	16.57	0.0
J	normal human immunoglobulins for intravascular administration	0.39	8.3	0.02	>100	48.64	-82.8
L,S	aflibercept	0.38	1.5	<0.005	57.4	333.73	-35.5
L	secukinumab	0.37	9.5	0.03	11.7	29.24	-2.0
L	nivolumab	0.37	54.8	0.10	>100	10.24	-89.7
L	risankizumab	0.36	33.4	0.04	>100	26.27	-37.3
L	dimethyl fumarate	0.35	-7.5	0.04	7.6	27.63	-14.0
L	canakinumab	0.34	25.2	0.01	30.5	136.96	-4.0
L	ixekizumab	0.34	24.8	0.03	24.5	30.37	0.2
L	natalizumab	0.33	-5.6	0.02	1.0	47.88	-6.5
L	fingolimod	0.33	-20.7	0.02	-2.8	43.77	-18.4
L	ibrutinib	0.31	-9.4	0.01	-5.9	120.42	-3.7
L	daratumumab	0.30	19.5	0.01	37.5	84.76	-13.1
L	trastuzumab emtansine	0.29	-0.8	0.01	-43.0	153.51	73.9
M	nusinersen	0.28	20.4	<0.005	20.9	397.09	-0.4
D	dupilumab	0.27	5.3	0.03	4.8	27.93	0.5
L	eculizumab	0.26	16.8	<0.005	23.2	715.89	-5.2
L	abemaciclib	0.26	>100	0.01	>100	51.69	-26.3
L	palbociclib	0.24	10.3	0.01	27.6	52.62	-13.6
L	teriflunomide	0.23	5.0	0.02	9.5	25.16	-4.1
L	axicabtagene ciloleucel	0.23	-	<0.005	-	242,990.06	-
L	dabrafenib	0.22	>100	0.01	204.3	115.11	8.8
	Total top 30	**11.53**	**14.0**	**1.28**	**88.7**	**24.68**	**-65.5**

2.6 Out-of-pocket medicines consumption

In 2023, expenditure on class C medicines exceeded 7.1 billion euro, an increase of 9.8% compared to 2022; 54% of the expenditure (3.8 billion euro) relates to prescription medicines and the remaining 46% (3.03 billion euro) to self-medication medicines (SOP and OTC) including those dispensed in shops (Table 1.1.1).

Class C prescription medicines show a 9.0% increase in expenditure over 2022 driven by an increase in prices (+6.8%) and the prescription of more expensive medicines (mix effect: +2.1%), while consumption remains unchanged (Figure 2.6.1).

It should be noted that the increase in expenditure was mainly determined by the increase in prices foreseen in the month of January of each odd-numbered year pursuant to Article 1, paragraph 3 of Decree-Law No 87 of 27 May 2005. Among the top 20 highest-spending class C therapeutic categories with prescription in 2023 (Table 2.6.1), benzodiazepine derivatives (both anxiolytics and hypnotic-sedatives) and benzodiazepine analogues are confirmed as the categories with the highest private purchase, with an expenditure of about 617 million euro, equal to 16.1% of the total expenditure and representing 25.4% of the total consumption of class C prescription medicines. Benzodiazepine derivatives with anxiolytic activity are the category with the highest expenditure with 387.5 million euro, and a consumption of 25.3 DDD per 1000 inhabitants per day, down from 2022 (-3.0%). The second highest spending category is anilides, with 275.3 million euro or 7.2% of total expenditure, with a slight increase in expenditure (+1.0%) and a decrease in consumption (-7.1%) compared to 2022. Other categories with an expenditure value of more than 200 million euro are medicines used in erectile dysfunction (250.0 million euro) and fixed oestrogen-progestin combinations (228.3 million euro); for both categories there is an increase in average DDD costs, while consumption remains stable compared to 2022 (Table 2.6.1 and Figure 2.6.2). Overall, the top 20 therapeutic categories show important increases in expenditure, with the exception of influenza vaccines, which record a reduction in pharmacy purchases (consumption -22.4%; expenditure -8.3%). Among the top 10 highest expenditure categories, the medicines used in erectile dysfunction present the highest average DDD cost (5.11 euro), while for the other 9 categories, the average DDD cost fluctuates between a minimum value of 0.33 euro and a maximum value of 1.80 euro, registering a slightly increasing trend compared to the previous year (Figure 2.6.2).

Among the top 20 highest consumption therapeutic categories, we find vitamin B12 with 26.7 doses dispensed per 1000 inhabitants per day, followed by anxiolytics with 25.3 DDD and hypnotics and sedatives with 20.3 DDD per 1000 inhabitants per day; all of them show a decreasing trend in consumption compared with 2022 (Table 2.6.2).

The top five highest expenditure active ingredients (Table 2.6. 3) remain unchanged compared to the previous year: paracetamol, with an expenditure of 259.7 million euro equal to 6.8% of the total class C with prescription, ranks first although it shows a decrease in consumption (-8.3%), while expenditure is stable (-0.1%), suggesting an increase in the cost of the packages. This is followed by two benzodiazepines, alprazolam and lorazepam, in second and fourth place respectively at 139.2 and 109.5 million, although both show a decrease in consumption (-1.8% and -3.2% respectively), and two phospho-diesterase type 5 inhibitors (PDE5I): tadalafil (129.7 million euro) and sildenafil (96.1 million euro), used in the treatment of erectile dysfunction, whose expenditure increased by 7.9% and 1.4% respectively. In addition to alprazolam and lorazepam, among the most expensive substances there are several benzodiazepines placed as follows: 8th zolpidem, 9th lormetazepan, 15th delorazepam, 16th

triazolam and 18th bromazepam. There was a marked increase in the private purchase of liraglutide-containing specialities, used in the management of body weight in addition to a healthy diet and physical activity, which reached 44.7 million euro with an increase, compared to last year, of 69.3% in expenditure and 71.0% in consumption; acetylcysteine-based specialities also recorded an increase in both indicators: expenditure +22.7% and consumption +10.6%. Among the top 30 highest consumption active ingredients of class C with prescription (Table 2.6.4), we find in first place cyanocobalamin with 26.7 DDD per 1000 inhabitants per day, a decrease of 7.3% compared to the previous year, followed by three benzodiazepines lormetazepam, alprazolam and lorazepam, which all record a decrease in consumption (-7.1%, -1.9% and -3.1% respectively). The most important increases in consumption, compared to 2022, concern two medicines indicated for the treatment of ocular inflammation, the antibacterial tobramycin eye drops (+33.3%) and the dexamethasone/tobramycin combination (+23.1%). In addition, the upward trend for mometasone in an inhaled formulation (+23.8%) and cholecalciferol (+21.4%) is also confirmed in 2023. Among the top 20 highest expenditure categories of self-medication medicines, anti-propellants are those that register the greatest increase (+58.3%) compared to the previous year and reach an expenditure of 66.5 million euro, while propionic acid derivatives confirm themselves as the category with the highest expenditure (416.3 million euro), representing 12.6% of the total expenditure, up by 6.9% compared to 2022 (Table 2.6.5). These are also among the top 20 most consumed self-medication categories, together with sympathomimetics and non-steroidal anti-inflammatory medicines for topical use (Table 2.6.6). Nasal decongestants based on sympathomimetics, mucolytics and other cough sedatives are the categories that show the most significant increases in both expenditure and consumption (Table 2.6.5). Again in 2023, ibuprofen is the self-medication molecule with the highest expenditure with 275.7 euro (+21.5% compared to 2022), followed by diclofenac which has an expenditure of 181.3 million euro (+10.3%), and by paracetamol, whose expenditure comes to 146.1 million euro (Table 2.6.7). On the consumption side, we find nafazoline, diclofenac and flurbiprofen in the top three positions. Also in 2023, nafazolin and flurbiprofen show a considerable increase in consumption compared with the previous year, by 27.9% and 21.7% respectively, while diclofenac shows a reduction of 2.0% (Table 2.6.8). At regional level, consumption of class C prescription medicines remains fairly stable compared to the previous year, with Sardinia and Basilicata recording the highest increase among the Regions, 6.3% and 4.0% respectively. The remaining Regions show variations ranging from -2.5% in Valle d'Aosta and Marche to +3.0% in Calabria (Table 2.6.9). For self-medication medicines, compared with the previous year, the Southern Regions show the greatest variations in consumption (+7.0%) compared with those of the Centre (+3.1%) and the North (+1.4%). In all Regions there is an increase in expenditure both for self-medication medicines and for class C prescription medicines; this trend, as previously mentioned, is due to the increase in prices to the public. Overall, for all class C medicines, the North and the Centre spend more than the South, which registers an expenditure that is 6.4% lower (class C with prescription) and 9.6% lower (SOP and OTC) than the national average.

The widest differences between the Regions emerge from the analysis of the private purchase of class A medicines, with Sardinia holding the record with a per capita expenditure of 116.2 euro, almost seven times higher than Molise (16.98 euro per capita) and, in general, with an expenditure in the Regions of the Centre (41.52 euro per capita) greater than that in the Regions of the South and the North (39.32 euro and 27.79 euro, respectively) (Table and Figure 2.6.10). In 2023, the Regions Sardinia, Basilicata and Sicily, record a notable increase in con-

sumption (81.3%, 57.7% and 44.4% respectively), while Friuli Venezia Giulia and Piedmont represent the Regions with the greatest reductions compared to the previous year (-43.0% and -12.2%) (Table 2.6.10). The top highest expenditure therapeutic categories of class A purchased by the citizen are proton pump inhibitors with over 146.3 million euro, propionic acid derivatives with 128.4 million euro, vitamin D and analogues with 76.6 million and the combination of penicillins including beta-lactamase inhibitors with 75.8 million euro, representing over a fifth (22.4%) of the total expenditure of class A medicines purchased privately by the citizen (Table 2.6.11). Three of these are also among the top highest consumption class A therapeutic categories purchased by the citizen: vitamin D and analogues (61.6 DDD per 1000 inhabitants per day), propionic acid derivatives (17.8 DDD) and proton pump inhibitors (16.8 DDD), to which is added the category of platelet aggregation inhibitors, excluding heparin (16.4 DDD per 1000 inhabitants per day) (Table 2.6.12). Among the class A active ingredients purchased privately by the citizen, amoxicillin/clavulanic acid, cholecalciferol, ibuprofen, pantoprazole, ketoprofen and semaglutide, rank at the top with a total expenditure of more than 324 euro million. Ketoprofen (79.1%) and ibuprofen (72.5%) are the substances with the highest percentage of private purchase, calculated on the total expenditure for the molecule. As for pump inhibitors, in addition to the aforementioned pantoprazole, among the top 20 highest expenditure active ingredients, there are esomeprazole, lansoprazole and omeprazole, whose share of private expenditure is around 17.5% (Table 2.6.13). The percentage of private purchase for the antibiotic amoxicillin/clavulanic acid, which reaches almost one third of the expenditure of the active ingredient (28.2%), could represent a wake-up call, suggesting an inappropriate use of this medicine. Among the first 30 class A active ingredients purchased privately by the citizen, those with the highest consumption are represented by cholecalciferol with 61.5 DDD (+14.1% compared to 2022), acetylsalicylic acid with 14.5 DDD (-32.9%) and ketoprofen with 9.6 DDD per 1000 population days (-3.0%) (Table 2.6.14).

A closer look at the breakdown of the consumption of class A medicines by price range shows that approximately 60% of private purchases relate to medicines with a price lower than 6 euro and only 16.5% relate to medicines with a price higher than 10 euro. There is, however, a wide regional variability in the distribution of consumption, mainly in the price range above 10 euro, which reaches its maximum in the central Regions with 19.3% of consumption. The consumption of medicines with a price lower than 6 euro accounted for about 61.6% of consumption in the Southern Regions (Table 2.6.15).

In 2023, expenditure on self-medication medicines dispensed by commercial shops amounted to 367.6 euro, increasing by 12.7% over the previous year. The highest *per capita* expenditure is recorded in Sardinia (9.8 euro) and Campania (9.3 euro), while the lowest values were observed in the Province of Bolzano and Sicily (0.9 euro and 3.2 euro respectively). There are no particular differences in expenditure between the geographical areas, with values ranging from 5.2 euro per capita in the Centre to 6.6 euro in the North (Table 2.6.16). In terms of per capita expenditure, the top five medicines dispensed by shops are ibuprofen (0.5 euro), followed by diclofenac, paracetamol, diosmin/hexperidine and flurbiprofen (0.3 euro), which account for 26.7% of the total expenditure (Table 2.6.17). As far as consumption is concerned, among the top active ingredients most frequently supplied by commercial shops, we find nafazolin, as a nasal decongestant (1.7 DDD per 1000 inhabitants per day), diclofenac (1.1 DDD per 1000 inhabitants per day) and glycerol (0.8 DDD per 1000 inhabitants per day) (Table 2.6.18).

Figure 2.6.1 Trend of local expenditure on Class C medicines with prescription in the period 2012-2023: consumption, price and mix effect

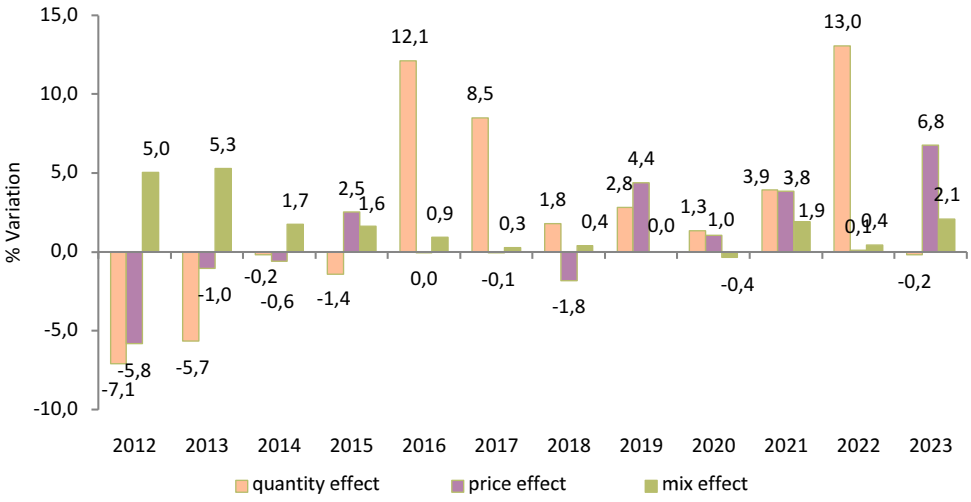
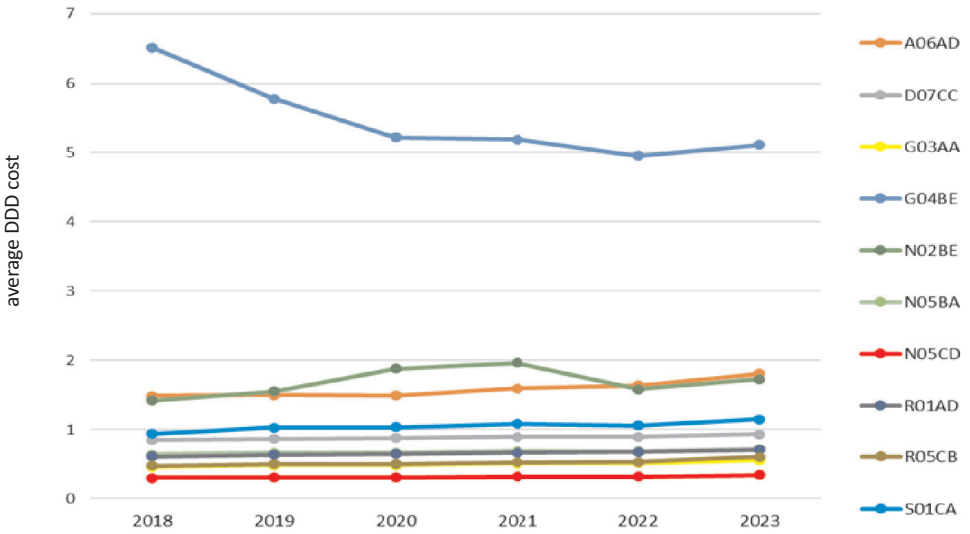


Table 2.6.1 Top 20 highest expenditure class C therapeutic categories with prescription in 2023: comparison 2023-2022

ATC 1st level	Therapeutic category	Expenditure *(million)*	Δ % 23-22	%*	DDD/ 1000 inhab. per day	Δ % 23-22
N	Benzodiazepine derivatives (anxiolytics)	387.5	2.2	10.1	25.34	-3.0
N	Anilides	275.3	1.0	7.2	7.42	-7.1
G	Medicines used in erectile dysfunctions	250.0	3.9	6.5	2.28	1.0
G	Fixed-dose oestrogen/progestogen combinations	228.3	5.9	5.9	19.51	-1.7
N	Benzodiazepine derivatives (hypnotics and sedatives)	146.1	1.2	3.8	20.29	-5.9
D	Active corticosteroids, in combination with antibiotics	100.4	6.7	2.6	4.99	2.8
R	Mucolytics	96.0	22.1	2.5	7.54	8.3
S	Corticosteroid and antimicrobial combinations	89.8	22.0	2.3	3.63	12.5
R	Corticosteroids	89.0	11.9	2.3	5.94	7.6
A	Osmotic laxatives	87.2	13.4	2.3	2.25	3.0
N	Benzodiazepine analogues	83.2	11.7	2.2	6.26	4.7
M	Other centrally acting muscle relaxants	75.6	13.7	2.0	1.32	8.4
J	Influenza vaccines	73.0	-8.3	1.9	0.12	-22.4
N	Other psychostimulants and nootropics	68.3	2.2	1.8	1.30	-3.6
M	Other muscle relaxants with peripheral action	66.1	2.3	1.7	0.02	-0.7
J	Protease inhibitors	54.2	85.6	1.4	0.01	88.2
N	Antivertigo preparations	53.7	4.7	1.4	2.76	-1.5
B	Heparins	53.5	0.2	1.4	2.25	-2.5
S	Antibiotics	49.3	30.4	1.3	3.04	21.5
G	Estrogen-progestogen, sequential combinations	47.5	1.5	1.2	3.49	-3.8
	Total top 20	**2,373.8**	**6.7**	**61.8**	**119.8**	**-0.6**
	Total	**3,841.5**	**9.0**	**100.0**	**204.2**	**0.1**

* Calculated on overall expenditure

Figure 2.6.2 Annual trend in average DDD cost of highest-spending class C therapeutic categories with prescription - top 10 (2018-2023)



A06AD – Osmotic laxatives	S01CA – Corticosteroid and antimicrobial combinations	G03AA – Fixed-dose oestrogen/ progestogen combinations
G04BE – Medicines used for erectile dysfunction	D07CC – Active corticosteroids, in combination with antibiotics	N05BA – Benzodiazepine derivatives (anxiolytics)
N05CD – Benzodiazepine derivatives (hypnotics and sedatives)	N02BE – Anilides	R05CB - Mucolytics
	R01AD – Corticosteroids	

Table 2.6.2 Top 20 highest consumption class C therapeutic categories with prescription in 2023: comparison 2023-2022

ATC 1st level	Therapeutic category	DDD/1000 inhab. per day	Δ % 23-22	Expenditure *(million)*	%*	Δ % 23-22
B	Vitamin B12 (cyanocobalamin and derivatives)	26.7	-8.2	5.5	0.1	-9.8
N	Benzodiazepine derivatives (anxiolytics)	25.3	-3.1	387.5	10.1	2.2
N	Benzodiazepine derivatives (hypnotics and sedatives)	20.3	-6.0	146.1	3.8	1.2
G	Fixed-dose oestrogen/ progestogen combinations	19.5	-1.5	228.3	5.9	5.9
R	Mucolytics	7.5	7.1	96.0	2.5	22.1
N	Anilides	7.4	-7.5	275.3	7.2	1.0
N	Benzodiazepine analogues	6.3	5.0	83.2	2.2	11.7
R	Corticosteroids	5.9	7.3	89	2.3	11.9
D	Active corticosteroids, in combination with antibiotics	5.0	2.0	100.4	2.6	6.7
S	Corticosteroid and antimicrobial combinations	3.6	12.5	89.8	2.3	22.0
G	Estrogen-progestogen, sequential combinations	3.5	-2.8	47.5	1.2	1.5
A	Vitamin D and analogues	3.4	21.4	8.7	0.2	33.8
G	Intrauterine contraceptives	3.3	10.0	9.1	0.2	12.3
D	Other antibiotics for topical use	3.2	0.0	39.4	1.0	8.2
G	Progestinic	3.1	19.2	32.1	0.8	26.9
S	Antibiotics	3.0	20.0	49.3	1.3	30.4
D	Corticosteroids, active (group III)	2.9	0.0	32.1	0.8	4.9
N	Antivertigo preparations	2.8	0.0	53.7	1.4	4.7
G	Intrauterine contraceptives	2.5	4.2	35.0	0.9	6.4
G	Medicines used in erectile dysfunctions	2.3	0.0	250.0	6.5	3.9
	Total top 20	**157.6**	**-1.0**	**2058.0**	**53.6**	**6.4**
	Total	**204.2**	**0.1**	**3,841.5**	**100.0**	**9.0**

* calculated on overall consumption

Table 2.6.3 Top 30 highest expenditure class C active ingredients with prescription in 2023: comparison 2023-2022

ATC 1st level	Active ingredient	Expenditure *(million)*	Δ % 23-22	%*	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost
N	paracetamol	259.7	-0.1	6.8	7.0	-8.3	1.7
N	alprazolam	139.2	4.9	3.6	10.1	-1.8	0.6
G	tadalafil	129.7	7.9	3.4	1.4	4.9	4.3
N	lorazepam	109.5	0.6	2.9	9.4	-3.2	0.5
G	sildenafil	96.1	1.4	2.5	0.7	-3.5	6.0
R	acetylcysteine	85.4	22.7	2.2	6.9	10.6	0.6
D	gentamicin/betamethasone	83.1	5.7	2.2	4.3	2.5	0.9
N	zolpidem	79.8	11.3	2.1	6.0	4.2	0.6
N	lormetazepam	67.0	-1.3	1.7	14.5	-7.3	0.2
M	*Clostridium botulinum* Type A toxin	66.1	2.3	1.7	<0.05	-0.6	204.5
G	drospirenone/ethinylestradiol	64.8	-4.3	1.7	4.9	-9.3	0.6
A	macrogol 3350/sodium chloride/ sodium bicarbonate/ potassium chloride	57.9	13.8	1.5	2.0	4.4	1.4
J	nirmatrelvir/ritonavir	54.2	85.6	1.4	<0.05	86.0	264.0
G	dienogest/ethinylestradiol	50.0	11.4	1.3	4.3	6.8	0.5
N	delorazepam	48.6	3.4	1.3	2.5	-2.0	0.9
N	triazolam	47.0	5.1	1.2	3.6	-2.1	0.6
N	bromazepam	46.4	-1.3	1.2	1.3	-5.9	1.7
M	thiocolchicoside	46.1	10.0	1.2	0.5	3.6	3.9
N	levo-acetylcarnitine	45.9	-2.3	1.2	0.9	-5.4	2.5
A	liraglutide	44.7	69.3	1.2	0.4	71	5.0
G	dienogest/estradiol	42.6	1.9	1.1	2.8	-4.1	0.7
R	mometasone	40.7	20.1	1.1	2.6	19.4	0.7
N	betahistine	37.6	3.9	1.0	2.2	-1.8	0.8
G	etonogestrel/ethinylestradiol	35.0	6.4	0.9	2.5	3.0	0.7
J	tetravalent influenza vaccine inactivated virus, surface antigen, adjuvanted	34.5	1.8	0.9	<0.05	2.3	34.0
S	dexamethasone/tobramycin	34.4	30.3	0.9	1.6	20.8	1.0
N	choline alfoscerate	34.4	12.8	0.9	0.3	9.9	4.7
B	mesoglycan	33.4	2.5	0.9	1.6	-0.7	1.0
S	tobramycin	33.1	35.1	0.9	2.0	26.7	0.8
J	tetravalent influenza vaccine, inactivated, split virus	32.5	-17.7	0.8	0.1	-34.4	24.0
	Total top 30	**1,979.7**		**51.5**	**96.2**		**1.00**
	Total	**3,841.5**	**9.0**	**100.0**	**204.2**	**0.1**	**0.90**

* calculated on overall expenditure

Table 2.6.4 Top 30 highest consumption class C active ingredients with prescription in 2023: comparison 2023-2022

ATC 1st level	Active ingredient	DDD/1000 inhab. per day	Δ % 23-22	Expenditure *(million)*	Δ % 23-22	%*	Average DDD cost
B	cyanocobalamin	26.7	-7.3	4.2	0.0	0.1	0.01
N	lormetazepam	14.5	-7.1	67.0	-1.3	1.7	0.22
N	alprazolam	10.1	-1.9	139.2	4.9	3.6	0.64
N	lorazepam	9.4	-3.1	109.5	0.6	2.9	0.54
N	paracetamol	7.0	-7.9	259.7	-0.1	6.8	1.74
R	acetylcysteine	6.9	11.3	85.4	22.7	2.2	0.58
N	zolpidem	6.0	3.4	79.8	11.3	2.1	0.62
G	drospirenone/ethinylestradiol	4.9	-10.9	64.8	-4.3	1.7	0.61
G	dienogest/ethinylestradiol	4.3	7.5	50.0	11.4	1.3	0.54
D	gentamicin/betamethasone	4.3	2.4	83.1	5.7	2.2	0.90
N	triazolam	3.6	-2.7	47.0	5.1	1.2	0.61
A	cholecalciferol	3.4	21.4	8.7	33.8	0.2	0.12
G	levonorgestrel	3.3	10.0	9.1	12.3	0.2	0.13
G	gestodene/ethinylestradiol	3.1	-8.8	22.8	-0.4	0.6	0.34
G	dienogest/estradiol	2.8	-3.4	42.6	1.9	1.1	0.71
D	gentamicin	2.7	0.0	24.7	4.7	0.6	0.43
G	levonorgestrel/ethinylestradiol	2.6	-3.7	28.5	5.9	0.7	0.51
R	mometasone	2.6	23.8	40.7	20.1	1.1	0.74
G	etonogestrel/ethinylestradiol	2.5	4.2	35	6.4	0.9	0.65
N	delorazepam	2.5	0.0	48.6	3.4	1.3	0.92
N	betahistine	2.2	0.0	37.6	3.9	1.0	0.81
A	macrogol 3350/sodium chloride/ sodium bicarbonate/ potassium chloride	2.0	5.3	57.9	13.8	1.5	1.37
S	tobramycin	2.0	33.3	33.1	35.1	0.9	0.79
G	desogestrel	1.9	5.6	18.0	7.8	0.5	0.44
D	clortetracyclines	1.9	0.0	7.5	8.7	0.2	0.19
R	bilastine	1.8	12.5	21.9	14.7	0.6	0.56
R	budesonide	1.8	0.0	9.6	3.2	0.3	0.25
G	nomegestrol/estradiol	1.6	0.0	25.9	12.6	0.7	0.75
S	dexamethasone/tobramycin	1.6	23.1	34.4	30.3	0.9	1.00
J	bacterial lysate	1.6	6.7	20.7	10.7	0.5	0.61
	Total top 30	**141.4**		**1,517.2**		**39.5**	**0.50**
	Total	**204.2**	**0.1**	**3,841.5**	**9.0**	**100.0**	**0.88**

* calculated on overall consumption

Table 2.6.5 Top 20 highest expenditure self-medication therapeutic categories (SOP and OTC) in 2023: comparison 2023-2022

ATC 1st level	Therapeutic category	Expenditure *(million)*	Δ % 23-22	%*	DDD/1000 inhab. per day	Δ % 23-22
M	Propionic acid derivatives	416.3	6.9	12.6	7.7	-1.3
N	Anilides	241.0	7.3	7.3	5.2	0.0
M	Nonsteroidal anti-inflammatory medicines for topical use	227.0	-3.4	6.9	11.9	-12.5
A	Other agents for local oral treatment	181.8	11.7	5.5	7.5	7.1
A	Antidiarrheal microorganisms	166.1	13.4	5.0	2.7	8.0
R	Mucolytics	158.5	25.6	4.8	6.7	17.5
C	Bioflavonoids	110.2	1.4	3.3	5.4	-1.8
R	Sympathomimetics, not in combination	100.1	13.8	3.0	16.4	14.7
R	Antiseptics	86.7	19.6	2.6	1.4	7.7
D	Imidazole and triazole derivatives	84.3	25.8	2.6	3.4	9.7
N	Salicylic acid and derivatives	71.8	-9.2	2.2	1.5	-11.8
A	Antipropulsives	66.5	58.3	2.0	0.6	50.0
A	Enemas	62.4	8.0	1.9	2.3	4.5
R	Other cough suppressants	62.2	15.2	1.9	3.0	15.4
G	Imidazole derivatives	61.3	12.1	1.9	1.6	6.7
A	Other anti-peptic antiulcer and gastroesophageal reflux disease (GERD)	51.5	39.2	1.6	0.7	16.7
A	Contact laxatives	49.5	0.2	1.5	3.9	-7.1
S	Sympathomimetics used as decongestants	44.1	16.4	1.3	7.8	18.2
M	Acetic acid derivatives and related substances	40.7	14.0	1.2	0.8	14.3
C	Corticosteroids	40.4	5.5	1.2	2.3	4.5
	Total top 20	**2,322.2**	**10.2**	**70.3**	**92.8**	**4.5**
	Total	**3,304.7**	**10.8**	**100.0**	**143.6**	**3.4**

*calculated on overall expenditure

Table 2.6.6 Top 20 highest consumption self-medication therapeutic categories (SOP and OTC) in 2023: comparison 2023-2022

ATC 1st level	Therapeutic category	DDD/1000 inhab. per day	Δ % 23-22	Expenditure *(million)*	Δ % 23-22	%*
R	Sympathomimetics, not in combination	16.4	14.7	100.1	13.8	3.0
M	Topical nonsteroidal anti-inflammatory medicines	11.9	-12.5	227.0	-3.4	6.9
S	Sympathomimetics used as decongestants	7.8	18.2	44.1	16.4	1.3
M	Propionic acid derivatives	7.7	-1.3	416.3	6.9	12.6
A	Other agents for local oral treatment	7.5	7.1	181.8	11.7	5.5
R	Mucolytics	6.7	17.5	158.5	25.6	4.8
C	Bioflavonoids	5.4	-1.8	110.2	1.4	3.3
N	Anilides	5.2	0.0	241.0	7.3	7.3
A	Other medicines for constipation	4.8	11.6	33.4	25.6	1.0
A	Contact laxatives	3.9	-7.1	49.5	0.2	1.5
D	Imidazole and triazole derivatives	3.4	9.7	84.3	25.8	2.6
R	Other cough suppressants	3.0	15.4	62.2	15.2	1.9
A	Osmotic laxatives	2.9	0.0	25.6	2.4	0.8
A	Antidiarrheal microorganisms	2.7	8.0	166.1	13.4	5.0
C	Corticosteroids	2.3	4.5	40.4	5.5	1.2
A	Enemas	2.3	4.5	62.4	8.0	1.9
D	Sulfonamides	1.9	5.6	23.4	4.0	0.7
D	Other antiseptics and disinfectants	1.8	0.0	15.4	9.2	0.5
D	Iodine derivatives	1.8	-5.3	29.2	4.3	0.9
D	Other quaternary ammonium derivatives	1.6	-5.9	6.4	10.3	0.2
	Total top 20	**100.9**	**4.2**	**2,077.0**	**8.9**	**62.8**
	Total	**143.6**	**3.4**	**3,304.7**	**10.8**	**100.0**

* calculated on overall consumption

Table 2.6.7 Top 30 highest expenditure self-medication active ingredients (SOP and OTC) in 2023: comparison 2023-2022

ATC 1st level	Active ingredient	Expenditure *(million)*	Δ % 23-22	%*	DDD/1000 inhab. per day	Δ % 23-22	% SOP (no prescription required)	% OTC	Average DDD cost
M	ibuprofen	275.7	21.5	8.3	4.2	16.7	14.6	85.4	3.05
M	diclofenac	181.3	10.3	5.5	9.6	-2.0	6.2	93.8	0.88
N	paracetamol	146.1	8.1	4.4	3.1	3.3	93.2	6.8	2.23
A	flurbiprofen	139.1	26.9	4.2	5.6	21.7	0.0	100.0	1.16
A	antidiarrheal microorganisms	121.2	23.2	3.7	2.1	16.7	0.0	100.0	2.67
C	diosmin/hesperidin	95.4	17.3	2.9	4.6	15.0	100.0	0.0	0.98
M	ketoprofen	73.3	21.4	2.2	1.7	21.4	0.0	100.0	2.07
R	naphazoline	69.3	33.8	2.1	11.0	27.9	0.0	100.0	0.29
A	loperamide	64.8	70.5	2.0	0.6	50.0	15.7	84.3	5.1
R	carbocisteine	62.6	36.1	1.9	3.2	28.0	8.3	91.7	0.9
N	acetylsalicylic acid/ascorbic acid	62.2	2.5	1.9	1.3	0.0	0.0	100.0	2.18
N	paracetamol/ascorbic acid/phenylephrine	42.3	36.9	1.3	0.7	16.7	0.0	100.0	2.64
R	acetylcysteine	41.8	31.9	1.3	1.8	28.6	1.7	98.3	1.07
M	diclofenac (M01AB05)	40.7	30.0	1.2	0.8	33.3	0.0	100.0	2.4
R	dichlorophenyl carbinol/amylmetacresol/ascorbic acid	38.9	30.1	1.2	0.5	25.0	0.0	100.0	3.42
R	dextromethorphan/guaiaphenesin	34.3	45.3	1.0	0.6	50.0	0.0	100.0	2.76
A	glycerol (A06AX01)	33.4	52.5	1.0	4.8	41.2	1.2	98.8	0.33
A	glycerol (A06AG04)	32.9	34.3	1.0	1.7	30.8	0.2	99.8	0.93
A	*Saccharomyces boulardii*	31.6	49.8	1.0	0.4	33.3	24.6	75.4	3.76
G	clotrimazole/metronidazole	31.2	20.0	0.9	1.0	11.1	100.0	0.0	1.42
R	bromhexine	29.9	61.6	0.9	0.9	50.0	0.0	100.0	1.56
D	tioconazole	29.5	84.4	0.9	0.6	100.0	0.0	100.0	2.4
M	ibuprofen/pseudoephedrine	29.3	36.9	0.9	0.2	0.0	0.0	100.0	6.72
A	magnesium hydroxide/algeldrate/dimethicone	28.8	29.1	0.9	0.3	0.0	0.0	100.0	4.04
A	sodium alginate/sodium bicarbonate	28.2	80.8	0.9	0.5	66.7	0.0	100.0	2.86

continued

Table 2.6.7 – *continued*

ATC 1st level	Active ingredient	Expenditure *(million)*	Δ % 23-22	%*	DDD/1000 inhab. per day	Δ % 23-22	% SOP (no prescription required)	% OTC	Average DDD cost
A	butylscopolamine	28.1	39.8	0.9	0.5	25.0	0.0	100.0	2.61
R	cloperastine	27.9	23.5	0.8	1.4	16.7	10.6	89.4	0.95
D	povidone iodine	27.4	11.8	0.8	1.7	6.3	0.0	100.0	0.76
A	sodium citrate/potassium citrate/vitamin complex	27.2	27.7	0.8	0.3	50.0	0.0	100.0	4.27
R	levodropropyzine	27.1	15.8	0.8	1.3	30.0	0.0	100.0	0.99
	Total top 30	**1,901.7**	**-36.3**	**57.5**	**66.8**	**-51.9**	**18.0**	**82.0**	**1.33**
	Total	**3,304.7**	**10.8**	**100.0**	**143.6**	**3.4**	**20.3**	**79.7**	**1.07**

* calculated on overall expenditure

Table 2.6.8 Top 30 highest consumption self-medication active ingredients (SOP and OTC) in 2023: comparison 2023-2022

ATC 1st level	Active ingredient	DDD/1000 inhab. per day	Δ % 23-22	Expenditure *(million)*	Δ % 23-22	%*	% SOP (no prescription required)	% OTC	Average DDD cost
R	naphazoline (R01AA08)	11.0	27.9	69.30	33.80	2.10	-	100.00	0.29
M	diclofenac	9.6	-2.0	181.30	10.30	5.50	6.20	93.80	0.88
A	flurbiprofen	5.6	21.7	139.10	26.90	4.20	-	100.00	1.16
S	naphazoline (S01GA01)	5.6	47.4	24.70	44.40	0.70	-	100.00	0.21
A	glycerol	4.8	41.2	33.40	52.50	1.00	1.20	98.80	0.33
C	diosmin/hesperidin	4.6	15.0	95.40	17.30	2.90	100.00	-	0.98
M	ibuprofen	4.2	16.7	275.70	21.50	8.30	14.60	85.40	3.05
R	oxymetazoline	3.9	69.6	4.50	25.00	0.10	-	100.00	0.05
R	carbocisteine	3.2	28.0	62.60	36.10	1.90	8.30	91.70	0.90
N	paracetamol	3.1	3.3	146.10	8.10	4.40	93.20	6.80	2.23
A	antidiarrheal microorganisms	2.1	5.0	121.20	9.50	3.70	-	100.00	2.67
A	lactulose	2.1	16.7	11.10	16.80	0.30	21.30	78.70	0.25

continued

Table 2.6.8 – *continued*

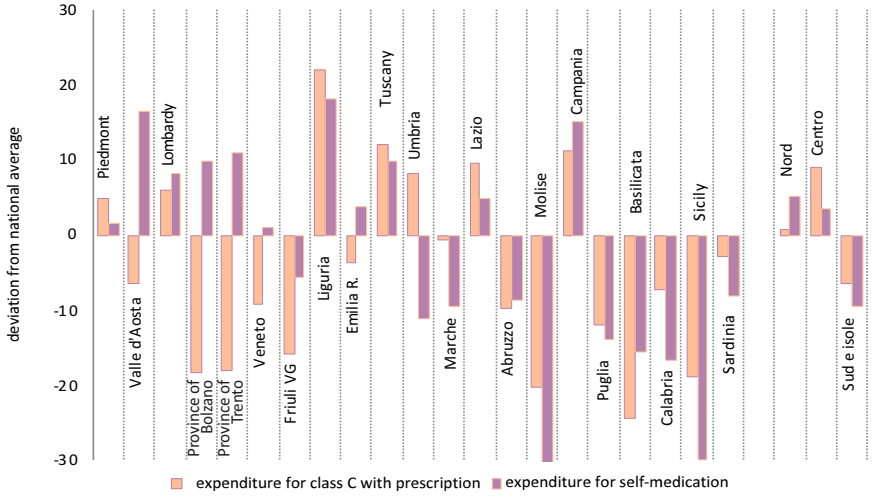
ATC 1st level	Active ingredient	DDD/1000 inhab. per day	Δ % 23-22	Expenditure *(million)*	Δ % 23-22	%*	% SOP (no prescription required)	% OTC	Average DDD cost
R	acetylcysteine	1.8	28.6	41.80	31.90	1.30	1.70	98.30	1.07
D	povidone iodine	1.7	6.3	27.40	11.80	0.80	-	100.00	0.76
A	glycerol	1.7	30.8	32.90	34.30	1.00	0.20	99.80	0.93
M	ketoprofen	1.7	21.4	73.30	21.40	2.20	-	100.00	2.07
A	bisacodyl	1.6	23.1	22.80	27.40	0.70	-	100.00	0.65
M	ibuprofen	1.5	-6.3	20.40	-8.90	0.60	7.60	92.40	0.62
A	senna	1.5	0.0	16.70	8.40	0.50	-	100.00	0.52
A	sodium bicarbonate	1.4	7.7	2.90	-3.30	0.10	100.00	-	0.10
R	cloperastine	1.4	16.7	27.90	23.50	0.80	10.60	89.40	0.95
D	silver sulfadiazine	1.4	16.7	11.70	19.40	0.40	100.00	-	0.40
N	acetylsalicylic acid/ascorbic acid	1.3	0.0	62.20	2.50	1.90	-	100.00	2.18
C	heparinoids	1.3	18.2	17.70	20.40	0.50	95.80	4.20	0.64
R	levodropropyzine	1.3	30.0	27.10	15.80	0.80	-	100.00	0.99
A	thiamine	1.3	18.2	2.50	13.60	0.10	100.00	-	0.09
C	fluocinolone/ketocaine	1.2	9.1	23.00	21.10	0.70	-	100.00	0.86
R	xylometazoline	1.2	50.0	21.80	50.30	0.70	-	100.00	0.83
A	ascorbic acid	1.2	-25.0	3.80	-20.80	0.10	-	100.00	0.15
S	tetrizoline/pheniramine	1.0	42.9	7.40	39.60	0.20	69.60	30.40	0.33
	Total top 30	**85.0**	**-38.8**	**1,607.80**	**-46.10**	**48.70**	**23.50**	**76.50**	**0.88**
	Total	**143.6**	**3.4**	**3,304.70**	**10.80**	**100.00**	**20.30**	**79.70**	**1.07**

* calculated on overall consumption

Table 2.6.9 Local pharmaceutical prescription 2023 of class C medicines with prescription and self-medication (Table) and % deviation of gross expenditure from the national average (Figure): comparison 2023-2022

Region	Class C with prescription				Self-medication (SOP and OTC)			
	Per capita expenditure	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22	Per capita expenditure	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22
Piedmont	68.5	8.2	225.4	-1.9	57.0	8.4	144.9	1.5
Valle d'Aosta	61.0	7.2	230.9	-2.5	65.5	11.0	160.6	3.2
Lombardy	69.2	8.0	215.8	-0.1	60.8	11.4	152.1	4.5
Province of Bolzano	53.3	14.4	153.9	0.3	61.7	8.8	144.7	3.6
Province of Trento	53.6	8.7	187.5	1.0	62.4	7.8	148.9	0.5
Veneto	59.3	5.3	201.4	-0.7	56.7	6.2	141.2	-0.6
Friuli VG	55.0	7.4	186.1	-0.5	53.0	8.4	130.3	-1.1
Liguria	79.7	6.6	274.7	-2.0	66.4	7.3	177.8	-0.3
Emilia R.	62.8	7.0	209.1	-1.9	58.3	5.0	149.2	-1.9
Tuscany	73.2	18.8	236.3	0.3	61.7	9.8	160.9	2.5
Umbria	70.7	12.0	196.1	2.3	49.9	9.2	126.4	1.5
Marche	64.9	5.5	202.8	-2.5	50.8	5.8	131.8	-1.6
Lazio	71.6	12.8	209.8	2.4	58.9	13.7	153.8	4.9
Abruzzo	58.9	7.3	164.7	2.2	51.4	12.7	130.7	3.6
Molise	52.0	8.6	150.9	1.7	38.9	9.9	101.5	1.1
Campania	72.6	5.1	207.1	-0.9	64.6	13.5	173.1	4.7
Puglia	57.5	7.1	171.4	-0.4	48.4	12.3	121.9	5.1
Basilicata	49.3	16.3	155.0	4.0	47.4	23.1	115.7	12.1
Calabria	60.5	11.8	210.6	3.0	46.8	17.6	118.3	9.0
Sicily	53.0	12.1	148.2	2.7	39.4	22.4	103.7	13.8
Sardinia	63.5	16.9	225.2	6.3	51.7	14.9	125.4	7.0
Italy	**65.3**	**9.2**	**204.2**	**0.1**	**56.2**	**11.1**	**143.6**	**3.4**
North	65.7	7.5	214.3	-0.9	59.1	8.4	148.9	1.4
Centre	71.2	13.7	216.4	1.1	58.1	11.1	151.1	3.1
South and Islands	61.1	9.1	182.5	1.4	50.8	15.7	131.3	7.0

* Including medicines classified in Class C-Non-Negotiated



Class A medicines - private purchase

Table 2.6.10 2023 expenditure and consumption of Class A out-of pocket medicines (Table) and deviation (%) of gross expenditure from national average (Figure)

Region	Per capita expenditure	Δ % 23-22	DDD/1000 inhabitants per day	Δ % 23-22
Piedmont	39.52	-5.7	233.4	-12.2
Valle d'Aosta	75.06	-5.4	256.3	-1.6
Lombardy	27.59	0.7	257.0	-1.8
Province of Bolzano	23.60	-1.0	261.9	-2.6
Province of Trento	17.63	-44.3	139.0	-7.6
Veneto	25.81	-3.6	309.0	-6.0
Friuli VG	16.88	-22.5	150.0	-43.0
Liguria	35.40	-4.2	316.0	-3.2
Emilia R.	19.40	-8.7	173.2	-6.6
Tuscany	26.39	12.6	270.6	8.8
Umbria	31.36	2.6	202.6	13.2
Marche	27.48	-10.2	206.0	-6.5
Lazio	57.09	23.8	217.6	8.2
Abruzzo	21.92	-68.8	171.3	-1.3
Molise	16.98	23.4	142.6	20.7
Campania	29.35	-10.7	239.4	-10.4
Puglia	23.57	13.6	184.4	9.5
Basilicata	36.06	>100	133.9	57.7
Calabria	43.70	57.9	268.0	30.2
Sicily	41.19	23.2	161.9	44.4
Sardinia	116.29	65.9	211.9	81.3
Italy	**34.35**	**6.2**	**228.1**	**0.8**
North	27.79	-4.8	245.3	-7.0
Centre	41.52	16.4	232.0	6.8
South and Islands	39.32	12.9	201.0	13.1

* Including medicines classified in Class C-Non-Negotiated

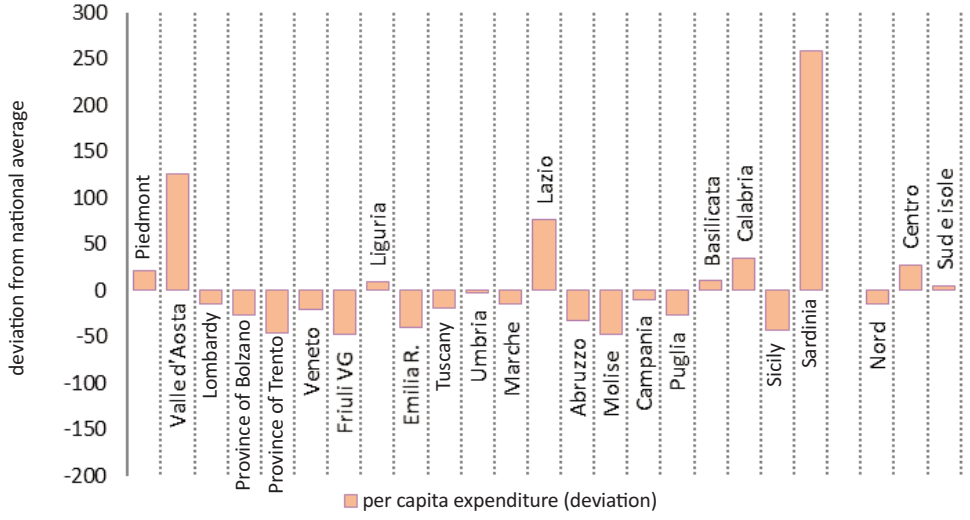


Table 2.6.11 Top 20 class A therapeutic categories purchased privately by the citizen in descending order of expenditure in 2023: comparison 2023-2022

ATC 1st level	Therapeutic category	Expenditure *(million)*	Δ% 23-22	%*	DDD/1000 inhab. per day	Δ% 23-22	% medicines paid out of pocket**
A	Proton pump inhibitors	146.3	0.7	7.7	16.8	3.7	18.0
M	Propionic acid derivatives	128.4	-0.6	6.7	17.8	-1.1	73.9
A	Vitamin D and analogues	76.6	22.8	4.0	61.6	13.9	24.4
J	Penicillin combinations, including betalactamase inhibitors	75.8	16.2	4.0	2.4	14.3	25.3
B	Direct Xa factor inhibitors	65.2	16.3	3.4	0.7	16.7	9.7
A	GLP-1 (glucagon-like peptide-1) receptor analogues	64.9	33.1	3.4	0.5	25.0	11.6
C	HMG-CoA reductase inhibitors	52.8	6.3	2.8	8.5	3.7	10.0
B	Other antianemic preparations	45.3	20.8	2.4	0.2	100.0	19.3
H	Glycocorticoids	44.2	- 0.4	2.3	6.2	3.3	27.8
B	Blood coagulation factors	43.7	32.6	2.3	<0.05	0.0	9.0
R	Glycocorticoids	40.7	13.1	2.1	1.7	13.3	27.3
B	Platelet aggregation inhibitors, excl. heparin	38.8	-21.6	2.0	16.4	-30.2	11.1
M	Acetic acid derivatives and related substances	35.4	6.4	1.9	3.9	8.3	41.8
A	Insulins and injectable analogues, long-acting	31.8	21.5	1.7	0.5	25.0	13.1
R	Piperazine derivatives	26.3	9.2	1.4	4.2	10.5	51.6
A	SGLT2 cotransporter inhibitors (sodium-glucose type 2)	24.8	64.8	1.3	0.5	66.7	12.2
C	Other lipid modifying agents	24.5	-0.7	1.3	0.7	0.0	5.1
N	Diazepines, oxazepines, thiazepines and oxepins	24.2	13.4	1.3	0.5	25.0	21.8
A	Oral hypoglycemic agents, in combination	23.1	21.7	1.2	0.6	50.0	11.3
J	Macrolides	22.8	-23.8	1.2	0.8	-27.3	21.0
	Total of the top 20	**1,035.3**	**9.0**	**54.2**	**144.6**	**2.2**	**16.6**
	Total	**1,909.2**	**5.9**	**100.0**	**228.1**	**0.8**	**6.8**

* Calculated on the total expenditure of Class A medicines paid out of pocket by citizens

** Calculated on total expenditure (under approved care regime, out of pocket expenses and purchases by public health facilities) of the active ingredient

Table 2.6.12 Top 20 class A therapeutic categories purchased privately by the citizen in descending order of consumption in 2023: comparison 2023-2022

ATC 1st level	Therapeutic category	DDD/1000 inhab. per day	Δ% 23-22	Expenditure *(million)*	Δ% 23-22	%*	% medicines paid out of pocket**
A	Vitamin D and analogues	61.6	13.9	76.6	22.8	4.0	24.4
M	Propionic acid derivatives	17.8	-1.1	128.4	-0.6	6.7	73.9
A	Proton pump inhibitors	16.8	3.7	146.3	0.7	7.7	18.0
B	Platelet aggregation inhibitors, excl. heparin	16.4	-30.2	38.8	-21.6	2.0	11.1
C	HMG-CoA reductase inhibitors	8.5	3.7	52.8	6.3	2.8	10.0
H	Thyroid hormones	7.6	5.6	17.8	0.9	0.9	16.6
C	ACE inhibitors, not in combination	7.2	-23.4	18.2	-17.6	1.0	8.3
H	Glycocorticoids	6.2	3.3	44.2	-0.4	2.3	27.8
R	Piperazine derivatives	4.2	10.5	26.3	9.2	1.4	51.6
M	Acetic acid derivatives and related substances	3.9	8.3	35.4	6.4	1.9	41.8
C	Sulfonamides, not in combination	3.6	2.9	7.5	2.4	0.4	13.3
N	Selective serotonin reuptake inhibitors	3.0	-9.1	17.9	-12.5	0.9	8.2
R	Other antihistamines for systemic use	2.7	3.8	18.2	2.8	1.0	31.9
B	Folic acid and derivatives	2.6	8.3	10.2	10.6	0.5	24.4
C	Angiotensin II receptor blockers (ARBs), not in combination	2.6	4.0	13.2	8.0	0.7	4.3
C	Dihydropyridine derivatives	2.5	-21.9	9.5	-27.1	0.5	3.9
C	Beta blockers, selective	2.5	-19.4	18.4	-22.2	1.0	5.7
J	Penicillin combinations, incl. beta-lactamase inhibitors	2.4	14.3	75.8	16.2	4.0	25.3
D	Corticosteroids, very active (group IV)	2.3	15.0	8.1	16.3	0.4	63.6
D	Corticosteroids, active (group III)	2.2	10.0	9.3	10.4	0.5	66.0
	Total of the top 20	**176.7**	**0.1**	**772.9**	**1.5**	**40.5**	**17.7**
	Total	**228.1**	**0.8**	**1,909.2**	**5.9**	**100.0**	**6.8**

* Calculated on the total expenditure of Class A medicines paid out of pocket by citizens
** Calculated on total consumption (under approved care regime, out of pocket expenses and purchases by public health facilities) of the active ingredient

Table 2.6.13 Top 30 class A active ingredients purchased privately by the citizen in descending order of expenditure in 2023: comparison 2023-2022

ATC 1st level	Active ingredient	Expenditure *(million)*	Δ% 23-22	%*	DDD/1000 inhab. per day	Δ% 23-22	% medicines paid out of pocket**	Average DDD cost
J	amoxicillin/ clavulanic acid	73.4	16.9	3.8	2.4	14.3	28.2	1.41
A	cholecalciferol	71.0	21.5	3.7	61.5	14.1	26.3	0.10
M	ibuprofen	65.7	2.1	3.4	7.1	2.9	72.5	0.43
A	pantoprazole	59.7	3.3	3.1	6.5	4.8	17.9	0.43
M	ketoprofen	54.5	-3.6	2.9	9.6	-3.0	79.1	0.26
A	semaglutide	35.7	44.6	1.9	0.2	0.0	13.4	7.79
M	diclofenac	30.4	9.4	1.6	3.6	12.5	44.2	0.40
C	rosuvastatin	29.7	16.7	1.6	4.8	9.1	24.1	0.29
A	esomeprazole	29.1	15.5	1.5	3.4	17.2	18.1	0.40
A	lansoprazole	27.0	-6.1	1.4	2.8	-3.4	18.4	0.45
A	omeprazole	25.8	-11.8	1.3	3.6	-5.3	17.0	0.33
A	dulaglutide	25.3	31.6	1.3	0.2	0.0	9.5	4.91
R	beclomethasone	25.1	8.3	1.3	1.1	10.0	38.6	1.08
B	apixaban	24.5	8.1	1.3	0.3	50.0	9.2	4.27
B	rivaroxaban	24.1	15.3	1.3	0.3	0.0	10.5	3.89
B	acetylsalicylic acid	23.4	-34.2	1.2	14.5	-32.9	24.7	0.08
H	betamethasone	23.0	-5.6	1.2	2.6	-3.7	53.4	0.41
B	epoetin alfa	22.4	18.7	1.2	0.1	0.0	23.1	11.54
R	cetirizine	22.1	9.4	1.2	3.6	12.5	54.7	0.29
C	omega-3	19.1	2.0	1.0	0.4	0.0	12.8	2.23
H	levothyroxine	17.4	0.7	0.9	7.6	5.6	16.6	0.11
J	fosfomycin	16.9	5.9	0.9	0.2	100.0	24.5	4.95
B	edoxaban	16.5	32.9	0.9	0.2	100.0	9.4	4.45
B	enoxaparin	16.2	11.9	0.8	0.4	33.3	7.0	2.13
B	electrolytes for intravenous solutions	15.9	57.3	0.8	0.4	33.3	18.2	1.74
N	quetiapine	15.2	8.4	0.8	0.2	0.0	23.6	3.26
J	azithromicyn	15.0	-27.5	0.8	0.5	-28.6	24.0	1.50
C	valsartan/sacubitril	13.7	69.5	0.7	0.1	0.0	9.3	7.21
A	insulin glargine	13.6	12.0	0.7	0.3	0.0	13.3	1.99
C	atorvastatin	13.3	7.7	0.7	2.3	0.0	4.6	0.26
	Total top 30	**864.8**	**7.8**	**45.3**	**140.6**	**2.1**	**19.1**	**0.29**
	Total	**1,909.2**	**5.9**	**100.0**	**228.1**	**0.8**	**6.8**	**0.39**

* Calculated on the total expenditure of Class A medicines paid out of pocket by citizens
** Calculated on total expenditure (under approved care regime, out of pocket expenses and purchases by public health facilities) of the active ingredient

Table 2.6.14 Top 30 class A active ingredients purchased privately by the citizen in descending order of consumption in 2023: comparison 2023-2022

ATC 1st level	Active ingredient	DDD/1000 inhab. per day	Δ% 23-22	Expenditure *(million)*	Δ% 23-22	%*	% medicines paid out of pocket**	Average DDD cost
A	cholecalciferol	61.5	14.1	70.9	21.5	3.7	26.3	0.10
B	acetylsalicylic acid	14.5	-32.9	23.3	-34.2	1.2	24.7	0.08
M	ketoprofen	9.6	-3.0	54.0	-3.6	2.9	79.1	0.30
H	levothyroxine	7.6	5.6	17.3	0.7	0.9	16.6	0.11
M	ibuprofen	7.1	2.9	65.7	2.1	3.4	72.5	0.43
A	pantoprazole	6.5	4.8	59.7	3.3	3.1	17.9	0.43
C	ramipril	5.4	-27.0	10.7	-24.5	0.6	8.7	0.10
C	rosuvastatin	4.8	9.1	29.7	16.7	1.6	24.1	0.29
A	omeprazole	3.6	-5.3	25.8	-11.8	1.3	17.0	0.33
R	cetirizine	3.6	12.5	22.1	9.4	1.2	54.7	0.29
M	diclofenac	3.6	12.5	30.4	9.4	1.6	44.2	0.40
C	furosemide	3.4	3.0	6.6	2.3	0.3	13.5	0.10
A	esomeprazole	3.4	17.2	29.1	15.5	1.5	18.1	0.40
A	lansoprazole	2.8	-3.4	27.0	-6.1	1.4	18.4	0.50
B	folic acid	2.6	8.3	10.2	10.6	0.5	24.4	0.20
H	betamethasone	2.6	-3.7	23.1	-5.6	1.2	53.4	0.41
J	amoxicillin/clavulanic acid	2.4	14.3	73.4	16.9	3.8	28.2	1.40
C	atorvastatin	2.3	0.0	13.3	7.7	0.7	4.6	0.26
D	clobetasol	2.3	15.0	8.1	16.4	0.4	63.6	0.20
A	metformin	2.2	-4.3	8.4	-4.9	0.4	7.8	0.20
M	nimesulide	2.1	-8.7	11.1	-7.6	0.6	58.5	0.20
M	allopurinol	2.0	5.3	5.1	8.3	0.3	18.8	0.10
R	salbutamol	2.0	0.0	8.0	-1.0	0.4	40.8	0.20
H	prednisone	2.0	11.1	10.4	6.6	0.5	19.8	0.20
B	cyanocobalamin	1.9	18.8	0.8	17.2	-	13.3	-
C	amlodipine	1.9	-5.0	5.8	-9.7	0.3	5.8	0.10
M	etoricoxib	1.4	27.3	12.9	20.1	0.7	26.3	0.40
R	beclomethasone	1.1	10.0	25.1	8.3	1.3	38.6	1.08
R	ebastine	1.1	22.2	7.3	14.9	0.4	30.9	0.30
B	lysine acetylsalicylate	1.0	11.1	1.8	10.5	0.1	14.0	0.10
	Total top 30	**168.1**	**1.1**	**697.8**	**3.3**	**36.5**	**23.6**	**0.29**
	Total	**228.1**	**0.8**	**1,909.2**	**5.9**	**100.0**	**6.8**	**0.39**

* Calculated on the total expenditure of Class A medicines paid out of pocket by citizens

** Calculated on total expenditure (under approved care regime, out of pocket expenses and purchases by public health facilities) of the active ingredient

Table 2.6.15 Breakdown of consumption by price range of Class A medicines paid out of pocket by citizens in 2023

Region	<2 € %	≥2 <3 € %	≥3 <6 € %	≥6 <10 € %	≥10 <30 € %	≥30 € %
Piedmont	8.8	11.3	32.9	26.5	15.8	4.6
Valle d'Aosta	10.0	16.6	25.8	21.9	14.9	10.8
Lombardy	13.5	19.4	30.1	22.9	12.8	1.2
Province of Bolzano	8.9	14.8	34.2	24.0	15.6	2.4
Province of Trento	13.0	8.0	31.5	27.7	16.9	2.9
Veneto	13.3	19.1	31.5	21.9	13.0	1.2
Friuli VG	7.8	8.4	35.7	29.3	17.1	1.7
Liguria	12.2	18.1	30.2	24.5	14.0	1.0
Emilia R.	10.8	8.5	36.3	27.3	15.9	1.1
Tuscany	11.0	11.7	35.1	25.8	15.2	1.1
Umbria	10.3	8.9	34.9	27.6	16.0	2.3
Marche	11.7	8.7	31.1	28.4	17.3	2.8
Lazio	12.0	13.2	29.8	23.7	15.3	6.0
Abruzzo	13.5	12.6	32.3	26.3	13.6	1.7
Molise	11.2	14.4	33.3	27.0	13.2	0.9
Campania	12.6	23.9	31.1	20.3	10.9	1.2
Puglia	13.9	13.3	33.7	23.1	14.2	1.8
Basilicata	11.8	13.3	32.1	22.3	12.0	8.5
Calabria	9.5	21.2	31.4	23.0	12.4	2.6
Sicily	11.2	21.9	28.4	27.8	10.4	0.3
Sardinia	10.9	8.5	20.8	17.1	15.4	27.3
Italy	**12.0**	**16.3**	**31.3**	**23.9**	**13.7**	**2.8**
North	12.1	16.2	31.7	24.2	14.0	1.8
Centre	11.5	11.9	32.0	25.2	15.5	3.8
South and Islands	12.0	19.2	30.4	22.8	12.1	3.4

Table 2.6.16 Expenditure and consumption of OTC self-medication medicines provided by retail pharmacies by Region in 2023 and deviation (%) from national average (Table and Figure)

Region	Expenditure *(million)*	Δ % 23-22	Per capita expenditure	DDD/1000 inhab. per day
Piedmont	25.4	3.1	5.7	14.6
Valle d'Aosta	0.6	-19.7	4.7	11.8
Lombardy	81.3	36.6	8.3	21.3
Province of Bolzano	0.5	16.5	0.9	2.3
Province of Trento	2.0	2.2	3.8	9.0
Veneto	22.9	3.6	4.7	11.8
Friuli VG	5.5	10.9	4.4	10.8
Liguria	9.3	-5.2	5.7	16.3
Emilia R.	34.5	-0.2	7.7	20.5
Tuscany	29.7	6.7	7.8	20.6
Umbria	4.8	0.2	5.4	14.8
Marche	6.8	-2.9	4.5	12.5
Lazio	20.0	0.4	3.5	9.7
Abruzzo	7.4	10.7	5.7	14.7
Molise	1.3	10.2	4.2	11.3
Campania	48.2	19.2	9.3	26.7
Puglia	20.7	6.7	5.4	14.7
Basilicata	4.5	29.2	8.2	20.8
Calabria	11.2	13.8	6.2	16.2
Sicily	14.9	16.5	3.2	9.9
Sardinia	16.3	13.4	9.8	24.4
Italy	**367.6**	**12.7**	**6.2**	**16.7**
North	181.9	14.7	6.6	17.0
Centre	61.3	2.9	5.2	13.9
South and Islands	124.4	15.1	6.4	17.9

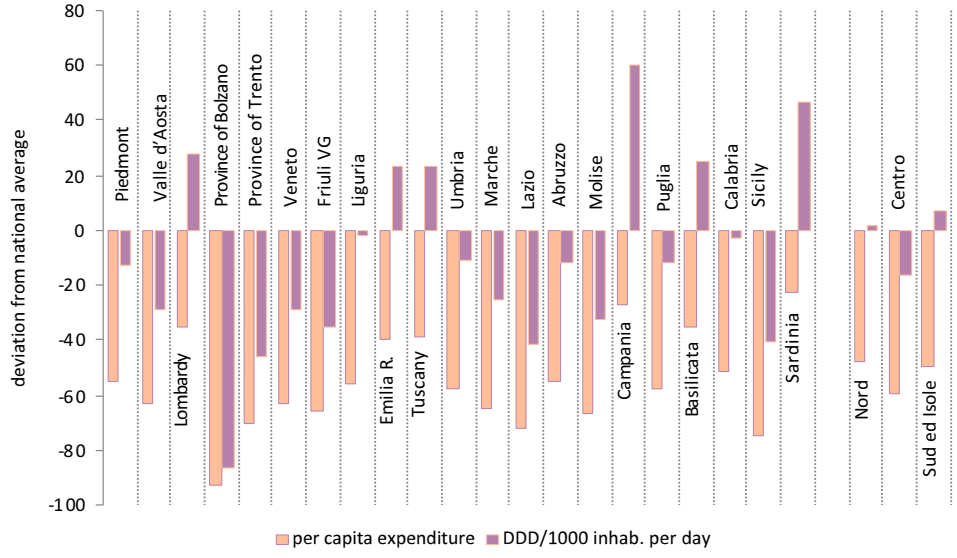


Table 2.6.17 Top 30 self-medication active ingredients supplied by commercial shops in descending order of expenditure in 2023: comparison 2023-2022

ATC	Active substances	Per capita expenditure	Expenditure *(million)*	Δ % 23-22	Inc. %	% cum	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost
M	ibuprofen	0.5	31.1	16.3	8.5	8.5	0.5	10.2	2.85
M	diclofenac	0.3	20.0	-1.0	5.5	13.9	1.1	-13.0	0.88
N	paracetamol	0.3	17.2	-5.8	4.7	18.6	0.4	-18.4	1.82
C	diosmin/hesperidin	0.3	15.1	30.3	4.1	22.7	0.8	30.4	0.92
A	flurbiprofen	0.3	14.8	8.6	4.0	26.7	0.6	-2.2	1.24
A	antidiarrheal microorganisms	0.2	12.5	1.3	3.4	30.1	0.2	-4.0	2.74
M	ketoprofen	0.2	12.3	5.0	3.4	33.5	0.3	5.0	2.02
R	naphazoline	0.2	10.9	6.4	3.0	36.4	1.7	2.1	0.29
A	glycerol	0.1	6.3	10.1	1.7	38.2	0.3	2.2	0.93
N	acetylsalicylic acid/ ascorbic acid	0.1	6.3	1.8	1.7	39.9	0.1	-12.4	2.18
A	loperamide	0.1	6.1	58.2	1.6	41.5	0.1	40.0	4.89
A	glycerol	0.1	5.8	20.9	1.6	43.1	0.8	-2.8	0.33
M	diclofenac	0.1	4.9	12.7	1.3	44.4	0.1	6.7	2.39
R	carbocisteine	0.1	4.6	18.8	1.3	45.7	0.2	12.3	0.87
N	paracetamol/ascorbic acid/phenylephrine	0.1	4.6	32.2	1.3	46.9	0.1	27.7	2.61
R	dichlorophenyl carbinol/amylmetacresol/ ascorbic acid	0.1	4.4	11.9	1.2	48.1	0.1	4.2	3.41
R	xylometazoline	0.1	4.0	32.2	1.1	49.2	0.2	26.9	0.83
A	bisacodyl	0.1	3.9	9.0	1.0	50.3	0.3	3.7	0.64
N	nicotine	0.1	3.8	53.6	1.0	51.3	0.0	38.0	6.15
D	minoxidil	0.1	3.8	76.1	1.0	52.3	0.2	55.0	1.04
A	sodium alginate/ sodium bicarbonate	0.1	3.7	35.6	1.0	53.3	0.1	21.1	2.79
A	magnesium hydroxide/ algeldrate/dimethicone	0.1	3.7	17.8	1.0	54.3	<0.05	3.1	4.01
R	acetylcysteine	0.1	3.6	27.0	1.0	55.3	0.2	14.2	1.00
S	naphazoline	0.1	3.6	38.1	1.0	56.3	0.8	39.3	0.21
M	ibuprofen/ pseudoephedrine	0.1	3.5	34.2	0.9	57.2	<0.05	23.4	6.62
R	dextromethorphan/ guaiaphenesin	0.1	3.5	42.1	0.9	58.2	0.1	25.5	2.77
D	escin/l-thyroxine	0.1	3.1	19.8	0.8	59.0	0.1	20.2	2.14
A	sodium alginate/ sodium bicarbonate/ calcium carbonate	<0.05	2.9	8.8	0.8	59.8	<0.05	7.6	3.78
D	tioconazole	<0.05	2.8	95.9	0.8	60.6	0.1	98.4	2.62
M	naproxen	<0.05	2.7	-6.3	0.7	61.3	0.1	-15.0	1.38
	Total top 30	**3.8**	**225.4**	**13.8**	**61.3**	**61.3**	**9.5**	**5.0**	**1.11**
	Total	**6.2**	**367.6**	**12.7**	**100.0**	**100.0**	**16.7**	**4.7**	**1.03**

Table 2.6.18 Top 30 self-medication active ingredients supplied by commercial shops in descending order of consumption in 2023: comparison 2023-2022

ATC	Active substances	DDD/1000 inhab. per day	Δ % 23-22	Per capita expenditure	Expenditure *(million)*	Δ % 23-22	Inc. %	% cum.	Average DDD cost
R	naphazoline	1.7	0.0	0.18	10.87	6.4	3.0	3.0	0.29
M	diclofenac	1.1	-8.3	0.34	20.04	-1.0	5.5	8.4	0.88
A	glycerol	0.8	0.0	0.10	5.77	20.9	1.6	10.0	0.33
S	naphazoline	0.8	33.3	0.06	3.61	38.1	1.0	11.0	0.21
C	diosmin/hesperidin	0.8	33.3	0.26	15.09	30.3	4.1	15.1	0.92
R	oxymetazoline	0.6	20.0	0.01	0.83	-3.0	0.2	15.3	0.06
A	flurbiprofen	0.6	0.0	0.25	14.76	8.6	4.0	19.3	1.24
M	ibuprofen	0.5	0.0	0.53	31.11	16.3	8.5	27.8	2.85
N	paracetamol	0.4	-20.0	0.29	17.23	-5.8	4.7	32.5	1.82
A	glycerol	0.3	0.0	0.11	6.31	10.1	1.7	34.2	0.93
M	ketoprofen	0.3	0.0	0.21	12.32	5.0	3.4	37.5	2.02
A	bisacodyl	0.3	0.0	0.07	3.86	9.0	1.0	38.6	0.64
R	carbocisteine	0.2	0.0	0.08	4.63	18.8	1.3	39.8	0.87
R	xylometazoline	0.2	0.0	0.07	4.02	32.2	1.1	40.9	0.83
A	lactulose	0.2	0.0	0.02	1.45	16.3	0.4	41.3	0.32
A	antidiarrheal microorganisms	0.2	0.0	0.21	12.54	1.3	3.4	44.7	2.74
A	senna	0.2	0.0	0.04	2.19	-3.5	0.6	45.3	0.51
D	silver sulfadiazine	0.2	100.0	0.02	1.24	25.3	0.3	45.7	0.33
R	acetylcysteine	0.2	100.0	0.06	3.63	27.0	1.0	46.7	1.00
D	minoxidil	0.2	100.0	0.06	3.76	76.1	1.0	47.7	1.04
M	ibuprofen	0.2	0.0	0.03	2.04	-16.2	0.6	48.2	0.58
C	fluocinolone/ketocaine	0.1	0.0	0.04	2.62	5.9	0.7	48.9	0.87
D	povidone iodine	0.1	0.0	0.04	2.08	1.8	0.6	49.5	0.71
A	ascorbic acid	0.1	-50.0	0.01	0.45	-8.9	0.1	49.6	0.15
N	acetylsalicylic acid/ ascorbic acid	0.1	-50.0	0.11	6.31	1.8	1.7	51.3	2.18
D	benzalkonium chloride	0.1	0.0	0.02	0.92	22.5	0.3	51.6	0.35
C	phosphatidylcholine/ escin	0.1	0.0	0.03	1.50	-7.2	0.4	52.0	0.65
A	sodium bicarbonate	0.1	0.0	<0.005	0.15	-5.0	0.0	52.0	0.07
S	nafazoline/tonzilamine	0.1	0.0	0.02	1.20	4.8	0.3	52.4	0.56
A	ketoprofen	0.1	0.0	0.03	2.01	15.6	0.5	52.9	0.96
	Total top 30	**11.0**	**4.8**	**3.31**	**194.50**	**9.4**	**52.9**	**52.9**	**0.82**
	Total	**16.7**	**5.0**	**6.25**	**367.60**	**12.7**	**100.0**	**100.0**	**1.03**

Benzodiazepine

In 2023, the consumption of benzodiazepines reached 45.6 DDD/1000 inhabitants per day, a decrease of 4.3% compared to the previous year, returning to the same levels observed before 2020. However, there has been an average annual variation of +1.5% over the last 8 years (Figure 2.6.19a). Over the same period, the average cost per therapy day has remained stable with values ranging from 0.49 euro in 2016 to 0.54 euro in 2023. When assessing consumption, it should be borne in mind that, compared to previous reports, this category does not include so-called 'Z drugs' (e.g. zolpidem and zopiclone) non-benzodiazepine hypnotic medicines.

The total expenditure exceeded 530 euro, corresponding to a per capita value of 9.07 euro, a slight increase (+2.2%) compared to 2022 (Table 2.6.19a).

Anxiolytics with 390 million euro represent the category with the highest expenditure (6.58 euro per capita) and account for 72% of total expenditure showing a 2.5% reduction compared to 2022. They also confirm themselves as the first category in terms of consumption, in fact, every thousand inhabitants, 25.3 daily doses are used (-2.9% compared to 2022). They are followed, with a decidedly lower expenditure, by hypnotics which in 2023 stand at 2.48 euro per capita, up 1.6% (Table 2.6.19a); consumption is slightly lower than anxiolytics and has a value of 20.3 DDD. The average cost per day of therapy for anxiolytics is more than double that of hypnotics (0.71 vs 0.33 euro). The use of benzodiazepines, particularly in the elderly population, can cause excessive sleepiness during the day, increasing the risk of falls and accidents, and can worsen memory and cognitive function, increasing the risk of confusion and dementia. For these reasons, their use in the elderly with cognitive and physical deficits should be carefully monitored and evaluated.

Alprazolam and lorazepam are confirmed in 2023 as the substances with the highest expenditure (respectively 2.37 and 1.86 euro per capita) and account for 46.4% of the total, both increasing by 5.2% and 1.0% respectively, while the highest increase in expenditure is recorded for triazolam (+5.5%) (Table 2.6.10a). Lormetazepam is the most widely used molecule in the population with a value of 14.5 DDD, and also has the lowest cost per day of therapy of the entire category (0.22 euro).

At the level of geographical area, a wide variability in terms of consumption is observed, with Northern Regions showing a 57% higher consumption than Southern Regions. The greatest contraction in consumption is recorded in the North (-6.1%), followed by the Centre (-4.2%), in the South no difference is observed compared to the previous year. Liguria is the Italian Region with the highest use of benzodiazepines (70.2 DDD), a value approximately three times higher than that of Basilicata (25.4 DDD) and the Province of Bolzano (26.2 DDD). All Regions, with the exception of Calabria (+6.0%), Basilicata (+5.0%), Sardinia (+2.5%) and Sicily (+1.9%), recorded a decrease in use with values ranging from -8.3% in Friuli Venezia Giulia to -1.6% in Abruzzo and Molise (Table 2.6.19b).

Figure 2.6.19a Benzodiazepine, trend 2016-2023 in local consumption and average DDD cost

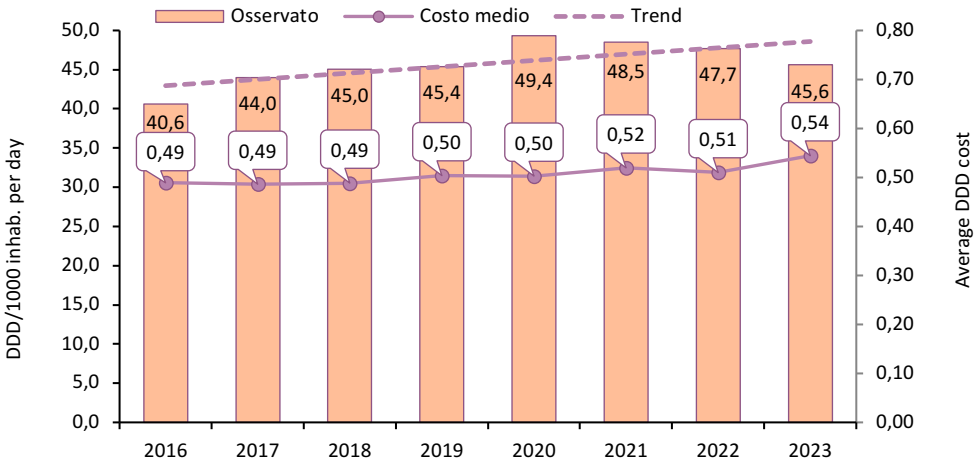


Table 2.6.19a Benzodiazepine, per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and by substance: comparison 2016-2023

Subgroups and substances	Expenditure (million)	Per capita expenditure	Δ % 23-22	CAGR % 16-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 16-23	Average DDD cost	Δ % 23-22
Anxiolytics	387.5	6.58	2.5	2.5	25.3	-2.9	0.9	0.71	5.6
Hypnotics	145.8	2.48	1.6	3.8	20.3	-5.9	2.1	0.33	7.9
Sedatives	0.3	<0.005	-12.4	-15.2	0.0	-1.3	-6.7	7.84	-11.2
Benzodiazepine	**533.5**	**9.07**	**2.2**	**2.8**	**45.6**	**-4.3**	**1.5**	**0.54**	**6.8**
alprazolam	139.2	2.37	5.2	5.0	10.1	-1.8	2.9	0.64	7.1
lorazepam	109.5	1.86	1.0	0.7	9.4	-3.1	-0.6	0.54	4.3
lormetazepam	67.0	1.14	-1.0	4.3	14.5	-7.2	2.4	0.22	6.6
delorazepam	48.6	0.83	3.6	3.6	2.5	-2.0	2.3	0.92	5.7
bromazepam	46.4	0.79	-1.0	1.1	1.3	-5.8	-0.6	1.73	5.1
triazolam	47.0	0.80	5.5	4.2	3.6	-2.0	2.0	0.61	7.6
diazepam	22.0	0.37	4.4	2.4	1.2	-3.9	1.0	0.84	8.7
brotizolam	19.6	0.33	1.2	3.0	1.4	-3.3	1.1	0.66	4.7
flurazepam	8.9	0.15	2.9	2.9	0.6	-1.2	1.4	0.64	4.2
etizolam	8.7	0.15	1.5	2.9	0.3	-3.3	1.1	1.29	4.9

Table 2.6.19b Benzodiazepine, regional trend of weighted DDD/1000 inhab. day: comparison 2016-2023

Region	2016	2017	2018	2019	2020	2021	2022	2023	Δ % 23-22
Piedmont	61.4	60.8	63.9	63.1	67.5	66.5	66.9	63.1	-5.7
Valle d'Aosta	60.4	60.4	64.9	65.7	64.1	61.6	61.2	59.1	-3.5
Lombardy	41.4	50.3	52.0	53.0	55.4	53.9	53.3	50.6	-5.1
Province of Bolzano	30.9	30.4	30.6	28.7	29.2	27.9	28.5	26.2	-8.2
Province of Trento	54.3	53.6	54.3	52.7	52.5	51.4	51.0	48.5	-4.8
Veneto	52.2	64.8	63.2	64.7	66.4	64.5	64.7	59.8	-7.5
Friuli VG	52.0	55.9	55.3	55.1	56.5	54.8	56.2	51.6	-8.3
Liguria	69.7	68.2	71.3	71.3	76.6	74.4	73.7	70.2	-4.7
Emilia R.	47.9	49.7	47.1	48.4	51.2	50.2	49.7	46.4	-6.6
Tuscany	37.9	39.9	42.7	40.8	43.2	42.3	40.9	38.7	-5.3
Umbria	28.2	28.2	28.2	26.3	41.4	47.6	47.9	45.8	-4.4
Marche	27.9	27.8	26.1	28.8	48.2	55.2	54.5	51.5	-5.5
Lazio	33.6	37.6	41.1	44.0	46.5	45.3	45.5	44.1	-3.1
Abruzzo	35.2	34.6	33.9	35.7	37.7	37.5	38.0	37.4	-1.6
Molise	28.6	28.4	29.3	28.3	28.7	28.7	27.6	27.2	-1.6
Campania	32.6	33.6	34.3	33.4	39.0	38.2	36.3	35.1	-3.3
Puglia	25.2	25.2	26.6	28.0	29.9	29.4	29.0	28.2	-2.5
Basilicata	24.7	24.8	25.3	25.4	26.5	25.9	24.2	25.4	5.0
Calabria	29.7	30.3	31.3	30.8	36.1	38.2	36.9	39.2	6.0
Sicily	26.5	28.5	29.0	27.3	35.3	32.6	28.3	28.8	1.9
Sardinia	58.5	57.5	59.3	59.5	61.8	61.5	59.5	60.9	2.5
Italy	**40.6**	**44.0**	**45.0**	**45.4**	**49.4**	**48.5**	**47.7**	**45.6**	**-4.3**
North	50.0	55.5	56.2	56.7	59.4	58.0	57.8	54.3	-6.1
Centre	33.8	36.3	38.7	39.7	45.3	45.8	45.4	43.4	-4.2
South and Islands	31.4	32.1	33.0	32.7	37.4	36.5	34.6	34.6	-0.1

Contraceptive medicines

From 2016 to 2023, there has been a slow but steady increase in the use of pharmacological contraception, with doses rising from 109.9 DDD/1000 inhabitants per day to 145.6, representing an average annual change (CAGR) of 3.6%. Over the same period, the average cost per DDD increased by 18.0% to 0.54 euro in 2023 (Figure 2.6.20a). Total expenditure reached 373 million euro in 2023, equal to 28.85 euro per capita (female population aged 12-50) with an average annual growth of 5.7% since 2016 and an increase of 8.6% compared to 2022 (Table 2.6.20a).

Fourth- and third-generation estrogen-progestin oral contraceptives account for 62% of consumption, the former stable and the latter decreasing by 3.6% compared to 2022. In terms of expenditure, the two categories account for 65% of the entire category (15.23 and 3.25 euro respectively), the former increasing by 6.1% and the latter by 7% (Table 2.6.20a). All subgroups show an increase in consumption (CAGR 2016-2023) with the exception of third-generation estrogen-progestin oral contraceptives (-3.8%). Systemic contraceptives with subcutaneous implant, oral progestin, intrauterine and emergency oral contraceptives show significant increases in expenditure (between 31 and 13%) and consumption (between 31 and 4%) compared to the previous year, while second and third generation oral contraceptives are the only categories to show a reduction in consumption compared to the previous year (-1.2% and -3.6% respectively). Emergency oral contraceptives show the highest cost per DDD (26 euro), while all other categories have a value lower than one euro.

The drospirenone/ethinylestradiol combination maintains, also in 2023, the highest expenditure and consumption values, reaching 5.01 euro per capita (about 65 million euro) and 22.5 DDD/1000 inhabitants per day, both indicators in sharp decline compared to 2022 (-3.2% and -8.4% respectively). Dienogest, in combination with ethinylestradiol or oestradiol, ranks second and third in terms of expenditure with 3.87 and 3.30 euro respectively; both combinations show increases in expenditure compared to the previous year. Ulipristal (emergency contraceptive to be taken within 5 days of unprotected sexual intercourse or the failure of another contraceptive method) is the molecule with the greatest increase in expenditure (+16.6%), while the variation observed in terms of consumption (+9.0%) is second only to that of levonorgestrel (+12.8%). On the contrary, in addition to the aforementioned reduction in consumption of the drospirenone/ethinylestradiol combination, the reductions for gestodene/ethinylestradiol (-11.5%) and dienogest/estradiol (-3.2%; Table 2.6.20a) should be mentioned.

Confirming the national data, 2023 consumption in this category increased particularly in the macro-geographic areas of the South (+4.6%) and of the Centre (+4.2), and to a lesser extent in the North (+0.9%) (Table 2.6.20b). Despite this trend, the use of contraception in the Northern Regions remains more than double compared to the Southern Regions (189.4 vs 86.4 DDD), however, analysing the regional variability, differences of approximately 5 times are noted, with Sardinia reaching the highest value with 294 DDD and Campania, Molise and Basilicata recording the lowest levels of consumption (around 60 DDD). The latter, together with Sardinia and Lazio, is the Region with the greatest increase in consumption (+11.5%, +9.1% and +8.1% respectively); Province of Bolzano (-4.3%) and Emilia-Romagna (-1.1%) are, instead, the only two Regions with a reduction in doses (Table 2.6.20b).

All indicators presented in this section are calculated on the female population (12-50 years)

Figure 2.6.20a Contraceptive medicines, temporal trend (2016-2023) of consumption and average DDD cost

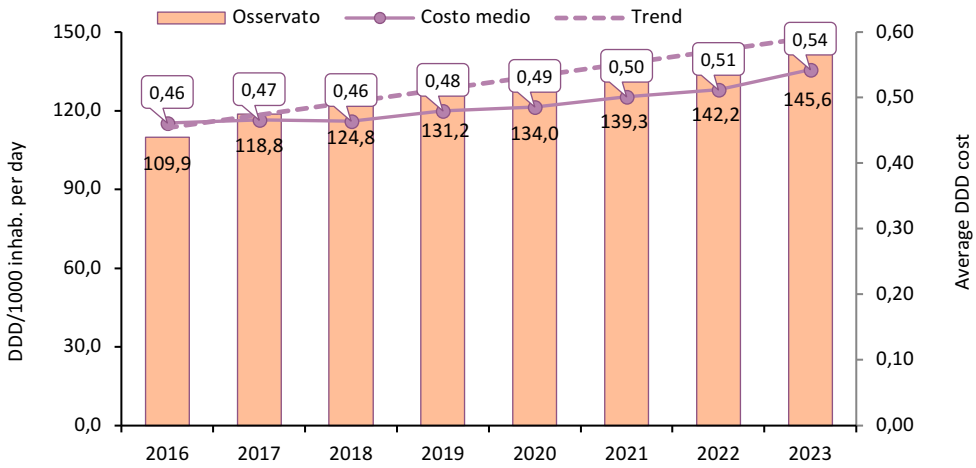


Table 2.6.20a Contraceptive medicines, per capita expenditure and consumption (DDD/1000 inhab. per day) by therapeutic category and substance: comparison 2016-2023

Subgroups and substances	Expenditure million	Per capita expenditure	Δ % 23-22	CAGR % 16-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 16-23	Average DDD cost	Δ % 23-22
Fourth-generation estrogen-progestin oral contraceptives	196.6	15.23	6.1	6.4	66.8	-0.3	4.8	0.62	6.5
Third-generation estrogen-progestin oral contraceptives	41.9	3.25	7.0	-0.4	23.1	-3.6	-3.8	0.39	11.0
Intravaginal contraceptives	35.0	2.71	7.6	3.5	11.4	4.0	4.3	0.65	3.4
Second-generation estrogen-progestin oral contraceptives	28.5	2.20	7.0	4.3	11.9	-1.2	2.6	0.51	8.3
Progestin oral contraceptives	31.1	2.41	28.0	17.3	12.9	19.0	15.4	0.51	7.5
Emergency oral contraceptives	20.5	1.59	12.7	12.9	0.2	4.3	10.0	26.00	8.1
Transdermal estrogen-progestin contraceptives	8.7	0.68	7.0	1.1	3.0	3.7	0.3	0.61	3.2
Intrauterine contraceptives	9.1	0.71	13.7	9.4	15.2	12.9	9.8	0.13	0.7
Systemic subcutaneous implant contraceptives	1.0	0.08	30.8	13.8	1.1	30.8	13.9	0.20	0.0
Contraceptive medicines	**372.5**	**28.85**	**8.6**	**5.7**	**145.6**	**2.4**	**3.6**	**0.54**	**6.0**
drospirenone/ ethinylestradiol	64.8	5.01	-3.2	-0.6	22.5	-8.4	-1.8	0.61	5.7
dienogest/ ethinylestradiol	50.0	3.87	12.8	14.6	19.7	7.8	13.6	0.54	4.6
dienogest/ estradiol	42.6	3.30	3.1	11.3	12.8	-3.2	9.5	0.71	6.5
ethonogestrel/ ethinylestradiol	35.0	2.71	7.6	3.5	11.4	4.0	4.3	0.65	3.4
levonorgestrel/ ethinylestradiol	28.5	2.20	7.0	4.3	11.9	-1.2	2.6	0.51	8.3
gestodene/ ethinylestradiol	24.4	1.89	-2.6	-4.5	15.7	-11.5	-6.6	0.33	10.1
nomegestrol/ estradiol	25.9	2.01	14.2	10.7	7.4	-0.5	7.5	0.75	14.8
desogestrel	18.0	1.39	9.0	9.5	8.7	7.6	9.9	0.44	1.3
levonorgestrel	15.4	1.19	9.9	9.1	15.3	12.8	9.8	0.21	-2.6
ulipristal	14.3	1.10	16.6	15.2	0.1	9.0	14.3	28.72	7.0

Table 2.6.20b Contraceptive medicines, regional trend of weighted DDD/1000 inhab. day: comparison 2016-2023

Region	2016	2017	2018	2019	2020	2021	2022	2023	Δ % 23-22
Piedmont	167.3	170.7	182.5	188.5	189.4	195.8	200.5	200.9	0.2
Valle d'Aosta	207.0	217.8	216.5	212.4	220.5	221.9	233.4	238.9	2.4
Lombardy	131.3	162.4	179.5	189.1	186.9	194.3	199.9	202.7	1.4
Province of Bolzano	212.3	202.8	202.3	194.3	184.8	184.4	186.6	178.7	-4.3
Province of Trento	150.1	155.3	164.7	172.9	167.1	177.1	188.3	193.7	2.8
Veneto	114.9	146.0	152.6	159.6	156.0	160.8	165.8	169.3	2.1
Friuli VG	128.7	143.0	149.4	151.1	154.1	160.2	163.9	163.5	-0.2
Liguria	183.1	186.9	195.6	206.1	208.5	208.0	211.1	215.0	1.9
Emilia R.	148.7	159.7	152.6	161.5	159.7	166.4	169.9	168.1	-1.1
Tuscany	125.9	137.1	151.5	156.3	157.3	164.3	174.1	174.4	0.2
Umbria	66.0	64.6	65.5	66.8	104.5	124.3	130.4	134.6	3.2
Marche	53.2	49.1	46.3	57.8	90.6	110.6	114.2	115.3	1.0
Lazio	78.5	91.7	104.9	117.5	117.8	120.5	132.9	143.7	8.1
Abruzzo	90.3	88.1	84.1	93.2	93.0	94.8	99.1	100.9	1.8
Molise	62.4	60.9	58.8	58.9	60.1	59.8	58.9	61.1	3.7
Campania	69.8	52.2	49.1	51.4	55.5	60.0	58.7	59.6	1.6
Puglia	69.0	68.2	71.6	77.8	77.9	78.2	79.6	81.2	1.9
Basilicata	56.9	56.2	56.4	58.1	56.9	59.8	55.9	62.3	11.5
Calabria	58.4	56.3	57.0	58.5	61.8	66.6	65.4	68.8	5.2
Sicily	59.6	61.6	60.6	59.5	75.3	74.5	64.1	67.9	5.8
Sardinia	269.8	268.6	270.3	274.3	274.2	281.4	269.6	294.0	9.1
Italy	**109.9**	**118.8**	**124.8**	**131.2**	**134.0**	**139.3**	**142.2**	**145.6**	**2.4**
North	141.6	161.7	170.7	178.4	176.8	182.9	187.7	189.4	0.9
Centre	88.7	98.2	108.8	118.2	125.4	132.9	143.0	148.9	4.2
South and Islands	81.9	76.6	76.0	78.5	83.8	86.1	82.6	86.4	4.6

Medicines for erectile dysfunction

In the last eight years, the consumption in this category shows a steady growth with an increase of 56% between 2016 and 2023 and an average annual variation of +5.7%; in the same period, the average cost per DDD of the category has almost halved (from 8.00 euro to 5.11 euro) due to the patent expiry of the main molecules (Figure 2.6.21a). In 2023, expenditure stood at 250 million euro or 10.38 euro per capita (figure calculated on the male population aged 18 years and over), up 3.9% compared to 2022.

Tadalafil and sildenafil remained the substances with the highest expenditure (5.38 and 3.99 euro per capita respectively) and consumption (3.4 and 1.8 DDD respectively), accounting for over 90% of expenditure and doses in this category. These two medicines are the only ones in the category to show an increase in expenditure compared to 2022 (+7.8% and +1.4% respectively), whereas tadalafil alone also shows an increase in consumption (+4.6%) (Table 2.6.21a). On the other hand, alprostadil, a medicine administered by intracavernous injection, recorded a drop in expenditure of 3.4% (together with vardenafil and avanafil: -7% and 0.7%), while still maintaining, although with reduced consumption, the highest cost per DDD in the category (27.89 euro). In the Central Regions, consumption is 25% higher than the average (7.0 vs. 5.6 DDD), while the values in the South are in line with the national value; those in the North are 12% lower. Campania and Lazio register the highest consumption with 7.6 and 7.3 DDD respectively, Sardinia (+14.4%) and Calabria (+8.5%) show the highest increases (Table 2.6.21b).

All indicators presented in this section are calculated on the male population over the age of 18

Figure 2.6.21a Erectile dysfunction medicines, temporal trend (2016-2023) of consumption and average DDD cost

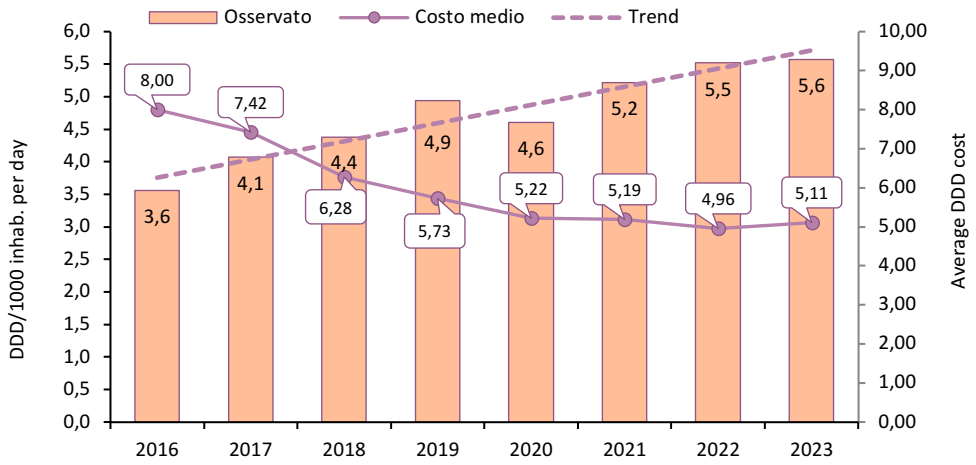


Table 2.6.21a Medicines for erectile dysfunction, per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and substance: comparison 2016-2023

Subgroups and substances	Expenditure million	Per capita expenditure	Δ % 23-22	CAGR % 16-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 16-23	Average DDD cost	Δ % 23-22
Medicines for erectile dysfunction	**250.0**	**10.38**	**3.9**	**-0.1**	**5.6**	**0.8**	**5.7**	**5.11**	**250.0**
tadalafil	129.7	5.38	7.8	0.9	3.4	4.6	11.2	4.35	3.1
sildenafil	96.1	3.99	1.4	3.0	1.8	-3.8	3.2	5.98	5.3
vardenafil	15.4	0.64	-7.0	-10.4	0.2	-12.3	-7.6	7.56	6.0
avanafil	4.8	0.20	-0.7	-9.4	0.1	-1.8	-9.5	5.55	1.1
alprostadil	4.0	0.17	-3.4	-6.1	<0.05	-0.1	-8.9	27.89	-3.3

Table 2.6.21b Medicines for erectile dysfunction, regional trend of weighted DDD/1000 inhab. day: comparison 2016-2023

Region	2016	2017	2018	2019	2020	2021	2022	2023	Δ % 23-22
Piedmont	4.1	4.3	4.7	5.0	4.5	5.1	5.3	5.2	-2.6
Valle d'Aosta	3.9	4.6	4.8	4.4	4.1	4.4	4.4	4.4	0.9
Lombardy	3.3	4.3	4.8	5.2	4.0	4.4	4.7	4.6	-1.3
Province of Bolzano	3.1	3.1	3.4	3.5	3.2	3.2	3.5	3.6	2.8
Province of Trento	2.7	2.7	2.9	3.1	2.7	3.0	3.4	3.2	-4.1
Veneto	2.7	3.6	3.8	4.3	3.8	4.1	4.3	4.3	-1.4
Friuli VG	2.8	3.2	3.3	3.7	3.3	3.7	4.0	3.9	-2.0
Liguria	5.0	5.4	5.8	6.1	5.8	6.4	6.5	6.7	2.1
Emilia R.	4.7	5.1	5.0	5.6	5.1	5.6	6.0	5.8	-1.9
Tuscany	4.8	5.5	5.9	6.2	5.8	6.4	6.7	7.0	4.7
Umbria	3.1	3.2	3.2	3.6	4.3	5.7	6.0	6.0	0.3
Marche	2.8	3.0	2.7	3.7	4.4	5.7	6.1	6.2	0.8
Lazio	3.8	4.4	5.1	5.9	5.6	6.2	7.1	7.3	2.9
Abruzzo	4.1	4.5	4.6	5.6	4.6	5.3	5.9	5.8	-1.2
Molise	2.9	3.2	3.3	4.1	3.5	4.3	4.5	4.8	5.4
Campania	4.4	4.5	4.9	5.7	6.0	7.3	7.7	7.6	-0.6
Puglia	3.1	3.4	3.7	4.5	4.2	4.7	5.1	5.1	0.0
Basilicata	2.1	2.2	2.4	2.7	2.7	3.3	3.5	3.7	3.8
Calabria	2.4	2.7	2.7	3.3	3.3	4.1	4.3	4.6	8.5
Sicily	2.6	3.2	3.3	3.8	4.5	5.0	4.9	5.0	2.4
Sardinia	3.2	3.3	3.5	4.1	3.6	4.2	4.1	4.7	14.4
Italy	**3.6**	**4.1**	**4.4**	**4.9**	**4.6**	**5.2**	**5.5**	**5.6**	**0.8**
North	3.6	4.3	4.6	5.0	4.3	4.7	4.9	4.9	-1.4
Centre	3.9	4.4	4.9	5.5	5.4	6.2	6.8	7.0	3.1
South and Islands	3.3	3.6	3.8	4.5	4.6	5.4	5.6	5.7	1.8

NSAIDs and antipyretics

From 2016 to 2023, the consumption of antipyretic medicines increased from 19.2 to 26.5 DDD/1000 inhabitants per day (Figure 2.6.22a) with an average annual variation of 4.1%, while between 2022 and 2023 there was a reduction of 1.9%. The average DDD cost, on the other hand, recorded an increase, moving from 1.65 euro in 2016 to 2.01 in 2023 (+21.6%) (Figure 2.6.22a).

Total expenditure in the year 2023 was equal to 1.14 billion euro corresponding to 19.42 euro per capita, an increase of 5.2% compared to the previous year (Table 2.6.22a).

Paracetamol alone or in combination and traditional NSAIDs represent over 80% of consumption and expenditure for the entire category, both categories show an increase in expenditure (+4.2% and 8.0% respectively) but, while the first decreases in terms of consumption by 4.5%, the second increases (+2.8%). The other categories show levels of expenditure lower than 80 million euro and dissimilar trends: the prescription of salicylic acid and derivatives (-13.3%) as well as of pyrazolones (-14.7%) is decreasing, while the NSAIDs associated with decongestant and Coxibs are increasing (+12.1% and +19.5% respectively). Significant increases in consumption are noted for the combination paracetamol/ascorbic acid/phenylephrine (+18.0%), for ketorolac (+19.6%) and for bromfenac (+15.1%).

Paracetamol is the substance with the highest expenditure with over 405 million euro equal to 6.90 euro per capita and a consumption of 10.0 DDD (-9.6% compared to 2022), followed by ibuprofen (4.69 euro and 4.2 DDD/1000 inhabitants per day, both indicators increasing by 9.0% and 3.4% respectively), which accounts for about 50% of all NSAIDs and is also, at 3.05 euro, the medicine with the highest cost per DDD. The change in ibuprofen consumption (alone +3.4% or in combination +12.1%) could depend on the high incidence of flu-like syndromes in the paediatric age group during the 2022-2023 and 2023-2024 seasons and on a residual use of home treatment for COVID-19 (Table 2.6.22a).

In the macro areas of the North there is higher consumption than the national average (28.7 DDD), while the Centre (26.1 DDD) and in particular the South and Islands (23.5 DDD) show lower than average consumption (Table 2.6.22b). Compared to 2022, the North and Centre show decreasing consumption (-3.2% and -2.5% respectively) while in the South there is a slight increase (+0.9%). In regional detail, Sicily, with 17.8 DDD, has a value about half lower than that of the Valle d'Aosta (35.0 DDD).

Figure 2.6.22a NSAIDs and antipyretics, temporal trend (2016-2023) of consumption and average DDD cost

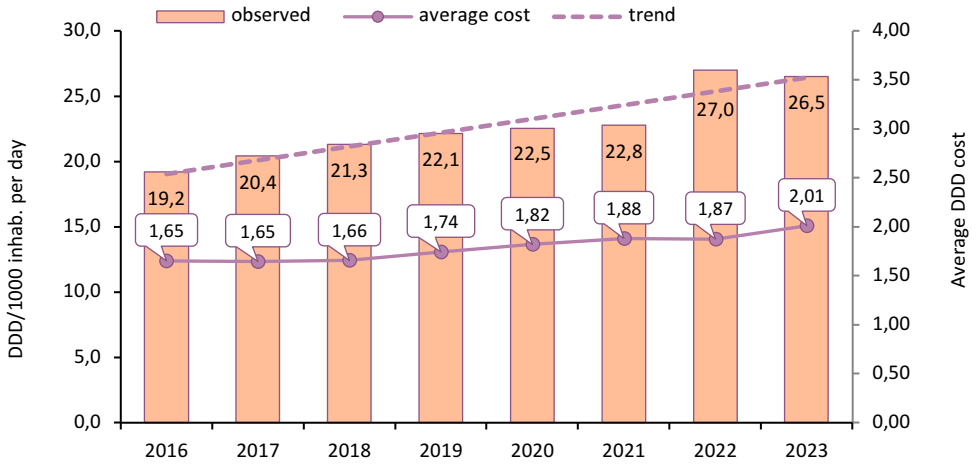


Table 2.6.22a NSAIDs and antipyretics, per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and by substance: comparison 2016-2023

Subgroups and substances	Expenditure million	Per capita expenditure	Δ % 23-22	CAGR % 16-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 16-23	Average DDD cost	Δ % 23-22
Paracetamol plain and in combination	516.3	8.77	4.2	6.5	12.6	-4.5	4.5	1.91	9.1
Traditional NSAIDs	498.9	8.48	8.0	7.8	11.3	2.8	4.6	2.05	5.1
Other antipiretics - salicylic acid and derivatives	72.9	1.24	-8.9	1.5	1.5	-13.3	-1.0	2.26	5.1
NSAIDs combined with decongestant	29.3	0.50	22.4	16.5	0.2	12.1	13.3	6.72	9.2
Other antipiretics - Pyrazolones	12.4	0.21	-2.4	-1.8	0.2	-14.7	-5.6	2.66	14.4
Other nonsteroidal anti-inflammatory/anti-rheumatic medicines	12.6	0.21	5.2	3.7	0.6	5.3	7.3	0.92	0.0
Coxib	0.6	0.01	25.1	6.0	<0.05	19.5	3.2	1.28	4.7
Oxicam	<0.05	<0.005	-68.7	-32.7	<0.05	-68.7	-35.0	1.24	0.0
NSAIDs and antipyretics	**1,143.1**	**19.42**	**5.2**	**6.7**	**26.5**	**-1.9**	**4.1**	**2.01**	**7.2**
paracetamol	405.8	6.90	-1.5	6.5	10.0	-9.6	4.8	1.89	9.0
ibuprofen	275.8	4.69	9.0	9.1	4.2	3.4	7.3	3.05	5.4
ketoprofen	74.7	1.27	1.8	9.2	1.7	1.3	8.0	2.01	0.6
acetylsalicylic acid/ ascorbic acid	62.2	1.06	-6.7	2.8	1.3	-11.2	0.1	2.18	5.0
diclofenac	50.3	0.85	12.5	7.6	1.4	2.4	4.6	1.73	9.9
paracetamol/ascorbic acid/phenylephrine	42.3	0.72	23.1	4.6	0.7	18.0	2.5	2.64	4.3
naproxen	24.8	0.42	-2.7	4.5	0.8	-11.9	0.7	1.43	10.5
ibuprofen/ pseudoephedrine	29.3	0.50	22.4	16.5	0.2	12.1	13.3	6.72	9.2
ketorolac	15.8	0.27	6.7	6.7	0.6	19.6	14.1	1.14	-10.8
bromfenac	16.7	0.28	19.5	9.4	0.5	15.1	8.3	1.47	3.8

Table 2.6.22b NSAIDs and antipyretics, regional trend of weighted DDD/1000 inhab. day: comparison 2016-2023

Region	2016	2017	2018	2019	2020	2021	2022	2023	Δ % 23-22
Piedmont	23.7	24.5	25.5	24.9	26.0	24.6	30.3	28.9	-4.6
Valle d'Aosta	29.4	31.0	31.5	30.4	31.5	27.6	35.1	35.0	-0.2
Lombardy	20.4	23.4	24.2	24.6	25.1	24.4	29.1	28.7	-1.5
Province of Bolzano	21.4	22.2	22.8	22.9	21.4	21.6	28.3	27.8	-1.7
Province of Trento	22.5	23.0	24.2	24.0	23.0	22.5	29.6	28.8	-2.6
Veneto	21.9	25.1	25.5	25.8	25.0	24.9	30.0	28.7	-4.3
Friuli VG	22.0	23.9	24.7	24.6	24.6	24.5	28.9	28.7	-0.9
Liguria	23.4	24.0	25.1	25.6	24.9	25.0	29.3	27.9	-4.8
Emilia R.	22.6	23.6	23.5	25.0	24.5	25.4	30.2	28.8	-4.6
Tuscany	17.6	18.4	19.5	20.2	21.0	21.9	26.5	25.9	-2.5
Umbria	16.9	16.8	16.9	17.0	21.9	24.3	28.4	28.5	0.5
Marche	13.8	13.4	13.7	14.7	18.0	20.5	24.7	23.2	-6.3
Lazio	17.6	19.3	21.2	23.2	22.4	22.4	27.1	26.6	-2.0
Abruzzo	17.8	17.8	18.7	20.5	19.4	20.0	23.9	23.4	-2.0
Molise	14.9	14.9	15.8	16.5	16.1	16.1	19.0	19.1	0.7
Campania	18.8	18.2	19.2	20.8	24.4	26.2	28.7	28.6	-0.3
Puglia	18.1	17.8	18.9	21.0	20.5	20.6	24.7	24.6	-0.4
Basilicata	18.0	17.9	18.5	20.2	18.7	19.3	23.5	24.6	4.6
Calabria	15.1	15.7	16.6	17.1	17.4	18.8	21.9	22.0	0.6
Sicily	12.5	13.5	14.4	14.8	15.6	15.3	17.0	17.8	4.5
Sardinia	19.1	19.8	20.8	21.4	19.4	19.7	23.1	23.8	2.9
Italy	**19.2**	**20.4**	**21.3**	**22.1**	**22.5**	**22.8**	**27.0**	**26.5**	**-1.9**
North	21.9	24.0	24.6	25.0	25.0	24.6	29.7	28.7	-3.2
Centre	17.0	18.1	19.4	20.7	21.3	22.1	26.7	26.1	-2.5
South and Islands	16.6	16.8	17.8	19.0	19.8	20.4	23.3	23.5	0.9

2.7 AIFA Notes for the Appropriate Use of Medicines

Introduced in 1993 following the establishment of the new Therapeutic Handbook (Law no. 537 of 24 December 1993) of the National Health Service (SSN), initially developed by the Single Medicine Commission (CUF), the AIFA Notes define the only therapeutic indications for which some medicines are reimbursed by the NHS. They have become a regulatory tool aimed at ensuring their appropriate use, directing the prescribing activity of doctors on the basis of the best evidence of efficacy in the literature.

Notes may be introduced if the relevant medicine is authorised for several clinical indications, of which only some concern relevant diseases, or in the case in which the medicine is used to prevent a significant risk in one or more population groups as well as when the medicine may lend itself to any improper uses which go beyond proven efficacy or may reduce its safety of use. The process of reviewing and updating the Notes occurs continuously based on the availability of new scientific evidence, making this regulatory instrument flexible in response to the needs of daily medical practice throughout the country. Amendments are aimed at a simpler and more direct management of the patient by the GP, better correspondence between indications of proven efficacy and those eligible for full reimbursement by the NHS, and prevention of misuse or significant risk only for one or more population groups.

The AIFA Notes currently in force are 39 compared to the 71 initially introduced by the CUF in 1994 with the drafting of the new National Health Service Handbook and the reclassification of medicines pursuant to art. 8, paragraph 10, of Law no. 537 of 24 December 1993. The Notes have undergone important revisions over time, taking into account the efficacy of individual medicines in different pathologies, possible reactions to treatments, but, above all, the evidence of the most recent scientific studies. Some medicines, previously covered by a Note, have been admitted directly to class A without limitations on reimbursement while others have moved from class C (paid by the citizen) to prescription at the expense of the NHS, limited to the cases provided for by the relevant Note.

During 2023, nine Notes were revised and, with AIFA Decision no. DG/507/2023 of 19 December 2023 published in the Official Journal on 12 January 2024, Note 93 concerning medicines used in the acute treatment of epilepsy seizures (oromucosal midazolam) was abolished, so that this can be prescribed by the NHS without any limitations since January 2024.

In addition, AIFA Decision No. DG/385/2023 of 5 October 2023 established Note 101 on the prescription of oral anticoagulants vitamin K inhibitors (AVK) and direct thrombin or factor Xa inhibitors (NAO/DOAC) in the home treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and in the prevention of relapses of PE and DVT. However, following the request received from the National Pharmaceutical Coordination of the Regions (note Prot. 126344 of 13 October 2023), the suspension of the effects of AIFA decision no. DG/385/2023 establishing AIFA Note 101 was ordered; deferral occurred with AIFA decision no. DG/394/2023 of 13/10/2023. Below are availabel the Note updates that took place during 2023.

Note 13

Note 13 defines the criteria for the prescription of lipid-lowering medicines to be charged to the NHS. AIFA Decision no. DG/26/2023 of 19 January 2023 replaces the text of AIFA Note 13 (AIFA Decision no. DG/560/2022 of 01/12/2022, Official Journal General Series no. 286

of 07/12/2022). In particular, in Annex 1 "Insights and theoretical basis of the note", in the chapter "Continuation of treatment with statins in combination therapies with non-lipid-lowering medicines", the triple association "ramipril, amlodipine and atorvastatin" has been introduced in the list of combinations of fixed-dose active ingredients eligible for reimbursement, limited to adult patients suffering from dyslipidemia already included in Note 13 and exclusively in cases in which the patient is already adequately treated and controlled by the simultaneous and extemporaneous intake of the same active ingredients, at the same doses, present in the fixed combinations, in compliance with the therapeutic indications reported in the respective Summaries of Product Characteristics (SPC).

Note 39

Note 39 defines the criteria for the prescription of growth hormone (GH) somatotropin and analogues at the expense of the NHS, on the basis of the diagnosis and treatment plan from specialised centres, Universities, Hospitals, Health Authorities, IRCCS, identified by the Regions and autonomous Provinces of Trento and Bolzano, limited to certain conditions defined on the basis of the age of the subject being treated. With AIFA Decision no. DG/104/2023 of 21 March 2023, published in the Official Journal General Series no. 74 of 28 March 2023, AIFA Note 39 was updated (pursuant to Decision no. 390/2021 of 6 April 2021) with the inclusion of the active ingredient somatrogon. In the same Official Journal, in fact, AIFA Decision no. 13/2023 of 13/03/2023 was published to reclassify the medicine for human use NGENLA (somatrogon).
Somatrogon is indicated for the treatment of children and adolescents from 3 years of age with growth disorders due to insufficient secretion of somatotropic hormone and is administered once a week subcutaneously. The reimbursable packages are available as 24 mg/1.2 ml and 60 mg/1.2 ml solution for injection in a pre-filled pen, and the classification for the purposes of reimbursability and supply is the same as for somatropins (class A/RRL, hypostatalism/PT/PHT centres).
The Note also points out that somatrogon is not indicated for the long-term treatment of paediatric patients with poor growth due to genetically confirmed Prader-Willi syndrome, unless they have also been diagnosed with growth hormone deficiency.
Note 39 calls for compliance with the RCP of the different medicines where this contains more restrictive indications and/or recommendations than those given in the Note.

Note 51

Note 51 establishes, on the basis of the main available evidence, the criteria for prescription and reimbursability by the NHS of gonadotropin-releasing hormone (LHRH) analogues (buserelin, goserelin, leuprorelin triptorelin), selective progesterone receptor modulators (ulipristal acetate) and gonadotropin-releasing hormone antagonists, oestrogen and progestin in combination (relugolix, estradiol and norethisterone acetate). The update of the Note, which took place with AIFA Decision no. DG/236/2023 of 23 May 2023 published in the OJ General Series no. 126 of 31/05/2023, concerns the inclusion of the combination consisting of relugolix (40 mg) in combination with oestradiol (as hemihydrate; 1 mg) (E2) and norethisterone acetate (NETA; 0.5 mg), for the treatment up to a maximum of 24 continuous months of moderate to severe symptoms of uterine fibroids in adult women of childbearing age when surgical treatment is not the option of choice on the basis of an individual clinical evaluation. Further courses of treatment may be considered on the basis of clinical evaluation.

Note 79

Note 79 regulates the prescription of medicines for the treatment of osteoporosis at the charge of the National Health Service in secondary prevention in subjects with previous osteoporotic fractures and in primary prevention in postmenopausal women or men aged ≥50 years at high risk of fracture limited to certain osteoporotic fracture risk conditions listed in the above note. With AIFA Decision no. DG/28/2023 of 19 January 2023 'Update of AIFA Note 79' referred to in Decision no. 363/2022 of 5 August 2022', published in the Official Journal General Series no. 31 of 07/02/23, the part concerning the medicine teriparatide, in the table "Secondary prevention in subjects with previous osteoporotic fractures - vertebral or femur fractures", is modified with regard to its use as first-choice treatment. The new update provides that for teriparatide the Note applies following a diagnosis and treatment plan, lasting 6 months renewable for further periods of 6 months no more than three times (for a grand total of 24 months), on prescription from hospital centres or specialist physicians (internist, rheumatologist, endocrinologist, gynaecologist, geriatrician, orthopaedist, physiatrist, nephrologist).

Note 83

Note 83 defines the criteria for the prescription at the expense of the NHS of medicines for the topical treatment of xerophthalmia (dry eye syndrome-DED) in Sjögren's disease. The update, introduced by AIFA Decision No. DG/29/2023 of 19 January 2023 published in the OJ General Series No. 31 of 7-2-2023, provides for the inclusion of cyclosporine A eye drops for the treatment of severe keratitis in adult patients with Sjögren's disease with dry eye syndrome when tear substitutes are not sufficiently effective. In addition, the 'Background' chapter of the note has been implemented with more information about the treatment of the condition.

Note 85

Note 85 defines the criteria for the prescription of acetylcholinesterase (AChE) inhibitors (donepezil, galantamine, rivastigmine) and glutamate receptor antagonists (memantine), for the treatment of patients with Alzheimer's disease, to be charged to the NHS. The new Note, updated by AIFA Decision no. DG/105/2023 of 21 March 2023, published in the Official Gazette General Series no. 73 of 27.03.2023, introduces the AIFA therapeutic plan (PT) for the medicines donepezil, galantamine, rivastigmine and memantine which must be filled out, for the purposes of NHS reimbursability, by the Centres for Cognitive Disorders and Dementia (CDCD) identified by the Regions and Autonomous Provinces. For patients on their first prescription, the treatment plan is adopted 30 days after the date of publication of this measure in the Official Journal. For patients already under treatment, the plan must be drawn up at the first possible specialist visit.
The treatment plan, which must be formulated on the basis of the initial diagnosis of probable Alzheimer's dementia (AD) according to the NIA-AA criteria, 2011, indicates the prescription of inhibitors in the mild (MMSE between 21 and 26) and moderate (MMSE between 10 and 20) forms and that of memantine in the moderate (MMSE between 10 and 20) and severe (MMSE <10) forms. In addition, the updated note allows the Therapeutic Plan to be renewed within a maximum of 12 months, exclusively in cases of clinical stability.

Note 95

Note 95, established by AIFA Decision no. DG/1466/2016, refers to the prescription of topical medicines for the treatment of actinic keratosis (AK) to be charged to the NHS, limited to adult patients with multiple lesions in number ≥6 and for non-hypertrophic actinic keratosis. By AIFA Decision DG/261/2023, published in the Official Journal General Series no. 152 of 1/7/2023, the medicinal product diclofenac 3% in sodium hyaluronate, already present in the Note in forms of AK localised to the trunk and/or extremities, is also included in actinic keratoses localised to the face and/or scalp. For the treatment of non-hyperkeratotic non-hypertrophic AK, the use of imiquimod 3.75% cream, 5-fluorouracil 4% cream, and tirbanibulin 10 mg/g ointment continues.

Note 96

Note 96, established by AIFA Decision no. DG/1533/2019, updated by AIFA Decision no. DG/48/2023, published in OJ General Series no. 43 of 20 February 2023, defines the reimbursement by NHS for medicines containing cholecalciferol, cholecalciferol/calcium salts and calcifediol, in the prevention and treatment of vitamin D deficiency in adults (<18 years), according to two different clinical scenarios that take into account or not the determination of serum levels of 25(OH) vitamin D.

The update of the Note, established in 2019, became necessary following the publication of new scientific evidence that further clarified the role of vitamin D in the absence of concomitant risk conditions. In particular, the results of two large randomised clinical trials, the American VITAL study and the European DO-HEALTH study, were taken into account. Both studies concluded that supplementation with more than adequate doses of vitamin D (2000 IU per day of cholecalciferol) over several years (more than 5 years in the first study and 3 years in the second) was not able to alter the risk of fracture in healthy populations without risk factors for osteoporosis. These results were also confirmed among subjects with lower vitamin 25(OH)D levels. In addition to these main studies, there is a rich literature regarding the use in COVID-19 which has not demonstrated any benefit of vitamin D, even in this condition. On this occasion, a number of improving clarifications have been included in the text of the Note at the suggestion of clinicians or scientific societies. The changes introduced with the update include the addition of the new risk category 'persons with severe motor deficits or bedridden persons living at home', in the prescription of the above-mentioned medicines regardless of the 25(OH)D determination, in addition to the other risk categories already provided for in the previous version, i.e., institutionalised persons, pregnant and breastfeeding women, persons suffering from osteoporosis, regardless of the cause, or established osteopathy, who are not candidates for remineralising therapy. Whereas, in the second scenario, i.e. medicines reimbursable by the NHS subject to a 25(OH)D determination, the changes relate to:

- The reduction from 20 to 12 ng/mL (or from 50 to 30 nmol/L) of the maximum serum vitamin 25(OH)D level values, in subjects with symptoms attributable to hypovitaminosis (intense asthenia, myalgia, widespread or localised pain, frequent unmotivated falls);
- The inclusion of asymptomatic subjects presenting with maximum serum vitamin 25(OH)D level values from 20 to 12 ng/mL (or <30 nmol/L);
- The specification of differentiated serum vitamin 25(OH)D levels in the presence of certain risk conditions (e.g. malabsorption disease, hyperparathyroidism) already present in the first version of the Note.

In addition, the update includes revisions of the most recent evidence mentioned above, the addition of a short paragraph on vitamin D and COVID-19, and a new paragraph on the potential risks associated with the misuse of vitamin D preparations.
The note refers to the adult population (18 years and over); therefore, there are no restrictions on reimbursability in the paediatric age group.

Note 98

Note 98, introduced with AIFA Decision no. DG/1379/2020 of 28 December 2020, published in the Official Journal General Series no. 323 of 31/12/2020, defines the prescription methods, intravitreal administration, as well as the use by the NHS of anti-VEGF medicines in age-related macular degeneration (nAMD) or diabetic macular edema (DME). During 2023, the Note underwent two updates: the first, with AIFA Decision no. DG/382/2023 of 29 September 2023, published in the Official Journal General Series no. 235 of 7.10.2023, concerns the inclusion of the active ingredient faricimab among those subject to AIFA Resolution 98, in the treatment of nAMD or DME, and a revision of the text of the Note; the second update, implemented with AIFA Decision n. DG/500/2023 of 14 December 2023, published in the Official Journal General Series n. 297 of 21/12/2023, takes into account the reimbursement of the medicine XIMLUCI (ranibizumab), and extends the reimbursement of the active ingredient brolucizumab, an inhibitor of vascular endothelial growth factor (VEGF), for the treatment of DME.

Analysis of consumption and expenditure of medicines included in AIFA Notes

In 2023 the local expenditure (including expenditure under approved care regime and expenditure in direct distribution (DD) and "on behalf" distribution (DPC) of medicines included in AIFA Notes was equal to 5.5 billion euro, a slight increase over 2022 of 2.8% (Table 2.7.1). This value is mainly attributable to the approved care regime (63.7%) and for a smaller share to direct and "on behalf" distribution (36.3%). However, for some Notes, the largest share of expenditure and consumption is attributable to alternative forms of medicine distribution (DD/DPC), as in the case of Note 39 concerning somatropin and somatrogon, of Note 65 concerning medicines for multiple sclerosis, of Note 74 on medicines for infertility (female and male) and preservation of female fertility in women (≥45 years) who have to undergo cancer therapies that may cause transient or permanent infertility, and of Note 51 on medicines used in certain forms of carcinoma and fibroma, as well as in early puberty. For Note 98, relating to medicines used in age-related macular degeneration (nAMD) or diabetic macular oedema (DME), expenditure and consumption are almost exclusively attributable to public health facilities.

Local expenditure was higher for medicines in Note 13 (lipid-lowering medicines) and Note 100 (antidiabetics), with absolute values of 981.6 and 953.6 million euro, respectively. However, in the case of lipid-lowering medicines, all of the supply was carried out through the conventional channel, while in the case of antidiabetics, approximately 79% is attributable to direct or "on behalf" distribution. The next highest expenditure levels are for COPD medicines included in Note 99 (680.4 million), oral anticoagulants included in Note 97 (648.7 million), supplied almost exclusively through the DD and DPC channel, and those for peptic ulcer and gastroesophageal reflux disease included in Note 1 or 48 (637.7 million), whose supply takes place almost entirely through the conventional channel. With regard to the medicines of the latter, particularly interesting is the figure for misoprostol, which is only included in Note 1 and presents an expenditure of 0.3 million, and for H2 antagonists, whose prescription restriction is only present in Note 48 and which show an expenditure of 20.6 million.

In 2023, the local consumption of medicines included in the AIFA Notes (Table 2.7.2) was equal to 449.3 DDD/1000 inhabitants per day, slightly decreasing (-1.3%) compared to the previous year.

With a per capita expenditure at national level of 94.4 euro, there is a marked regional variability (Table 2.7.3) ranging from 112.0 euro in Campania to 62.0 euro in Valle d'Aosta. The Northern Regions (90.4 euro), with the exception of Lombardy (103.2 euro), spent less than the Central (91.4 euro) and the Southern Regions (101.9 euro). The highest consumption is recorded in Campania (542.3 DDD/1000 inhabitants per day) and in Basilicata (511.9 DDD/1000 inhabitants per day), while Umbria (345.9 DDD/1000 inhabitants per day) and Valle d'Aosta (351.3 DDD/1000 inhabitants per day) have the lowest.

The top 20 active ingredients by expenditure (Table 2.7.4) include five from Note 13, four from Note 1-48, three from Note 97, two from Note 99, and two from Note 100. The active ingredients that recorded the greatest increase in expenditure were semaglutide (+50.5%) and the combination rosuvastatin/ezetimibe (+47.0%), with an increase in consumption of 70.2% and 47.7% respectively. The molecules which, on the other hand, showed the greatest decreases were cholecalciferol (-17.1%), the combination formoterol/beclomethasone (-11.6%) and dimethylfumarate (-15.1%). In the first case the reduction in expenditure is associated with a contraction in consumption (-14.3%), while in the second case with a reduc-

tion in the average DDD cost (-13.3%). For dimethyl fumarate, however, the reduction in expenditure is mainly attributable to the decrease in the average DDD cost (-11.7%) and to a lesser extent to that of consumption (-3.5%).

Figure 2.7.1 shows the temporal trend of the top 10 AIFA Notes by expenditure, which represent 90% of the local expenditure on all the medicines included in AIFA Notes. In particular, there is an increasing trend in the expenditure in Note 97 (oral anticoagulants), Note 100 (antidiabetics) and Note 13 (lipid-lowering medicines). The latter saw the introduction in 2023 of the triple combination ramipril, amlodipine and atorvastatin. For Note 96, concerning the prescription of vitamin D-based medicines, a reduction in expenditure is observed in 2020 due to the introduction of the prescription limitation introduced in the previous year, while in the years 2021 and 2022 there was again an increase. In 2023, on the other hand, following the update of Note 96, which provided for the reduction from 20 to 12 ng/mL (or from 50 to 30 nmol/L) of the values of the maximum level of serum vitamin 25(OH)D, expenditure fell again (-15.7%). For Note 99 relating to medicines for the treatment of COPD, a progressive reduction in expenditure has been observed since 2021, the year in which the Note was introduced. Similar trends are recorded on the consumption side (Figure 2.7.2).

Analysing, instead, the cost per day of therapy of the medicines included in the top 10 Notes by expenditure, a downward trend is observed in the period 2019-2023 for almost all Notes, especially for Note 79 (medicines for osteoporosis), probably due to the patent expiry of teriparatide, for Notes 1-48 and for Note 99 (COPD), attributable to the renegotiation of prices and the introduction of new molecules on the Transparency List (Figure 2.7.3).

Table 2.7.1 Expenditure on medicines included in AIFA Notes: comparison 2023-2022

Note	Approved care regime (A)		DD/DPC (B)		Public local (C=A+B)		Public health facilities		% under approved care regime*	% DD+DPC*	% expenditure Note**
	(million)	Δ % 23-22	(million)	Δ % 23-22	(million)	Δ % 23-22	(million)	Δ % 23-22			
Note 1	0.3	-15.3	<0.05	76.6	0.3	-15.1	<0.05	3.6	99.6	0.4	0.0
Note 1+48	635.9	-2.8	1.9	15.3	637.7	-2.8	3.4	13.5	99.7	0.3	4.2
Note 2	57.8	5.1	0.7	14.4	58.5	5.2	1.0	14.3	98.9	1.1	0.4
Note 4	158.4	6.1	1.4	7.5	159.8	6.1	1.6	5.4	99.1	0.9	1.1
Note 8	0.4	2.2	0.3	-4.8	0.7	-1.3	0.3	-0.6	52.2	47.8	0.0
Note 11	-		<0.05		<0.05		-				0.0
Note 13	980.5	8.1	1.1	36.4	981.6	8.1	1.7	32.7	99.9	0.1	6.5
Note 15	14.1	-0.7	0.6	-13.8	14.7	-1.2	7.8	-12.6	96.1	3.9	0.1
Note 28	2.5	-4.8	<0.05	9.7	2.5	-4.5	<0.05	1.5	98.2	1.8	0.0
Note 31	1.1	-0.9	0.1	16.7	1.1	-0.2	0.2	6.5	95.1	4.9	0.0
Note 36	1.5	3.8	2.1	-8.1	3.6	-3.5	2.4	7.9	41.0	59.0	0.0
Note 39	1.1	-51.0	63.1	-6.6	64.2	-8.1	64.4	-5.4	1.8	98.2	0.4
Note 41	-		<0.05	-100.0	<0.05	-100.0	-				0.0
Note 42	0.3	-4.4	<0.05	37.5	0.3	-4.3	<0.05	-17.3	99.5	0.5	0.0
Note 48	20.6	-5.0	<0.05	12.0	20.6	-4.9	0.1	9.5	99.9	0.1	0.1
Note 51	1.3	-21.6	118.1	3.1	119.4	2.7	129.9	6.2	1.1	98.9	0.8
Note 55	16.6	5.0	0.4	-24.4	17.1	4.0	3.1	-36.6	97.5	2.5	0.1
Note 56	4.0	-0.6	0.2	-3.3	4.2	-0.7	1.8	-23.9	94.1	5.9	0.0
Note 65	0.2	-40.8	275.7	-10.2	275.8	-10.2	273.2	-11.2	0.1	99.9	1.8
Note 66	140.7	-5.6	0.4	-1.0	141.1	-5.6	1.7	8.5	99.7	0.3	0.9

continued

Table 2.7.1 – *continued*

Note	Approved care regime (A)		DD/DPC (B)		Public local (C=A+B)		Public health facilities		% under approved care regime*	% DD+DPC*	% expenditure Note**
	(million)	Δ % 23-22	(million)	Δ % 23-22	(million)	Δ % 23-22	(million)	Δ % 23-22			
Note 74	8.4	-9.4	57.4	8.8	65.7	6.1	63.1	17.3	12.8	87.2	0.4
Note 75	6.0	8.1	2.9	-29.5	8.9	-7.8	2.9	-21.6	67.7	32.3	0.1
Note 79	144.0	1.5	94.0	20.2	238.0	8.2	106.4	21.4	60.5	39.5	1.6
Note 82	27.1	-0.1	<0.05	-22.9	27.1	-0.1	<0.05	3.4	100.0	0.0	0.2
Note 83	1.7	-5.7	0.5	48.1	2.2	3.0	0.5	40.8	76.8	23.2	0.0
Note 84	31.8	3.1	1.4	-1.5	33.2	2.9	2.1	0.9	95.8	4.2	0.2
Note 85	11.0	-8.8	7.8	-5.0	18.8	-7.3	7.5	-9.4	58.7	41.3	0.1
Note 87	6.1	21.2	<0.05	25.9	6.2	21.3	<0.05	10.1	99.6	0.4	0.0
Note 88	8.7	1.8	<0.05	16.0	8.8	1.8	0.1	11.1	99.4	0.6	0.1
Note 89	63.1	-1.8	0.1	18.1	63.2	-1.8	0.2	29.3	99.9	0.1	0.4
Note 90	7.2	35.4	0.3	40.7	7.5	35.6	0.8	62.0	95.6	4.4	0.0
Note 91	34.7	7.0	0.1	-22.7	34.8	7.0	0.1	-21.8	99.8	0.2	0.2
Note 92	0.1	20.0	0.2	39.4	0.2	33.0	0.4	20.5	29.5	70.5	0.0
Note 93§	2.6	3.1	0.3	11.4	2.9	4.1	0.5	12.2	88.2	11.8	0.0
Note 95	9.8	23.1	1.7	19.2	11.5	22.5	1.6	18.9	85.4	14.6	0.1
Note 96	228.1	-15.7	0.5	5.8	228.6	-15.7	0.8	3.3	99.8	0.2	1.5
Note 97	31.1	5.1	617.7	6.9	648.7	6.8	658.0	13.3	4.8	95.2	4.3
Note 98	-		11.3	-45.6	11.3	-45.6	138.2	-16.9	0.0	100.0	0.1
Note 99	675.4	-3.2	5.0	-10.7	680.4	-3.2	8.7	-7.4	99.3	0.7	4.5
Note 100	202.5	1.5	751.1	21.1	953.6	16.3	795.5	22.5	21.2	78.8	6.3
Total Notes	**3,537.0**	**0.1**	**2,018.4**	**7.9**	**5,555.0**	**2.8**	**2,280.1**	**9.0**	**63.7**	**36.3**	**36.6**

*calculated on total expenditure on medicines in the relevant Note under approved care regime and in DD and DPC
**calculated on total expenditure under approved care regime and in DD and DPC
§Note 93 was abolished with DG Decision no. 507/2023 of 19 December 2023 published in the Official Journal on 12 January 2024.

Table 2.7.2 Consumption (DDD/1000 inhabitants per day) of medicines included in AIFA Notes: comparison 2023-2022

Note	Under approved care regime (A)		DD/DPC (B)		Public local (C=A+B)		Public health facilities		% under approved care regime*	% DD+DPC*	% consumption Note**
	DDD	Δ% 23-22	DDD	Δ% 23-22	DDD	Δ% 23-22	DDD	Δ% 23-22			
Note 1	<0.05	-15.0	<0.05	83.7	<0.05	-14.6	<0.05	4.1	99.1	0.9	0.0
Note 1+48	75.0	-1.0	1.7	3.8	76.6	-0.9	3.1	4.0	97.8	2.2	6.2
Note 2	2.9	5.3	0.1	8.8	3.0	5.4	0.1	8.5	96.6	3.4	0.2
Note 4	6.6	6.2	0.4	4.7	7.1	6.2	0.6	11.8	93.8	6.2	0.6
Note 8	<0.05	3.4	<0.05	1.1	<0.05	1.9	<0.05	3.2	36.5	63.5	0.0
Note 11	<0.05						<0.05				0.0
Note 13	119.5	7.6	1.4	4.8	120.9	7.6	2.2	5.0	98.8	1.2	9.8
Note 15	<0.05	-2.6	<0.05	12.3	<0.05	-0.2	<0.05	-16.0	81.4	18.6	0.0
Note 28	0.1	-3.7	<0.05	22.8	0.1	-2.2	<0.05	30.0	93.1	6.9	0.0
Note 31	0.1	0.0	<0.05	17.5	0.1	1.7	<0.05	9.1	88.9	11.1	0.0
Note 36	<0.05	27.8	0.1	17.4	0.1	20.5	0.1	37.7	31.5	68.5	0.0
Note 39	<0.05	-38.7	0.3	-2.7	0.3	-3.1	0.3	-2.4	0.7	99.3	0.0
Note 41	<0.05						<0.05				0.0
Note 42	<0.05	-2.9	<0.05	-5.9	<0.05	-2.9	<0.05	-11.4	98.6	1.4	0.0
Note 48	1.9	-3.3	<0.05	0.6	2.0	-3.3	0.1	22.3	99.6	0.4	0.2
Note 51	<0.05	7.1	1.2	6.5	1.2	6.5	1.3	8.9	0.9	99.1	0.1
Note 55	<0.05	8.7	<0.05	-14.8	<0.05	6.0	<0.05	-25.8	90.9	9.1	0.0
Note 56	<0.05	15.6	<0.05	-1.8	<0.05	8.0	<0.05	-8.9	60.0	40.0	0.0
Note 65	<0.05	-48.2	0.7	-7.7	0.7	-7.7	0.7	-4.0	0.0	100.0	0.1
Note 66	17.0	-5.6	0.2	12.8	17.2	-5.4	0.5	8.0	99.1	0.9	1.4

continued

Table 2.7.2 – *continued*

Note	Under approved care regime (A)		DD/DPC (B)		Public local (C=A+B)		Public health facilities		% under approved care regime*	% DD+DPC*	% consumption Note**
	DDD	Δ% 23-22	DDD	Δ% 23-22	DDD	Δ% 23-22	DDD	Δ% 23-22			
Note 74	<0.05	22.3	0.1	-14.4	0.1	-11.7	0.1	-4.8	10.0	90.0	0.0
Note 75	0.1	14.6	0.3	12.2	0.3	12.7	0.3	6.1	20.5	79.5	0.0
Note 79	9.6	4.1	4.6	11.1	14.2	6.3	5.3	14.7	67.4	32.6	1.2
Note 82	2.0	-0.1	<0.05	-7.1	2.0	-0.1	<0.05	3.1	99.7	0.3	0.2
Note 83	0.4	-0.9	<0.05	-66.0	0.4	-13.5	<0.05	13.0	92.4	7.6	0.0
Note 84	0.3	4.4	0.1	7.3	0.3	4.9	0.1	4.2	80.1	19.9	0.0
Note 85	0.6	-4.9	1.5	4.7	2.2	1.7	1.6	2.3	29.1	70.9	0.2
Note 87	0.6	26.9	<0.05	8.9	0.6	26.6	<0.05	13.1	98.5	1.5	0.0
Note 88	2.0	2.6	<0.05	19.0	2.1	2.8	0.1	7.9	98.7	1.3	0.2
Note 89	10.2	-0.8	0.1	10.1	10.4	-0.7	0.3	10.8	98.9	1.1	0.8
Note 90	0.1	45.5	<0.05	38.9	0.1	44.9	<0.05	75.5	91.1	8.9	0.0
Note 91	2.4	7.5	<0.05	22.5	2.4	7.6	<0.05	17.5	99.2	0.8	0.2
Note 92	<0.05	20.3	<0.05	40.6	<0.05	36.1	<0.05	20.8	19.8	80.2	0.0
Note 93§	<0.05	4.9	<0.05	14.4	<0.05	6.4	<0.05	17.7	83.0	17.0	0.0
Note 95	0.1	-8.5	0.1	10.7	0.2	-2.2	0.1	10.9	63.0	37.0	0.0
Note 96	119.9	-14.4	2.1	7.1	122.0	-14.1	3.2	4.4	98.3	1.7	9.9
Note 97	2.4	-11.8	17.1	8.5	19.6	5.5	18.8	12.8	12.5	87.5	1.6
Note 98	<0.05		<0.05	-58.8	<0.05	-58.8	0.1	-22.2	0.0	100.0	0.0
Note 99	19.5	0.0	0.2	-11.1	19.7	-0.1	0.4	-6.7	98.8	1.2	1.6
Note 100	2.4	21.5	21.0	25.3	23.5	24.9	23.5	26.6	10.4	89.6	1.9
Total Notes	**395.8**	**-3.0**	**53.5**	**13.6**	**449.3**	**-1.3**	**63.1**	**15.3**	**88.1**	**11.9**	**36.5**

*calculated on total consumption of medicines in the relevant Note under approved care regime and in DD and DPC
** calculated on total consumption under approved care regime and in DD and DPC
§Note 93 was abolished with DG Decision no. 507/2023 of 19 December 2023 published in the Official Journal on 12 January 2024.

Table 2.7.3 Consumption (DDD/1000 inhabitants per day) and expenditure on medicines included in AIFA Notes by Region: comparison 2023-2022

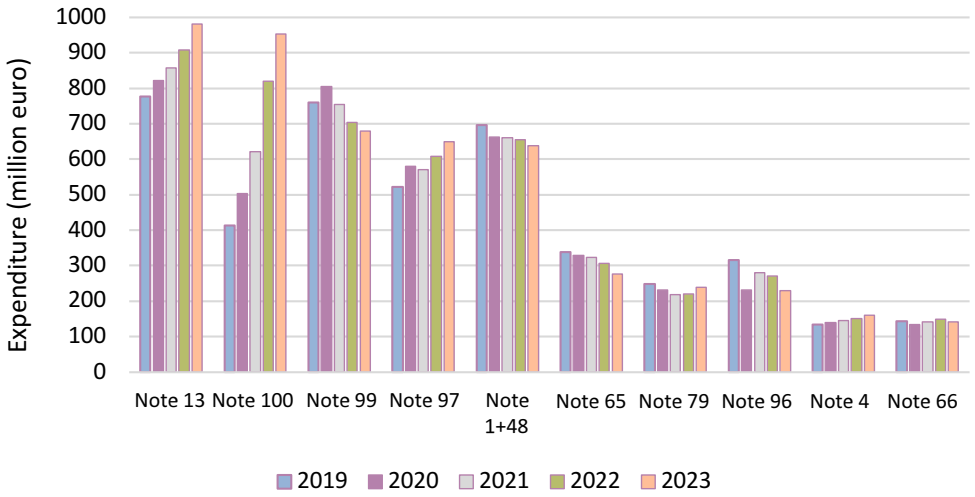
Region	Public local	Δ % 23-22	Per capita expenditure	% DD/DPC*	Public local	Δ % 23-22
Piedmont	358	3.8	80.9	41.0	398.4	-0.4
Valle d'Aosta	8	6.7	62.0	23.5	351.3	3.3
Lombardy	1,016	4.2	103.2	24.2	464.1	0.0
Province of Bolzano	36	3.0	73.0	45.4	411.8	4.0
Province of Trento	46	13.5	86.5	38.1	465.2	4.5
Veneto	404	4.0	82.9	44.5	431.8	0.7
Friuli VG	114	5.3	90.7	43.1	470.5	1.7
Liguria	145	3.0	88.3	38.7	432.4	-1.8
Emilia R.	375	5.9	83.8	43.3	440.5	0.0
Tuscany	298	0.2	78.4	44.1	359.0	-4.8
Umbria	74	-5.3	83.1	46.6	345.9	-10.2
Marche	143	5.0	93.7	41.6	423.9	2.0
Lazio	569	3.4	100.8	37.9	436.9	-2.9
Abruzzo	138	5.5	106.3	42.1	469.3	-0.4
Molise	32	5.5	104.9	43.2	465.0	1.6
Campania	583	-0.1	112.0	32.7	542.3	-3.7
Puglia	407	-1.7	105.3	40.4	491.1	-3.6
Basilicata	57	0.8	105.6	33.6	511.9	0.2
Calabria	179	0.5	98.7	35.0	459.9	-1.6
Sicily	444	4.5	95.4	37.6	441.8	-0.8
Sardinia	131	0.8	79.5	20.2	496.9	1.2
Italy	**5,555**	**2.8**	**94.4**	**36.3**	**449.3**	**-1.3**
North	2,500	4.5	90.4	35.0	441.1	0.2
Centre	1,084	2.1	91.4	40.7	403.5	-3.3
South and Islands	1,971	1.2	101.9	35.6	489.3	-2.0

*calculated on total expenditure on medicines in the relevant Note under approved care regime and in DD and DPC

Table 2.7.4 Expenditure and consumption (DDD/1000 inhabitants per day) for the top 20 active ingredients by expenditure included in AIFA Notes: comparison 2023-2022

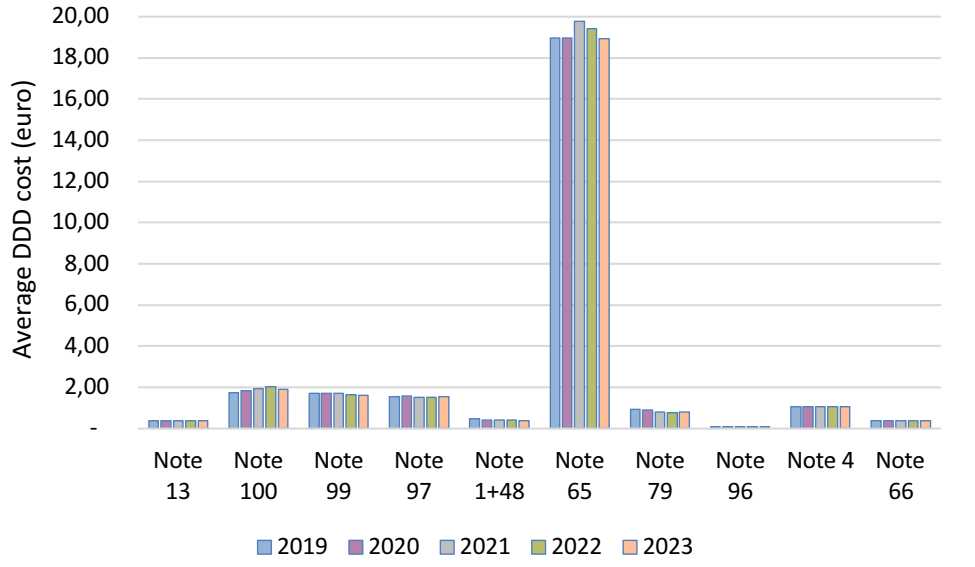
ATC 1st level	Active ingredient	Public local	Δ % 23-22	Public local	Δ % 23-22	Average DDD cost	Δ% 23-22
C	atorvastatin	274.4	-0.6	51.6	-0.4	0.25	0.1
A	pantoprazole	265.9	-0.2	30.0	1.7	0.41	-1.6
A	dulaglutide	228.2	-1.3	4.3	10.9	2.50	-10.7
B	apixaban	222.1	9.5	5.8	11.6	1.78	-1.6
A	semaglutide	217.5	50.5	2.7	70.2	3.70	-11.3
A	cholecalciferol	198.4	-17.1	118.8	-14.3	0.08	-3.0
B	rivaroxaban	192.9	3.6	5.5	3.9	1.62	0.0
B	edoxaban	145.6	18.5	3.8	22.6	1.79	-3.1
C	rosuvastatin/ezetimibe	134.0	47.0	15.8	48.7	0.39	-0.8
R	formoterol/ beclomethasone	133.0	-11.6	4.2	2.3	1.48	-13.3
A	esomeprazole	131.3	-0.8	16.0	0.9	0.38	-1.4
C	omega-3	130.7	2.6	2.7	4.9	2.25	-1.9
L	dimethyl fumarate	126.4	-15.1	0.2	-3.5	25.64	-11.7
R	vilanterol/ fluticasone furoate	125.1	-0.1	3.7	2.4	1.57	-2.2
A	omeprazole	121.6	-4.8	17.5	-2.2	0.32	-2.4
A	lansoprazole	119.0	-7.9	13.1	-6.6	0.42	-1.1
C	ezetimibe	109.1	7.9	7.0	9.1	0.72	-0.8
C	rosuvastatin	93.2	6.3	16.8	6.5	0.26	0.2
N	pregabalin	87.9	8.6	2.9	9.4	1.39	-0.5
M	denosumab	85.3	15.1	4.5	11.0	0.88	4.0
	Top 20	**3141.7**	**3.1**	**327.2**	**-2.9**	**0.45**	**6.6**
	Total	**5,555.0**	**2.8**	**449.3**	**-1.3**	**0.58**	**4.4**

Figure 2.7.1 Temporal trend (2019-2023) of local expenditure* on the top 10 AIFA Notes with the highest expenditure in 2023



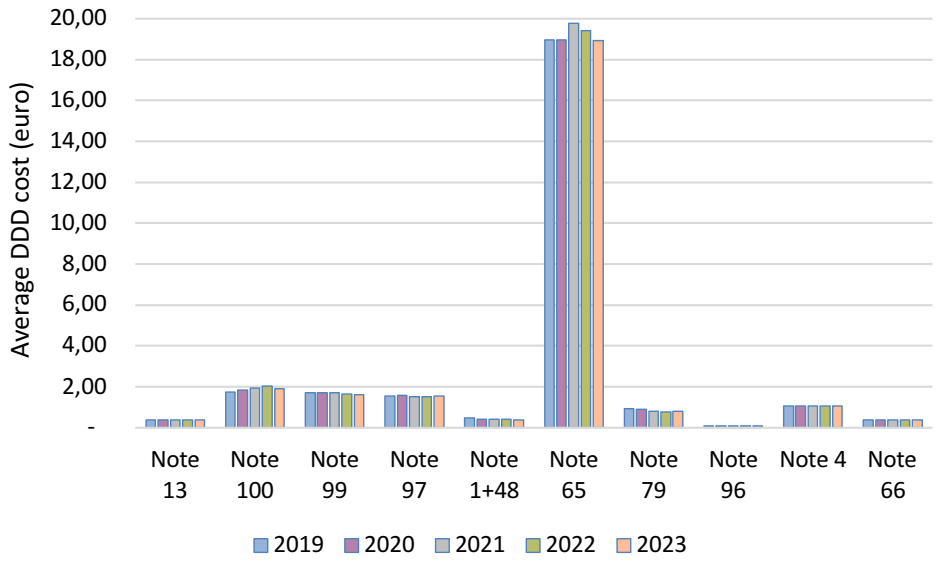
*includes expenditure under approved care regime and DD/DPC expenditure
Note 100 introduced in 2022, Note 99 introduced in 2021, Note 97 introduced in 2020, Note 96 introduced in 2019.
Notes 13, 1/48, 65, 79, 4 and 66 were introduced before the start of the observation period.

Figure 2.7.2 Temporal trend (2019-2023) of local consumption* of the top 10 AIFA Notes with the highest expenditure in 2023



*includes expenditure under approved care regime and DD/DPC expenditure
Note 100 introduced in 2022, Note 99 introduced in 2021, Note 97 introduced in 2020, Note 96 introduced in 2019.
Notes 13, 1/48, 65, 79, 4 and 66 were introduced before the start of the observation period.

Figure 2.7.3 Temporal trend (2019-2023) of the average cost per day of therapy at local level* of the top 10 AIFA Notes with the highest expenditure in 2023



*includes expenditure under approved care regime and DD/DPC expenditure
Note 100 introduced in 2022, Note 99 introduced in 2021, Note 97 introduced in 2020, Note 96 introduced in 2019. Notes 13, 1/48, 65, 79, 4 and 66 were introduced before the start of the observation period.

Note 1: pantoprazole, omeprazole, misoprostol, lansoprazole, esomeprazole.

Note 2: chenoursodeoxycholic acid, tauroursodeoxycholic acid, ursodeoxycholic acid.

Note: 4: duloxetine, gabapentin, pregabalin.

Note 8: levocarnitine.

Note 11: calcium folinate.

Note 13: bezafibrate, fenofibrate, gemfibrozil, simvastatin, pravastatin, fluvastatin, lovastatin, atorvastatin, rosuvastatin, ezetimibe.

Note 15: human albumin.

Note 28: megestrol, medroxyprogesterone.

Note 31: levodropropizine, dihydrocodeine, benzoic acid, dihydrocodeine.

Note 36: testosterone.

Note 39: somatropin, somatrogon.

Note 41: calcitonin.

Note 42: etidronic acid, clodronic acid.

Note 48: oxatidine, ranitidine, rabeprazole, pantoprazole, omeprazole, nizatidine, lansoprazole, famotidine, esomeprazole, cimetidine.

Note 51: buserelin, goserelin, leuprorelin, triptorelin, ulipristal acetate, relugolix, estradiol (as hemihydrate) (e2), norethisterone acetate (neta).

Note 55: tobramycin, piperacillin + tazobactam, piperacillin, netilmicin, mezlocillin, gentamicin, ceftazidime, cefepime, ampicillin + sulbactam, amikacin; Note 56: teicoplanin, rifabutin, imipenem + cilastatin, aztreonam.

Note 65: glatiramer, interferon β-1a, interferon β-1b, teriflunomide, dimethyl fumarate, peginterferon beta-1.

Note 66: tenoxicam, sulindac, proglumethacin, piroxicam, oxaprozine, nimesulide, naproxen, nabumetone, meloxicam, lornoxicam, ketoprofen, indomethacin, ibuprofen, furprofen, flurbiprofen, fentiazac, etoricoxib, diclofenac + misoprostol, diclofenac, dexibuprofen, codeine and ibuprofen, cinnoxicam, celecoxib, amtolmetin, tiaprofenic acid, mefenamic acid, acetamethacin, aceclofenac.

Note 74: urofollitropin, menotropin, lutropin alfa, follitropin delta, follitropin beta, follitropin alfa/lutropin alfa, follitropin alfa, choriogonadotropin alfa, corifollitropin alfa.

Note 75: vardenafil, tadalafil, sildenafil, avanafil, alprostadil.

Note 79: alendronate, bazedoxifene, denosumab, ibandronate, raloxifene, risedronate, romosozumab, teriparatide, zoledronate.

Note 82: zafirlukast, montelukast.

Note 83: carbomer.

Note 84: valaciclovir, famciclovir, brivudine, aciclovir.

Note 85: donepezil galantamine, rivastigmine, memantine.

Note 87: fesoterodine, oxybutynin, solifenacin, tolterodine.

Note 88: corticosteroids, dermatological preparations.

Note 89: promethazine, oxatomide, mizolastine, loratadine, levocetirizine, ketotifen, fexofenadine, ebastine, desloratadine, cetirizine, acrivastine, rupatadine.

Note 90: naloxegol, methylnaltrexone, naldemedine.

Note 91: febuxostat.

Note 92: benzathine benzylpenicillin.

Note 93 - abolished since January 2024: midazolam oromucosale.

Note 95: diclofenac 3% in sodium hyaluronate, 5-fluorouracil/salicylic acid (for actinic keratosis), imiquimod cream 3.75%, 5-fluorouracil 4%, tirbanibulin 10 mg/g ointment (for non-hyperkeratotic non-hypertrophic actinic keratosis).

Note 96: cholecalciferol, cholecalciferol/calcium salts, calcifediol.

Note 97: warfarin, acenocoumarol, dabigatran, apixaban, edoxaban, rivaroxaban.

Note 98: aflibercept**,** bevacizumab (Law 648/96), brolucizumab, faricimab, ranibizumab.

Note 99: Inhalation medicines (limited to dosages/formulations for maintenance inhalation therapy of COPD) based on the following active substances: LABA: formoterol, indacaterol, olodaterol, salmeterol - LAMA: Aclidinium, glycopyrronium, tiotropium, umeclidinium - LABA + ICS (single actuator) - formoterol/beclomethasone, formoterol/budesonide, salmeterol/fluticasone propionate, vilanterol/fluticasone furoate - LABA + LAMA (single actuator): indacaterol/glycopyrronium, vilanterol/ umeclidinium, olodaterol/tiotropium, formoterol/aclidinium - ICS + LABA + LAMA (single actuator): beclomethasone dipropionate/formoterol fumarate dihydrate/ glycopyrronium bromide, fluticasone furoate/ umeclidinium bromide/ vilanterol trifenatate, budesonide/glycopyrronium bromide/ formoterol fumarate dihydrate.

Note 100: SGLT2 inhibitors: canagliflozin, dapagliflozin, empagliflozin, ertugliflozin GLP1 receptor agonists: dulaglutide, exenatide, exenatide LAR, liraglutide, lixisenatide, oral semaglutide, subcutaneous semaglutide - DPP4 inhibitors: alogliptin, linagliptin, saxagliptin, sitagliptin, vildagliptin - pre-established combinations: canagliflozin/metformin, apagliflozin/ metformin, empagliflozin/metformin, empagliflozin/linagliptin, ertugliflozin/ metformin, ertugliflozin/sitagliptin, saxagliptin/dapagliflozin, degludec/liraglutide, glargine/lixisenatide, alogliptin/metformin, alogliptin/pioglitazone, linagliptin/metformin, saxagliptin/metformin, sitagliptin/metformin, vildagliptin/ metformin.

Section 3

Consumption and expenditure by therapeutic class

BACK TO CONTENTS

General data on expenditure and consumption by ATC group

This section presents the trend of NHS-covered pharmaceutical expenditure and consumption, including the prescription under approved care and the supply of medicines purchased directly from public health facilities. National and regional data are analysed by ATC level I, by therapeutic category and by active ingredient.

In 2023, the NHS pharmaceutical expenditure, expressed as a per capita value, was 441.37 euros, with a 5.3% increase compared to the previous year (Table 3.1). This was entirely due to the increase in expenditure by public health facilities (+8.5%; 275.16 euros per capita, more than 62% of total expenditure) while expenditure on class A medicines under approved care regime remained stable (+0.3%; 166.22 euros).

With the exception of 'Various' medicines, the category with the largest increase under approved care regime is that of antimicrobials for systemic use (+6.1%), while medicines for the gastrointestinal tract recorded the largest decrease (-5.8%). As already highlighted in previous years, once again in 2023 cardiovascular system drugs are the category with the highest per capita expenditure (52.25 euros, equal to 87% of the total NHS expenditure). As regards the medicines dispensed by public health facilities, antineoplastic and immunomodulators reached 120.47 euros per capita in 2023, constantly increasing since 2018 and a stable average cost per DDD over the same period (Figures 3.1 and 3.3). Among the most expensive categories, increases of more than 20% are recorded for musculoskeletal and respiratory systems drugs (Table 3.1).

Consumption under approved care regime accounts for 85% of total consumption (1322.95 DDD/1000 inhabitants per day), stable compared to the previous year (Table 3.2). Cardiovascular drugs (513.91 DDD) account for 39% of the overall doses consumed, entirely represented by the prescription under approved care regime) and have been stable in the past 6 years (Figure 3.2).

Public and private expenditure by ATC 1st level (Table 3.3) show that antineoplastic and immunomodulating agents have the highest expenditure, with a value of 7.4 billion, an incidence of 21.2% on total pharmaceutical expenditure and a per capita value of 125.03 euros. As expected for this category, the largest share of expenditure (95.3%) refers to purchases by public health facilities. Gastrointestinal drugs account for 14.1% of total expenditure and represent, in absolute values, the most privately purchased category in the case of both class A medicines (448 million euros), class C medicines (303 million), and self-medication drugs (898 million euros). Medicines acting on the central nervous system have the highest absolute expenditure value of class C drugs sold upon prescription (1.26 billion euros) and in fact represent 33.0% of the total expenditure in this reimbursement range. As for purchases by public health facilities, 43.8% (equal to 7.1 billion euros) refers to antineoplastics and immunomodulators; as for class A drugs, 31.4% relates to cardiovascular drugs, for a total expenditure of 3.1 billion euros. Among the class C drugs with prescription, 32.8% refers to central nervous system drugs (1.3 billion euros); as for self-medication drugs, after gastrointestinal drugs, the most expensive category concerns drugs for musculoskeletal disorders with 708 million euros, equal to 21.4%.

Cardiovascular drugs are the highest consumption category with 561.4 DDD/1000 inhabitants per day, equal to 29.6% of total consumption (Table 3.4). Among these, the highest incidence (88.2%) relates to class A drugs reimbursed by the NHS. Gastrointestinal drugs rank second (433.0 DDD; 22.8% of the total), followed by blood and haematopoietic organs drugs (198.1

DDD; 10.4%), 45% of which are in class A-NHS, 27.6% by public health facilities and 14.9% in class C with prescription. The most consumed privately purchased class A drugs (Table 3.4) are gastrointestinal system drugs (86.4 DDD/1000 inhabitants per day, 37.9% of the total), while drugs acting on the central nervous system are the most used within class C drugs with prescription (68.2 DDD/1000 inhabitants per day, 33.4%); gastrointestinal drugs rank first for consumption within self-medication drugs (36.1 DDD/1000 inhabitants per day, 25.2%), followed by respiratory system drugs (33.9 DDD, 23.6%).

Table 3.5 shows the distribution of gross per capita expenditure under approved care regime of class A drugs, classified by Region and geographical area. Overall, compared to the national value of 166.2 euros, the Northern and Central Regions report lower values, respectively 154.9 and 162.0 euros, while the Southern Regions show a higher value, equal to 184.9 euros (+11% compared to the national average). As in 2022, blood and haematopoietic organs drugs report a high variability (CV: 54%), probably due to the different use by the Regions of alternative drug dispensing methods (e.g. direct and "on-behalf" distribution).

The trend in drug consumption (Table 3.6) shows a greater use in the South (1,216.8 DDD/1000 inhabitants per day, 8.6% higher than the national average) and in the Centre (1,127.9 DDD) compared to the North (1,066.1 DDD, 5% below the average). For ATC "Antimicrobics for systemic use" (CV 19%) the highest consumption is observed in Campania (21.6 DDD/1000 inhab. per day) and the lowest in the Province of Bolzano (9.4 DDD). The first three categories with the highest consumption (ATC A, B and C) account for over 75% of the doses in all regions (Table 3.6 and Figure).

When analysing the trend of regional per capita expenditure on drugs purchased by public health facilities by ATC 1st level, the Central and Southern Regions show a higher per capita expenditure (respectively 275.3 euros and 289.9 euros), compared to the Northern Regions (264.7 euros). The antineoplastics and immunomodulators category, in almost all the Regions, accounts for about half of the expenditure by public health facilities (Table 3.7 and Figure).

However, when analysing consumption, the greatest heterogeneity between the Regions is observed for genitourinary drugs (CV 94%), with a maximum value of 12 DDD/1000 inhabitants per day of Emilia Romagna and a minimum value (0.6 DDD/1000 inhabitants per day) of Molise. The category with the highest consumption in all Regions is ATC B, which, together with ATC A and N accounts for over 65% of the consumption for drugs purchased by public health facilities in all the Regions (Table 3.8 and Figure).

For class A medicines provided under approved care regime, there was no change in expenditure compared to 2022, even if there was a shift towards more expensive products (mix effect: +2.7%), but offset by a reduction in consumption and prices (both -1.3%) (Table 3.9). However, there are marked differences between the categories (Figure 3.4). As regards cardiovascular system drugs, the increase in expenditure was due almost exclusively to a positive mix effect (+2.4%) and to an increase in consumption (+1.3%). For antimicrobial medicines, the increase in expenditure (+5.8%) is driven exclusively by an increase in consumption (+6%).

When analysing the individual therapeutic categories, acid pump inhibitors show the highest value of per capita expenditure (11.09 euros), with a -3% reduction due to a shift towards less expensive products (mix effect: -1.6%) and a decrease in consumption (-1.4%). In 2023, there was a decrease in expenditure and consumption of vitamin D and similar products by around 15%, probably due to the impact of the AIFA Note 96. As for the triple combination

drugs (adrenergics associated with anticholinergics and corticosteroids), belonging to respiratory system drugs, they show an increase in expenditure and consumption of about 24%, with a shift towards more expensive products (mix effect: +4%) and a reduction in prices. As already mentioned, the increase in antibiotic consumption concerns in particular the associations of penicillins including beta-lactamase inhibitors and third-generation cephalosporins (approximately +16%).

As for cardiovascular medicines, atorvastatin accounts for the highest percentages of gross expenditure per capita and consumption in the category (8.9% of expenditure and 10.2% of doses), while ramipril although representing 12.3% of doses, accounts for only 3.6% of expenditure. As regards the central nervous system, three SSRI antidepressants (sertraline, paroxetine and escitalopram) individually represent more than 10% of the doses and an expenditure of around 4%. Finally, the formoterol/beclomethasone and vilanterol/fluticasone furoate associations account for 28% of the expenditure on respiratory drugs, just as the amoxicillin/clavulanic acid association represents 37.5% of the consumption and 26.2% of the expenditure on antimicrobial drugs. This category records, inter alia, the highest average cost per DDD (1.96 euros) (Table 3.10).

The first thirty active ingredients for class A approved care expenditure (Table 3.11) represent 37.8% of the total class A-NHS expenditure, equal to an absolute value of 3700.2 million euros. Overall, thirteen molecules belong to the category of medicines acting on the cardiovascular system and are mainly represented by atorvastatin (274.4 million), bisoprolol (171.4 million), and the combination ezetimibe/rosuvastatin (134 million), going from 21nd rank in 2022 to 6th in 2023 (it ranked 42nd in 2021). Another eight belong to the category of drugs acting on the gastrointestinal system and metabolism, including pantoprazole (265.5 million), cholecalciferol (198 million), esomeprazole (131.1 million). The average cost of direct purchases is an indicator that provides an estimate of the effect of regional purchasing procedures for individual active ingredients. For all medicines, the average cost of direct purchases is significantly lower than for purchases under approved care regime, with the exception of rifaximin, where the average cost of direct purchases is 2.27 euros compared to 2.08 euros under approved care regime. For instance, cholecalciferol goes from 0.01 euros in direct purchases to 0.08 euros under approved care regime (+0.07 euros), while amoxicillin/clavulanic acid shows a difference of 1.13 euros, the only exception being for rifaximin, whose average cost per DDD in the two distribution channels is similar.

In 2023, the drugs supplied under approved care regime with the highest average cost per day of therapy were ceftriaxone (11.63 euros), teriparatide (11.08 euros; a 15% decrease compared to 2022), and semaglutide (9.34 euros), which shows the highest increase (+18.2%) compared to 2022 (Table 3.12). Among the top 30 active ingredients with the lowest average cost per day of therapy, there are acetylsalicylic acid (0.07 euros), cholecalciferol and furosemide (0.08 euros); more than half of the substances listed belong to the category of cardiovascular drugs (17 out of 30) (Table 3.13).

The top 30 active ingredients with the greatest increase in expenditure include ranolazine (Table 3.14), and the combinations vilanterol/umeclidinium (+58.8% compared to 2022) and ezetimibe/rosuvastatin (+47.4%). As for ranolazine, the increase in expenditure and consumption is due to the shift from direct purchases to approved care regime. On the other hand, dulaglutide is the first of the active substances with the highest reduction in expenditure (-19.9%), followed by insulin lispro (-17.6%) and by the naloxone/oxycodone combination used for pain therapy (-17.4%) (Table 3.15). For dulaglutide, the reduction in

expenditure is mainly attributable to the reduction in consumption, while for the other two drugs there is a reduction in consumption and a sharp decrease of the average DDD cost. In the case of the naloxone/oxycodone combination, the reduction in the average cost is due to the recent inclusion in the AIFA transparency list.

Table 3.16 shows the top 30 most consumed active ingredients; cholecalciferol with 136.8 DDD ranks 1st and accounts for 10.3% of the total consumption in class A-NHS approved care regime, showing a 2.7% reduction compared to 2022; it is followed by ramipril with less than half of DDD (60.7), atorvastatin (50.6 DDD) and acetylsalicylic acid (46 DDD). The first thirty substances represent more than 58.1% of the total expenditure. As expected, direct purchases show an average cost that is always lower than approved care regime.

Table 3.17 shows, with regard to purchases by health facilities (ATC 1st level), the therapeutic subgroups in descending order of expenditure by public health facilities, up to 0.10 euros of gross per capita expenditure. In 2023, the gross per capita expenditure on drugs purchased directly by public health facilities was 275.16 euros, increasing by 8.2% compared to the previous year. This trend is due to an increase in consumption (+4.9%) and to a shift towards more expensive medicines (mix effect: +7.1%), offset by a 3.7% drop in prices. The expenditure on immunomodulatory and immunostimulant drugs (ATC L) increased by 6.3% due to both an increase in consumption (+9.6%) and a positive mix effect (+1.9%), while there was a reduction in prices by 4.8% (Figure 3.5).

Table 3.18 shows the most prescribed active ingredients by ATC 1st level in public health facilities. The drugs with the greatest expenditure impact by category include the following: dupilumab, which accounts for about 85% of dermatologicals, atovaquone (51.0% of antiparasitic drugs), aflibercept (46.6% of sensory organs drugs), and the combination elexacaftor/tezacaftor/ivacaftor (38.4% of respiratory system drugs).

With reference to the first thirty most expensive active ingredients, which represent 33% of the total expenditure by healthcare facilities, 15 molecules belong to the category of antineoplastic and immunomodulatory drugs and 5 to blood and blood-forming organs drugs (Table 3.19). Pembrolizumab and daratumumab recorded the highest values of per capita expenditure, equal to 7.76 and 7.75 euros respectively, with a total expenditure of 456.5 and 456.2 million respectively (3.1% of total expenditure). This is followed by the association elexacaftor/tezacaftor/ivacaftor with 4.83 euros per capita and apixaban with 3.80 euros. Semaglutide, an antidiabetic administered weekly, ranked 10th in 2023 compared to 27th rank in 2022.

By analysing the first 30 active substances with the greatest increase in expenditure, twelve belong to the category of antineoplastic and immunosuppressants, with ravulizumab and acalabrutinib showing the largest increases (>100%), followed by ciloleucel axicabtagene (>100%) indicated for the treatment of diffuse large B-cell lymphoma (DLBCL) and refractory or relapsing primary large B-cell mediastinal lymphoma (PMBCL), with an average cost per DDD of over 282 thousand euros in 2023 (Table 3.20). The change recorded in the average DDD cost in 2023 compared to 2022 (+70.7%) is due to the change in the methods of accounting for the expenditure of the drug that were subject to conditional reimbursement agreements, payment at result, which provided for the allocation and for the attribution of fractions of the cost of treatment over time following the verification of the maintenance of therapeutic success. Subsequently, the amendment provided for the revision of the negotiating agreement and for accounting the full cost of the infusion treatment. The drugs with the greatest expenditure reduction (Table 3.21) are fingolimod (-29.2%), octocog alfa (-

24.0%) and paliperidone (-23.2%). Axicabtagene ciloleucel remains among the first active substances with an average cost per DDD of more than 1,000 euros (Table 3.22) followed by imiglucerase (1,096.5 euros), indicated for Gaucher disease, albutrepenonacog alfa, used to prevent or stop bleeding caused by factor IX deficiency in patients of all age groups with haemophilia B (also known as congenital factor IX deficiency or Christmas disease), and by algucosidase alfa indicated in Pompe disease. Table 3.23 shows the lowest average cost drugs per day of therapy, including electrolytes for intravenous solutions (0.45 euros), showing an increase of about 13%, followed by enoxaparin (0.85 euros) and denosumab (0.86 euros); significant reductions in this indicator were observed for paliperidone (26.3%), adalimumab (14.4%) and etanercept (14.3%), due to a reduction in expenditure compared to 2022. Within the most consumed drugs, the first six active ingredients, with more than 5 DDD, belong to the blood and blood-forming organs category: semaglutide, with 2.9 DDD shows an increase in consumption by over 96%, going from 27th rank in 2022 to 14th rank in 2023 (Table 3.24). Tables 3.25 and 3.26 show the top 30 active ingredients by expenditure and consumption in relation to the approved care regime and purchases by public health facilities. In detail, two antineoplastic drugs (pembrolizumab and daratumumab) rank 1st and 2nd in terms of expenditure and an average cost per DDD higher than 80 euros, followed by atorvastatin, pantoprazole and apixaban with an expenditure ranging between 274.5 and 241.1 million euros (average cost per DDD lower than 0.5 euros for the first two substances). Atorvastatin is also among the molecules with the highest consumption (52.1 DDD), while cholecalciferol ranks first with 119.8 DDD.

Table 3.1 NHS expenditure of approved care regime (A-NHS) and public health facilities by ATC 1st level in descending order of total NHS expenditure: comparison 2023-2022 (Table and Figure)

ATC 1st level	Per capita expenditure Approved care regime (a)	Δ% 23-22	Per capita expenditure Public health facilities (b)	Δ% 23-22	*Per capita* expenditure NHS (a+b)	Δ% 23-22
L	4.55	1.6	120.47	6.6	125.03	6.4
C	52.25	4.0	8.18	11.4	60.43	4.9
A	30.73	-5.8	25.66	13.7	56.39	2.2
J	11.64	6.1	35.28	5.3	46.92	5.5
B	7.19	-3.2	36.76	7.6	43.95	5.7
N	23.65	-0.6	11.23	15.0	34.88	3.9
R	15.56	-1.9	12.55	21.1	28.12	7.2
M	5.36	-0.5	5.90	30.0	11.26	13.4
H	4.05	1.9	4.09	-4.9	8.14	-1.6
G	5.70	2.1	1.48	14.2	7.17	4.4
S	3.76	3.1	3.04	-7.3	6.80	-1.8
V	0.19	35.4	6.19	-2.9	6.37	-2.1
D	1.35	4.2	4.29	37.3	5.64	27.6
P	0.24	2.6	0.04	38.6	0.28	6.7
Total	166.22	0.3	275.16	8.5	441.37	5.3

A Gastrointestinal system and metabolism
B Blood and blood-forming organs
C Cardiovascular system
D Dermatologicals
G Genito-urinary system and sex hormones
H Systemic hormonal preparations, excluding sex hormones
J Antimicrobials for systemic use
L Antineoplastic and immunomodulatory pharmaceuticals
M Musculo-skeletal system
N Central nervous system
P Antiparasitic products
R Respiratory system
S Sensory organs
V Various

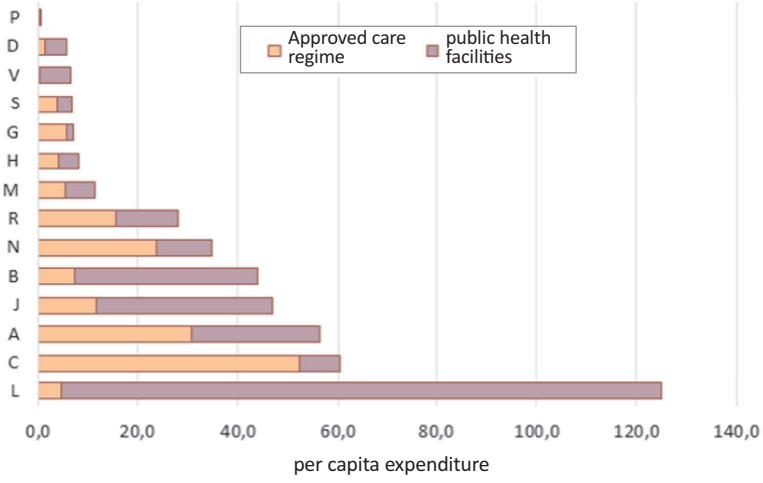


Table 3.2 NHS Consumption (DDD/1000 inhab. per day) of approved care regime (A-NHS) and public health facilities by ATC 1st level in descending order of total NHS consumption: comparison 2023-2022 (Table and Figure)

ATC 1st level	DDD/1000 inhab. per day Approved care regime (a)	Δ% 23-22	DDD/1000 inhab. per day Public health facilities (b)	Δ% 23-22	DDD/1000 inhab. per day NHS (a+b)	Δ% 23-22
C	494.98	1.6	18.93	5.5	513.91	1.8
A	254.92	-8.7	43.69	13.0	298.61	-6.1
B	89.77	-0.9	54.70	3.5	144.47	0.7
N	71.80	2.3	25.99	-4.9	97.79	0.3
G	46.35	3.6	3.16	14.1	49.52	4.2
M	38.75	-0.9	7.05	11.8	45.81	0.9
H	39.88	2.7	5.16	-0.2	45.04	2.3
R	40.72	-0.2	2.46	8.9	43.18	0.2
S	21.81	2.4	1.84	-3.4	23.65	1.9
J	16.25	6.4	6.15	5.5	22.40	6.1
L	6.58	1.6	13.51	9.9	20.09	7.1
D	5.10	3.0	8.73	-0.3	13.83	0.9
V	0.10	1.2	3.49	10.6	3.59	10.3
P	1.05	2.5	0.03	>100	1.08	4.5
Total	**1128.06**	**-1.0**	**194.89**	**5.2**	**1322.95**	**-0.1**

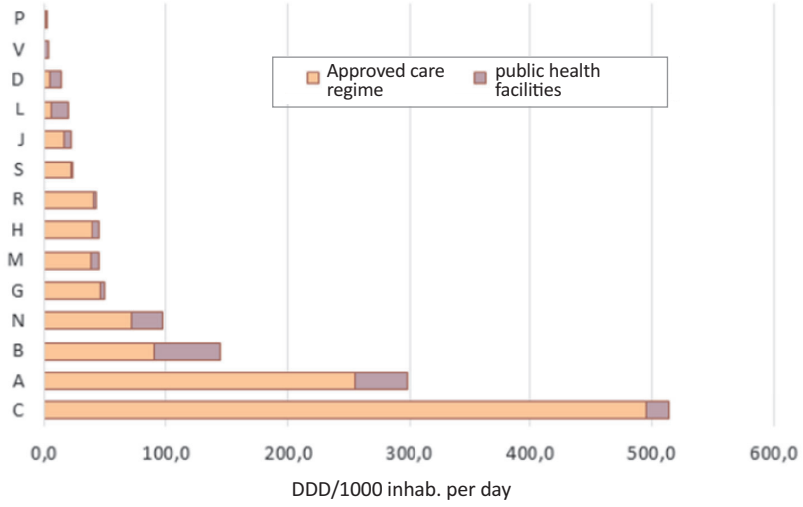


Table 3.3 Composition of 2023 pharmaceutical expenditure by ATC 1st level and reimbursement class (descending order for total expenditure)

ATC 1st level	Class A-NHS^		Private purchase of class A		Class C with prescription		Self-medication pharmaceuticals (OTC and without prescription)		Public health Facilities§		Total	
	€°	%*	€°	%*	€°	%*	€°	%*	€°	%*	€°	%*
L	268	2.7	55	2.7	24	0.6	<0.05	0.0	7,090	43.8	7,437	21.2
A	1,808	18.5	448	22.2	303	7.9	898	27.1	1,510	9.3	4,967	14.1
C	3,075	31.4	222	11.0	34	0.9	194	5.8	481	3.0	4,006	11.4
N	1,392	14.2	154	7.6	1,261	32.8	352	10.6	661	4.1	3,820	10.9
J	685	7.0	192	9.5	247	6.4	<0.05	0.0	2,076	12.8	3,200	9.1
B	423	4.3	276	13.7	88	2.3	5	0.2	2,164	13.4	2,956	8.4
R	916	9.4	157	7.8	235	6.1	598	18.1	739	4.6	2,645	7.5
M	316	3.2	216	10.7	256	6.7	708	21.4	347	2.1	1,843	5.2
G	335	3.4	52	2.6	721	18.8	105	3.2	87	0.5	1,301	3.7
D	79	0.8	32	1.6	294	7.7	342	10.3	253	1.6	1,000	2.8
S	221	2.3	16	0.8	261	6.8	103	3.1	179	1.1	779	2.2
H	238	2.4	79	3.9	53	1.4	<0.05	0.0	240	1.5	611	1.7
V	11	0.1	118	5.8	47	1.2	3	0.1	364	2.2	543	1.5
P	14	0.1	4	0.2	15	0.4	1	0.0	2	0.0	36	0.1
Tot	9,782	100	2,021	100	3,839	100	3,308	100	16,192	100	35,144	100

^ Expenditure on Class A net of Class C reimbursed (17 million); § Not including oxygen; # includes commercial businesses; ° Gross in million euros; * calculated according to reimbursement class
Source: OsMed, Tracciabilità del farmaco

Table 3.4 Composition of 2023 consumption (in terms of DDD/1000 inhabitants per day), by ATC 1st level and reimbursement class (descending order of consumption)

ATC 1st level	Class A-NHS^		Private purchase of class A		Class C with prescription		Self-medication pharmaceuticals# (OTC and without prescription)		Public health Facilities§		Total	
	DDD	%*	DDD	%*	DDD	%*	DDD	%*	DDD	%*	DDD	%*
C	495.0	43.9	36.0	15.8	1.0	0.5	10.5	7.3	18.9	9.7	561.4	29.6
A	254.9	22.6	86.4	37.9	11.8	5.8	36.1	25.2	43.7	22.5	433.0	22.8
B	89.8	8.0	23.9	10.5	29.6	14.5	0.1	0.1	54.7	28.1	198.1	10.4
N	71.8	6.4	8.0	3.5	68.2	33.4	7.9	5.5	26.0	13.4	181.9	9.6
R	40.7	3.6	13.1	5.7	16.3	8.0	33.9	23.6	2.5	1.3	106.5	5.6
M	38.8	3.4	28.9	12.7	3.5	1.7	21.6	15.0	7.1	3.6	99.9	5.3
G	46.4	4.1	4.6	2.0	38.3	18.8	2.5	1.8	3.2	1.6	95.0	5.0
H	39.9	3.5	14.0	6.1	2.3	1.1	<0.05	0.0	5.2	2.7	61.3	3.2
D	5.1	0.5	5.0	2.2	17.6	8.6	19.1	13.3	8.7	4.5	55.6	2.9
S	21.8	1.9	2.0	0.9	12.1	5.9	11.6	8.1	1.8	0.9	49.4	2.6
J	16.3	1.4	5.5	2.4	2.2	1.1	<0.05	0.0	6.1	3.2	30.0	1.6
L	6.6	0.6	0.5	0.2	0.1	0.1	<0.05	0.0	13.5	6.9	20.7	1.1
V	0.1	0.0	0.1	0.0	1.0	0.5	0.1	0.0	3.5	1.8	4.7	0.2
P	1.0	0.1	0.2	0.1	0.1	0.0	<0.05	0.0	<0.05	0.0	1.4	0.1
Tot	1128.1	100	228.1	100	204.2	100	143.6	100	194.4	100	1898.9	100

^ Expenditure on Class A net of Class C reimbursed; § Not including oxygen; # includes commercial businesses; ° Gross in million euros; * calculated according to reimbursement class
Source: OsMed, Tracciabilità del farmaco

Figure 3.1 Trend of per capita expenditure of approved care regime (A-NHS) and public health facilities in the period 2018-2023 by ATC 1st level (*first 10 ATC with highest expenditure in 2023*)

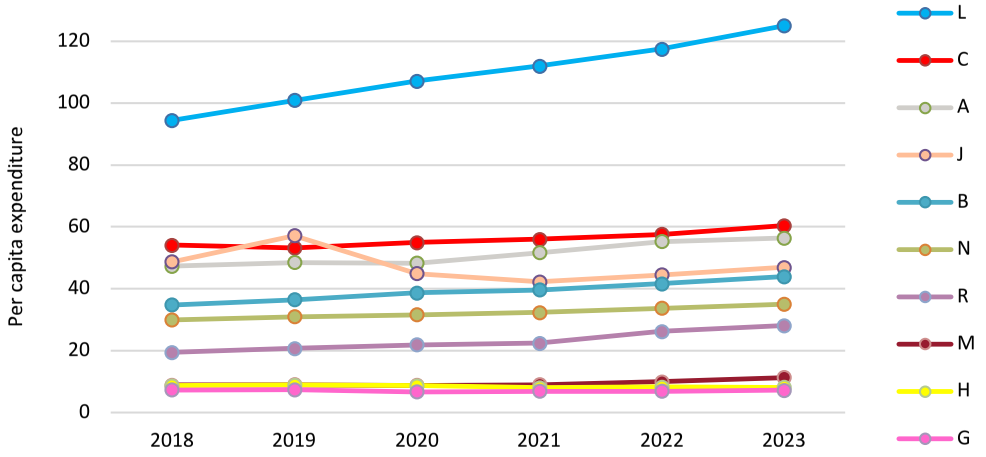


Figure 3.2 Trend of consumption of approved care regime (A-NHS) and public health facilities in the period 2018-2023 by ATC 1st level (*first 10 ATC with highest consumption in 2023*)

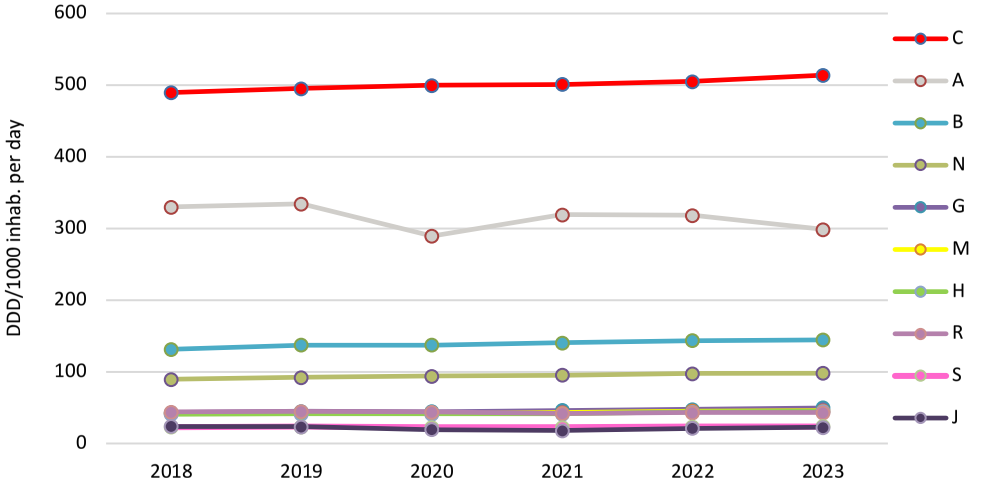


Figure 3.3 Trend of the average DDD cost of medicines of approved care regime (A-NHS) and public health facilities in the period 2018-2023 by ATC 1st level (*first 10 ATC with highest average cost in 2023*))

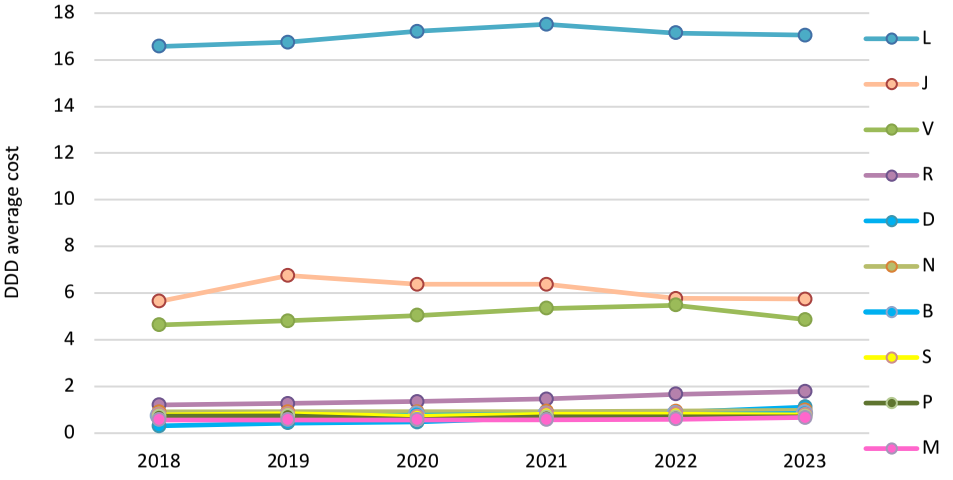


Table 3.5 Regional distribution by ATC 1st level of gross per capita approved care expenditure (on weighted population) for class A-NHS medicines: year 2023 (Table and Figure)

Region	A	B	C	D	G	H	J	L	M	N	P	R	S	V	Total
Piedmont	23.3	2.9	45.6	1.3	5.0	4.0	8.7	4.6	4.4	23.3	0.2	13.5	4.1	0.0	140.9
Valle d'Aosta	23.6	2.4	40.2	1.1	5.4	3.4	7.8	3.8	4.6	23.1	0.2	13.4	3.4	0.1	132.5
Lombardy	46.9	12.1	49.7	1.2	6.0	3.8	9.7	6.8	4.2	28.2	0.3	14.9	3.2	0.5	187.4
Province of Bolzano	17.0	6.0	34.5	1.1	3.6	3.1	5.9	3.5	3.4	24.1	0.2	11.1	2.7	0.1	116.3
Province of Trento	25.7	5.3	41.9	1.6	5.3	4.2	8.7	5.1	4.7	23.4	0.3	15.0	2.9	0.0	144.1
Veneto	20.8	2.6	46.7	1.2	4.9	3.8	7.5	4.4	3.9	21.3	0.3	12.8	3.3	0.0	133.5
Friuli V.G.	26.0	5.2	47.8	1.4	4.7	3.9	7.2	4.9	4.7	22.7	0.3	13.0	4.1	0.0	146.0
Liguria	26.9	2.1	45.2	1.3	5.5	2.9	8.8	4.5	4.4	24.7	0.1	15.5	4.0	0.0	145.9
Emilia R.	20.6	3.4	49.0	1.2	5.6	3.0	8.0	1.2	4.2	17.5	0.3	13.8	4.8	0.0	132.7
Tuscany	19.6	5.8	44.8	1.3	5.2	3.9	8.9	0.6	3.9	21.8	0.3	15.2	4.7	0.0	135.9
Umbria	19.1	3.2	53.8	1.1	6.0	4.5	11.7	4.5	4.3	22.5	0.3	13.3	4.5	0.1	148.8
Marche	25.3	3.2	57.0	1.2	6.5	4.5	13.3	4.6	5.6	23.3	0.2	13.9	5.4	0.0	164.0
Lazio	29.1	11.8	56.4	1.3	5.8	5.0	13.9	4.7	6.4	24.6	0.2	17.8	3.9	0.1	181.2
Abruzzo	30.6	8.1	55.6	1.3	6.0	5.0	15.5	5.0	7.0	29.1	0.2	15.1	4.7	0.1	183.4
Molise	31.1	5.3	56.0	1.3	5.8	4.2	15.1	5.0	7.1	21.7	0.1	13.7	3.0	0.1	169.5
Campania	37.9	6.9	62.1	1.9	6.3	4.2	17.8	5.2	7.0	21.8	0.2	21.5	3.4	0.1	196.1
Puglia	31.4	10.1	58.7	1.4	6.3	4.7	15.6	5.0	7.5	24.6	0.1	16.7	3.4	0.1	185.7
Basilicata	40.5	10.1	59.1	1.5	6.7	4.7	14.9	4.8	8.0	24.2	0.2	17.0	3.9	0.1	195.6
Calabria	34.6	11.5	59.2	1.6	5.8	4.3	17.8	5.1	7.6	22.5	0.2	15.0	3.4	0.5	189.0
Sicily	31.6	6.6	58.7	1.4	5.8	4.2	14.1	4.4	6.5	21.9	0.2	15.6	3.1	0.1	174.2
Sardinia	32.7	4.3	50.8	1.6	5.7	4.0	12.1	5.5	7.0	28.3	0.2	16.8	3.5	1.9	174.1
Italy	**30.7**	**7.2**	**52.3**	**1.4**	**5.7**	**4.1**	**11.6**	**4.6**	**5.4**	**23.6**	**0.2**	**15.6**	**3.8**	**0.2**	**166.2**
North	31.1	6.4	47.6	1.2	5.4	3.6	8.6	4.8	4.2	23.8	0.3	14.0	3.7	0.2	154.9
Centre	24.8	8.1	52.6	1.3	5.7	4.6	12.1	3.3	5.3	23.4	0.3	16.1	4.4	0.1	162.0
South and Islands	33.8	7.8	58.7	1.6	6.1	4.4	15.7	4.9	7.1	23.6	0.2	17.4	3.4	0.3	184.9

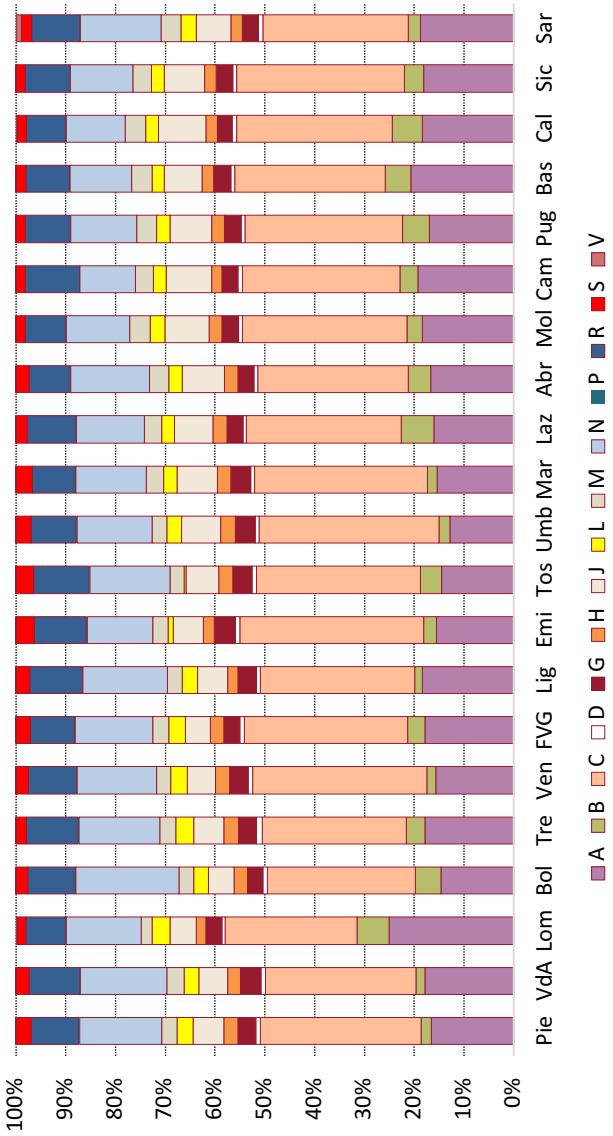

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Table 3.6 Regional distribution by ATC 1st level of DDD/1000 inhabitants per day (on weighted population) for class A-NHS medicines under approved care regime: year 2023 (Table and Figure)

Region	A	B	C	D	G	H	J	L	M	N	P	R	S	V	Total
Piedmont	222.1	83.2	461.1	4.3	43.1	38.6	12.9	6.9	33.5	77.4	1.0	34.0	24.3	0.0	1042.5
Valle d'Aosta	232.6	63.1	382.6	3.7	41.8	32.5	12.5	5.8	34.1	68.4	1.0	34.5	19.6	0.1	932.2
Lombardy	293.7	79.5	467.7	3.8	43.5	29.6	14.0	8.8	28.6	76.3	1.2	37.3	18.2	0.3	1102.6
Province of Bolzano	213.7	55.2	364.8	3.7	31.4	30.7	9.4	5.8	23.9	78.2	0.8	27.3	16.4	0.0	861.3
Province of Trento	262.8	99.8	432.2	5.9	44.3	45.3	14.2	7.7	33.5	69.2	1.0	42.7	17.2	0.0	1075.8
Veneto	226.7	51.8	474.7	4.6	40.3	33.9	11.9	7.0	27.7	65.4	1.1	32.8	19.6	0.0	997.5
Friuli V.G.	267.3	80.8	494.2	5.3	39.6	40.6	12.6	7.7	36.1	61.5	1.3	34.0	23.9	0.0	1104.8
Liguria	238.8	54.7	422.8	4.1	45.7	23.8	12.6	6.6	30.2	82.9	0.6	40.0	21.5	0.0	984.3
Emilia R.	223.7	105.9	516.8	4.8	47.1	44.5	13.7	2.7	32.8	69.0	1.1	37.5	28.5	0.0	1128.0
Tuscany	175.5	103.2	488.1	4.4	44.7	48.4	14.5	1.4	32.0	86.6	1.3	38.0	27.0	0.0	1065.2
Umbria	166.1	85.3	586.0	4.0	50.6	50.9	18.5	7.0	35.2	77.1	1.4	33.0	25.4	0.1	1140.5
Marche	214.2	87.4	521.8	4.0	54.2	46.0	18.4	6.7	43.8	74.1	1.0	33.5	31.9	0.1	1137.1
Lazio	243.3	112.9	499.4	5.1	48.4	46.3	18.6	7.1	45.1	69.6	1.1	45.9	22.6	0.1	1165.5
Abruzzo	262.6	115.1	487.6	4.9	48.3	47.7	21.5	6.9	52.4	79.1	1.0	39.7	27.3	0.1	1194.2
Molise	279.4	101.7	491.6	5.2	45.2	49.4	19.7	6.8	52.9	65.8	0.7	36.3	16.9	0.1	1171.6
Campania	312.6	85.7	545.0	8.3	51.2	37.0	21.6	6.7	49.3	62.3	0.9	59.7	19.2	0.1	1259.7
Puglia	274.1	113.4	520.3	5.4	51.9	50.0	20.7	7.1	54.5	67.5	0.7	46.9	20.3	0.1	1232.8
Basilicata	320.6	118.0	516.9	6.7	53.5	51.8	20.8	6.7	58.2	69.0	0.7	44.0	22.5	0.1	1289.5
Calabria	271.0	117.7	511.2	6.3	46.9	41.5	20.8	7.1	52.8	69.4	0.9	37.8	20.1	0.2	1203.7
Sicily	258.8	87.4	533.2	6.2	48.1	39.0	18.8	6.4	44.6	63.9	0.9	42.3	18.3	0.1	1168.1
Sardinia	318.1	84.3	472.1	5.7	49.2	47.7	15.1	8.5	48.6	81.8	1.1	45.4	20.8	0.2	1198.6
Italy	**254.9**	**89.8**	**495.0**	**5.1**	**46.4**	**39.9**	**16.3**	**6.6**	**38.8**	**71.8**	**1.0**	**40.7**	**21.8**	**0.1**	**1128.1**
North	252.4	78.0	471.5	4.3	43.2	34.7	13.2	6.9	30.4	73.0	1.1	35.9	21.5	0.1	1066.1
Centre	212.1	104.4	505.1	4.6	48.1	47.3	17.3	5.2	40.0	76.2	1.2	40.8	25.4	0.1	1127.9
South and Islands	284.9	97.7	522.4	6.5	49.8	42.8	20.0	6.9	50.0	67.4	0.9	47.5	20.0	0.1	1216.8

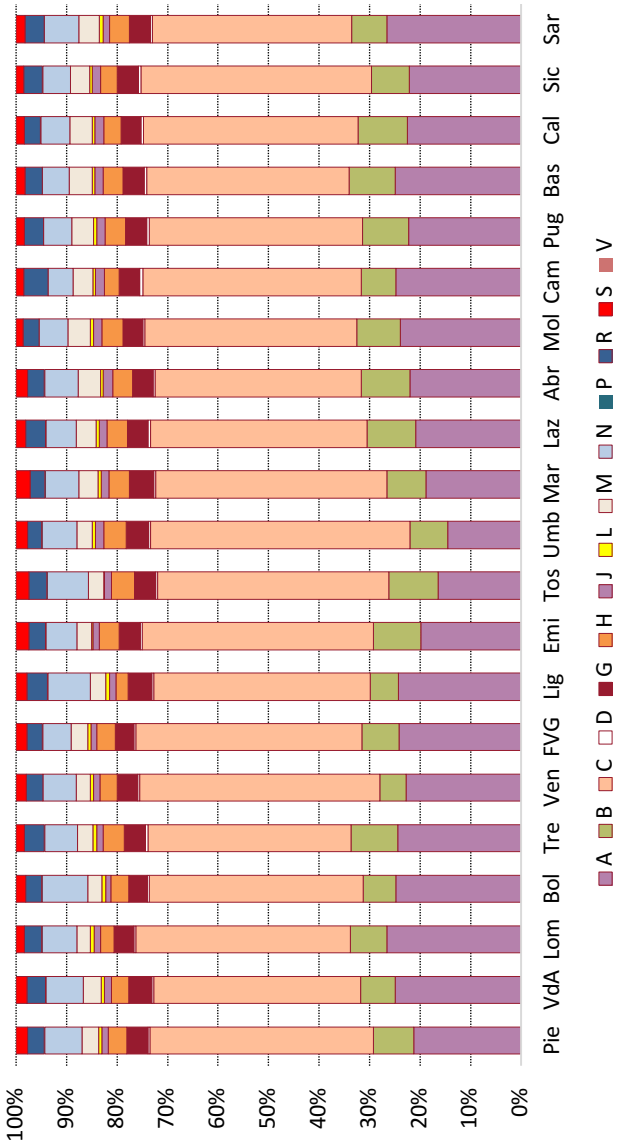
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Table 3.7 Regional distribution by ATC 1st level of per capita expenditure (on weighted population) for medicines purchased by public health facilities: year 2023 (Table and Figure)

Region	A	B	C	D	G	H	J	L	M	N	P	R	S	V	Total
Piedmont	25.5	37.0	8.8	5.2	1.4	3.8	33.8	116.2	5.1	10.3	0.1	12.0	3.7	5.7	268.6
Valle d'Aosta	14.8	36.9	7.6	3.7	1.2	2.7	27.3	86.6	2.8	10.7	<0.05	8.8	6.9	7.7	217.7
Lombardy	17.5	31.4	5.6	3.5	1.2	3.7	41.8	99.5	6.5	8.2	0.1	12.6	3.0	6.2	240.6
Province of Bolzano	15.4	31.8	6.9	3.6	1.5	3.8	34.3	125.5	9.0	13.6	<0.05	17.9	4.4	6.4	274.2
Province of Trento	28.3	30.5	4.5	4.2	1.9	3.9	33.8	92.0	5.7	11.3	0.1	10.1	3.5	4.5	234.3
Veneto	24.6	35.9	6.5	3.7	1.4	4.0	36.4	110.6	6.3	12.4	<0.05	11.6	3.9	6.4	263.8
Friuli V.G.	24.8	33.8	8.3	3.9	1.1	4.0	36.4	140.5	7.7	12.0	0.1	12.0	5.2	6.4	296.2
Liguria	22.0	40.3	10.5	3.1	1.0	4.4	40.9	130.1	6.1	12.7	<0.05	13.7	4.2	5.5	294.6
Emilia R.	27.0	39.5	7.7	4.1	2.1	4.5	39.1	133.5	5.4	15.1	0.1	11.3	2.7	7.0	299.2
Tuscany	23.1	37.5	8.7	4.2	1.6	4.4	35.8	122.1	5.0	13.6	<0.05	12.2	1.7	7.0	276.9
Umbria	27.2	41.1	8.1	3.4	1.4	4.2	38.8	131.5	5.0	13.7	<0.05	10.3	2.7	5.8	293.1
Marche	21.9	39.6	9.5	5.5	1.4	4.9	32.4	139.4	7.9	15.3	<0.05	12.6	3.0	7.0	300.3
Lazio	26.2	34.8	7.2	4.1	1.6	3.9	38.0	111.8	6.9	11.9	<0.05	11.8	1.8	4.6	264.7
Abruzzo	28.1	45.6	8.1	4.2	1.3	5.0	33.3	141.9	5.7	14.3	0.1	12.5	3.5	7.1	310.7
Molise	23.1	36.5	6.8	6.0	1.1	3.5	23.1	130.2	6.4	10.4	<0.05	10.7	5.0	4.7	267.6
Campania	35.0	43.0	15.2	6.0	2.0	4.9	31.1	145.8	5.8	9.6	<0.05	11.2	3.2	4.7	317.5
Puglia	32.4	39.2	9.2	4.6	1.3	4.0	30.5	123.8	5.9	11.8	<0.05	14.1	3.6	6.5	286.8
Basilicata	28.7	35.3	12.3	5.5	1.3	4.0	22.3	130.6	2.8	9.3	<0.05	21.7	3.6	10.0	287.4
Calabria	32.5	39.2	9.9	5.3	1.5	4.7	27.9	131.1	5.1	10.0	<0.05	14.9	2.6	8.8	293.5
Sicily	28.5	33.8	6.0	3.9	1.4	3.4	28.8	111.7	4.8	10.0	<0.05	16.0	2.6	5.9	256.6
Sardinia	24.8	39.2	6.8	4.3	1.1	3.5	30.9	142.8	5.6	9.6	<0.05	9.3	2.9	8.5	289.2
Italy	**25.7**	**36.8**	**8.2**	**4.3**	**1.5**	**4.1**	**35.3**	**120.5**	**5.9**	**11.2**	**0.0**	**12.6**	**3.0**	**6.2**	**275.2**
North	22.3	35.1	7.0	3.9	1.4	4.0	38.5	113.6	6.1	11.0	0.1	12.2	3.4	6.2	264.7
Centre	24.7	36.8	8.0	4.3	1.6	4.2	36.6	120.1	6.3	13.0	<0.05	11.9	2.0	5.8	275.3
South and Islands	31.0	39.2	9.9	4.9	1.5	4.2	29.9	130.6	5.4	10.5	<0.05	13.5	3.1	6.4	289.9

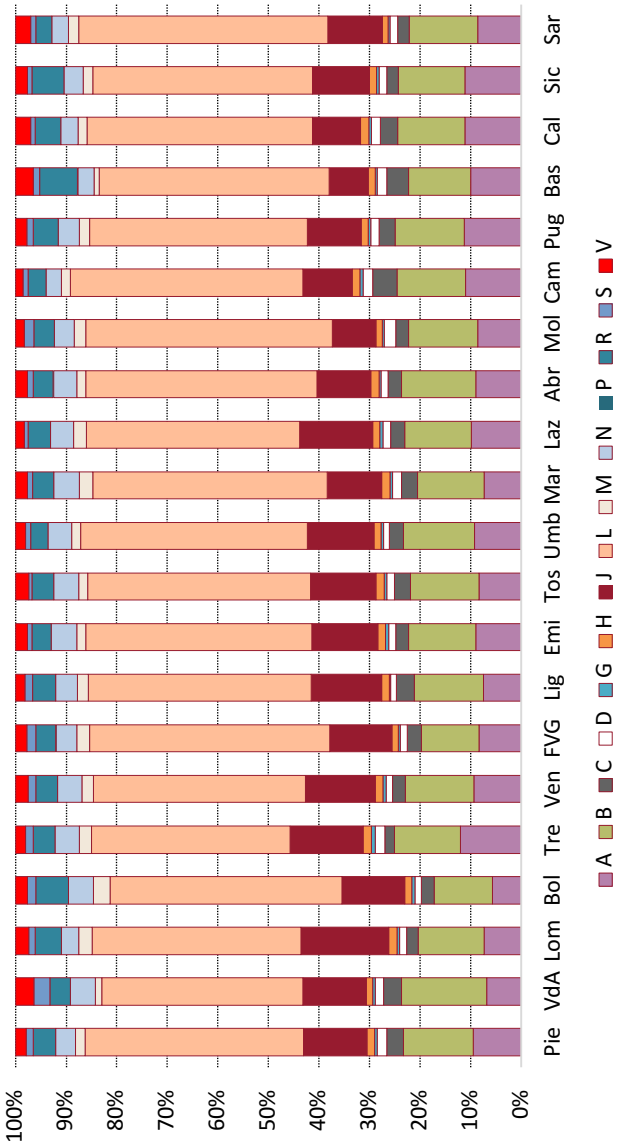
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Table 3.8 Regional distribution by ATC 1st level of DDD/1000 inhabitants per day (on weighted population) of medicines purchased by public health facilities: year 2023 (Table and Figure)

Region	A	B	C	D	G	H	J	L	M	N	P	R	S	V	Total
Piedmont	53.8	63.3	33.3	7.8	3.0	6.2	6.5	13.3	7.3	29.6	0.1	3.2	1.9	4.9	234.0
Valle d'Aosta	39.0	60.0	20.6	8.8	6.7	6.4	6.4	9.9	6.7	30.9	0.1	5.2	1.7	4.7	207.1
Lombardy	25.4	33.8	10.8	4.9	2.5	3.2	7.0	10.2	6.9	11.6	<0.05	2.2	1.7	3.4	123.5
Province of Bolzano	61.4	40.3	24.7	10.4	2.3	7.6	5.7	14.2	10.8	33.5	<0.05	3.3	2.8	4.8	221.9
Province of Trento	57.0	50.1	21.4	7.2	4.1	5.4	5.4	11.5	6.3	28.3	<0.05	2.5	2.2	7.8	209.4
Veneto	56.4	60.8	24.7	15.8	2.2	5.6	6.6	12.6	6.6	39.6	<0.05	3.6	2.7	5.9	243.1
Friuli V.G.	49.0	54.4	22.4	11.5	2.5	4.2	6.5	14.5	6.9	36.5	<0.05	3.5	2.5	2.4	216.7
Liguria	48.2	71.1	24.5	6.1	2.2	6.8	6.4	13.2	7.7	35.6	0.1	3.1	2.5	4.3	231.6
Emilia R.	67.5	84.2	41.0	10.6	12.0	8.6	9.2	18.0	8.0	47.6	0.1	5.3	3.1	6.4	321.7
Tuscany	40.7	62.9	20.1	7.2	8.0	7.2	7.0	19.2	5.9	36.3	<0.05	3.3	2.2	3.2	223.2
Umbria	46.5	74.3	25.7	15.7	2.6	5.9	6.2	14.0	5.0	43.2	0.1	2.4	2.6	4.0	248.2
Marche	39.4	91.5	16.2	10.4	2.9	5.6	5.6	14.8	8.2	25.0	<0.05	1.8	1.8	4.4	227.7
Lazio	38.2	41.0	13.1	5.2	1.7	3.8	6.0	12.0	7.6	20.0	<0.05	1.2	1.2	2.0	153.1
Abruzzo	44.0	42.6	12.3	7.0	0.8	5.5	5.2	14.9	8.5	19.1	<0.05	1.6	1.7	2.2	165.5
Molise	38.6	54.6	11.7	4.5	0.6	2.8	3.8	13.1	7.1	20.1	<0.05	1.0	1.9	2.4	162.1
Campania	45.8	63.2	16.0	10.2	1.2	4.5	4.7	14.5	6.9	22.1	<0.05	1.6	1.3	1.9	193.9
Puglia	44.5	44.8	12.0	10.5	1.9	5.2	5.0	13.6	6.4	18.0	<0.05	1.7	2.0	2.2	167.9
Basilicata	41.2	47.7	11.3	15.1	1.3	4.5	4.1	13.3	6.6	17.4	<0.05	2.3	1.6	2.8	169.3
Calabria	40.9	41.5	11.7	9.2	0.9	4.3	3.9	12.3	6.4	18.2	<0.05	1.2	0.9	1.8	153.3
Sicily	39.9	52.9	14.6	8.1	1.4	5.3	4.7	12.7	6.2	22.3	<0.05	1.5	0.9	1.7	172.2
Sardinia	40.9	58.6	12.3	11.9	1.3	3.6	5.3	14.6	9.6	30.3	<0.05	1.5	1.5	4.2	195.6
Italy	**43.7**	**54.7**	**18.9**	**8.7**	**3.2**	**5.2**	**6.1**	**13.5**	**7.1**	**26.0**	**<0,05**	**2.5**	**1.8**	**3.5**	**194.9**
North	45.9	55.1	23.6	8.7	4.1	5.4	7.1	12.8	7.2	28.6	0.1	3.3	2.2	4.7	208.7
Centre	39.8	57.0	16.7	7.3	3.9	5.3	6.3	14.8	6.9	27.6	<0.05	2.1	1.7	2.9	192.3
South and Islands	42.9	52.7	13.7	9.6	1.3	4.8	4.7	13.7	6.9	21.3	<0.05	1.6	1.4	2.2	176.7

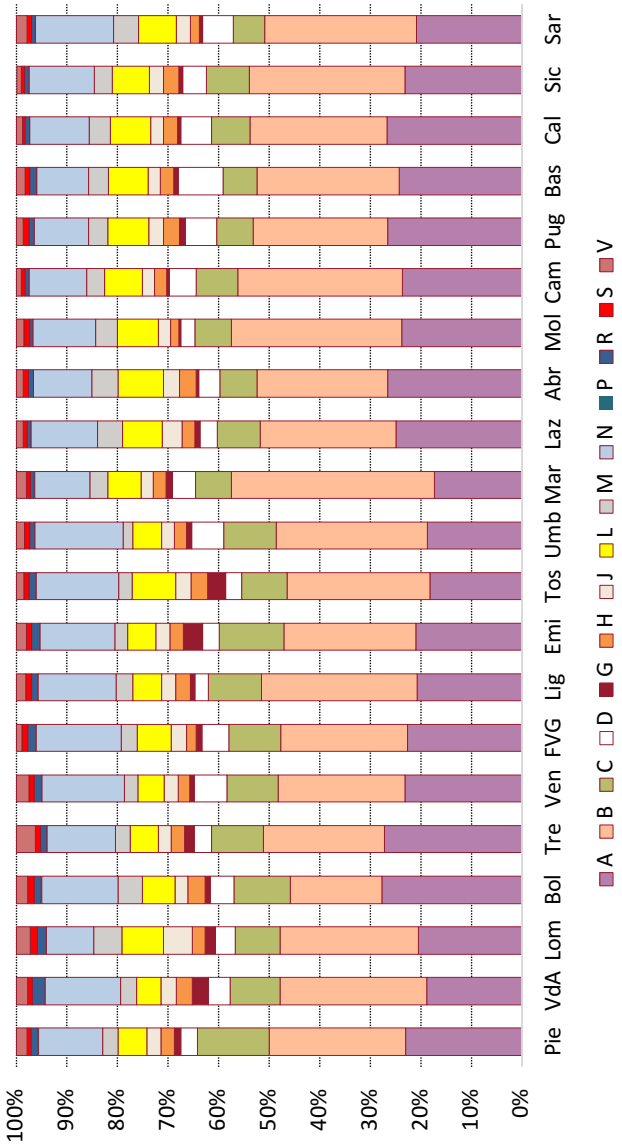
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Figure 3.4 Consumption, price and mix effect on variation of class A-NHS approved care pharmaceutical expenditure by ATC 1st level: comparison 2023-2022

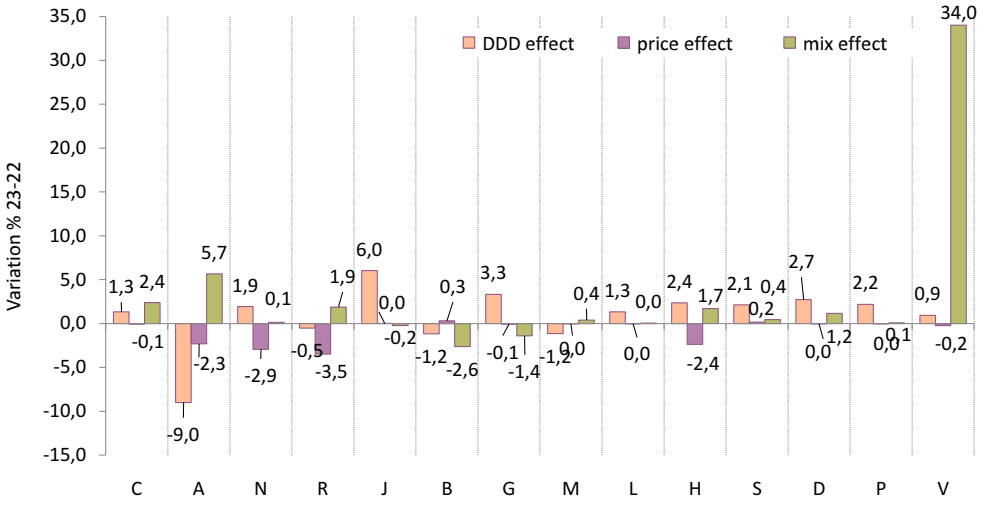

Table 3.9 Consumption, price and mix effect on variation of class A-NHS approved care pharmaceutical expenditure: comparison 2023-2022

(Any ATC category includes the therapeutic subgroups in decreasing order of per capita expenditure, up to the value of 0.10 euros)

ATC 1st level ATC 4th level	Gross per capita expenditure	DDD/1000 inhab. per day	Δ % 23-22				Δ % average DDD cost
			Expenditure	DDD	Prices	Mix	
Italy	**166.22**	**1128.1**	**0.0**	**-1.3**	**-1.3**	**2.7**	**1.4**
C - Cardiovascular system	**52.25**	**495.0**	**3.7**	**1.3**	**-0.1**	**2.4**	**2.3**
HMG-CoA reductase inhibitors	8.09	82.0	-0.9	-0.6	0.0	-0.3	-0.3
Beta-blockers, selective	5.10	41.9	2.1	1.3	0.0	0.8	0.8
Angiotensin II receptor blockers (ARBs), not in combination	5.01	58.6	1.7	0.8	0.0	0.9	0.9
Other lipid modifying agents	4.12	9.7	6.2	7.8	0.0	-1.5	-1.5
Lipid modifying agents in combination	4.08	24.4	39.8	46.2	0.0	-4.4	-4.4
Dihydropyridines derivatives	3.95	49.3	-3.0	-0.6	-0.6	-1.8	-2.4
Angiotensin II receptor blockers (ARBs) and diuretics	3.72	31.3	-1.9	-1.6	0.0	-0.2	-0.3
ACE inhibitors, not in combination	3.43	78.6	-3.8	-2.5	-0.2	-1.2	-1.4
ACE inhibitors and diuretics	2.25	17.8	-5.1	-4.4	0.0	-0.6	-0.7
Angiotensin II receptor blockers (ARBs) and calcium channel blockers	1.72	11.9	12.5	13.2	0.0	-0.6	-0.6
ACE inhibitors and calcium channel blockers	1.64	12.3	-0.4	0.9	0.0	-1.3	-1.3
Alpha-adrenoreceptor blockers	1.22	7.5	-1.2	-0.8	0.0	-0.4	-0.4
Antiarrhythmic agents, class Ic	1.11	4.7	1.4	-0.2	0.0	1.6	1.6
Other cardiac preparations	0.98	1.5	>100	>100	-1.8	83.6	80.3
ACE inhibitors, other combinations	0.87	6.5	13.8	11.9	0.0	1.7	1.7
Sulphonamides, not in combination	0.78	23.5	-4.3	-4.1	0.0	-0.2	-0.2
Aldosterone antagonists	0.60	3.4	6.9	1.6	-0.2	5.4	5.2
Selective beta-blockers and thiazides	0.60	6.1	0.7	1.0	0.0	-0.2	-0.2
Organic nitrates	0.43	4.1	-12.0	-11.9	0.0	-0.1	-0.1
Alpha and beta adrenoreceptor antagonists	0.43	2.4	-6.8	-6.5	0.0	-0.3	-0.3
Fibrates	0.41	2.9	0.8	1.3	0.0	-0.4	-0.4
Angiotensin II receptor blockers (ARBs), other combinations	0.33	0.3	-35.5	34.0	0.0	-51.9	-51.9
Antiarrhythmic agents, class III	0.26	2.8	0.7	-0.2	0.0	0.9	0.9
Imidazoline receptor agonists	0.17	1.2	-6.7	-6.4	0.0	-0.3	-0.3
Benzothiazepine derivatives	0.13	0.8	-9.4	-8.3	0.0	-1.2	-1.2
Beta-blockers, not selective	0.13	1.5	-3.7	-2.7	0.0	-1.1	-1.1
High-ceiling diuretics in combination with potassium-sparing agents	0.11	0.6	-0.9	-1.2	0.0	0.2	0.2
Sulphonamides, not in combination	0.10	1.5	-6.6	-7.2	0.6	0.1	0.6
Selective beta-blockers and other diuretics	0.10	1.4	-7.5	-7.3	0.0	-0.2	-0.2
Phenylalkylamine derivatives	0.10	0.8	-8.3	-8.4	0.0	0.1	0.1
A - Gastrointestinal system and metabolism	**30.73**	**254.9**	**-6.1**	**-9.0**	**-2.3**	**5.7**	**3.2**
Proton pump inhibitors	11.09	76.6	-3.0	-1.4	0.0	-1.6	-1.6
Vitamin D and analogues	4.01	119.1	-14.9	-14.6	0.0	-0.4	-0.4
Insulins and injectable analogues, fast-acting	2.78	6.8	-14.0	-3.6	-11.1	0.3	-10.9

continued

Table 3.9 - *continued*

ATC 1st level ATC 4th level	Gross per capita expenditure	DDD/1000 inhab. per day	Δ % 23-22				Δ % costo medio DDD
			Expenditure	DDD	Prices	Mix	
Aminosalicylic acid and analogues	2.23	5.8	1.2	2.5	-0.8	-0.4	-1.2
GLP-1 (glucagon-like peptide-1) receptor analogues	1.83	0.8	-16.4	-20.8	0.4	5.1	5.5
Biguanides	1.68	23.0	1.0	-0.8	0.0	1.8	1.8
Antibiotics	1.47	2.0	-1.4	-1.5	0.0	0.1	0.1
Bile acids and derivatives	0.98	2.9	5.1	4.9	0.0	0.1	0.1
Oral hypoglycemic agents, in combination	0.72	1.4	18.0	-3.5	-0.8	23.3	22.3
Insulins and injectable analogues, slow-acting	0.54	0.2	16.1	-7.7	0.0	25.9	25.9
Aluminium, calcium and magnesium compounds in combination	0.49	2.2	-12.4	-10.7	0.0	-1.8	-1.8
Dipeptil Peptidase 4 Inhibitors (DPP-4)	0.37	0.7	67.0	>100	-2.5	-31.0	-32.7
Sulfonylureas	0.35	4.8	-17.9	-19.5	-0.1	2.1	2.0
Calcium, combinations with vitamin D and/or other pharmaceuticals	0.29	3.0	-5.0	-5.1	0.0	0.2	0.2
Corticosteroids for topical use	0.28	0.4	-6.2	-1.5	0.0	-4.8	-4.8
Enzyme preparations	0.25	0.6	-1.2	-1.4	0.0	0.1	0.1
Serotonin antagonists (5HT3)	0.22	0.0	6.6	6.2	0.0	0.4	0.4
SGLT2 cotransporter inhibitors	0.15	0.2	19.9	23.0	0.0	-2.6	-2.6
Other hypoglycaemic agents, excluding insulins	0.14	1.0	-22.9	-23.7	0.0	1.1	1.1
Peripheral opioid receptor antagonists	0.12	0.1	35.4	45.1	-6.2	-0.5	-6.7
Thiazolidinediones	0.12	0.5	-2.2	-3.3	0.0	1.1	1.1
Alpha Glucosidase Inhibitors	0.11	0.4	-9.9	-10.0	0.0	0.1	0.1
Osmotic laxatives	0.10	0.9	-8.6	-10.0	0.0	1.6	1.6
N- Central nervous system	**23.65**	**71.8**	**-0.9**	**1.9**	**-2.9**	**0.1**	**-2.8**
Other antidepressants	3.61	12.9	5.5	5.0	0.0	0.5	0.5
Selective serotonin reuptake inhibitors	3.41	31.1	0.3	1.8	-2,-0,4	-1.0	-1.5
Other antiepileptics	3.03	3.9	-5.9	2.4	-7.8	-0.3	-8.1
Gabapentinoids	1.85	3.2	7.7	8.8	-0.1	-1.0	-1.0
Other opioids	1.24	1.0	-3.4	-3.6	-4.1	4.4	0.2
Phenylpiperidine derivatives	1.16	0.6	-9.9	-1.4	-6.8	-2.0	-8.6
Diazepines, oxazepines, thiazepines and oxepins	1.12	1.4	9.4	7.1	0.0	2.1	2.1
Fatty acid derivatives	1.02	2.4	1.8	2.3	0.0	-0.4	-0.4
5HT1 selective receptor agonists	1.01	0.9	0.8	0.8	0.0	0.0	0.0
Dopamine agonists	0.99	0.9	-6.3	-4.6	-1.5	-0.2	-1.7
Type B monoamine oxidase inhibitors	0.79	1.6	1.5	0.8	0.0	0.6	0.6
DOPA and derivatives	0.73	2.1	1.0	1.3	0.0	-0.3	-0.3
Natural opium alkaloids	0.68	0.5	-21.1	-4.0	-17.1	-0.8	-17.8

continued

Table 3.9 - *continued*

ATC 1st level ATC 4th level	Gross per capita expenditure	DDD/1000 inhab. per day	Δ % 23-22				Δ % average DDD cost
			Expenditure	DDD	Prices	Mix	
Opioids in combination with non-opioid analgesics	0.53	1.4	-0.8	-1.5	0.0	0.7	0.7
Carboxamide derivatives	0.45	1.7	-4.2	-2.6	-0.9	-0.7	-1.6
Oripavine derivatives	0.39	0.2	16.3	11.3	0.8	3.6	4.5
Other antipsychotics	0.27	0.5	-0.4	-3.7	-0.1	3.5	3.4
Amides	0.22	0.3	-37.7	0.6	-38.1	0.0	-38.1
Non-selective monoamine reuptake inhibitors	0.16	1.0	0.1	1.3	0.0	-1.2	-1.2
R- Respiratory system	**15.56**	**40.7**	**-2.2**	**-0.5**	**-3.5**	**1.9**	**-1.7**
Adrenergics in combination with corticosteroids or others, excluding anticolinergics	6.64	12.3	-8.0	-1.4	-5.9	-0.8	-6.7
Combination of adrenergics with anticolinergics including triple combinations with corticosteroids	2.90	3.8	23.7	24.0	-4.1	4.0	-0.2
Anticholinergics	2.21	4.3	-13.0	-11.9	-1.0	-0.2	-1.2
Glucocorticoids	1.82	4.8	4.8	4.2	0.0	0.6	0.6
Other antihistamines for systemic use	0.66	6.0	-2.3	-1.8	0.0	-0.5	-0.5
Leukotriene receptor antagonists	0.46	2.0	-0.1	-0.4	0.0	0.3	0.3
Piperazine derivatives	0.41	4.3	-0.9	0.0	0.0	-0.9	-0.9
Selective agonists of beta2-adrenergic receptors	0.39	2.8	-14.0	-7.4	-1.7	-5.5	-7.2
J- General antimicrobials for systemic use	**11.64**	**16.3**	**5.8**	**6.0**	**0.0**	**-0.2**	**-0.2**
Penicillin combinations, including betalactamase inhibitors	3.19	6.1	16.9	16.4	0.0	0.4	0.4
Third-generation cephalosporins	2.82	2.0	14.6	15.7	0.0	-1.0	-1.0
Macrolides	1.43	3.3	-10.0	-9.2	0.0	-0.8	-0.9
Fluoroquinolones	1.11	1.5	-2.9	-1.1	-0.1	-1.6	-1.7
Triazole and tetrazole derivatives	0.84	0.5	0.3	1.5	0.0	-1.1	-1.1
Other antibacterials	0.64	0.4	-0.2	0.1	0.0	-0.2	-0.2
Nucleosides and nucleotides excl. reverse transcriptase inhibitors	0.58	0.3	2.9	4.0	0.0	-1.0	-1.1
Specific immunoglobulins	0.36	<0.05	-2.0	2.1	0.1	-4.1	-4.0
Broad-spectrum penicillins	0.17	0.9	-6.2	6.3	1.3	-12.9	-11.8
B - Blood and blood-forming organs	**7.19**	**89.8**	**-3.5**	**-1.2**	**0.3**	**-2.6**	**-2.3**
Platelet aggregation inhibitors, excl. heparin	3.07	61.6	2.7	0.6	0.0	2.1	2.1
Heparins	1.92	2.4	-14.9	-13.3	0.5	-2.4	-1.9
Folic acid and derivatives	0.53	7.0	2.2	2.5	0.0	-0.3	-0.3
Bivalent iron, oral preparations	0.39	3.1	4.8	5.3	-0.6	0.0	-0.6
Direct Xa factor inhibitors	0.36	0.3	8.8	9.2	0.0	-0.3	-0.3
Blood substitutes and plasma protein fractions	0.24	<0.05	-0.7	-2.9	0.0	2.4	2.3
Vitamin K antagonists	0.16	2.2	0.8	-13.9	17.2	-0.1	17.1
Solutions affecting the electrolyte balance	0.15	0.2	-3.4	-2.3	-1.3	0.1	-1.1
Vitamin B12 (cyanocobalamin and derivatives)	0.10	12.7	-4.8	-7.0	0.0	2.4	2.4

continued

Table 3.9 - *continued*

ATC 1st level ATC 4th level	Gross per capita expenditure	DDD/1000 inhab. per day	Δ % 23-22				Δ % costo medio DDD
			Expenditure	DDD	Prices	Mix	
G - Genito-urinary system and sex hormones	**5.70**	**46.4**	**1.8**	**3.3**	**-0.1**	**-1.4**	**-1.5**
Alpha adrenergic receptor antagonists	3.04	29.8	2.9	3.7	0.0	-0.7	-0.7
Testosterone-5-alpha reductase inhibitors	1.59	11.2	0.5	1.6	0.0	-1.2	-1.2
Prolactin inhibitors	0.17	0.1	-0.3	-2.1	0.0	1.9	1.9
Gonadotropins	0.14	<0.05	-9.4	21.9	0.0	-25.7	-25.7
Other estrogens	0.14	0.8	4.2	4.8	0.0	-0.5	-0.5
Pregnene derivatives (4)	0.11	1.0	-4.1	5.0	-0.2	-8.5	-8.7
Medicines for urinary frequency and incontinence	0.10	0.6	21.2	26.5	0.0	-4.2	-4.2
Medicines used in erectile dysfunctions	0.10	0.1	8.1	14.3	-2.0	-3.5	-5.4
M - Musculo-skeletal system	**5.36**	**38.8**	**-0.8**	**-1.2**	**0.0**	**0.4**	**0.4**
Bisphosphonates	1.43	7.5	4.5	5.1	0.0	-0.6	-0.6
Preparations inhibiting formation of uric acid	0.96	11.1	4.7	2.3	0.0	2.4	2.4
Acetic acid derivatives and related substances	0.81	5.0	-1.3	-0.8	-0.1	-0.4	-0.5
Propionic acid derivatives	0.73	5.6	-9.6	-10.1	0.0	0.5	0.5
Coxib	0.72	4.3	-0.5	0.4	0.0	-0.9	-0.9
Bisphosphonates, combinations	0.40	1.9	-0.7	-1.9	0.0	1.1	1.1
Other non-steroidal anti-inflammatory/ anti-rheumatic pharmaceuticals	0.14	1.6	-12.9	-12.6	0.0	-0.4	-0.4
L- Antineoplastic and immunomodulating agents	**4.55**	**6.6**	**1.3**	**1.3**	**0.0**	**0.0**	**0.0**
Aromatase inhibitors	2.43	3.3	3.1	2.8	0.0	0.3	0.3
Other immunosuppressants	0.86	1.8	4.2	3.4	0.0	0.8	0.8
Calcineurin inhibitors	0.51	0.2	-4.0	-3.1	0.0	-0.9	-0.9
Other antineoplastics	0.19	0.3	2.4	2.5	0.0	-0.1	-0.1
Colony stimulating factors	0.13	<0.05	-0.2	7.4	0.0	-7.1	-7.1
Antiandrogens	0.11	0.2	-5.4	-4.9	0.0	-0.5	-0.5
H - Systemic hormonal preparations, excluding sex hormones	**4.05**	**39.9**	**1.6**	**2.4**	**-2.4**	**1.7**	**-0.7**
Glucocorticoids	1.53	14.7	0.2	1.0	0.0	-0.7	-0.7
Thyroid hormones	1.51	23.5	5.8	3.2	0.0	2.5	2.5
Parathyroid hormones and analogues	0.66	0.2	-2.2	15.0	-14.1	-1.0	-15.0
Vasopressin and analogues	0.14	0.1	1.1	0.7	0.0	0.4	0.4
S-Sensory organs	**3.76**	**21.8**	**2.8**	**2.1**	**0.2**	**0.4**	**0.6**
Beta-blockers	2.14	12.2	3.3	2.3	-0.3	1.3	1.0
Prostaglandins analogues	1.21	5.8	1.5	2.4	0.0	-0.9	-0.9
Carbonic anhydrase inhibitors	0.28	1.8	5.1	0.4	4.6	0.0	4.6
Sympathomimetics for treatment of glaucoma	0.10	1.6	2.2	2.4	-0.1	-0.1	-0.2
D - Dermatologicals	**1.35**	**5.1**	**3.9**	**2.7**	**0.0**	**1.2**	**1.1**
Other antipsoriatic agents for topical use	0.91	2.6	2.7	3.9	0.0	-1.2	-1.2
Retinoids for acne treatment	0.11	0.2	-2.2	-2.1	0.0	-0.1	-0.1
P - Antiparasitic, insecticide and repellent pharmaceuticals	**0.24**	**1.0**	**2.3**	**2.2**	**0.0**	**0.1**	**0.1**
Aminoquinolines	0.17	0.9	1.4	1.6	0.0	-0.2	-0.2
V - Various	**0.19**	**0.1**	**35.0**	**0.9**	**-0.2**	**34.0**	**33.7**
Pharmaceuticals for treatment of hyperkalemia and hyperphosphatemia	0.12	0.1	2.1	-0.4	0.0	2.5	2.5

Table 3.10 2023 expenditure, consumption and average cost per day of therapy under approved care regime (class A-NHS): most prescribed active ingredients by ATC 1st level (up to 75% of the category expenditure)

Therapeutic category	Gross *per capita* expenditure	%*	Δ % 23-22	DDD/1000 inhab. per day	%*	Δ % 23-22	Average DDD cost	Δ % 23-22
C - Cardiovascular system	**52.25**		**4.0**	**494.98**		**1.6**	**0.29**	**2.3**
atorvastatin	4.66	8.9	-0.3	50.6	10.2	-0.4	0.25	0.1
bisoprolol	2.91	5.6	3.3	13.2	2.7	3.4	0.60	-0.1
ezetimibe/rosuvastatin	2.28	4.4	47.4	15.8	3.2	48.5	0.40	-0.7
omega-3	2.21	4.2	2.9	2.7	0.5	5.0	2.27	-2.0
olmesartan	2.07	4.0	7.9	18.0	3.6	7.8	0.31	0.1
ramipril	1.90	3.6	-2.5	60.7	12.3	-1.2	0.09	-1.3
ezetimibe	1.85	3.5	8.3	7.0	1.4	8.9	0.73	-0.6
olmesartan/amlodipine	1.62	3.1	11.2	11.0	2.2	11.4	0.40	-0.2
amlodipine	1.60	3.1	-0.1	28.3	5.7	1.5	0.15	-1.5
nebivolol	1.59	3.0	2.2	17.2	3.5	2.3	0.25	-0.1
rosuvastatin	1.58	3.0	6.6	16.8	3.4	6.4	0.26	0.2
olmesartan/hydrochlorothiazide	1.31	2.5	3.5	10.8	2.2	3.8	0.33	-0.3
simvastatin	1.26	2.4	-7.4	10.6	2.1	-7.2	0.33	-0.2
ezetimibe/simvastatin	1.25	2.4	2.3	5.2	1.1	2.9	0.66	-0.6
doxazosin	1.22	2.3	-1.0	7.5	1.5	-0.6	0.45	-0.4
flecainide	0.95	1.8	3.4	3.2	0.7	4.0	0.81	-0.6
ranolazine	0.88	1.7	>100	1.2	0.2	>100	2.08	-8.4
perindopril/amlodipine	0.82	1.6	0.5	5.3	1.1	0.9	0.42	-0.4
barnidipine	0.79	1.5	-8.4	4.6	0.9	-4.9	0.47	-3.6
lercanidipine	0.77	1.5	0.5	9.4	1.9	0.7	0.22	-0.1
perindopril/indapamide/amlodipine	0.72	1.4	13.5	5.2	1.0	10.4	0.38	2.8
valsartan	0.72	1.4	5.2	10.5	2.1	4.7	0.19	0.4
losartan	0.68	1.3	-4.5	6.5	1.3	-4.2	0.29	-0.3
furosemide	0.67	1.3	-3.4	22.5	4.5	-3.7	0.08	0.3
zofenopril	0.66	1.3	-1.2	4.4	0.9	-1.6	0.41	0.4
valsartan/hydrochlorothiazide	0.64	1.2	-1.3	5.8	1.2	-1.0	0.30	-0.3
irbesartan	0.61	1.2	-4.1	7.5	1.5	-4.2	0.22	0.1
zofenopril/hydrochlorothiazide	0.61	1.2	-2.8	3.9	0.8	-2.7	0.43	-0.1
ramipril/hydrochlorothiazide	0.53	1.0	-2.7	6.3	1.3	-1.9	0.23	-0.8
A - Gastrointestinal tract and metabolism	**30.73**		**-5.8**	**254.9**		**-8.7**	**0.33**	**3.2**
pantoprazole	4.51	14.7	0.0	29.4	11.5	1.6	0.42	-1.5
cholecalciferol	3.36	10.9	-16.9	116.7	45.8	-14.6	0.08	-2.7
esomeprazole	2.23	7.3	-0.5	15.9	6.3	0.9	0.38	-1.4
mesalazine	2.16	7.0	1.5	5.5	2.2	2.8	1.08	-1.2
omeprazole	2.06	6.7	-4.6	17.1	6.7	-2.6	0.33	-2.1
lansoprazole	2.00	6.5	-7.7	12.5	4.9	-6.4	0.44	-1.3
metformin	1.68	5.5	1.3	23.0	9.0	-0.5	0.20	1.8
rifaximin	1.36	4.4	-1.5	1.8	0.7	-1.4	2.08	0.0
insulin lispro	1.15	3.8	-17.6	3.0	1.2	-3.6	1.04	-14.6
insulin aspart	1.13	3.7	-14.0	2.7	1.1	-2.9	1.15	-11.4
dulaglutide	1.05	3.4	-19.9	0.6	0.2	-18.9	4.88	-1.2
ursodeoxycholic acid	0.96	3.1	5.5	2.8	1.1	5.4	0.92	0.1

continued

Table 3.10 - *continued*

Therapeutic category	Gross *per capita* expenditure	%*	Δ % 23-22	DDD/1000 inhab. per day	%*	Δ % 23-22	Average DDD cost	Δ % 23-22
N- Central nervous system	**23.65**		**-0.6**	**71.8**		**2.3**	**0.90**	**-2.8**
levetiracetam	1.69	7.2	1.1	2.3	3.2	1.5	2.01	-0.4
pregabalin	1.48	6.3	8.8	2.7	3.7	9.8	1.51	-0.9
fentanyl	1.16	4.9	-9.6	0.6	0.9	-1.1	5.16	-8.6
tapentadol	1.04	4.4	-1.1	0.6	0.8	4.3	4.92	-5.1
valproic acid	0.99	4.2	2.2	2.4	3.3	2.6	1.15	-0.4
paroxetine	0.97	4.1	-2.5	7.9	11.0	0.0	0.34	-2.4
escitalopram	0.97	4.1	0.1	7.7	10.7	0.8	0.34	-0.6
vortioxetine	0.93	3.9	13.6	2.2	3.1	13.5	1.14	0.1
sertraline	0.87	3.7	5.7	9.7	13.5	6.1	0.25	-0.4
duloxetine	0.84	3.6	3.0	3.5	4.8	3.8	0.67	-0.7
venlafaxine	0.83	3.5	2.2	3.9	5.4	3.7	0.59	-1.4
quetiapine	0.67	2.8	13.8	0.5	0.7	14.9	3.42	-0.9
rotigotine	0.55	2.3	-9.0	0.3	0.4	-6.5	5.17	-2.7
naloxone/oxycodone	0.52	2.2	-17.4	0.4	0.5	-1.8	3.94	-15.9
lamotrigine	0.49	2.1	5.0	0.8	1.1	5.5	1.76	-0.5
lacosamide	0.44	1.8	-33.4	0.4	0.6	9.0	2.85	-38.9
trazodone	0.44	1.8	5.0	1.2	1.7	5.1	0.98	-0.2
safinamide	0.41	1.7	2.8	0.3	0.4	4.7	4.22	-1.9
citalopram	0.39	1.7	-1.3	3.8	5.3	-0.8	0.28	-0.5
buprenorphine	0.39	1.6	16.7	0.2	0.3	11.7	4.82	4.5
gabapentin	0.37	1.6	4.7	0.5	0.7	5.4	2.13	-0.7
levodopa/benserazide	0.37	1.6	3.9	1.1	1.5	2.2	0.96	1.7
mirtazapine	0.36	1.5	3.2	1.8	2.5	2.6	0.56	0.6
pramipexole	0.36	1.5	-0.6	0.4	0.6	-1.5	2.34	0.9
olanzapine	0.28	1.2	6.6	0.6	0.8	7.6	1.37	-0.9
R - Respiratory system	**15.56**		**-1.9**	**40.7**		**-0.2**	**1.05**	**-1.7**
formoterol/beclomethasone	2.24	14.4	-11.3	4.1	10.1	2.3	1.49	-13.3
vilanterol/fluticasone furoate	2.12	13.6	0.2	3.7	9.1	2.5	1.57	-2.2
formoterol/budesonide	1.19	7.7	-10.3	2.0	4.9	-2.1	1.65	-8.4
tiotropium	0.81	5.2	-17.3	1.5	3.7	-14.8	1.46	-2.9
formoterol/glycopyrronium/ beclomethasone	0.79	5.1	20.5	0.8	2.0	37.1	2.65	-12.1
salmeterol/fluticasone	0.77	5.0	-12.1	1.8	4.4	-10.9	1.18	-1.4
umeclidinium	0.70	4.5	-1.8	1.3	3.1	-1.8	1.51	0.0
beclomethasone	0.65	4.2	1.6	1.7	4.3	0.4	1.04	1.2
vilanterol/umeclidinium	0.65	4.2	58.8	0.9	2.3	64.3	1.91	-3.3
vilanterol/umeclidinium/ fluticasone furoate	0.64	4.1	17.9	0.6	1.6	18.4	2.72	-0.4
budesonide	0.51	3.3	14.1	0.9	2.1	10.5	1.61	3.2
montelukast	0.46	3.0	0.2	2.0	5.0	-0.1	0.62	0.3
aclidinium	0.43	2.8	-11.3	0.8	1.9	-11.3	1.51	0.0

continued

Table 3.10 - *continued*

Therapeutic category	Gross *per capita* expenditure	%*	Δ % 23-22	DDD/1000 inhab. per day	%*	Δ % 23-22	Average DDD cost	Δ % 23-22
J - Antimicrobials	**11.64**		**6.1**	**16.3**		**6.4**	**1.96**	**-0.2**
amoxicillin/clavulanic acid	3.05	26.2	17.6	6.1	37.5	16.8	1.37	0.6
cefixime	1.15	9.8	15.3	1.3	8.3	15.0	2.34	0.3
ceftriaxone	1.04	9.0	11.3	0.2	1.5	14.2	11.63	-2.5
azithromycin	0.79	6.8	-16.2	1.5	9.1	-18.4	1.47	2.6
fluconazole	0.66	5.7	0.2	0.3	2.0	1.1	5.48	-0.9
fosfomycin	0.64	5.5	0.0	0.4	2.3	0.4	4.60	-0.4
ciprofloxacin	0.62	5.3	-2.2	0.7	4.1	-1.7	2.55	-0.5
clarithromycin	0.59	5.0	0.8	1.8	11.0	0.7	0.90	0.1
levofloxacin	0.39	3.3	-0.7	0.7	4.5	1.1	1.44	-1.8
B - Blood and blood-forming organs	**7.19**		**-3.2**	**89.8**		**-0.9**	**0.22**	**-2.3**
enoxaparin	1.76	24.4	-13.8	2.2	2.5	-12.1	2.16	-1.9
clopidogrel	1.28	17.8	5.5	6.4	7.2	7.5	0.55	-1.9
acetylsalicylic acid	1.20	16.7	0.7	46.0	51.2	0.8	0.07	-0.2
folic acid	0.53	7.4	2.6	7.0	7.8	2.8	0.21	-0.3
apixaban	0.30	4.2	12.5	0.2	0.2	12.8	3.82	-0.2
ferrous sulfate	0.28	3.9	5.5	2.5	2.8	5.5	0.31	0.0
human albumin	0.24	3.3	-0.4	<0.05	0.0	-2.6	53.38	2.3
G - Genito-urinary system and sex hormones	**5.70**		**2.1**	**46.4**		**3.6**	**0.34**	**-1.5**
tamsulosin	1.17	20.5	2.5	11.6	25.0	3.7	0.28	-1.1
dutasteride	1.03	18.2	0.2	8.5	18.3	1.3	0.33	-1.1
alfuzosin	0.97	17.0	5.7	10.3	22.2	5.5	0.26	0.1
silodosin	0.76	13.3	3.4	6.7	14.5	4.1	0.31	-0.7
finasteride	0.56	9.7	1.8	2.7	5.9	3.9	0.56	-2.0
M - Musculo-skeletal system	**5.36**		**-0.5**	**38.8**		**-0.9**	**0.38**	**0.4**
alendronic acid	0.87	16.2	7.0	4.7	12.1	8.3	0.51	-1.1
diclofenac	0.64	12.0	0.7	4.4	11.3	0.6	0.40	0.1
etoricoxib	0.62	11.5	1.1	3.7	9.6	1.9	0.46	-0.8
febuxostat	0.59	11.0	7.4	2.4	6.3	7.5	0.67	-0.1
alendronic acid/cholecalciferol	0.40	7.4	-0.4	1.9	4.8	-1.6	0.59	1.1
ibuprofen	0.39	7.2	-8.7	2.5	6.5	-9.3	0.42	0.7
allopurinol	0.37	6.9	1.6	8.7	22.4	1.3	0.12	0.3
risendronic acid	0.37	6.9	1.6	2.1	5.5	2.3	0.47	-0.7
L - Antineoplastic and immunomodulating agents	**4.55**		**1.6**	**6.6**		**1.6**	**1.90**	**-0.0**
letrozole	1.57	34.4	3.9	1.9	29.1	4.4	2.24	-0.5
methotrexate	0.77	16.9	5.1	1.5	22.4	4.7	1.43	0.4
exemestane	0.52	11.5	9.2	0.6	9.9	9.7	2.21	-0.4
cyclosporine	0.42	9.3	-5.2	0.1	2.2	-4.5	8.05	-0.8
anastrozole	0.34	7.4	-6.2	0.7	10.5	-5.4	1.34	-0.9

continued

Table 3.10 - *continued*

Therapeutic category	Gross *per capita* expenditure	%*	Δ % 23-22	DDD/1000 inhab. per day	%*	Δ % 23-22	Average DDD cost	Δ % 23-22
H - Systemic hormones	**4.05**		**1.9**	**39.9**		**2.7**	**0.28**	**-0.7**
levothyroxine	1.48	36.5	6.3	23.5	58.8	3.6	0.17	2.6
prednisone	0.70	17.2	-1.2	7.2	18.0	0.2	0.27	-1.4
teriparatide	0.66	16.3	-1.9	0.2	0.4	15.3	11.08	-15.0
betamethasone	0.33	8.1	4.1	2.2	5.4	3.9	0.42	0.2
methylprednisolone	0.21	5.1	2.5	3.3	8.3	3.5	0.17	-1.0
S - Sensory organs	**3.76**		**3.1**	**21.8**		**2.4**	**0.47**	**0.6**
dorzolamide/timolol	0.55	14.7	15.4	3.6	16.6	13.9	0.42	1.3
tafluprost	0.52	13.7	-0.5	1.7	7.6	-0.1	0.85	-0.4
timolol	0.39	10.4	4.1	3.2	14.6	1.8	0.34	2.3
bimatoprost	0.32	8.6	1.0	1.8	8.3	1.4	0.49	-0.4
timolol/bimatoprost	0.32	8.5	3.6	1.4	6.5	1.2	0.62	2.3
tafluprost/timolol	0.30	8.1	9.0	0.9	4.0	8.9	0.96	0.1
latanoprost	0.21	5.6	22.4	1.5	6.9	16.9	0.38	4.7
timolol/brinzolamide	0.19	5.0	-10.3	1.0	4.4	-10.3	0.53	0.0
travoprost	0.16	4.3	-10.0	0.8	3.7	-9.7	0.54	-0.3
D - Dermatologicals	**1.35**		**4.2**	**5.1**		**3.0**	**0.73**	**1.1**
calcipotriol/betamethasone	0.87	64.4	4.2	2.5	49.5	5.7	0.95	-1.4
isotretinoin	0.11	7.8	-1.9	0.2	4.1	-1.8	1.37	-0.1
clobetasol	0.08	5.7	4.0	1.0	20.1	4.1	0.21	-0.1
diclofenac	0.06	4.4	-8.8	0.1	1.1	-8.6	2.88	-0.2
terbinafine	0.05	3.9	5.1	0.1	2.0	7.2	1.39	-1.9
P - Antiparasitic products	**0.24**		**2.6**	**1.0**		**2.5**	**0.62**	**0.1**
hydroxychloroquine	0.17	73.1	1.7	0.9	87.6	1.9	0.52	-0.2
mefloquine	0.02	9.6	10.1	0.0	0.4	10.1	13.27	0.0
mebendazole	0.02	8.9	17.4	0.1	7.9	12.2	0.70	4.6
metronidazole	0.01	5.6	6.6	<0.05	3.4	6.6	1.03	0.0
albendazole	<0.005	1.9	10.0	<0.05	0.5	10.0	2.26	0.0
V - Various	**0.19**		**35.4**	**0.1**		**1.2**	**5.29**	**33.7**
sevelamer	0.06	32.3	5.1	<0.05	31.9	5.7	5.35	-0.5
deferasirox	0.05	27.5	>100	<0.05	2.1	>100	68.50	-12.5
polystyrene sulfonate	0.04	20.6	-4.9	<0.05	39.1	-4.8	2.78	-0.1
sucroferric oxyhydroxide	0.02	8.5	9.7	<0.05	5.3	9.7	8.44	0.0
calcium acetate/magnesium carbonate	0.01	2.9	-2.3	<0.05	15.0	-2.3	1.02	0.0

* The expenditure and DDD percentages are calculated on the total of ATC 1st level category

Table 3.11 First thirty active ingredients by expenditure under approved care regime (A-NHS): comparison 2023-2022

ATC	Active ingredient	Expenditure *(million)*	%*	Gross *per capita* expenditure	Rank 2023	Rank 2022	Average DDD cost	Δ % 23-22	Average DDD cost direct purchases
C	atorvastatin	274.4	2.8	4.66	1	1	0.25	0.1	<0.005
A	pantoprazole	265.5	2.7	4.51	2	2	0.42	-1.5	0.03
A	cholecalciferol	198.0	2.0	3.36	3	3	0.08	-2.7	0.01
J	amoxicillin/ clavulanic acid	179.7	1.8	3.05	4	5	1.37	0.6	0.24
C	bisoprolol	171.4	1.8	2.91	5	4	0.60	-0.1	0.09
C	ezetimibe/ rosuvastatin	134.0	1.4	2.28	6	21	0.40	-0.7	0.01
R	formoterol/ beclomethasone	131.9	1.3	2.24	7	6	1.49	-13.3	0.94
A	esomeprazole	131.1	1.3	2.23	8	7	0.38	-1.4	0.14
C	omega-3	130.3	1.3	2.21	9	10	2.27	-2.0	0.40
A	mesalazine	127.1	1.3	2.16	10	11	1.08	-1.2	0.24
R	vilanterol/ fluticasone furoate	124.6	1.3	2.12	11	12	1.57	-2.2	0.81
C	olmesartan	121.6	1.2	2.07	12	15	0.31	0.1	0.11
A	omeprazole	121.3	1.2	2.06	13	9	0.33	-2.1	0.04
A	lansoprazole	117.9	1.2	2.00	14	8	0.44	-1.3	0.08
C	ramipril	111.7	1.1	1.90	15	14	0.09	-1.3	0.01
C	ezetimibe	109.0	1.1	1.85	16	16	0.73	-0.6	0.11
B	enoxaparin	103.4	1.1	1.76	17	13	2.16	-1.9	0.85
N	levetiracetam	99.6	1.0	1.69	18	17	2.01	-0.4	0.69
A	metformin	98.9	1.0	1.68	19	18	0.20	1.8	0.05
C	olmesartan/ amlodipine	95.1	1.0	1.62	20	24	0.40	-0.2	0.23
C	amlodipine	94.1	1.0	1.60	21	19	0.15	-1.5	<0.005
C	nebivolol	93.6	1.0	1.59	22	20	0.25	-0.1	0.05
C	rosuvastatin	93.2	1.0	1.58	23	23	0.26	0.2	0.05
L	letrozole	92.2	0.9	1.57	24	22	2.24	-0.5	0.24
N	pregabalin	87.2	0.9	1.48	25	28	1.51	-0.9	0.09
H	levothyroxine	87.0	0.9	1.48	26	26	0.17	2.6	0.04
A	rifaximin	80.1	0.8	1.36	27	27	2.08	0.0	2.27
C	olmesartan/ hydrochlorothiazide	76.8	0.8	1.31	28	34	0.33	-0.3	0.17
B	clopidogrel	75.3	0.8	1.28	29	37	0.55	-1.9	0.05
C	simvastatin	74.1	0.8	1.26	30	29	0.33	-0.2	0.03
	Total top 30	**3,700.2**	**37.8**	**62.88**			**0.32**	**2.8**	**0.27**
	Total	**9,782.0**	**100.0**	**166.22**			**0.40**	**1.4**	**1.55**

* Calculated on overall expenditure under approved care regime

TTable 3.12 First thirty active ingredients* with highest average cost per day of therapy under approved care regime (A-NHS): comparison 2023-2022

ATC	Active ingredient	Average DDD cost	Δ % 23-22	Gross *per capita* expenditure	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22
J	ceftriaxone	11.63	-2.5	1.04	11.3	0.2	14.2
H	teriparatide	11.08	-15.0	0.66	-1.9	0.2	15.3
A	semaglutide	9.34	18.2	0.78	-10.5	0.2	-24.3
J	fluconazole	5.48	-0.9	0.66	0.2	0.3	1.1
N	rotigotine	5.17	-2.7	0.55	-9.0	0.3	-6.5
N	fentanyl	5.16	-8.6	1.16	-9.6	0.6	-1.1
N	tapentadol	4.92	-5.1	1.04	-1.1	0.6	4.3
A	dulaglutide	4.88	-1.2	1.05	-19.9	0.6	-18.9
J	fosfomycin	4.60	-0.4	0.64	0.0	0.4	0.4
N	naloxone/oxycodone	3.94	-15.9	0.52	-17.4	0.4	-1.8
N	quetiapine	3.42	-0.9	0.67	13.8	0.5	14.9
R	vilanterol/umeclidinium/ fluticasone furoate	2.72	-0.4	0.64	17.9	0.6	18.4
R	formoterol/glycopyrronium /beclomethasone	2.65	-12.1	0.79	20.5	0.8	37.1
J	ciprofloxacin	2.55	-0.5	0.62	-2.2	0.7	-1.7
J	cefixime	2.34	0.3	1.15	15.3	1.3	15.0
C	omega-3	2.27	-2.0	2.21	2.9	2.7	5.0
L	letrozole	2.24	-0.5	1.57	3.9	1.9	4.4
L	exemestane	2.21	-0.4	0.52	9.2	0.6	9.7
B	enoxaparin	2.16	-1.9	1.76	-13.8	2.2	-12.1
C	ranolazine	2.08	-8.4	0.88	>100	1.2	>100
A	rifaximin	2.08	0.0	1.36	-1.5	1.8	-1.4
N	levetiracetam	2.01	-0.4	1.69	1.1	2.3	1.5
R	vilanterol/umeclidinium	1.91	-3.3	0.65	58.8	0.9	64.3
R	formoterol/budesonide	1.65	-8.4	1.19	-10.3	2.0	-2.1
R	budesonide	1.61	3.2	0.51	14.1	0.9	10.5
R	vilanterol/ fluticasone furoate	1.57	-2.2	2.12	0.2	3.7	2.5
R	umeclidinium	1.51	0.0	0.70	-1.8	1.3	-1.8
N	pregabalin	1.51	-0.9	1.48	8.8	2.7	9.8
R	formoterol/beclomethasone	1.49	-13.3	2.24	-11.3	4.1	2.3
J	azithromycin	1.47	2.6	0.79	-16.2	1.5	-18.4
	Total top 30	**2.31**	**-3.8**	**31.62**	**1.4**	**37.5**	**5.4**
	Total	**0.40**	**1.4**	**166.22**	**0.3**	**1128.1**	**-1.0**

* selected among the top 100 active ingredients with highest per capita expenditure

Table 3.13 First thirty active ingredients* with lowest average cost per day of therapy under approved care regime (A-NHS): comparison 2023-2022

ATC	Active ingredient	Average DDD cost	Δ % 23-22	Gross expenditure *(in million)*	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22
B	acetylsalicylic acid	0.07	-0.2	70.7	0.7	46.0	0.8
A	cholecalciferol	0.08	-2.7	198.0	-16.9	116.7	-14.6
C	furosemide	0.08	0.3	39.6	-3.4	22.5	-3.7
C	ramipril	0.09	-1.3	111.7	-2.5	60.7	-1.2
C	amlodipine	0.15	-1.5	94.1	-0.1	28.3	1.5
H	levothyroxine	0.17	2.6	87.0	6.3	23.5	3.6
C	valsartan	0.19	0.4	42.1	5.2	10.5	4.7
A	metformin	0.20	1.8	98.9	1.3	23.0	-0.5
B	folic acid	0.21	-0.3	31.4	2.6	7.0	2.8
C	lercanidipine	0.22	-0.1	45.4	0.5	9.4	0.7
C	irbesartan	0.22	0.1	36.1	-4.1	7.5	-4.2
C	ramipril/hydrochlorothiazide	0.23	-0.8	31.2	-2.7	6.3	-1.9
N	sertraline	0.25	-0.4	51.2	5.7	9.7	6.1
C	atorvastatin	0.25	0.1	274.4	-0.3	50.6	-0.4
C	nebivolol	0.25	-0.1	93.6	2.2	17.2	2.3
G	alfuzosin	0.26	0.1	57.0	5.7	10.3	5.5
C	rosuvastatin	0.26	0.2	93.2	6.6	16.8	6.4
H	prednisone	0.27	-1.4	41.1	-1.2	7.2	0.2
G	tamsulosin	0.28	-1.1	68.9	2.5	11.6	3.7
C	nebivolol/hydrochlorothiazide	0.28	-0.5	29.2	2.0	4.9	2.5
C	losartan	0.29	-0.3	39.8	-4.5	6.5	-4.2
C	valsartan/hydrochlorothiazide	0.30	-0.3	37.7	-1.3	5.8	-1.0
G	silodosin	0.31	-0.7	44.6	3.4	6.7	4.1
C	olmesartan	0.31	0.1	121.6	7.9	18.0	7.8
C	irbesartan/hydrochlorothiazide	0.32	0.0	31.1	-5.1	4.6	-5.1
C	simvastatin	0.33	-0.2	74.1	-7.4	10.6	-7.2
A	omeprazole	0.33	-2.1	121.3	-4.6	17.1	-2.6
C	olmesartan/hydrochlorothiazide	0.33	-0.3	76.8	3.5	10.8	3.8
G	dutasteride	0.33	-1.1	60.9	0.2	8.5	1.3
N	paroxetine	0.34	-2.4	57.1	-2.5	7.9	0.0
	Total top 30	**0.18**	**1.7**	**2259.5**	**-1.2**	**586.0**	**-2.8**
	Total	**0.40**	**1.4**	**9872.2**	**0.3**	**1128.1**	**-1.0**

* selected among the top 100 active ingredients with highest per capita expenditure

Table 3.14 First thirty active ingredients* with highest variation in expenditure under approved care regime (A-NHS): comparison 2023-2022

ATC	Active ingredient	Gross *per capita* expenditure	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
C	ranolazine	0.88	>100	1.2	>100	2.08	-8.4
R	vilanterol/umeclidinium	0.65	58.8	0.9	64.3	1.91	-3.3
C	ezetimibe/rosuvastatin	2.28	47.4	15.8	48.5	0.40	-0.7
R	formoterol/glycopyrronium/ beclomethasone	0.79	20.5	0.8	37.1	2.65	-12.1
R	vilanterol/umeclidinium/ fluticasone furoate	0.64	17.9	0.6	18.4	2.72	-0.4
J	amoxicillin/clavulanic acid	3.05	17.6	6.1	16.8	1.37	0.6
S	dorzolamide/timolol	0.55	15.4	3.6	13.9	0.42	1.3
J	cefixime	1.15	15.3	1.3	15.0	2.34	0.3
R	budesonide	0.51	14.1	0.9	10.5	1.61	3.2
N	quetiapine	0.67	13.8	0.5	14.9	3.42	-0.9
N	vortioxetine	0.93	13.6	2.2	13.5	1.14	0.1
C	perindopril/indapamide/amlodipine	0.72	13.5	5.2	10.4	0.38	2.8
J	ceftriaxone	1.04	11.3	0.2	14.2	11.63	-2.5
C	olmesartan/amlodipine	1.62	11.2	11.0	11.4	0.40	-0.2
L	exemestane	0.52	9.2	0.6	9.7	2.21	-0.4
N	pregabalin	1.48	8.8	2.7	9.8	1.51	-0.9
C	ezetimibe	1.85	8.3	7.0	8.9	0.73	-0.6
C	olmesartan	2.07	7.9	18.0	7.8	0.31	0.1
M	febuxostat	0.59	7.4	2.4	7.5	0.67	-0.1
M	alendronic acid	0.87	7.0	4.7	8.3	0.51	-1.1
C	rosuvastatin	1.58	6.6	16.8	6.4	0.26	0.2
H	levothyroxine	1.48	6.3	23.5	3.6	0.17	2.6
G	alfuzosin	0.97	5.7	10.3	5.5	0.26	0.1
N	sertraline	0.87	5.7	9.7	6.1	0.25	-0.4
A	ursodeoxycholic acid	0.96	5.5	2.8	5.4	0.92	0.1
B	clopidogrel	1.28	5.5	6.4	7.5	0.55	-1.9
C	valsartan	0.72	5.2	10.5	4.7	0.19	0.4
L	methotrexate	0.77	5.1	1.5	4.7	1.43	0.4
D	calcipotriol/betamethasone	0.87	4.2	2.5	5.7	0.95	-1.4
L	letrozole	1.57	3.9	1.9	4.4	2.24	-0.5
	Total top 30	**33.91**	**15.1**	**171.7**	**11.3**	**0.54**	**3.4**
	Total	**166.22**	**0.3**	**1128.1**	**-1.0**	**0.40**	**1.4**

* selected among the top 100 active ingredients with highest per capita expenditure

Table 3.15 First thirty active ingredients* with highest variation in expenditure under approved care regime (A-NHS): comparison 2023-2022

ATC	Active ingredient	Gross *per capita* expenditure	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
A	dulaglutide	1.05	-19.9	0.6	-18.9	4.88	-1.2
A	insulin lispro	1.15	-17.6	3.0	-3.6	1.04	-14.6
N	naloxone/oxycodone	0.52	-17.4	0.4	-1.8	3.94	-15.9
R	tiotropium	0.81	-17.3	1.5	-14.8	1.46	-2.9
A	cholecalciferol	3.36	-16.9	116.7	-14.6	0.08	-2.7
J	azithromycin	0.79	-16.2	1.5	-18.4	1.47	2.6
A	insulin aspart	1.13	-14.0	2.7	-2.9	1.15	-11.4
B	enoxaparin	1.76	-13.8	2.2	-12.1	2.16	-1.9
R	salmeterol/fluticasone	0.77	-12.1	1.8	-10.9	1.18	-1.4
A	magaldrate	0.49	-12.1	2.2	-10.5	0.61	-1.8
R	formoterol/beclomethasone	2.24	-11.3	4.1	2.3	1.49	-13.3
A	semaglutide	0.78	-10.5	0.2	-24.3	9.34	18.2
R	formoterol/budesonide	1.19	-10.3	2.0	-2.1	1.65	-8.4
N	fentanyl	1.16	-9.6	0.6	-1.1	5.16	-8.6
N	rotigotine	0.55	-9.0	0.3	-6.5	5.17	-2.7
C	barnidipine	0.79	-8.4	4.6	-4.9	0.47	-3.6
A	lansoprazole	2.00	-7.7	12.5	-6.4	0.44	-1.3
C	simvastatin	1.26	-7.4	10.6	-7.2	0.33	-0.2
C	irbesartan/hydrochlorothiazide	0.53	-5.1	4.6	-5.1	0.32	0.0
A	omeprazole	2.06	-4.6	17.1	-2.6	0.33	-2.1
C	losartan	0.68	-4.5	6.5	-4.2	0.29	-0.3
C	irbesartan	0.61	-4.1	7.5	-4.2	0.22	0.1
C	furosemide	0.67	-3.4	22.5	-3.7	0.08	0.3
C	zofenopril/hydrochlorothiazide	0.61	-2.8	3.9	-2.7	0.43	-0.1
C	ramipril/hydrochlorothiazide	0.53	-2.7	6.3	-1.9	0.23	-0.8
C	ramipril	1.90	-2.5	60.7	-1.2	0.09	-1.3
N	paroxetine	0.97	-2.5	7.9	0.0	0.34	-2.4
J	ciprofloxacin	0.62	-2.2	0.7	-1.7	2.55	-0.5
H	teriparatide	0.66	-1.9	0.2	15.3	11.08	-15.0
R	umeclidinium	0.70	-1.8	1.3	-1.8	1.51	0.0
	Total top 30	**32.25**	**-10.1**	**306.5**	**-8.0**	**0.29**	**-2.3**
	Total	**166.22**	**0.3**	**1128.1**	**-1.0**	**0.40**	**1.4**

* selected among the top 100 active ingredients with highest per capita expenditure

Table 3.16 First thirty active ingredients by consumption under approved care regime (A-NHS): comparison 2023-2022

ATC	Active ingredient	DDD/1000 inhab. per day	%*	Rank 2023	Rank 2022	Average DDD cost	Δ % 23-22	Average DDD cost direct purchases
A	cholecalciferol	116.7	10.3	1	1	0.08	-2.7	0.01
C	ramipril	60.7	5.4	2	2	0.09	-1.3	0.01
C	atorvastatin	50.6	4.5	3	3	0.25	0.1	<0.005
B	acetylsalicylic acid	46.0	4.1	4	4	0.07	-0.2	0.02
A	pantoprazole	29.4	2.6	5	5	0.42	-1.5	0.03
C	amlodipine	28.3	2.5	6	6	0.15	-1.5	0.00
H	levothyroxine	23.5	2.1	7	9	0.17	2.6	0.04
A	metformin	23.0	2.0	8	8	0.20	1.8	0.05
C	furosemide	22.5	2.0	9	7	0.08	0.3	0.02
C	olmesartan	18.0	1.6	10	12	0.31	0.1	0.11
C	nebivolol	17.2	1.5	11	11	0.25	-0.1	0.05
A	omeprazole	17.1	1.5	12	10	0.33	-2.1	0.04
C	rosuvastatin	16.8	1.5	13	14	0.26	0.2	0.05
A	esomeprazole	15.9	1.4	14	13	0.38	-1.4	0.14
C	ezetimibe/rosuvastatin	15.8	1.4	15	20	0.40	-0.7	0.01
C	bisoprolol	13.2	1.2	16	16	0.60	-0.1	0.09
A	lansoprazole	12.5	1.1	17	15	0.44	-1.3	0.08
G	tamsulosin	11.6	1.0	18	19	0.28	-1.1	0.03
B	cyanocobalamin	11.3	1.0	19	17	0.02	2.1	0.01
C	olmesartan/amlodipine	11.0	1.0	20	23	0.40	-0.2	0.23
C	olmesartan/ hydrochlorothiazide	10.8	1.0	21	21	0.33	-0.3	0.17
C	simvastatin	10.6	0.9	22	18	0.33	-0.2	0.03
C	valsartan	10.5	0.9	23	22	0.19	0.4	<0.005
G	alfuzosin	10.3	0.9	24	24	0.26	0.1	0.06
N	sertraline	9.7	0.9	25	26	0.25	-0.4	<0.005
C	lercanidipine	9.4	0.8	26	25	0.22	-0.1	0.05
M	allopurinol	8.7	0.8	27	27	0.12	0.3	0.04
G	dutasteride	8.5	0.8	28	29	0.33	-1.1	0.08
C	candesartan	8.1	0.7	29	28	0.15	0.2	0.03
C	telmisartan	8.0	0.7	30	30	0.16	-0.2	0.01
	Total top 30	**655.6**	**58.1**			**0.20**	**2.6**	**0.02**
	Total	**1128.1**	**100.0**			**0.40**	**1.4**	

* calculated on overall expenditure under approved care regime

Figure 3.5 Consumption, price and mix effect on expenditure variation for medicines dispensed by public health facilities by ATC 1st level: comparison 2023-2022

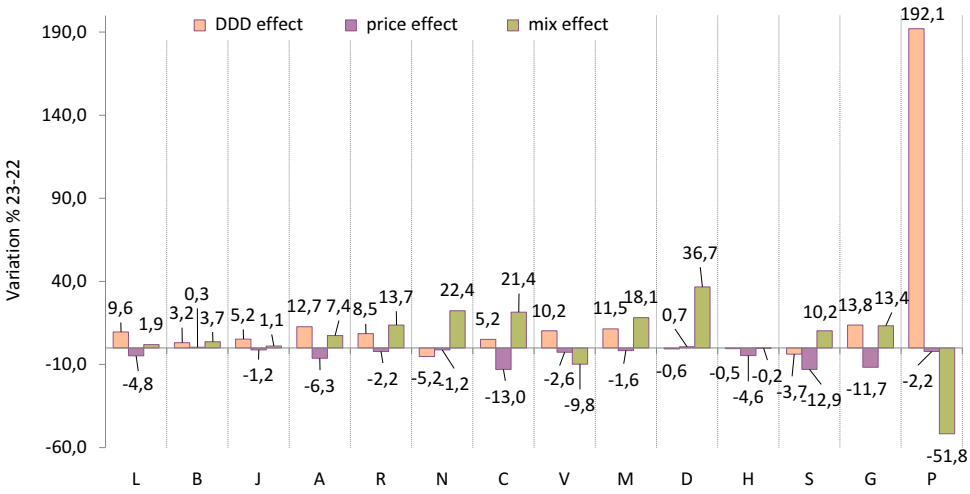

Figure 3.17 Consumption, price and mix effect on expenditure variation for medicines dispensed by public health facilities: comparison 2023-2022
(Any ATC category includes the therapeutic subgroups in decreasing order of per capita expenditure, up to the value of 0.10 euros)

ATC 1st level / ATC 4th level	Gross per capita expenditure	DDD/1000 inhab. per day	Δ % 23-22				Δ % Average DDD cost
			Expenditure	DDD	Prices	Mix	
Italy	**275.16**	**194.9**	**8.2**	**4.9**	**-3.7**	**7.1**	**3.1**
L- Antineoplastic and immunomodulatory drugs	**120.47**	**13.5**	**6.3**	**9.6**	**-4.8**	**1.9**	**-3.0**
PD-1/PD-L1 inhibitors	14.96	0.5	12.7	26.0	-6.0	-4.9	-10.6
Interleukin inhibitors	11.57	1.3	17.1	19.5	-1.6	-0.4	-2.0
CD38 inhibitors	8.21	0.3	18.7	32.8	-6.2	-4.7	-10.6
Monoclonal antibodies	6.90	0.4	17.5	13.7	-3.1	6.7	3.4
Other kinase protein inhibitors	4.93	0.1	13.4	15.5	-3.6	1.8	-1.8
HER2 inhibitors (human epid. growth factor 2 receptor)	4.68	0.2	-1.2	-4.8	-1.2	5.0	3.8
Bruton tyrosine kinase (BTK) inhibitors	4.52	0.1	18.7	20.5	-3.5	2.0	-1.5
Tumor necrosis factor alpha inhibitors (TNF-alpha)	4.49	1.8	-4.2	8.7	-5.5	-6.8	-11.9
Cyclin-dependent kinase inhibitors (CDK)	4.36	0.2	14.2	19.6	-2.6	-2.0	-4.5
Other immunosuppressants	4.26	0.5	-39.6	2.9	-9.2	-35.4	-41.3
Antiandrogens	3.73	0.6	43.7	4.4	-6.5	47.3	37.7
Other monoclonal antibodies and antibody-drug conjugates	3.36	0.0	31.1	65.5	-4.7	-16.9	-20.8
Epidermal growth factor receptor (EGFR) tyrosine kinase inhib.	3.01	0.1	2.2	6.9	-9.5	5.6	-4.4
Selective immunosuppressants	2.97	0.6	-4.4	6.3	-11.5	1.5	-10.1
Complement inhibitors	2.97	<0.05	29.2	40.0	-3.3	-4.6	-7.7
BCR-ABL tyrosine kinase inhibitors	2.63	0.2	-16.8	-0.4	-6.7	-10.6	-16.5
Janus kinase (JAK) inhibitors	2.49	0.1	16.7	17.5	0.3	-1.0	-0.7
Sphingosine 1-phosphate (S1P) receptor modulators	2.35	0.2	-7.6	11.6	-15.7	-1.8	-17.2
Gonadotropin-releasing hormone analogues	2.20	1.3	6.1	8.3	-0.8	-1.3	-2.0
Poly (ADP-RIBOSE) polymerase (PARP) inhibitors	2.15	<0.05	13.7	13.9	-1.5	1.3	-0.2
Other antineoplastics	1.90	0.1	21.5	12.5	-6.7	15.8	8.0
Antineoplastic cell and gene therapy	1.81	<0.05	51.1	17.3	26.5	1.8	28.8
Janus kinase (JAK) inhibitors	1.70	0.2	16.9	22.6	-3.9	-0.7	-4.6
Serine-threonine kinase B-RAF inhibitors	1.59	<0.05	5.8	4.5	-0.7	1.9	1.2
Anaplastic lymphoma kinase inhibitors (ALK)	1.49	<0.05	3.0	10.7	-7.3	0.3	-7.0
Interferons	1.29	0.3	-15.1	-16.9	-4.9	7.4	2.2
Dihydroorotate dehydrogenase (DHODH) inhibitors	1.24	0.3	19.4	19.8	-4.4	4.3	-0.3

continued

Table 3.17 - *continued*

ATC 1st level / ATC 4th level	Gross per capita expenditure	DDD/1000 inhab. per day	Δ % 23-22				Δ % Average DDD cost
			Expenditure	DDD	Prices	Mix	
VEGF/VEGFR inhibitors (angiogenic growth factor)	1.12	0.1	-12.4	13.5	-3.4	-20.1	-22.8
EGFR inhibitors (epidermal growth factor receptor)	1.05	<0.05	-0.8	3.6	-4.2	0.0	-4.3
CD20 inhibitors	1.02	0.5	-2.6	8.7	-7.9	-2.6	-10.4
Pyrimidine analogues	0.93	0.4	-4.9	-5.0	-4.3	4.7	0.2
Calcineurin inhibitors	0.90	0.4	0.9	2.7	0.4	-2.1	-1.8
Proteasome inhibitors	0.89	<0.05	4.4	7.3	-10.2	8.3	-2.7
Mammalian Target of Rapamycin (mTOR) Kinase Inhibitors	0.73	0.2	3.7	4.0	-0.3	0.0	-0.3
Mitogen-activated protein kinase (MEK) inhibitors	0.69	<0.05	-3.7	1.5	-0.1	-5.0	-5.1
Monoclonal antibodies + drug-conjugated antibodies	0.64	<0.05	>100	>100	46.5	-0.5	45.8
Other immunostimulating agents	0.59	0.1	-0.3	-10.9	-3.8	16.4	11.9
Other hormone antagonists and related substances	0.43	0.1	-73.1	4.3	-13.4	-70.2	-74.2
Taxanes	0.42	0.2	-5.9	1.0	-7.1	0.2	-6.9
Vascular endothelial growth factor receptor (VEGFR)- tyrosine kinase inhibitors	0.38	<0.05	-12.9	-9.5	-3.8	0.0	-3.8
Anthracyclines and related substances	0.36	0.1	-19.1	-9.6	-19.2	10.8	-10.5
Colony stimulating factors	0.35	0.1	-0.7	7.7	-1.3	-6.6	-7.8
Hedgehog pathway inhibitors	0.34	<0.05	13.0	17.6	-6.0	2.2	-3.9
Rapamycin and mammalian target of rapamycin (MTOR) inhibitors	0.23	<0.05	-37.8	-2.8	3.7	-38.2	-35.9
Antineoplastics in combination	0.21	<0.05	40.0	39.7	0.2	0.0	0.2
Folic acid analogues	0.16	0.1	-36.5	15.9	-1.1	-44.6	-45.2
Antiestrogens	0.13	0.3	4.8	78.6	-8.6	-35.8	-41.3
CD22 inhibitors	0.12	<0.05	6.4	6.3	0.1	0.0	0.1
Nitrogen mustard analogues	0.10	0.1	6.8	1.8	-2.2	7.4	5.0
B - Blood and blood-forming organs	**36.76**	**54.7**	**7.3**	**3.2**	**0.3**	**3.7**	**4.0**
Direct Xa factor inhibitors	9.95	16.3	15.7	15.1	-0.4	0.9	0.5
Blood coagulation factors	7.46	0.1	-2.2	-0.2	-1.6	-0.5	-2.1
Other hemostatics for systemic use	3.60	0.1	17.7	14.1	0.0	3.1	3.1
Other antianemic preparations	3.13	4.0	7.7	4.6	-3.2	6.4	3.0
Heparins	2.31	6.8	4.0	5.0	0.6	-1.5	-1.0
Platelet aggregation inhibitors, excl. heparin	2.20	9.3	-6.1	-3.7	-3.1	0.7	-2.5
Direct thrombin inhibitors	1.25	2.4	-2.4	-1.8	-1.1	0.4	-0.6
Solutions affecting the electrolyte balance	1.15	6.9	12.8	0.4	10.9	1.3	12.4

continued

Table 3.17 - *continued*

ATC 1st level ATC 4th level	Gross per capita expenditure	DDD/1000 inhab. per day	Δ % 23-22				Δ % Average DDD cost
			Expenditure	DDD	Prices	Mix	
Other antithrombotics	0.84	0.4	-9.5	-23.8	0.5	18.1	18.7
Medicines used in hereditary angioedema	0.79	<0.05	16.8	36.5	-15.6	1.4	-14.4
Iron, parenteral preparations	0.74	0.1	94.0	96.4	0.5	-1.7	-1.2
Parenteral nutritional solutions	0.72	0.6	-4.6	-16.3	41.5	-19.5	14.0
Local hemostatics	0.51	<0.05	14.8	11.2	1.5	1.7	3.2
Hypertonic solutions	0.47	0.2	6.1	14.7	-8.4	1.0	-7.5
Protease inhibitors	0.32	<0.05	11.1	-0.2	-0.6	12.1	11.4
Blood substitutes and plasma protein fractions	0.26	<0.05	-6.1	-13.3	0.8	7.6	8.4
Fibrinogen	0.26	<0.05	-9.1	-4.7	-4.8	0.2	-4.6
Enzymes	0.24	<0.05	14.5	-2.6	-0.8	18.6	17.6
Isotonic solutions	0.20	0.1	5.1	-15.1	8.8	13.7	23.8
Hemofiltrates	0.17	0.1	21.7	10.5	0.8	9.3	10.1
J- General antimicrobials for systemic use	**35.28**	**6.1**	**5.0**	**5.2**	**-1.2**	**1.1**	**-0.2**
Antivirals for treatment of HIV infections, combinations	8.66	1.5	-0.7	2.0	-1.5	-1.2	-2.6
Influenza vaccines	2.56	0.6	-3.5	-4.1	-7.4	8.6	0.6
Varicella Zoster vaccines	2.34	<0.05	46.4	5.8	-0.4	38.9	38.4
Human normal immunoglobulin	2.30	<0.05	17.9	5.7	6.9	4.4	11.6
Meningococcal vaccines	1.84	0.1	5.2	4.1	-0.3	1.3	1.1
Nucleosides and nucleotides excl. reverse transcriptase inhibitors	1.66	0.1	-21.7	1.7	-5.7	-18.4	-23.1
Human papillomavirus vaccines	1.64	0.1	13.3	13.2	0.1	0.0	0.1
Pneumococcal vaccines	1.51	0.1	15.9	11.1	0.5	4.3	4.3
Antivirals for treatment of HCV infections	1.32	<0.05	0.9	1.5	-0.5	-0.2	-0.6
Integrase inhibitors	1.27	0.3	3.0	2.6	0.2	0.2	0.4
Antibiotics	0.85	<0.05	2.9	3.0	-0.1	0.0	0.0
Bacterial and viral vaccines in combination	0.84	0.1	-1.3	2.5	-2.2	-1.5	-3.6
Other cephalosporins and penems	0.80	<0.05	7.2	7.0	-0.2	0.4	0.2
Other antivirals	0.73	<0.05	77.2	51.3	-1.8	19.2	17.1
Measles vaccines	0.68	<0.05	5.8	-0.1	0.8	5.1	5.9
Combinations of penicillins (including beta lactamase inhibitors)	0.61	0.5	-3.8	6.1	-8.1	-1.3	-9.3
Triazole and tetrazole derivatives	0.55	0.1	2.8	4.2	1.8	-3.0	-1.3
Third generation cephalosporins	0.54	0.3	1.7	8.9	0.2	-6.8	-6.6
Antiviral monoclonal antibodies	0.50	<0.05	7.5	-28.0	0.0	49.4	49.4
Carbapenems	0.48	0.1	11.6	-9.8	-1.7	26.0	23.8
Other antibacterials	0.47	0.1	-5.8	-5.1	2.8	-3.4	-0.8
Nucleosides and nucleotides inhibitors of reverse transcriptase	0.32	0.8	14.7	19.7	-5.7	1.8	-4.1

continued

Table 3.17 - *continued*

ATC 1st level ATC 4th level	Gross per capita expenditure	DDD/1000 inhab. per day	Δ % 23-22				Δ % Average DDD cost
			Expenditure	DDD	Prices	Mix	
Specific immunoglobulins	0.31	<0.05	3.0	4.2	0.7	-1.8	-1.2
Glycopeptide antibacterials	0.29	<0.05	8.4	-12.5	-3.7	28.7	23.9
Non-nucleosides inhibitors of reverse transcriptase	0.27	0.1	42.1	34.8	0.1	5.4	5.4
Rotavirus diarrhea vaccines	0.25	<0.05	-0.4	5.9	-2.5	-3.6	-6.0
Other antifungals for systemic use	0.21	<0.05	-25.1	-13.4	-4.8	-9.2	-13.5
Polymyxins	0.16	<0.05	-6.2	-10.3	-0.4	5.0	4.6
Pertussis vaccines	0.15	<0.05	13.7	17.8	-3.4	-0.1	-3.5
Hepatitis vaccines	0.13	<0.05	41.1	40.0	-0.2	1.0	0.8
Fluoroquinolones	0.11	0.2	-2.3	-2.7	6.5	-5.8	0.4
Other aminoglycosides	0.10	<0.05	8.8	-3.1	1.2	10.9	12.2
Broad-spectrum penicillins	0.10	<0.05	11.8	12.8	0.4	-1.2	-0.9
A- Gastrointestinal system and metabolism	**25.66**	**43.7**	**13.4**	**12.7**	**-6.3**	**7.4**	**0.6**
GLP-1 (glucagon-like peptide-1) receptor analogues	6.55	7.4	32.7	34.8	-5.5	4.2	-1.6
Enzymes	5.78	0.0	2.7	14.4	-6.1	-4.4	-10.2
Insulins and injectable analogues, slow-acting	3.04	6.8	0.1	0.4	-5.7	5.7	-0.3
SGLT2 cotransporter inhibitors (sodium-glucose type 2)	2.89	6.3	62.3	66.5	-4.3	1.9	-2.5
Oral hypoglycemic agents, in combination	2.34	6.6	-0.3	9.5	-9.5	0.6	-8.9
Various products for gastrointestinal system and metabolism	1.82	<0.05	16.3	6.9	-2.0	11.0	8.8
Dipeptil Peptidase 4 Inhibitors (DPP-4)	0.81	2.9	-35.4	-10.2	-27.2	-1.3	-28.1
Bile acids and derivatives	0.47	0.2	18.7	9.4	0.2	8.3	8.5
Antibiotics	0.31	0.3	25.7	4.0	2.4	18.0	20.9
Proton pump inhibitors	0.26	3.9	2.4	2.9	8.0	-7.9	-0.5
Serotonin antagonists (5HT3)	0.19	0.1	4.1	-4.0	-0.4	8.8	8.4
Amino acids and derivatives	0.17	0.1	10.4	4.3	-16.2	26.3	5.8
Insulins and injectable analogues, fast-acting	0.14	0.9	-15.4	-2.2	-12.2	-1.5	-13.5
Polyvitamins, not in combination	0.13	0.1	-2.5	-13.7	12.9	0.0	12.9
Enzyme preparations	0.11	0.2	47.1	8.7	1.3	33.5	35.3
Other drugs for biliary therapy	0.10	<0.05	>100	>100	-6.6	22.6	14.6
R- Respiratory system	**12.55**	**2.5**	**20.7**	**8.5**	**-2.2**	**13.7**	**11.2**
Other preparations for the respiratory system	8.79	0.1	22.9	23.7	-1.2	0.5	-0.7
Other systemic drugs for obstructive airway disorders	3.21	0.3	20.2	25.8	-5.1	0.7	-4.4
Mucolytics	0.23	0.3	-2.2	19.0	0.1	-17.8	-17.8

continued

Table 3.17 - *continued*

ATC 1st level / ATC 4th level	Gross per capita expenditure	DDD/1000 inhab. per day	Δ % 23-22				Δ % Average DDD cost
			Expenditure	DDD	Prices	Mix	
N- Central nervous system	**11.23**	**26.0**	**14.7**	**-5.2**	**-1.2**	**22.4**	**20.9**
Other medicines for the nervous system	3.26	0.2	62.4	39.4	-1.0	17.8	16.5
Other antipsychotics	2.80	3.0	-9.2	3.9	-9.3	-3.6	-12.5
Other antiepileptics	0.87	1.0	21.1	14.9	-12.7	20.7	5.4
Calcitonin gene-related peptide antagonists	0.55	0.3	16.5	20.3	-7.3	4.5	-3.1
DOPA and derivatives	0.54	0.2	2.5	-4.5	-0.2	7.5	7.3
Medicines used in opioid addiction	0.48	2.5	4.8	-6.4	-2.2	14.6	12.0
Diazepines, oxazepines, thiazepines and oxepins	0.36	3.5	0.9	-2.3	11.2	-7.1	3.3
Halogenated hydrocarbons	0.20	0.0	-2.4	0.3	-1.4	-1.4	-2.7
Amides	0.18	2.1	2.0	-3.9	0.8	5.3	6.1
Other general anesthetics	0.18	0.2	19.4	2.2	3.1	20.5	16.8
Other dopaminergic substances	0.17	0.1	13.8	14.1	0.0	-0.4	-0.3
Other antidepressants	0.16	0.8	>100	9.2	8.9	85.1	>100
Anilides	0.15	2.4	31.5	-42.1	>100	-34.7	>100
Indole derivatives	0.13	0.2	14.7	20.2	-1.4	-3.1	-4.5
Anticholinesterases	0.10	0.9	-10.4	-2.0	5.1	-13.0	-8.6
Other analgesics and antipyretics	0.10	<0.05	1.7	2.0	-0.2	-0.1	-0.3
C - Cardiovascular system	**8.18**	**18.9**	**11.1**	**5.2**	**-13.0**	**21.4**	**5.6**
Other lipid modifying agents	3.67	1.3	56.0	72.6	-3.9	-6.0	-9.7
Angiotensin II receptor blockers, other combinations	1.96	1.5	26.9	45.0	-12.5	0.0	-12.5
Antihypertensives for pulmonary arterial hypertension	1.48	0.1	7.8	4.4	-4.8	8.4	3.2
Other cardiac preparations	0.19	1.2	-84.8	-47.6	-44.3	-48.0	-71.0
Vasopressin antagonists	0.16	<0.05	-7.3	17.8	-22.2	1.2	-21.3
Adrenergics and dopaminergics	0.16	0.8	15.9	-16.9	11.9	24.7	39.6
V - Various	**6.19**	**3.5**	**-3.2**	**10.2**	**-2.6**	**-9.8**	**-12.2**
Radiological contrast media water-soluble, nephrotropic, low osmolar radiological contrast media	1.36	0.1	2.3	-2.2	2.1	2.4	4.6
Antidotes	1.18	0.1	0.1	-6.3	-4.0	11.2	6.8
Iron chelating agents	0.53	0.1	-49.3	-4.2	-4.7	-44.4	-47.0
Other diagnostic radiopharmaceuticals for cancer detection	0.53	<0.05	11.8	7.5	-1.6	5.7	4.0
Paramagnetic contrast agents	0.46	<0.05	2.2	2.3	-0.2	0.0	-0.1
Pharmaceuticals for treatment of hyperkalemia and hyperphosphatemia	0.45	0.3	70.0	28.5	0.9	31.2	32.3

continued

Table 3.17 - *continued*

ATC 1st level ATC 4th level	Gross per capita expenditure	DDD/1000 inhab. per day	Δ % 23-22				Δ % Average DDD cost
			Expenditure	DDD	Prices	Mix	
Detoxifying substances for cytostatic treatments	0.27	0.2	-10.8	2.3	1.2	-13.9	-12.8
Various therapeutic radiopharmaceuticals	0.23	<0.05	-17.6	-7.6	-19.5	10.7	-10.8
Iodine-123I compounds	0.20	<0.05	15.4	16.7	0.1	-1.3	-1.1
Various thyroid diagnostic radiopharmaceuticals	0.17	<0.05	39.3	31.7	9.2	-3.2	5.7
Allergenic extracts	0.16	0.2	18.3	13.7	-7.6	12.7	4.1
Other diagnostics	0.13	<0.05	16.4	3.3	2.2	10.3	12.7
Solvents and thinners, including cleaning solutions	0.11	2.4	-5.0	11.0	-12.6	-2.1	-14.4
M - Musculo-skeletal system	**5.90**	**7.1**	**29.6**	**11.5**	**-1.6**	**18.1**	**16.2**
Other drugs for musculoskeletal system disorders	2.85	<0.05	23.5	10.4	0.0	11.8	11.8
Other drugs acting on bone structure and mineralization	2.44	5.2	43.8	14.5	-4.0	30.7	25.6
Other muscle relaxants with peripheral action	0.30	<0.05	20.3	16.3	3.9	-0.5	3.4
D - Dermatologicals	**4.29**	**8.7**	**36.9**	**-0.6**	**0.7**	**36.7**	**37.7**
Substances for dermatitis, excluding corticosteroids	3.80	0.4	41.2	36.8	0.2	3.0	3.2
Biguanides and amidines	0.14	1.3	25.7	3.4	5.0	15.9	21.6
H - Systemic hormonal preparations, excl. sex hormones	**4.09**	**5.2**	**-5.2**	**-0.5**	**-4.6**	**-0.2**	**-4.7**
Somatostatin and analogues	1.43	0.2	-12.0	2.9	-9.6	-5.4	-14.5
Somatropin and somatropin agonists	1.10	0.3	-5.3	-2.7	-2.8	0.0	-2.6
Other antiparathyroid substances	0.55	0.4	-1.5	3.2	-2.0	-2.6	-4.5
Glucocorticoids	0.42	3.7	7.4	-1.8	3.1	6.0	9.3
S-Sensory organs	**3.04**	**1.8**	**-7.5**	**-3.7**	**-12.9**	**10.2**	**-4.0**
Antineovascularization substances	2.15	0.1	-12.2	-12.1	-18.6	22.9	0.0
Corticosteroids, not in	0.53	0.3	13.8	8.2	6.4	-1.1	5.2
Other ophthalmological drugs	0.19	0.1	-9.1	10.2	0.8	-18.1	-17.5
G - Genito-urinary system and sex hormones	**1.48**	**3.2**	**13.8**	**13.8**	**-11.7**	**13.4**	**0.1**
Gonadotropins	1.07	0.1	17.3	-4.9	-17.7	49.9	23.3
Prostaglandins	0.11	<0.05	8.3	-11.1	3.3	17.8	21.8
P - Antiparasitic, insecticide and repellent pharmaceuticals	**0.04**	**<0,05**	**38.2**	**192.1**	**-2.2**	**-51.8**	**-52.7**

Table 3.18 2023 expenditure, consumption and average cost per day of therapy for medicines supplied by public health facilities: most prescribed active ingredients by ATC 1st level (up to 75% of the category expenditure)

ATC 1st level Substances	NHS per capita expenditure	%*	Δ % 23-22	DDD/1000 inhab. per day	%*	Δ % 23-22	Average DDD cost	Δ % 23-22
L- Antineoplastic and immunomodulating agents	**120.47**		**6.6**	**13.5**		**9.9**	**24.43**	**-3.0**
pembrolizumab	7.76	6.4	3.0	0.2	1.8	8.3	87.70	-4.9
daratumumab	7.75	6.4	17.2	0.3	1.9	32.4	83.48	-11.5
nivolumab	3.78	3.1	14.5	0.1	0.7	22.5	109.12	-6.5
ibrutinib	3.40	2.8	-0.8	0.1	0.6	2.8	119.24	-3.5
osimertinib	2.94	2.4	3.6	0.1	0.5	11.6	130.71	-7.2
ocrelizumab	2.68	2.2	19.7	0.2	1.2	21.0	44.72	-1.2
ustekinumab	2.60	2.2	13.9	0.5	3.7	16.4	14.11	-2.1
enzalutamide	2.52	2.1	25.2	0.1	0.8	32.0	65.62	-5.2
ruxolitinib	2.36	2.0	12.8	0.1	0.4	12.0	111.23	0.6
pertuzumab	2.32	1.9	-11.5	0.1	0.4	-11.5	105.55	0.0
secukinumab	2.12	1.8	4.9	0.2	1.5	6.4	28.95	-1.4
dimethyl fumarate	2.11	1.8	-18.0	0.2	1.7	1.5	25.57	-19.3
nintedanib	2.05	1.7	28.9	0.1	0.5	30.1	91.01	-0.9
eculizumab	2.01	1.7	0.3	<0.05	0.1	2.8	710.85	-2.5
natalizumab	1.81	1.5	-4.4	0.1	0.8	4.4	45.83	-8.4
ribociclib	1.71	1.4	22.0	0.1	0.5	22.2	67.98	-0.2
palbociclib	1.52	1.3	-7.7	0.1	0.5	-9.6	67.13	2.1
fingolimod	1.48	1.2	-29.2	0.1	0.7	-12.3	43.23	-19.2
vedolizumab	1.46	1.2	9.1	0.1	1.0	11.8	30.18	-2.4
ixekizumab	1.41	1.2	14.5	0.1	0.9	14.5	30.31	0.1
adalimumab	1.36	1.1	-6.2	0.9	6.3	9.6	4.37	-14.4
venetoclax	1.34	1.1	28.8	<0.05	0.2	31.3	155.82	-1.9
olaparib	1.29	1.1	14.2	<0.05	0.2	15.2	127.99	-0.8
atezolizumab	1.28	1.1	26.9	<0.05	0.3	37.1	82.43	-7.5
canakinumab	1.24	1.0	16.2	<0.05	0.2	21.3	141.56	-4.2
teriflunomide	1.23	1.0	19.9	0.1	1.0	27.3	24.72	-5.8
dabrafenib	1.14	0.9	-2.3	<0.05	0.2	-2.1	105.57	-0.1
abemaciclib	1.13	0.9	49.1	0.1	0.4	76.2	52.10	-15.4
etanercept	1.11	0.9	-8.2	0.3	2.4	7.2	9.38	-14.3
trastuzumab emtansine	1.10	0.9	-14.5	<0.05	0.1	-14.5	152.80	0.0
triptorelin	1.10	0.9	8.9	1.1	8.3	8.6	2.70	0.2
alectinib	1.10	0.9	3.3	<0.05	0.2	15.7	141.40	-10.8
pomalidomide	1.09	0.9	5.9	<0.05	0.1	13.9	225.52	-7.0
leuprorelin	1.09	0.9	4.2	0.2	1.5	9.5	15.20	-4.8
apalutamide	1.05	0.9	>100	0.1	0.4	>100	56.06	-9.7
nilotinib	1.01	0.8	-10.3	<0.05	0.2	-3.1	91.13	-7.4
guselkumab	0.99	0.8	43.7	0.1	0.8	43.7	24.39	0.0
acalabrutinib	0.98	0.8	>100	<0.05	0.1	>100	137.34	1.7
axicabtagene ciloleucel^	0.96	0.8	>100	<0.05	0.0	27.8	282,923.31	70.7
risankizumab	0.95	0.8	41.3	0.1	0.7	49.1	26.99	-5.2
abatacept	0.91	0.8	-22.9	0.1	0.5	10.1	34.64	-30.0
tocilizumab	0.91	0.8	0.5	0.1	0.8	9.6	22.18	-8.3

continued

Table 3.18 - *continued*

ATC 1st level Substances	NHS per capita expenditure	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
ravulizumab	0.91	0.8	>100	<0.05	0.0	>100	548.33	-9.7
brentuximab vedotin	0.86	0.7	15.2	<0.05	0.1	15.2	293.24	0.0
tacrolimus	0.84	0.7	1.9	0.4	2.9	4.2	5.88	-2.2
cladribine	0.83	0.7	4.0	<0.05	0.4	3.9	46.85	0.1
golimumab	0.81	0.7	-7.8	0.1	0.9	-0.9	18.19	-7.0
interferon beta 1a	0.80	0.7	-19.5	0.2	1.5	-18.2	10.60	-1.6
cabozantinib	0.77	0.6	24.4	<0.05	0.1	27.7	135.94	-2.6
cemiplimab	0.75	0.6	16.1	<0.05	0.1	42.7	107.94	-18.6
apremilast	0.71	0.6	8.2	0.1	0.6	8.2	22.63	0.0
carfilzomib	0.71	0.6	12.7	<0.05	0.1	26.5	117.56	-10.9
niraparib	0.70	0.6	19.7	<0.05	0.1	19.8	153.69	0.0
ipilimumab	0.68	0.6	19.9	<0.05	0.0	23.0	313.61	-2.5
everolimus	0.67	0.6	4.9	0.2	1.2	4.8	11.06	0.0
trametinib	0.67	0.6	-3.6	<0.05	0.2	-3.6	64.30	0.0
B - Blood and blood-forming organs	**36.76**		**7.6**	**54.7**		**3.5**	**1.84**	**4.0**
apixaban	3.80	10.3	21.5	6.2	11.3	21.8	1.68	-0.2
rivaroxaban	3.47	9.4	6.8	6.0	10.9	5.1	1.59	1.6
edoxaban	2.68	7.3	21.9	4.2	7.6	23.6	1.76	-1.3
enoxaparin	1.91	5.2	6.1	6.1	11.2	7.6	0.85	-1.5
emicizumab	1.91	5.2	20.6	<0.05	0.0	20.5	683.35	0.0
dabigatran	1.23	3.4	-2.4	2.4	4.4	-1.5	1.42	-0.9
epoetin alfa	1.21	3.3	4.1	2.7	5.0	9.6	1.21	-5.1
electrolytes for intravenous solutions	1.09	3.0	13.4	6.7	12.2	0.6	0.45	12.8
efmoroctocog alfa	1.05	2.9	-1.7	<0.05	0.0	-1.7	357.07	0.0
eltrombopag	1.04	2.8	10.6	0.1	0.1	10.6	49.35	0.0
albutrepenonacog alfa	0.93	2.5	3.7	<0.05	0.0	12.0	979.51	-7.4
ticagrelor	0.91	2.5	-4.9	1.1	2.0	-2.8	2.28	-2.2
octocog alfa	0.88	2.4	-24.0	<0.05	0.0	-22.7	320.61	-1.6
darbepoetin alfa	0.87	2.4	-2.8	0.4	0.8	-1.2	5.78	-1.6
damoctocog alfa pegol	0.79	2.2	20.0	<0.05	0.0	20.1	329.77	-0.1
carboxymaltose iron	0.73	2.0	92.9	0.1	0.2	96.9	22.14	-2.1
luspatercept	0.66	1.8	56.0	<0.05	0.0	55.7	107.80	0.2
pegylated turoctocog alfa	0.62	1.7	28.7	<0.05	0.0	30.5	253.75	-1.4
parenteral nutrition solutions	0.59	1.6	-4.2	0.1	0.2	-37.4	14.96	52.9
caplacizumab	0.50	1.4	-9.2	<0.05	0.0	-9.4	3402.90	0.2
lanadelumab	0.48	1.3	36.9	<0.05	0.0	37.0	555.46	-0.1
hypertonic solutions for peritoneal dialysis	0.47	1.3	6.4	0.2	0.3	15.1	8.37	-7.5
J- General antimicrobials for systemic use	**35.28**		**5.3**	**6.1**		**5.5**	**15.72**	**-0.2**
emtricitabine/tenofovir alafenamide/bictegravir	2.68	7.6	17.5	0.4	6.0	17.5	19.96	0.0
adjuvanted recombinant varicella zoster virus vaccine	2.10	5.9	66.6	<0.05	0.3	41.0	321.38	18.2
dolutegravir/lamivudine	1.98	5.6	20.6	0.3	5.3	20.6	16.60	0.0

continued

Table 3.18 - *continued*

ATC 1st level Substances	NHS per capita expenditure	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
human papillomavirus vaccine (human types 6, 11, 16, 18, 31, 33, 45, 52, 58)	1.64	4.6	13.6	0.1	1.1	13.5	69.37	0.1
remdesivir	1.55	4.4	-22.8	<0.05	0.2	-17.9	356.96	-5.9
meningococcal group B (MenB) vaccine	1.46	4.1	8.7	0.1	1.0	7.8	62.66	0.8
tetravalent influenza vaccine (surface antigen, adjuvanted)	1.40	4.0	4.8	0.3	4.1	3.9	15.00	0.9
human normal immunoglobulin for extravascular administration	1.32	3.7	9.6	<0.05	0.1	-6.1	530.97	16.8
emtricitabine/rilpivirine/ tenofovir alafenamide	1.02	2.9	-22.8	<0.05	2.5	-16.5	17.96	-7.5
human normal immunoglobulin for intravascular administration	0.98	2.8	32.3	<0.05	0.1	21.3	385.38	9.0
amphotericin B	0.85	2.4	3.2	<0.05	0.4	3.3	101.55	0.0
inactivated, split virus tetravalent influenza vaccine	0.76	2.2	-23.2	0.2	3.6	-31.3	9.50	11.8
dolutegravir	0.75	2.1	-7.3	0.1	2.0	-7.3	16.42	0.0
emtricitabine/tenofovir alafenamide/ darunavir/cobicistat	0.72	2.0	-10.3	0.1	1.5	-10.3	21.85	0.0
measles/mumps/rubella/ varicella live attenuated vaccine	0.66	1.9	7.7	<0.05	0.6	6.8	48.02	0.9
sofosbuvir/velpatasvir	0.65	1.9	6.8	<0.05	0.4	6.8	71.91	0.0
glecaprevir/pibrentasvir	0.61	1.7	0.3	<0.05	0.3	1.1	107.12	-0.7
dolutegravir/rilpivirine	0.60	1.7	4.9	0.1	1.5	4.9	18.30	0.0
dolutegravir/abacavir/ lamivudine	0.57	1.6	-28.1	0.1	1.2	-28.1	21.48	0.0
20-valent pneumococcal vaccine	0.53	1.5	35.7	<0.05	0.5	34.2	48.99	1.1
hexavalent vaccine	0.50	1.4	-4.6	0.1	0.9	-0.8	25.51	-3.8
palivizumab	0.50	1.4	7.8	<0.05	0.0	7.6	810.07	0.2
piperacillin/tazobactam	0.46	1.3	-7.4	0.2	2.6	6.5	7.73	-13.1
13-valent pneumococcal vaccine	0.44	1.2	-38.4	<0.05	0.4	-38.6	48.84	0.3
15-valent pneumococcal vaccine	0.42	1.2	>100	<0.05	0.4	>100	45.84	0.0
ceftazidime/avibactam	0.40	1.1	1.3	<0.05	0.1	1.3	190.48	0.0
cefiderocol	0.38	1.1	6.4	<0.05	0.0	6.3	549.94	0.0
isavuconazole	0.37	1.0	13.4	<0.05	0.2	19.3	100.27	-4.9
letermovir	0.37	1.0	16.1	<0.05	0.0	12.2	353.52	3.5

continued

Table 3.18 - *continued*

ATC 1st level Substances	NHS per capita expenditure	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
A - Gastrointestinal system and metabolism	**25.66**		**13.7**	**43.7**		**13.0**	**1.61**	**0.6**
semaglutide	3.15	12.3	84.2	2.9	6.5	96.7	3.03	-6.4
dulaglutide	3.04	11.9	11.1	4.1	9.3	18.3	2.05	-6.1
dapagliflozin	1.57	6.1	70.1	3.6	8.4	81.3	1.18	-6.2
insulin glargine	1.48	5.8	-1.1	4.5	10.4	-0.3	0.89	-0.8
agalsidase alfa	1.41	5.5	-0.7	<0.05	0.0	9.9	960.53	-9.6
agalsidase beta	1.11	4.3	22.7	<0.05	0.0	22.7	483.63	0.0
empagliflozin	1.04	4.0	69.9	2.1	4.7	60.8	1.37	5.7
insulin degludec/liraglutide	0.87	3.4	24.5	0.7	1.6	34.0	3.46	-7.1
imiglucerase	0.85	3.3	8.4	<0.05	0.0	8.4	1,096.50	0.0
agalsidase alfa	0.76	3.0	-5.8	<0.05	0.0	-2.8	1,625.02	-3.1
dapagliflozin/metformin	0.63	2.5	11.2	1.5	3.3	18.3	1.18	-6.0
linagliptin	0.62	2.4	7.0	1.6	3.7	11.6	1.06	-4.1
insulin degludec	0.53	2.1	-23.0	1.4	3.1	-6.8	1.06	-17.4
migalastat	0.47	1.8	17.6	<0.05	0.0	22.3	447.75	-3.8
empagliflozin/metformin	0.45	1.8	26.5	1.2	2.7	30.2	1.07	-2.8
idursulfase	0.42	1.6	-14.5	<0.05	0.0	4.3	2,264.25	-18.0
eliglustat	0.41	1.6	7.8	<0.05	0.0	8.0	621.79	-0.1
linagliptin/empagliflozin	0.39	1.5	69.8	0.8	1.8	74.5	1.34	-2.7
obeticholic acid	0.38	1.5	24.8	<0.05	0.0	25.2	80.97	-0.3
R- Respiratory system	**12.55**		**21.1**	**2.5**		**8.9**	**13.98**	**11.2**
elexacaftor/tezacaftor/ivacaftor	4.83	38.4	38.1	<0.05	1.9	38.1	289.31	0.0
ivacaftor	3.73	29.7	22.7	<0.05	1.0	21.9	431.86	0.7
omalizumab	1.19	9.5	10.2	0.1	5.3	12.6	24.82	-2.1
mepolizumab	1.17	9.3	32.3	0.1	5.0	52.4	26.00	-13.2
benralizumab	0.85	6.8	22.0	0.1	3.3	22.0	28.98	0.0
N- Central nervous system	**11.23**		**15.0**	**26.0**		**-4.9**	**1.18**	**20.9**
tafamidis	2.09	18.6	85.0	0.1	0.4	95.4	61.20	-5.4
aripiprazole	1.26	11.2	8.8	1.2	4.7	4.3	2.81	4.3
paliperidone	1.22	10.9	-23.2	0.9	3.5	4.3	3.72	-26.3
patisiran	0.89	7.9	33.9	<0.05	0.0	33.9	516.03	0.0
levodopa/carbidopa	0.52	4.6	3.4	0.1	0.4	2.2	12.81	1.2
methadone	0.27	2.4	-7.5	2.1	8.2	-8.3	0.35	0.8
risperidon	0.27	2.4	-6.1	0.7	2.7	0.7	1.05	-6.8
cannabidiol	0.21	1.9	66.5	<0.05	0.0	64.0	48.28	1.5
galcanezumab	0.20	1.8	15.4	0.1	0.4	47.6	5.33	-21.8
fremanezumab	0.18	1.6	52.4	0.1	0.3	52.5	7.01	0.0
erenumab	0.17	1.5	-5.3	0.1	0.5	-5.8	3.79	0.5
quetiapine	0.17	1.5	7.5	1.5	5.6	-3.1	0.32	10.9
opicapone	0.16	1.5	15.9	0.1	0.5	15.9	3.23	0.0
paracetamol	0.15	1.3	31.7	2.4	9.3	-41.9	0.16	126.8
sevoflurane	0.13	1.2	2.5	<0.05	0.0	5.9	57.01	-3.2

continued

Table 3.18 - *continued*

ATC 1st level Substances	NHS per capita expenditure	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
levetiracetam	0.13	1.2	11.4	0.5	1.9	12.2	0.76	-0.7
perampanel	0.13	1.1	14.8	0.1	0.3	15.1	4.58	-0.2
lurasidone	0.13	1.1	15.5	0.2	0.7	20.8	1.99	-4.4
olanzapine	0.12	1.1	0.9	1.6	6.3	-1.8	0.20	2.8
propofol	0.12	1.0	29.7	0.2	0.8	7.3	1.62	20.9
C - Cardiovascular system	**8.18**		**11.4**	**18.9**		**5.5**	**1.18**	**5.6**
valsartan/sacubitril	1.96	24.0	27.2	1.5	8.0	45.4	3.57	-12.5
evolocumab	1.60	19.6	35.3	0.4	2.1	45.5	11.13	-7.0
alirocumab	1.46	17.8	48.8	0.6	2.9	62.4	7.18	-8.4
macitentan	1.04	12.8	4.2	<0.05	0.2	4.2	87.71	0.0
inclisiran	0.34	4.1	>100	0.1	0.6	>100	8.84	0.0
V - Various	**6.19**		**-2.9**	**3.5**		**10.6**	**4.85**	**-12.2**
sugammadex	0.89	14.4	-7.5	<0.05	1.0	8.2	69.54	-14.5
iomeprol	0.53	8.6	-2.5	<0.05	0.5	-4.2	76.83	1.8
deferasirox	0.44	7.1	-53.7	<0.05	0.9	-7.0	37.40	-50.2
fluoride deoxyglucose (18F)	0.41	6.7	16.4	<0.05	0.1	7.8	460.32	8.0
Iodinaxol	0.25	4.1	6.9	<0.05	0.2	4.3	79.57	2.5
gadobutrol	0.23	3.7	5.2	<0.05	0.2	5.2	77.79	0.0
lutetium oxodotreotide (177Lu)	0.20	3.2	-17.8	<0.05	0.0	6.3	12,858.52	-22.7
iodine ioflupane (123I)	0.20	3.2	15.7	<0.05	0.0	17.0	808.09	-1.1
iopromide	0.18	2.9	-2.0	<0.05	0.2	-10.0	59.77	8.8
andexanet alfa	0.18	2.9	63.5	<0.05	0.0	63.7	3515.33	-0.1
sodium zirconium cyclosilicate	0.18	2.9	>100	0.1	1.6	>100	8.96	6.7
tecnetium pertecnetate (99 mTc)	0.14	2.3	31.2	<0.05	0.0	36.6	372.16	-4.0
iobitridol	0.13	2.1	7.0	<0.05	0.2	-3.0	51.96	10.3
iopamidol	0.13	2.0	4.0	<0.05	0.3	-0.2	28.39	4.2
rasburicase	0.11	1.8	-28.6	<0.05	0.0	-32.9	892.39	6.3
ioexol	0.11	1.7	20.3	<0.05	0.2	5.8	37.28	13.7
indocyanine green	0.10	1.6	17.2	<0.05	0.0	17.8	162.57	-0.5
gadoxetic acid	0.09	1.4	-0.7	<0.05	0.0	-0.8	176.01	0.1
calcium levofolinate	0.09	1.4	-7.3	0.1	3.7	0.1	1.79	-7.4
thyrotropin	0.08	1.4	11.2	<0.05	0.0	11.2	339.74	0.0
M - Musculo-skeletal system	**5.90**		**30.0**	**7.1**		**11.8**	**2.29**	**16.2**
denosumab	1.62	27.4	16.2	5.1	72.8	14.4	0.86	1.6
risdiplam	1.24	20.9	72.0	<0.05	0.1	65.8	397.30	3.8
nusinersen	1.09	18.5	-2.2	<0.05	0.1	-0.7	396.05	-1.5
ataluren	0.38	6.4	14.1	<0.05	0.0	19.2	1490.27	-4.3
vosoritide	0.37	6.3	>100	<0.05	0.0	>100	455.84	-1.5

continued

Table 3.18 - *continued*

ATC 1st level Substances	NHS per capita expenditure	%	Δ % 23-22	DDD/1000 inhab. per day	%	Δ % 23-22	Average DDD cost	Δ % 23-22
D - Dermatologicals	**4.29**		**37.3**	**8.7**		**-0.3**	**1.35**	**37.7**
dupilumab	3.65	85.0	36.6	0.4	4.1	36.6	28.03	0.0
tralokinumab	0.14	3.3	>100	<0.05	0.0	>100	300.94	37.5
chlorhexidine/isopropyl alcohol	0.10	2.3	37.4	0.1	0.6	33.9	5.06	2.6
povidone iodine	0.07	1.6	11.6	0.8	9.1	-11.6	0.24	26.3
silver sulfadiazine	0.06	1.4	-0.8	0.7	7.7	0.3	0.24	-1.2
H - Systemic hormonal preparations, excl. sex hormones	**4.09**		**-4.9**	**5.2**		**-0.2**	**2.17**	**-4.7**
somatropin	1.09	26.6	-5.6	0.3	5.2	-2.6	11.08	-3.0
octreotide	0.73	17.8	0.3	0.1	2.1	-0.7	18.73	1.0
lanreotide	0.53	12.9	-28.4	0.1	2.4	6.9	11.77	-33.0
etelcalcetide	0.48	11.8	12.4	0.1	2.6	12.4	10.03	0.0
pegvisomant	0.38	9.2	-9.0	<0.05	0.3	-4.9	65.37	-4.3
S-Sensory organs	**3.04**		**-7.3**	**1.8**		**-3.4**	**4.52**	**-4.0**
aflibercept	1.42	46.6	-4.3	<0.05	0.5	17.8	400.79	-18.7
ranibizumab	0.52	17.2	-34.0	0.1	4.5	-15.0	17.39	-22.4
dexamethasone	0.52	17.2	17.7	0.3	15.8	9.3	4.90	7.7
brolucizumab	0.20	6.5	28.2	<0.05	0.1	28.0	401.52	0.1
voretigene neparvovec	0.11	3.7	-15.1	<0.05	0.0	-15.1	297000.00	0.0
G - Genito-urinary system and sex hormones	**1.48**		**14.2**	**3.2**		**14.1**	**1.28**	**0.1**
follitropin alfa/lutropin alfa	0.39	26.1	75.9	<0.05	0.1	52.9	335.55	15.1
follitropin alfa from recombinant DNA	0.33	22.2	15.1	0.1	1.7	20.6	16.40	-4.6
follitropin beta	0.11	7.7	30.9	<0.05	0.4	30.7	27.21	0.2
menotropin	0.11	7.1	-46.2	<0.05	0.6	-50.4	14.70	8.5
testosterone	0.07	4.7	5.4	0.2	5.3	23.8	1.13	-14.9
dinoprostone	0.07	4.7	-15.3	<0.05	1.1	-14.5	5.29	-1.0
mifepristone	0.05	3.5	11.0	<0.05	0.2	9.0	20.03	1.8
P - Antiparasitic, insecticide and repellent pharmaceuticals	**0.04**		**38.6**	**<0,05**		**192.9**	**3.57**	**-52.7**
atovaquone	0.02	51.0	16.6	<0.05	17.1	28.3	10.62	-9.1
permethrin	0.01	21.8	38.1	<0.05	7.7	37.3	10.06	0.6
atovaquone/proguanil	<0.005	7.4	99.7	<0.05	5.8	93.0	4.54	3.5
ivermectin	<0.005	7.4	>100	<0.05	1.2	>100	21.19	1.6
hydroxychloroquine	<0.005	3.9	>100	<0.05	37.8	0.0	0.37	785.8

* percentage calculated on overall expenditure
^ the change recorded in the average DDD cost in 2023 compared to 2022 due to the change in the methods of accounting for the expenditure of the drug that were subject to conditional reimbursement agreements, payment at result, which provided for the allocation and for the attribution of fractions of the cost of treatment over time following the verification of the maintenance of therapeutic success. Subsequently, the amendment provided for the revision of the negotiating agreement and for accounting the full cost of the infusion treatment.

Table 3.19 First thirty active ingredients purchased by public health facilities in terms of expenditure: comparison 2023-2022

ATC	Active ingredient	Expenditure *(million)*	%*	Expenditure *per capita*	Rank 2023	Rank 2022	Average DDD cost	Δ % 23-22	Average DDD cost under approved care regime
L	pembrolizumab	456.5	3.1	7.76	1	1	87.70	-4.9	—
L	daratumumab	456.2	3.1	7.75	2	2	83.48	-11.5	—
R	elexacaftor/tezacaftor/ivacaftor	284.0	1.9	4.83	3	3	289.31	0.0	—
B	apixaban	223.6	1.5	3.80	4	7	1.68	-0.2	3.8
L	nivolumab	222.4	1.5	3.78	5	5	109.12	-6.5	—
R	ivacaftor	219.4	1.5	3.73	6	8	431.86	0.7	—
D	dupilumab	214.5	1.4	3.65	7	11	28.03	0.0	83.6
B	rivaroxaban	204.1	1.4	3.47	8	6	1.59	1.6	4.3
L	ibrutinib	199.8	1.3	3.40	9	4	119.24	-3.5	—
A	semaglutide	185.6	1.2	3.15	10	27	3.03	-6.4	9.3
A	dulaglutide	179.0	1.2	3.04	11	10	2.05	-6.1	4.9
L	osimertinib	173.0	1.2	2.94	12	9	130.71	-7.2	—
L	ocrelizumab	157.9	1.1	2.68	13	17	44.72	-1.2	—
J	emtricitabine/tenofovir alafenamide/bictegravir	157.7	1.1	2.68	14	16	19.96	0.0	—
B	edoxaban	157.6	1.1	2.68	15	18	1.76	-1.3	4.6
L	ustekinumab	153.3	1.0	2.60	16	15	14.11	-2.1	—
L	enzalutamide	148.2	1.0	2.52	17	22	65.62	-5.2	—
L	ruxolitinib	139.2	0.9	2.36	18	19	111.23	0.6	—
L	pertuzumab	136.4	0.9	2.32	19	12	105.55	0.0	—
L	secukinumab	125.0	0.8	2.12	20	21	28.95	-1.4	—
L	dimethyl fumarate	124.5	0.8	2.11	21	13	25.57	-19.3	46.8
J	adjuvanted recombinant varicella zoster virus vaccine	123.4	0.8	2.10	22	48	321.38	18.2	—
N	tafamidis	123.2	0.8	2.09	23	61	61.20	-5.4	—
L	nintedanib	120.6	0.8	2.05	24	30	91.01	-0.9	—
L	eculizumab	118.5	0.8	2.01	25	24	710.85	-2.5	—
J	dolutegravir/lamivudine	116.4	0.8	1.98	26	29	16.60	0.0	—
C	valsartan/sacubitril	115.5	0.8	1.96	27	33	3.57	-12.5	7.2
B	enoxaparin	112.3	0.8	1.91	28	26	0.85	-1.5	2.2
B	emicizumab	112.3	0.8	1.91	29	32	683.35	0.0	1723.3
L	natalizumab	106.3	0.7	1.81	30	25	45.83	-8.4	—
	Total top 30	**5,366.1**	**33.1**	**105.07**			**0.96**	**13.1**	**0.34**
	Total	**16,193.2**	**100**	**275.16**			**3.90**	**3.1**	**0.40**

* Calculated on the total expenditure on medicines purchased by public health facilities

Table 3.20 First thirty active ingredients* with highest increase in expenditure relating to medicines purchased by public health facilities: comparison 2023-2022

ATC	Active ingredient	Expenditure *per capita*	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
L	ravulizumab	0.91	>100	<0.05	>100	548.33	-9.7
L	acalabrutinib	0.98	>100	<0.05	>100	137.34	1.7
L	axicabtagene ciloleucel^	0.96	>100	<0.05	27.8	282,923.31	70.7
L	apalutamide	1.05	>100	0.1	>100	56.06	-9.7
N	tafamidis	2.09	85.0	0.1	95.4	61.20	-5.4
A	semaglutide	3.15	84.2	2.9	96.7	3.03	-6.4
M	risdiplam	1.24	72.0	<0.05	65.8	397.30	3.8
A	dapagliflozin	1.57	70.1	3.6	81.3	1.18	-6.2
A	empagliflozin	1.04	69.9	2.1	60.8	1.37	5.7
J	adjuvanted recombinant varicella zoster virus vaccine	2.10	66.6	<0.05	41.0	321.38	18.2
L	abemaciclib	1.13	49.1	0.1	76.2	52.10	-15.4
C	alirocumab	1.46	48.8	0.6	62.4	7.18	-8.4
L	guselkumab	0.99	43.7	0.1	43.7	24.39	0.0
L	risankizumab	0.95	41.3	0.1	49.1	26.99	-5.2
R	elexacaftor/tezacaftor/ ivacaftor	4.83	38.1	<0.05	38.1	289.31	0.0
D	dupilumab	3.65	36.6	0.4	36.6	28.03	0.0
C	evolocumab	1.60	35.3	0.4	45.5	11.13	-7.0
N	patisiran	0.89	33.9	<0.05	33.9	516.03	0.0
J	human normal immunoglobulin for intravascular administration	0.98	32.3	<0.05	21.3	385.38	9.0
R	mepolizumab	1.17	32.3	0.1	52.4	26.00	-13.2
L	nintedanib	2.05	28.9	0.1	30.1	91.01	-0.9
L	venetoclax	1.34	28.8	<0.05	31.3	155.82	-1.9
C	valsartan/sacubitril	1.96	27.2	1.5	45.4	3.57	-12.5
L	atezolizumab	1.28	26.9	<0.05	37.1	82.43	-7.5
L	enzalutamide	2.52	25.2	0.1	32.0	65.62	-5.2
A	insulin degludec/liraglutide	0.87	24.5	0.7	34.0	3.46	-7.1
A	agalsidase beta	1.11	22.7	<0.05	22.7	483.63	0.0
R	ivacaftor	3.73	22.7	<0.05	21.9	431.86	0.7
L	ribociclib	1.71	22.0	0.1	22.2	67.98	-0.2
R	benralizumab	0.85	22.0	0.1	22.0	28.98	0.0
	Total top 30	**50.14**	**44.8**	**13.1**	**66.3**	**10.46**	**-12.9**
	Total	**275.16**	**8.5**	**194.9**	**5.2**	**3.90**	**3.1**

* selected among the top 100 active ingredients with highest per capita expenditure
^ the change recorded in the average DDD cost in 2023 compared to 2022 due to the change in the methods of accounting for the expenditure of the drug that were subject to conditional reimbursement agreements, payment at result, which provided for the allocation and for the attribution of fractions of the cost of treatment over time following the verification of the maintenance of therapeutic success. Subsequently, the amendment provided for the revision of the negotiating agreement and for accounting the full cost of the infusion treatment.

Table 3.21 First thirty active ingredients* with highest reduction in expenditure relating to medicines purchased by public health facilities: comparison 2023-2022

ATC	Active ingredient	Expenditure *per capita*	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22	Average DDD cost	Δ % 23-22
L	fingolimod	1.48	-29.2	0.1	-12.3	43.23	-19.2
B	octocog alfa	0.88	-24.0	<0.05	-22.7	320.61	-1.6
N	paliperidone	1.22	-23.2	0.9	4.3	3.72	-26.3
L	abatacept	0.91	-22.9	0.1	10.1	34.64	-30.0
J	emtricitabine/rilpivirine/ tenofovir alafenamide	1.02	-22.8	0.2	-16.5	17.96	-7.5
J	remdesivir	1.55	-22.8	<0.05	-17.9	356.96	-5.9
L	dimethyl fumarate	2.11	-18.0	0.2	1.5	25.57	-19.3
L	trastuzumab emtansine	1.10	-14.5	<0.05	-14.5	152.80	0.0
L	pertuzumab	2.32	-11.5	0.1	-11.5	105.55	0.0
L	nilotinib	1.01	-10.3	<0.05	-3.1	91.13	-7.4
L	etanercept	1.11	-8.2	0.3	7.2	9.38	-14.3
L	palbociclib	1.52	-7.7	0.1	-9.6	67.13	2.1
V	sugammadex	0.89	-7.5	<0.05	8.2	69.54	-14.5
L	adalimumab	1.36	-6.2	0.9	9.6	4.37	-14.4
H	somatropin	1.09	-5.6	0.3	-2.6	11.08	-3.0
B	ticagrelor	0.91	-4.9	1.1	-2.8	2.28	-2.2
L	natalizumab	1.81	-4.4	0.1	4.4	45.83	-8.4
S	aflibercept	1.42	-4.3	<0.05	17.8	400.79	-18.7
B	darbepoetin alfa	0.87	-2.8	0.4	-1.2	5.78	-1.6
B	dabigatran	1.23	-2.4	2.4	-1.5	1.42	-0.9
L	dabrafenib	1.14	-2.3	<0.05	-2.1	105.57	-0.1
M	nusinersen	1.09	-2.2	<0.05	-0.7	396.05	-1.5
B	efmoroctocog alfa	1.05	-1.7	<0.05	-1.7	357.07	0.0
A	insulin glargine	1.48	-1.1	4.5	-0.3	0.89	-0.8
L	ibrutinib	3.40	-0.8	0.1	2.8	119.24	-3.5
A	agalsidase alfa	1.41	-0.7	<0.05	9.9	960.53	-9.6
	Total active ingredients with highest reduction	**46.89**	**-7.7**	**12.5**	**0.3**	**10.24**	**-8.0**
	Total	**275.16**	**8.5**	**194.9**	**5.2**	**3.90**	**3.1**

* selected among the top 100 active ingredients with highest per capita expenditure

Table 3.22 First thirty active ingredients* by average cost per day of therapy for medicines purchased by public health facilities: comparison 2023-2022

ATC	Active ingredient	Average DDD cost	Δ % 23-22	Expenditure per capita	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22
L	axicabtagene ciloleucel^	282,923.3	70.7	0.96	>100	<0.05	27.8
A	imiglucerase	1,096.5	0.0	0.85	8.4	<0.05	8.4
B	albutrepenonacog alfa	979.5	-7.4	0.93	3.7	<0.05	12.0
A	agalsidase alfa	960.5	-9.6	1.41	-0.7	<0.05	9.9
L	eculizumab	710.9	-2.5	2.01	0.3	<0.05	2.8
B	emicizumab	683.4	0.0	1.91	20.6	<0.05	20.5
L	ravulizumab	548.3	-9.7	0.91	>100	<0.05	256.2
J	human normal immunoglobulin for extravascular administration	531.0	16.8	1.32	9.6	<0.05	-6.1
N	patisiran	516.0	0.0	0.89	33.9	<0.05	33.9
A	agalsidase beta	483.6	0.0	1.11	22.7	<0.05	22.7
R	ivacaftor	431.9	0.7	3.73	22.7	<0.05	21.9
S	aflibercept	400.8	-18.7	1.42	-4.3	<0.05	17.8
M	risdiplam	397.3	3.8	1.24	72.0	<0.05	65.8
M	nusinersen	396.1	-1.5	1.09	-2.2	<0.05	-0.7
J	human normal immunoglobulin for intravascular administration	385.4	9.0	0.98	32.3	<0.05	21.3
B	efmoroctocog alfa	357.1	0.0	1.05	-1.7	<0.05	-1.7
J	remdesivir	357.0	-5.9	1.55	-22.8	<0.05	-17.9
J	adjuvanted recombinant varicella zoster virus vaccine	321.4	18.2	2.10	66.6	<0.05	41.0
B	octocog alfa	320.6	-1.6	0.88	-24.0	<0.05	-22.7
L	brentuximab vedotin	293.2	0.0	0.86	15.2	<0.05	15.2
R	elexacaftor/tezacaftor/ivacaftor	289.3	0.0	4.83	38.1	<0.05	38.1
L	pomalidomide	225.5	-7.0	1.09	5.9	<0.05	13.9
L	venetoclax	155.8	-1.9	1.34	28.8	<0.05	31.3
L	trastuzumab emtansine	152.8	0.0	1.10	-14.5	<0.05	-14.5
L	canakinumab	141.6	-4.2	1.24	16.2	<0.05	21.3
L	alectinib	141.4	-10.8	1.10	3.3	<0.05	15.7
L	acalabrutinib	137.3	1.7	0.98	>100	<0.05	157.5
L	osimertinib	130.7	-7.2	2.94	3.6	0.1	11.6
L	olaparib	128.0	-0.8	1.29	14.2	<0.05	15.2
L	ibrutinib	119.2	-3.5	3.40	-0.8	0.1	2.8
	Total top 30	**259.6**	**-0.3**	**46.49**	**15.5**	**0.5**	**15.8**
	Total	**3.9**	**3.1**	**275.16**	**8.5**	**194.9**	**5.2**

* selected among the top 100 active ingredients with highest per capita expenditure
^ the change recorded in the average DDD cost in 2023 compared to 2022 due to the change in the methods of accounting for the expenditure of the drug that were subject to conditional reimbursement agreements, payment at result, which provided for the allocation and for the attribution of fractions of the cost of treatment over time following the verification of the maintenance of therapeutic success. Subsequently, the amendment provided for the revision of the negotiating agreement and for accounting the full cost of the infusion treatment.

Table 3.23 First thirty active ingredients* by average cost per day of therapy for medicines purchased by public health facilities^: comparison 2023-2022

ATC	Active ingredient	Average DDD cost	Δ % 23-22	Expenditure *per capita*	Δ % 23-22	DDD/1000 inhab. per day	Δ % 23-22
B	electrolytes for intravenous solutions	0.45	12.8	1.09	13.4	6.7	0.6
B	enoxaparin	0.85	-1.5	1.91	6.1	6.1	7.6
M	denosumab	0.86	1.6	1.62	16.2	5.1	14.4
A	insulin glargine	0.89	-0.8	1.48	-1.1	4.5	-0.3
A	dapagliflozin	1.18	-6.2	1.57	70.1	3.6	81.3
B	epoetin alfa	1.21	-5.1	1.21	4.1	2.7	9.6
A	empagliflozin	1.37	5.7	1.04	69.9	2.1	60.8
B	dabigatran	1.42	-0.9	1.23	-2.4	2.4	-1.5
B	rivaroxaban	1.59	1.6	3.47	6.8	6.0	5.1
B	apixaban	1.68	-0.2	3.80	21.5	6.2	21.8
B	edoxaban	1.76	-1.3	2.68	21.9	4.2	23.6
A	dulaglutide	2.05	-6.1	3.04	11.1	4.1	18.3
B	ticagrelor	2.28	-2.2	0.91	-4.9	1.1	-2.8
L	triptorelin	2.70	0.2	1.10	8.9	1.1	8.6
N	aripiprazole	2.81	4.3	1.26	8.8	1.2	4.3
A	semaglutide	3.03	-6.4	3.15	84.2	2.9	96.7
A	insulin degludec/liraglutide	3.46	-7.1	0.87	24.5	0.7	34.0
C	valsartan/sacubitril	3.57	-12.5	1.96	27.2	1.5	45.4
N	paliperidone	3.72	-26.3	1.22	-23.2	0.9	4.3
L	adalimumab	4.37	-14.4	1.36	-6.2	0.9	9.6
B	darbepoetin alfa	5.78	-1.6	0.87	-2.8	0.4	-1.2
L	tacrolimus	5.88	-2.2	0.84	1.9	0.4	4.2
C	alirocumab	7.18	-8.4	1.46	48.8	0.6	62.4
L	etanercept	9.38	-14.3	1.11	-8.2	0.3	7.2
H	somatropin	11.08	-3.0	1.09	-5.6	0.3	-2.6
C	evolocumab	11.13	-7.0	1.60	35.3	0.4	45.5
L	ustekinumab	14.11	-2.1	2.60	13.9	0.5	16.4
J	tetravalent influenza vaccine (surface antigen, inactivated, adjuvanted)	15.00	0.9	1.40	4.8	0.3	3.9
L	leuprorelin	15.20	-4.8	1.09	4.2	0.2	9.5
J	dolutegravir/lamivudine	16.60	0.0	1.98	20.6	0.3	20.6
	Total top 30	**2.03**	**-1.1**	**50.02**	**14.7**	**67.6**	**16.0**
	Total	**3.90**	**3.1**	**275.16**	**8.5**	**194.9**	**5.2**

* selected among the top 100 active ingredients with highest per capita expenditure

Table 3.24 First thirty active ingredients purchased by public health facilities in terms of consumption: comparison 2023-2022

ATC	Active ingredient	DDD/1000 inhab. per day	Δ % 23-22	Rank 2023	Rank 2022	Expenditure per capita	Δ % 23-22	Average DDD cost	Δ % 23-22	Average DDD cost under approved care regime
B	electrolytes for intravenous solutions	6.7	0.6	1	1	1.09	13.4	0.45	12.8	1.75
B	apixaban	6.2	21.8	2	6	3.80	21.5	1.68	-0.2	3.82
B	enoxaparin	6.1	7.6	3	3	1.91	6.1	0.85	-1.5	2.16
B	rivaroxaban	6.0	5.1	4	2	3.47	6.8	1.59	1.6	4.31
B	clopidogrel	5.4	-2.0	5	4	0.10	-7.2	0.05	-5.3	0.55
B	cyanocobalamin	5.3	0.8	6	5	0.01	0.6	0.00	-0.3	0.02
M	denosumab	5.1	14.4	7	8	1.62	16.2	0.86	1.6	1.80
A	insulin glargine	4.5	-0.3	8	7	1.48	-1.1	0.89	-0.8	1.94
C	furosemide	4.4	0.9	9	9	0.05	4.2	0.03	3.3	0.08
B	edoxaban	4.2	23.6	10	12	2.68	21.9	1.76	-1.3	4.63
A	dulaglutide	4.1	18.3	11	11	3.04	11.1	2.05	-6.1	4.88
A	dapagliflozin	3.6	81.3	12	18	1.57	70.1	1.18	-6.2	2.22
A	cholecalciferol	3.1	4.6	13	13	0.01	5.5	0.01	0.8	0.08
A	semaglutide	2.9	96.7	14	27	3.15	84.2	3.03	-6.4	9.34
B	epoetin alfa	2.7	9.6	15	15	1.21	4.1	1.21	-5.1	12.56
D	sodium hypochlorite	2.7	4.8	16	14	0.04	7.7	0.04	2.8	0.32
N	paracetamol	2.4	-41.9	17	10	0.15	31.8	0.16	>100	1.62
B	dabigatran	2.4	-1.5	18	16	1.23	-2.4	1.42	-0.9	4.10
N	methadone	2.1	-8.3	19	17	0.27	-7.5	0.35	0.8	1.25
A	empagliflozin	2.1	60.8	20	33	1.04	69.9	1.37	5.7	2.51
V	sodium chloride	2.0	11.9	21	19	0.06	15.6	0.08	3.2	0.59
A	pantoprazole	1.8	8.8	22	20	0.15	11.4	0.22	2.4	0.42
C	ramipril	1.7	4.7	23	22	0.01	46.4	0.01	39.8	0.09
N	olanzapine	1.6	-1.8	24	21	0.12	0.9	0.20	2.8	1.37
A	linagliptin	1.6	11.6	25	28	0.62	7.0	1.06	-4.1	2.21
C	atorvastatin	1.6	0.1	26	23	0.00	69.4	0.00	69.2	0.25
N	lidocaine	1.5	-0.1	27	24	0.09	0.6	0.16	0.7	2.23
C	valsartan/ sacubitril	1.5	45.4	28	39	1.96	27.3	3.57	-12.5	7.21
A	dapagliflozin/ metformin	1.5	18.3	29	34	0.63	11.3	1.18	-6.0	2.00
N	quetiapine	1.5	-3.1	30	25	0.17	7.5	0.32	10.9	3.42
	Total top 30	**98.3**	**8.2**			**31.73**	**19.8**	**0.88**	**10.6**	**0.20**
	Total	**194.9**	**5.2**			**275.16**	**8.5**	**3.90**	**3.1**	**0.40**

Table 3.25 Top thirty active ingredients with the highest expenditure on medicines under approved care regime (A-NHS) and purchased by public health facilities: comparison 2023-2022

ATC	Active ingredient	Expenditure *(million)*	%*	Expenditure *per capita*	Rank 2023	Rank 2022	Average DDD cost	Δ % 23-22
L	pembrolizumab	456.5	1.8	7.76	1	1	87.70	-4.9
L	daratumumab	456.2	1.8	7.75	2	2	83.48	-11.5
R	elexacaftor/tezacaftor/ ivacaftor	284.0	1.1	4.83	3	8	289.31	0.0
C	atorvastatin	274.5	1.1	4.66	4	3	0.25	0.1
A	pantoprazole	274.1	1.1	4.66	5	4	0.41	-1.6
B	apixaban	241.1	0.9	4.10	6	10	1.75	-0.5
A	dulaglutide	240.7	0.9	4.09	7	6	2.41	-9.6
A	semaglutide	231.5	0.9	3.93	8	19	3.50	-13.4
L	nivolumab	222.4	0.9	3.78	9	11	109.12	-6.5
R	ivacaftor	219.4	0.8	3.73	10	13	431.86	0.7
B	enoxaparin	215.8	0.8	3.67	11	7	1.20	-5.9
D	dupilumab	214.5	0.8	3.65	12	17	28.03	0.0
B	rivaroxaban	205.9	0.8	3.50	13	12	1.60	1.6
L	ibrutinib	199.8	0.8	3.40	14	9	119.24	-3.5
A	cholecalciferol	198.6	0.8	3.37	15	5	0.08	-3.1
J	amoxicillin/clavulanic acid	186.8	0.7	3.17	16	16	1.35	1.0
L	osimertinib	173.0	0.7	2.94	17	14	130.71	-7.2
C	bisoprolol	172.1	0.7	2.93	18	15	0.59	-0.2
B	edoxaban	159.7	0.6	2.71	19	28	1.77	-1.5
L	ocrelizumab	157.9	0.6	2.68	20	26	44.72	-1.2
J	emtricitabine/tenofovir alafenamide/bictegravir	157.7	0.6	2.68	21	24	19.96	0.0
L	ustekinumab	153.3	0.6	2.60	22	23	14.11	-2.1
L	enzalutamide	148.2	0.6	2.52	23	37	65.62	-5.2
L	ruxolitinib	139.2	0.5	2.36	24	33	111.23	0.6
L	pertuzumab	136.4	0.5	2.32	25	18	105.55	0.0
C	valsartan/sacubitril	134.0	0.5	2.28	26	35	3.84	-16.1
C	ezetimibe/rosuvastatin	134.0	0.5	2.28	27	55	0.39	-0.9
R	formoterol/beclomethasone	133.9	0.5	2.28	28	21	1.47	-13.4
A	esomeprazole	131.6	0.5	2.24	29	25	0.38	-1.4
C	omega-3	130.8	0.5	2.22	30	30	2.23	-2.0
	Total top 30	**6,183.4**	**23.8**	**105.07**			**0.96**	**13.1**
	Total	**25,975.2**	**100.0**	**441.37**			**0.91**	**6.2**

Table 3.26 Top thirty most consumed active ingredients for medicines under approved care regime and purchased by public health facilities: comparison 2023-2022

ATC	Active ingredient	DDD/1000 inhab. per day	Δ % 23-22	Rank 2023	Rank 2022	Expenditure per capita	Δ % 23-22	Average DDD cost	Δ % 23-22
A	cholecalciferol	119.8	-14.2	1	1	3.37	-16.8	0.08	-3.1
C	ramipril	62.3	-1.1	2	2	1.90	-2.4	0.08	-1.4
C	atorvastatin	52.1	-0.4	3	3	4.66	-0.3	0.25	0.1
B	acetylsalicylic acid	47.3	0.9	4	4	1.21	0.7	0.07	-0.2
A	pantoprazole	31.2	1.9	5	5	4.66	0.3	0.41	-1.6
C	amlodipine	29.5	1.7	6	6	1.60	0.0	0.15	-1.7
C	furosemide	26.9	-2.9	7	7	0.72	-2.9	0.07	0.0
H	levothyroxine	23.8	3.6	8	9	1.48	6.3	0.17	2.6
A	metformin	23.3	-0.5	9	8	1.69	1.3	0.20	1.8
A	omeprazole	18.1	-2.2	10	10	2.13	-4.7	0.32	-2.6
C	olmesartan	18.0	7.8	11	13	2.07	7.9	0.31	0.1
C	nebivolol	17.4	2.4	12	12	1.59	2.2	0.25	-0.1
C	rosuvastatin	16.9	6.6	13	15	1.59	6.7	0.26	0.1
B	cyanocobalamin	16.7	-5.0	14	11	0.09	-5.0	0.02	0.0
A	esomeprazole	16.0	0.8	15	14	2.24	-0.6	0.38	-1.4
C	ezetimibe/ rosuvastatin	15.8	48.7	16	21	2.28	47.4	0.39	-0.9
C	bisoprolol	13.6	3.5	17	17	2.93	3.3	0.59	-0.2
A	lansoprazole	13.4	-6.5	18	16	2.03	-7.5	0.42	-1.1
G	tamsulosin	11.9	3.8	19	20	1.17	2.5	0.27	-1.2
B	clopidogrel	11.8	3.0	20	19	1.38	4.5	0.32	1.5
C	olmesartan/ amlodipine	11.0	11.4	21	24	1.62	11.2	0.40	-0.2
C	olmesartan/ hydrochlorothiazide	10.8	3.8	22	22	1.31	3.5	0.33	-0.3
C	simvastatin	10.8	-7.1	23	18	1.26	-7.4	0.32	-0.3
C	valsartan	10.7	4.8	24	23	0.72	5.2	0.18	0.4
G	alfuzosin	10.4	5.7	25	25	0.97	5.7	0.26	0.1
N	sertraline	10.3	5.8	26	26	0.87	5.5	0.23	-0.2
C	lercanidipine	9.5	0.8	27	27	0.77	0.5	0.22	-0.2
M	allopurinol	9.0	1.2	28	28	0.38	1.6	0.11	0.4
G	dutasteride	8.6	1.6	29	29	1.04	0.3	0.33	-1.3
B	enoxaparin	8.4	1.5	30	32	3.67	-4.5	1.20	-5.9
	Total top 30	**685.3**	**-1.4**			**53.39**	**0.7**	**0.21**	**2.1**
	Total	**1322.95**	**-0.1**			**441.37**	**5.3**	**0.91**	**6.2**

Table 3.27 Expenditure and consumption by group and sub-group of medicines supplied under approved care regime and purchased by public facilities

ATC 1st level Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Antineoplastic medicines	**2.96**	**4.6**	**1.76**	**78.16**	**7.0**	**30.41**	**4773.9**	**249.9**	**45.4**	**2.5**
Monoclonal antibodies inhibiting immune check points				15.65	0.5	92.02	920.8	10.0	5.9	
Monoclonal antibodies acting on specific targets				9.93	0.8	35.52	584.2	16.4	9.4	
Monoclonal antibodies blocking growth factors				5.14	0.4	36.88	302.4	8.2	4.4	
Bruton tyrosine kinase (BTK) inhibitors				4.52	0.1	122.69	265.9	2.2	94.5	
VEGFR-associated multitarget tyrosine kinase inhibitors				4.43	0.1	90.58	261.0	2.9	96.6	
CDK protein kinase inhibitors 4/6				4.36	0.2	62.75	256.9	4.1	95.4	
Endocrine therapy – antiandrogens	0.11	0.2	1.37	3.73	0.6	17.14	226.1	17.4	95.0	0.6
Monoclonal antibodies conjugated with drugs				3.80	0.1	193.83	223.4	1.2	7.1	
EGFR tyrosine kinase inhibitors				3.01	0.1	121.86	177.2	1.5	97.5	
Endocrine therapy - aromatase inhibitors	2.43	3.3	2.05	0.47	0.7	1.76	170.5	85.5	15.4	3.6
BRC-ABL tyrosine kinase inhibitors	<0.005	<0.05	16.71	2.63	0.2	40.18	154.7	3.9	99.1	2.5
JAK tyrosine kinase inhibitors				2.49	0.1	109.30	146.3	1.3	92.9	
Endocrine therapy - hormones and GnRH analogues	0.06	0.1	2.88	2.20	1.3	4.55	133.4	29.8	7.2	81.2
Cytostatic antineoplastics - PARP inhibitors				2.15	<0.05	135.13	126.4	0.9	96.2	
Cytostatic antineoplastics - other cytostatics	0.19	0.3	1.71	1.83	0.1	75.29	119.4	8.1	65.4	0.4
CAR-T				1.81	<0.05	271450.37	106.7	<0.05	13.1	
BRAF tyrosine kinase inhibitors				1.59	<0.05	113.46	93.7	0.8	95.6	
ALK tyrosine kinase inhibitors				1.49	<0.05	131.63	87.5	0.7	97.0	
Cytostatic antineoplastics – antimetabolites	0.08	0.1	2.38	1.13	0.5	5.84	71.2	13.4	31.1	0.5

continued

Table 3.27 - *continued*

ATC 1st level Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Cytostatic antineoplastics - proteasome inhibitors				0.89	<0.05	58.56	52.2	0.9	18.4	
MEK tyrosine kinase inhibitors				0.69	<0.05	53.52	40.5	0.8	96.7	
Other protein kinase inhibitors				0.64	<0.05	2765.26	37.8	<0.05	0.9	
Cytotoxic antineoplastics of natural derivation – taxanes				0.61	<0.05	448.61	36.0	0.1	86.4	
Cytostatic antineoplastics - alkylating agents				0.42	0.2	6.31	25.0	4.0	4.6	
Cytotoxic antineoplastics – cytotoxic antibiotics - anthracyclines and related substances				0.36	0.1	11.09	21.0	1.9	2.9	
Hedgehog pathway inhibitors				0.34	<0.05	113.12	20.0	0.2	103.1	
MTOR protein kinase inhibitors	<0.005	<0.05	270.40	0.23	<0.05	42.98	13.5	0.3	100.4	3.2
Combination of antineoplastic agents				0.21	<0.05	3817.23	12.5	<0.05	2.1	
Cytotoxic antineoplastics of natural derivation – others	0.01	<0.05	56.92	0.20	0.1	10.14	11.9	1.1	37.0	2.4
Endocrine therapy - antiestrogens	0.06	0.6	0.28	0.13	0.3	1.40	11.8	19.4	50.5	0.1
RET protein kinase inhibitors				0.11	<0.05	139.66	6.5	<0.05	93.7	
NTRK protein kinase inhibitors				0.11	<0.05	181.74	6.3	<0.05	85.6	
Bispecific fusion protein (ImmTAC)				0.08	<0.05	294.60	4.5	<0.05		
Cytostatic antineoplastics – platinum compounds				0.07	0.2	0.99	4.4	4.4	1.3	
Cytotoxic antineoplastics – cytotoxic antibiotics - others				0.07	0.2	1.09	4.2	3.9	2.1	
Cytostatic antineoplastics - PI3K inhibitors				0.06	<0.05	97.67	3.6	<0.05	97.8	
IL-3 fusion protein and diphtheria toxin (anti-CD123 cytotoxin)				0.05	<0.05	1168.63	2.8	<0.05		
HER2 tyrosine kinase inhibitors				0.04	<0.05	70.56	2.5	<0.05	331.3	

continued

Table 3.27 - *continued*

ATC 1st level / Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
MET tyrosine kinase inhibitors				0.03	<0.05	155.17	1.9	<0.05	62.2	
FGFR tyrosine kinase inhibitors				0.02	<0.05	197.39	1.5	<0.05	85.1	
Monoclonal antibodies IgG1 bispecific against EGFR-MET				0.02	<0.05	131.14	1.3	<0.05	2.7	
Cytostatic antineoplastics - TOP1 inhibitors				0.02	<0.05	2.01	1.2	0.6	4.6	0.6
KIT and PDGFRA tyrosine kinase inhibitors				0.02	<0.05	428.60	1.1	<0.05	58.5	
KRAS G12C selective inhibitors				0.01	<0.05	277.09	0.6	<0.05	33.7	
CD20/CD3 bispecific monoclonal antibodies activating T lymphocytes				<0.005	<0.05	285.25	0.2	<0.05		
Alkylating agents				<0.005	<0.05	79.65	<0.05	<0.05		
IgG4-PAA BCMA/CD3 bispecific monoclonal antibodies				<0.005	<0.05	0.08	<0.05	<0.05	1.4	
Medicines for hypertension and heart failure	**32.63**	**361.1**	**0.25**	**2.27**	**12.5**	**0.50**	**2053.7**	**8025.7**	**1.4**	**3.9**
Beta-blockers	5.66	45.8	0.34	0.11	1.9	0.17	340.0	1023.9	0.5	0.1
Angiotensin II receptor blockers	5.01	58.6	0.23	<0.005	0.6	0.02	294.9	1270.3	0.0	0.0
Calcium channel blockers (dihydropyridines)	3.96	49.3	0.22	0.04	1.2	0.08	235.0	1085.6	0.1	0.0
Angiotensin II receptor blockers and diuretics (combinations)	3.72	31.3	0.33	<0.005	0.1	0.05	218.9	673.6	0.0	0.0
ACE inhibitors	3.43	78.6	0.12	0.01	1.9	0.01	202.4	1729.4	0.1	0.0
Angiotensin II receptor antagonists and niprilysin inhibitor (combinations)	0.31	0.1	7.21	1.96	1.5	3.57	134.0	34.9	17.9	58.8
ACE inhibitors and diuretics (combinations)	2.25	17.8	0.35	<0.005	0.1	0.05	132.5	383.7	0.0	0.0
Angiotensin II receptor blockers and calcium channel blockers (combinations)	1.72	11.9	0.40	<0.005	<0.05	0.23	101.3	254.9	0.0	0.0
ACE inhibitors and calcium channel blockers (combinations)	1.64	12.3	0.36	<0.005	<0.05	0.20	96.4	264.7	0.0	0.0
Alpha-blockers	1.22	7.5	0.45	0.01	0.3	0.12	72.4	166.9	0.0	0.0

continued

Table 3.27 - *continued*

ATC 1st level Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
High-ceiling diuretics, alone or in combination with potassium-sparing agents	0.90	24.1	0.10	0.07	4.5	0.04	56.6	614.4	1.2	0.0
ACE inhibitors, calcium channel blockers and diuretics (triple combination)	0.73	5.3	0.38	<0.005	<0.05	0.23	43.2	114.2	0.0	0.0
Beta-blockers and diuretics (combinations)	0.70	7.5	0.25	<0.005	<0.05	0.14	41.1	162.1	0.0	0.0
Potassium-sparing diuretics	0.60	3.4	0.48	0.04	0.3	0.33	37.8	80.7	2.0	0.0
Calcium channel blockers (not dihydropyridines)	0.23	1.6	0.39	<0.005	<0.05	0.26	13.9	35.7	0.6	0.0
Thiazides and similars (including combinations)	0.20	3.3	0.16	<0.005	0.1	0.06	11.8	73.1	0.5	0.0
Imidazoline receptor agonists	0.17	1.2	0.39	0.01	0.1	0.32	10.6	27.4	2.0	0.0
ACE inhibitors, other combinations	0.14	1.1	0.33	<0.005	<0.05	0.19	8.2	24.6	0.0	0.0
Aliskiren alone or in combination	0.02	0.1	0.88	<0.005	<0.05	0.58	1.2	1.4	0.3	
Angiotensin II receptor blockers, calcium channel blockers and diuretics (triple combination)	0.02	0.2	0.32	<0.005	<0.05	0.21	1.1	3.3		
Alpha-2 adrenergic receptor agonists	0.01	<0.05	0.37	<0.005	<0.05	0.24	0.3	0.9	0.6	
Immunosuppressants and immunomodulating agents	**1.54**	**2.0**	**2.14**	**29.34**	**5.3**	**15.14**	**1817.5**	**156.5**	**69.9**	**5.8**
Interleukin inhibitors				11.57	1.3	24.29	681.0	28.0	89.9	
Selective immunosuppressants (monoclonal antibodies)				4.66	0.2	69.84	274.0	3.9	25.6	
Tumor necrosis factor alpha inhibitors (TNF-alpha)				4.49	1.8	6.66	264.2	39.7	92.2	
Other immunosuppressants	0.86	1.8	1.34	2.16	0.3	18.46	177.9	44.6	70.5	0.6
JAK tyrosine kinase inhibitors				1.70	0.2	20.97	99.8	4.8	93.9	
Calcineurin inhibitors	0.51	0.2	8.34	0.90	0.4	5.79	82.9	12.7	16.1	41.5
Selective immunosuppressants	0.03	<0.05	2.03	1.26	0.6	5.62	76.0	14.1	47.7	36.1
Selective T cell co-stimulation modulators				0.94	0.1	34.10	55.3	1.6	99.4	
MTOR protein kinase inhibitors	<0.005	<0.05	17.09	0.73	0.2	11.06	43.1	3.9	21.6	66.6

continued

Table 3.27 - *continued*

ATC 1st level Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Growth factors	0.13	<0.05	54.36	0.35	0.1	7.98	28.3	2.7	14.7	48.6
Other immunomodulators	<0.005	<0.05	7.34	0.45	<0.05	181.54	26.6	0.2	2.4	
Interferons	<0.005	<0.05	44.70	0.14	<0.05	36.82	8.4	0.2	77.3	6.8
Antidiabetics	**8.83**	**39.8**	**0.61**	**15.82**	**31.6**	**1.37**	**1450.7**	**1533.6**	**2.2**	**58.2**
GLP-1 (glucagon-like one) analogues	1.83	0.8	6.13	6.55	7.4	2.44	493.4	175.8	2.1	70.8
Glifozins (SGLT2 inhibitors) alone	0.15	0.2	2.66	2.89	6.3	1.26	178.7	138.6	4.9	82.6
Fast acting insulins	2.78	6.8	1.12	0.14	0.9	0.43	171.9	164.8	2.0	2.0
Long acting insulins	0.03	<0.05	2.13	2.06	6.0	0.94	123.1	130.3	3.4	88.6
Metformin	1.68	23.0	0.20	0.01	0.3	0.05	99.3	500.7	0.3	0.0
Insulins combined with GLP-1 (glucagon-like one) analogues	0.51	0.2	9.20	0.98	0.8	3.46	87.3	19.9	1.6	60.7
Glifozins (SGLT2 inhibitors), combined with metformin	0.23	0.3	2.31	1.22	3.0	1.13	85.5	69.3	1.2	80.7
Gliptins (DPP-4 inhibitors) alone	0.37	0.7	1.47	0.81	2.9	0.77	69.4	76.8	2.1	67.8
Gliptins (DPP-4 inhibitors) in combination with glifozins (SGLT2 inhibitors)	0.28	0.2	3.65	0.49	1.0	1.34	45.1	25.8	1.6	57.3
Gliptins (DPP-4 inhibitors) in combination with metformin	0.05	0.1	1.29	0.53	2.1	0.71	34.4	46.6	1.2	93.6
Sulfonylureas alone	0.35	4.8	0.20	<0.005	0.1	0.01	20.5	104.5	0.0	0.0
Glitazones alone	0.12	0.5	0.69	0.04	0.4	0.27	9.1	18.7	0.4	20.9
Repaglinide	0.14	1.0	0.41	<0.005	<0.05	0.09	8.5	21.1	0.3	
Glitazones in combination with metformin	0.09	0.3	0.96	0.05	0.4	0.34	8.2	13.6	0.4	31.6
Acarbose	0.11	0.4	0.72	<0.005	<0.05	0.39	6.3	8.8	0.2	
Gliptins (DPP-4 inhibitors) in combination with pioglitazone	0.02	<0.05	2.00	0.05	0.1	0.96	4.3	3.8	0.7	67.2
Combined insulins (long/intermediate with fast-acting)	0.04	0.1	1.18	<0.005	<0.05	0.64	2.5	2.3	1.6	4.8

continued

Table 3.27 - *continued*

ATC 1st level Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Sulfonylureas in combination with metformin	0.04	0.5	0.21	<0.005	<0.05	0.08	2.2	10.9	0.2	
Sulfonylureas in combination with pioglitazone	<0.005	<0.05	1.82	0.01	<0.05	0.97	0.8	0.8	0.1	85.1
Intermediate acting insulins	<0.005	<0.05	0.59	<0.005	<0.05	0.11	0.1	0.3	1.0	
Lipid-lowering medicines	**16.75**	**119.5**	**0.38**	**3.74**	**3.5**	**2.92**	**1206.2**	**2642.4**	**16.7**	**0.2**
Statins, alone	8.09	82.0	0.27	0.01	1.9	0.01	476.5	1801.3	0.0	0.0
Ezetimibe and statins (combination)	4.02	24.4	0.45	0.01	0.2	0.13	236.8	526.8	0.2	0.0
PCSK9 inhibitors (monoclonal antibodies)	<0.005	<0.05	20.96	3.06	0.9	8.82	180.1	20.4	96.5	0.0
Omega 3	2.21	2.7	2.27	0.01	0.1	0.40	130.8	58.6	0.3	0.0
Ezetimibe	1.85	7.0	0.73	0.01	0.1	0.11	109.3	152.5	0.1	0.0
Fibrates	0.41	2.9	0.38	<0.005	0.0	0.18	24.3	63.7	0.2	0.0
PCSK9 inhibitors (siRNA)				0.34	0.1	8.84	19.9	2.3	65.6	
MTP inhibitor				0.14	<0.05	1079.74	8.0	<0.05	93.1	
Ezetimibe and bempedoic acid (combination)	0.06	<0.05	4.29	0.06	0.1	1.35	6.9	3.3	18.4	17.8
Adenosine triphosphate citrate lyase (ACL) inhibitors	0.05	<0.05	4.29	0.05	0.1	1.35	5.8	2.9	19.3	17.8
Drugs for the alteration of lipid metabolism of genetic origin				0.07	<0.05	8190.19	4.3	<0.05	89.0	
Statins, calcium channel blockers and ACE inhibitors (triple combination)	0.03	0.2	0.45	<0.005	<0.05	0.30	1.9	4.3	<0.05	
Statins in combination	0.03	0.3	0.24	<0.005	<0.05	0.22	1.5	6.4	<0.05	
ANGPTL3 inhibitors				<0.005	<0.05	318.64	<0.05	<0.05		
Asthma and COPD	**14.47**	**30.4**	**1.31**	**3.42**	**1.7**	**5.59**	**1052.6**	**688.4**	**11.7**	**5.2**
LABAs+ICS	6.54	12.0	1.49	0.06	0.2	0.72	388.7	263.4	0.5	0.0
Monoclonal antibodies	<0.005	<0.05	63.32	3.20	0.3	26.25	188.6	7.2	62.4	28.9
LAMAs	2.18	4.0	1.49	0.03	0.1	0.71	129.9	88.3	0.8	0.0

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Table 3.27 - *continued*

ATC 1st level Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
ICSs	1.82	4.8	1.04	0.03	0.2	0.33	108.6	107.4	0.3	0.0
LABAs+LAMAs+ICS	1.60	1.6	2.68	0.04	0.1	1.77	96.6	36.6	1.5	0.0
LABAs+LAMAs	1.17	1.7	1.93	0.01	<0.05	1.11	69.5	36.1	0.6	0.0
Antileukotrienics (LTRA)	0.46	2.0	0.62	<0.005	<0.05	0.09	27.1	43.8	0.0	
LABAs	0.21	0.6	0.95	<0.005	<0.05	0.50	12.3	13.0	0.6	0.0
SABAs	0.19	2.3	0.23	0.02	0.3	0.14	11.9	55.3	1.2	0.0
SABAs+SAMAs	0.13	0.5	0.67	<0.005	<0.05	0.23	8.0	12.5	0.3	0.0
SABAs+ICSs	0.10	0.2	1.21	<0.005	<0.05	0.71	5.8	4.9	0.1	0.0
SAMAs	0.04	0.3	0.29	0.01	0.3	0.12	2.8	12.9	2.8	0.0
Theophylline-based bronchodilators	0.04	0.3	0.37	<0.005	<0.05	0.30	2.5	6.9	0.7	0.0
PDE-4 inhibitors	<0.005	<0.05	2.20	<0.005	<0.05	1.46	0.2	0.1	12.6	69.4
Anticoagulants	**2.46**	**4.8**	**1.40**	**14.09**	**26.0**	**1.49**	**973.8**	**661.7**	**4.8**	**67.6**
NOACs	0.37	0.3	3.93	11.18	18.7	1.63	679.7	407.9	2.6	88.3
LMWH	1.90	2.4	2.21	2.08	6.4	0.89	234.4	188.5	11.3	21.4
Heparin and heparinoids	0.02	<0.05	2.63	0.23	0.4	1.73	14.5	8.2	2.4	0.8
Antithrombotic enzymes				0.24	<0.05	924.96	14.2	<0.05	2.6	
Fondaparinux	0.01	<0.05	6.61	0.21	0.4	1.58	13.5	8.1	10.5	61.1
Vitamin K antagonists	0.16	2.2	0.20	<0.005	0.1	0.08	9.4	49.0	1.3	0.0
Other antithrombotics				0.13	<0.05	4099.7	7.4	<0.05		
Antithrombotics - direct thrombin inhibitors				0.01	<0.05	203.41	0.8	<0.05		
Antibiotics	**9.90**	**15.4**	**1.77**	**4.08**	**1.8**	**6.26**	**822.6**	**368.4**	**2.9**	**0.0**
Combinations of penicillins (including beta lactamase inhibitors)	3.19	6.1	1.43	0.61	0.5	3.10	223.3	142.7	0.5	0.0
Third-generation cephalosporins	2.82	2.0	3.86	0.54	0.3	4.69	198.1	49.9	0.5	0.0

continued

Table 3.27 - *continued*

ATC 1st level Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Macrolides and lincosamides	1.46	3.3	1.20	0.04	0.2	0.60	88.2	75.3	0.3	0.0
Fluoroquinolones	1.11	1.5	2.04	0.11	0.2	1.77	71.8	35.7	5.6	0.0
Other antibacterials	0.64	0.4	4.61	0.47	0.1	10.22	65.2	10.8	1.8	0.2
Other cephalosporins and penems				0.80	<0.05	220.83	47.0	0.2	3.9	
Carbapenems				0.48	0.1	21.15	28.3	1.3	3.8	
Glycopeptides	0.06	<0.05	66.89	0.29	<0.05	19.22	21.1	1.0	3.5	0.0
Broad-spectrum penicillins	0.17	0.9	0.50	0.10	<0.05	7.22	15.7	20.7	0.8	0.0
Polymyxins				0.16	<0.05	38.53	9.6	0.2	65.0	
Tetracyclines	0.08	0.4	0.64	0.08	<0.05	6.53	9.3	8.2	0.8	
Aminoglycosides	0.05	<0.05	8.65	0.10	<0.05	9.59	8.6	0.9	47.6	0.0
First-generation cephalosporins	0.02	<0.05	2.04	0.09	0.1	2.77	6.5	2.5	0.5	
Beta-lactamase resistant penicillins	0.01	<0.05	1.84	0.08	<0.05	8.44	5.3	0.8	1.7	
Sulphonamides (alone or in combination)	0.07	0.4	0.47	0.02	0.1	0.86	5.1	9.6	3.3	0.0
Second-generation cephalosporins	0.07	0.1	1.52	0.01	<0.05	7.71	5.0	2.9	0.3	0.0
Other combinations	0.08	<0.05	6.74	<0.005	<0.05	4.50	4.8	0.7	0.8	
Nitrofuran derivatives	0.06	0.2	0.94	<0.005	<0.05	0.27	3.3	3.6	0.2	0.0
Fourth-generation cephalosporins	0.01	<0.05	34.17	0.04	<0.05	16.35	3.3	0.2	1.8	0.0
Monobactams				0.03	<0.05	88.12	1.7	<0.05	106.5	
Imidazole derivatives	<0.005	<0.05	16.82	0.02	<0.05	0.98	0.9	0.9	0.5	
Beta-lactamase sensitive penicillins	<0.005	<0.05	81.25	0.01	<0.05	47.29	0.6	<0.05	27.2	1.9
Amphenicols	<0.005	<0.05	4.22	<0.005	<0.05	6.63	<0.05	<0.05	39.8	0.2

continued

Table 3.27 - *continued*

ATC 1st level / Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Medicines for multiple sclerosis	**<0.005**	**<0,05**	**35.26**	**12.97**	**1.2**	**30.74**	**763.4**	**24.8**	**63.0**	**5.5**
Monoclonal antibodies				5.16	0.3	51.69	303.9	5.9	21.9	
Immunosuppressants	<0.005	<0.05	61.33	2.93	0.3	29.64	172.6	5.8	95.1	4.6
Fingolimod (S1P receptor modulators)				1.48	0.1	43.23	87.0	2.0	104.1	1.0
Pyrimidine synthesis inhibitors	<0.005	<0.05	54.67	1.23	0.1	24.72	72.3	2.9	85.4	14.3
Interferons	<0.005	<0.05	23.09	1.16	0.3	12.64	68.1	5.4	69.5	31.2
Other S1P receptor modulators				0.87	0.1	35.88	51.0	1.4	85.7	0.2
Glatiramer (AA copolymers)	<0.005	<0.05	38.72	0.14	0.1	6.04	8.4	1.4	82.0	19.9
Vaccines	**0.01**	**<0,05**	**28.42**	**12.09**	**1.2**	**27.88**	**712.2**	**25.5**	**0.3**	**0.1**
Adjuvanted recombinant varicella zoster vaccine				2.10	<0.05	321.38	123.4	0.4	0.4	
Human papillomavirus (HPV) vaccine	<0.005	<0.05	198.00	1.64	0.1	69.37	96.5	1.4	0.0	
Meningococcal B vaccine				1.46	0.1	62.66	85.6	1.4	0.0	0.0
Pneumococcal polysaccharide conjugate vaccine (adsorbed)	<0.005	<0.05	121.27	1.41	0.1	47.57	83.3	1.8	0.5	0.0
Adjuvanted tetravalent influenza vaccine	<0.005	<0.05	34.00	1.40	0.3	15.00	82.3	5.5	0.0	0.4
Non-adjuvanted tetravalent influenza vaccine	0.01	<0.05	24.39	0.98	0.3	7.75	58.0	7.4	1.7	0.1
MMRV vaccine (measles/mumps/rubella/varicella)				0.66	<0.05	48.02	38.7	0.8		
Hexavalent vaccine (diphtheria/tetanus/pertussis/haemophilus Influenzae B/poliomyelitis/hepatitis B)				0.50	0.1	25.51	29.6	1.2		
Tetravalent meningococcal conjugate vaccine				0.37	<0.05	25.16	21.6	0.9	0.0	0.0
Tetravalent vaccine (diphtheria/tetanus/pertussis/poliomyelitis)				0.33	0.1	17.75	19.5	1.1	0.0	
Live attenuated rotavirus vaccine				0.25	<0.05	18.97	14.8	0.8		
Live attenuated varicella zoster vaccine				0.19	<0.05	96.20	11.0	0.1		

continued

Table 3.27 - *continued*

ATC 1st level / Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Intranasal tetravalent influenza vaccine	<0.005	<0.05	33.50	0.18	<0.05	19.74	10.8	0.5	0.0	
DTP vaccine (diphtheria/tetanus/pertussis)				0.15	<0.05	11.43	8.8	0.8	0.1	0.0
Pneumococcal polysaccharide 23 vaccine	<0.005	<0.05	42.33	0.10	<0.05	21.27	5.6	0.3	1.0	0.7
Tick-borne encephalitis vaccine				0.08	<0.05	35.34	4.9	0.1	<0.05	
Hepatitis A vaccine				0.06	<0.05	17.36	3.8	0.2	0.1	
Live attenuated varicella vaccine				0.06	<0.05	30.88	3.6	0.1		
Hepatitis B vaccine	<0.005	<0.05	31.58	0.06	<0.05	16.99	3.4	0.2	0.5	
MMR vaccine (measles/mumps/rubella)				0.02	<0.05	8.90	1.1	0.1	0.0	
Meningococcal C conjugate vaccine				0.02	<0.05	11.96	1.0	0.1		
Yellow fever vaccine				0.01	<0.05	20.89	0.9	<0.05		
DT vaccine (diphtheria/tetanus)	<0.005	<0.05	11.56	0.01	<0.05	4.96	0.7	0.1	0.1	
Live attenuated typhus vaccine	<0.005	<0.05	31.52	0.01	<0.05	11.10	0.7	0.1		
Hepatitis A and B vaccine				0.01	<0.05	31.59	0.5	<0.05	0.1	
Cholera vaccine	<0.005	<0.05	64.00	0.01	<0.05	27.16	0.4	<0.05		
Tetanus vaccine	<0.005	<0.05	12.40	0.01	<0.05	4.71	0.4	0.1	0.2	0.0
Polysaccharide typhus vaccine				0.01	<0.05	12.05	0.4	<0.05		
Haemophilus influenzae B conjugate vaccine				0.01	<0.05	13.08	0.3	<0.05	0.0	
Inactivated polio vaccine (IPV)	<0.005	<0.05	15.44	<0.005	<0.05	7.54	0.3	<0.05		
Japanese encephalitis vaccine				<0.005	<0.05	170.18	0.3	<0.05		
Haemophilus influenzae B vaccine				<0.005	<0.05	15.85	0.2	<0.05	0.0	
Rabies vaccine				<0.005	<0.05	50.32	0.1	<0.05		
Dengue Disease Vaccine				<0.005	<0.05	88.00	0.1	<0.05		
Respiratory Syncytial Virus Vaccine				<0.005	<0.05	1.10	<0.05	<0.05		

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Table 3.27 - *continued*

ATC 1st level Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Medicines for peptic ulcer and gastroesophageal reflux disease (GERD)	**11.70**	**79.4**	**0.40**	**0.28**	**4.1**	**0.19**	**704.7**	**1792.8**	**0.3**	**0.0**
Proton pump inhibitors	11.09	76.6	0.40	0.26	3.9	0.18	667.9	1730.2	0.3	0.0
Antacids	0.50	2.2	0.60	0.02	0.1	0.34	30.1	51.2	1.0	0.0
H2 receptor antagonists	0.06	0.3	0.62	<0.005	<0.05	0.43	3.7	6.1	0.5	0.0
Other medicines for peptic ulcer and gastroesophageal reflux disease (GERD)	0.04	0.2	0.52	<0.005	<0.05	0.26	2.6	5.1	1.1	0.0
Prostaglandins	<0.005	<0.05	1.12	<0.005	<0.05	0.56	0.3	0.3	0.4	
Diseases due to altered functionality of cellular metabolism	**<0.005**	**<0,05**	**102.15**	**10.69**	**0.2**	**194.07**	**629.0**	**3.2**	**69.5**	**0.0**
Hereditary transthyretin-mediated amyloidosis				3.08	0.1	85.07	181.0	2.1	85.6	
Lysosomal storage diseases - Fabry disease - enzyme replacement therapy				1.87	<0.05	676.50	110.2	0.2	69.1	
Lysosomal storage diseases - Pompe disease - enzyme replacement therapy				1.41	<0.05	960.53	82.8	0.1	29.4	
Lysosomal storage diseases - type 1 Gaucher disease - enzyme replacement therapy				1.12	<0.05	1096.50	66.0	0.1	60.0	
Lysosomal storage diseases - Fabry disease - chaperone therapy				0.47	<0.05	447.75	27.5	0.1	92.9	
Lysosomal storage diseases - type 1 Gaucher disease - chaperone therapy	<0.005	<0.05	190.26	0.43	<0.05	362.92	25.6	0.1	96.0	
Lysosomal storage diseases - mucopolysaccharidosis II - enzyme replacement therapy				0.42	<0.05	2264.25	24.7	<0.05	77.7	
Lysosomal storage diseases - mucopolysaccharidosis IV-A (Morquio syndrome) - enzyme replacement therapy				0.29	<0.05	2744.48	16.9	<0.05	61.9	
Congenital amino-acid transport and metabolism defects - phenylketonuria				0.24	<0.05	144.10	14.2	0.1	94.3	
Acute hepatic porphyria				0.21	<0.05	854.52	12.1	<0.05	77.6	

continued

Table 3.27 - *continued*

ATC 1st level / Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Lysosomal storage diseases - mucopolysaccharidosis I - enzyme replacement therapy				0.19	<0.05	1296.72	11.1	<0.05	40.5	
Juvenile neuronal ceroid lipofuscinosis				0.18	<0.05	473.07	10.8	<0.05	46.1	
Primary hyperoxaluria (siRNA)				0.17	<0.05	1036.83	9.9	<0.05	60.8	
Lysosomal storage diseases - mucopolysaccharidosis VI - enzyme replacement therapy				0.12	<0.05	2517.58	7.3	<0.05	44.8	
Wilson disease	<0.005	<0.05	6.08	0.12	<0.05	46.74	7.1	0.2	92.7	0.2
Lysosomal storage diseases - Liposomal acid lipase deficiency - enzyme replacement therapy				0.10	<0.05	1181.17	5.7	<0.05	6.2	
Urea cycle disorders				0.08	<0.05	34.06	4.7	0.1	95.2	
Hypophosphatasia-enzyme replacement therapy				0.06	<0.05	2353.42	3.4	<0.05	73.4	
Lipodystrophy				0.05	<0.05	969.88	3.2	<0.05	89.3	
Congenital amino-acid transport and metabolism defects - homocystinuria				0.03	<0.05	13.27	2.1	0.2	84.2	0.4
Lysosomal storage diseases - alpha-mannosidosis - enzyme replacement therapy				0.02	<0.05	664.26	1.4	<0.05	52.5	
Congenital amino-acid transport and metabolism defects - type 1 hereditary tyrosinemia	<0.005	<0.05	159.54	0.02	<0.05	38.15	0.9	<0.05	98.5	
Congenital defects of amino acid metabolism and transport-manifest nephropathic cystinosis				0.01	<0.05	24.58	0.5	<0.05	94.4	1.4
Anti-HIV antivirals	**0.02**	**0.0**	**6.04**	**10.50**	**2.2**	**12.85**	**619.2**	**48.3**	**96.6**	**0.3**
Co-formulated regimens - 2 nucleoside/ nucleotide reverse transcriptase inhibitors + 1 integrase inhibitor (2 NRTIs + 1 INSTI)				3.32	0.4	20.21	195.3	9.7	96.9	
Co-formulated regimens - 1 nucleoside/ nucleotide reverse transcriptase inhibitors + 1 integrase inhibitor (1 NRTIs + 1 INSTI)				1.98	0.3	16.60	116.4	7.0	96.8	

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Table 3.27 - *continued*

ATC 1st level / Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Co-formulated regimens - 2 nucleoside/ nucleotide reverse transcriptase inhibitors + 1 non-nucleoside reverse transcriptase inhibitor (2 NRTI + 1 NNRTI)				1.37	0.2	16.36	80.7	4.9	101.0	
Integrase inhibitors (INSTI)				1.27	0.3	13.30	74.9	5.6	91.7	
Co-formulated regimens - 2 nucleoside/nucleotide reverse transcriptase inhibitors + 1 protease inhibitor (2 NRTIs + 1 PI)				0.72	0.1	21.85	42.2	1.9	99.6	
Co-formulated regimens - 1 non-nucleoside reverse transcriptase inhibitor + 1 integrase inhibitor (1 NNRTI + 1 INSTI)				0.60	0.1	18.30	35.4	1.9	98.2	
Nucleoside/nucleotide reverse transcriptase inhibitors (NRTI)	0.02	<0.05	6.04	0.51	0.5	2.60	31.2	11.8	89.9	5.1
Protease inhibitors (PIs)				0.36	0.1	8.80	21.2	2.4	103.3	
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)				0.27	0.1	5.58	16.2	2.9	84.5	
Other anti-HIV antivirals				0.10	<0.05	41.86	5.9	0.1	95.1	
Coagulation factors	**0.04**	**<0,05**	**398.24**	**9.36**	**0.1**	**404.22**	**553.4**	**1.4**	**75.1**	**12.9**
Haemophilia A (long acting-recombinant)	0.01	<0.05	594.17	2.84	<0.05	315.14	167.2	0.5	76.9	17.5
Haemophilia A (short acting-recombinant)	<0.005	<0.05	550.53	2.02	<0.05	330.48	118.9	0.4	72.2	19.3
Haemophilia A (monoclonal antibodies)	<0.005	<0.05	1723.27	1.91	<0.05	683.35	112.4	0.2	89.9	4.2
Haemophilia B (long acting-recombinant)	<0.005	<0.05	1320.03	1.35	<0.05	854.87	79.3	0.1	81.1	9.9
Factor VII deficiency (short acting-recombinant)				0.32	<0.05	3855.66	18.6	<0.05	27.4	
Haemophilia A (plasma derivatives)	0.02	<0.05	374.19	0.30	<0.05	247.47	18.5	0.1	79.6	18.7
Haemophilia B (short acting-recombinant)	<0.005	<0.05	568.96	0.20	<0.05	378.03	11.6	<0.05	70.4	14.7
Activated human antihemophilic prothrombin complex				0.16	<0.05	8496.29	9.2	<0.05	33.3	4.1

continued

Table 3.27 - *continued*

ATC 1st level / Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Combination of coagulation factors (plasma derivatives)				0.08	<0.05	102.00	5.0	<0.05	0.9	
Factor VIII deficiency (plasma derivatives)	<0.005	<0.05	376.39	0.08	<0.05	366.16	4.5	<0.05	32.6	25.3
Von Willebrand disease (plasma derivatives)				0.06	<0.05	71.65	3.5	<0.05	66.0	
Other deficiencies of coagulation factors (long-acting, recombinant)				0.06	<0.05	15524.20	3.2	<0.05	25.8	
Other deficiencies of coagulation factors (plasma derivatives)				0.02	<0.05	6169.18	1.0	<0.05	12.9	
Haemophilia B (plasma derivatives)	0.01	<0.05	236.68	<0.005	<0.05	196.51	0.5	<0.05	27.5	
Medicines for osteoporosis	**6.83**	**132.1**	**0.14**	**2.28**	**8.6**	**0.73**	**536.0**	**3022.0**	**8.8**	**12.6**
Vitamin D and analogues	4.01	119.1	0.09	0.02	3.2	0.01	236.8	2626.5	0.2	0.0
Monoclonal antibodies-denosumab	<0.005	<0.05	1.80	1.62	5.1	0.86	95.4	110.4	19.9	69.3
Bisphosphonates alone	1.38	7.5	0.50	0.08	0.1	3.42	86.0	162.2	0.4	0.0
Teriparatide	0.66	0.2	11.08	0.09	<0.05	5.86	44.3	4.4	9.5	0.3
Bisphosphonates in combination	0.40	1.9	0.59	<0.005	<0.05	0.35	23.5	40.1	0.0	
Monoclonal antibodies-burosumab				0.36	<0.05	142.18	21.3	0.1	92.1	
Calcium and vitamin D	0.29	3.0	0.26	<0.005	0.1	0.06	17.1	66.3	0.3	0.0
Calcium	<0.005	<0.05	34.96	0.10	<0.05	13.98	5.6	0.4	57.9	21.0
SERM (selective estrogen-receptor modulators)	0.08	0.4	0.53	0.01	0.1	0.32	5.3	10.6	1.7	0.0
Cystic fibrosis				**8.96**	**0.1**	**252.49**	**527.2**	**2.1**	**92.7**	**0.0**
CFTR modulators				8.75	0.1	339.52	515.1	1.5	92.8	
Specific action mucolytics				0.21	<0.05	21.31	12.2	0.6	87.9	0.2

continued

Table 3.27 - *continued*

ATC 1st level Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Antidepressants	**7.17**	**45.0**	**0.44**	**0.18**	**2.1**	**0.23**	**432.7**	**1012.3**	**1.4**	**0.0**
SSRI antidepressants	3.41	31.1	0.30	0.01	1.3	0.03	201.2	695.5	0.2	0.0
SNRI antidepressants	1.68	7.3	0.63	0.01	0.3	0.06	99.0	163.0	0.3	0.0
Other antidepressants	1.00	3.3	0.82	0.05	0.4	0.30	62.0	81.4	3.5	0.0
Vortioxetine	0.93	2.2	1.14	0.01	0.1	0.70	55.6	49.2	1.0	0.0
1st generation antidepressants, alone or in combination	0.16	1.0	0.42	<0.005	0.1	0.20	9.4	22.9	2.7	0.0
Esketamine				0.09	<0.05	19.23	5.5	0.3	43.4	
Medicines for eye disorders	**3.73**	**21.4**	**0.48**	**2.89**	**0.5**	**14.42**	**389.7**	**472.5**	**4.7**	**0.0**
Antiglaucoma preparations - beta blocking agents alone or in combination	2.19	12.7	0.47	<0.005	0.1	0.16	129.3	273.7	0.1	0.0
Recombinant anti-VEGF fusion proteins				1.42	<0.05	400.79	83.3	0.2	9.5	
Antiglaucoma preparations – prostaglandin analogues	1.21	5.8	0.57	<0.005	<0.05	0.22	71.3	124.8	0.1	
Monoclonal antibodies anti-VEGF - ranibizumab				0.52	0.1	17.39	30.9	1.8	7.8	
Corticosteroids (intravitreal implants)				0.52	0.3	5.03	30.8	6.1	6.0	
Antiglaucoma preparations – carbonic anhydrase inhibitors alone or in combination	0.22	1.4	0.44	<0.005	<0.05	0.29	13.3	30.5	0.4	0.0
Monoclonal anti-VEGF antibodies—brolucizumab				0.20	<0.05	401.52	11.6	<0.05	7.2	
Other ophthalmological medicines (gene therapy)				0.11	<0.05	297000.00	6.5	<0.05	22.7	
Antiglaucoma preparations – sympathomimetic drugs	0.10	1.6	0.18	<0.005	<0.05	0.06	6.0	34.0	0.1	
Other ophthalmological drugs	<0.005	<0.05	4.96	0.07	<0.05	8.51	4.3	0.5	83.8	0.6
Antiglaucoma preparations – parasympathomimetic drugs	<0.005	<0.05	0.10	0.01	<0.05	2.50	0.7	0.6	0.2	
Corticosteroids alone	<0.005	<0.05	0.87	0.01	<0.05	3.45	0.7	0.2	2.6	0.0
Antineovascularising agents (photodynamic therapy)				0.01	<0.05	797.05	0.5	<0.05	5.1	

continued

Table 3.27 - *continued*

ATC 1st level / Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Monoclonal anti-VEGF antibodies— faricimab				0.01	<0.05	91.41	0.4	<0.05	6.9	
Other ophthalmological medicines (cell therapy)				<0.005	<0.05	94310.54	0.1	<0.05		
Antiglaucoma preparations - others	<0.005	<0.05	0.81	<0.005	<0.05	0.36	<0.05	<0.05	8.3	
Pain therapy	**5.94**	**7.1**	**2.30**	**0.17**	**1.0**	**0.45**	**359.8**	**174.1**	**1.3**	**0.2**
Major opioids alone or in combination - oral	1.99	1.5	3.71	0.05	0.1	1.48	120.3	33.7	1.5	0.0
Medications for neuropathic pain	1.85	3.2	1.61	0.02	0.5	0.13	110.2	77.6	0.3	0.8
Minor opioids, alone or in combination	0.58	1.6	0.97	0.02	0.1	0.31	35.1	38.1	0.8	0.0
Fentanyl - transdermal	0.50	0.5	2.68	0.02	0.1	0.50	30.9	13.9	2.9	0.0
Fentanyl - oral	0.36	0.1	13.54	<0.005	<0.05	1.40	21.7	1.8	0.8	0.0
Major opioids alone or in combination - transdermal	0.34	0.2	5.37	0.01	<0.05	2.79	20.1	3.8	0.5	0.0
Fentanyl - nasal	0.30	<0.05	26.22	0.02	<0.05	17.22	18.5	0.7	4.1	0.0
Major opioids alone or in combination - parenteral	0.02	<0.05	2.50	0.03	0.2	0.41	2.9	4.6	8.5	
Platelet aggregation inhibitors	**3.07**	**61.6**	**0.14**	**2.70**	**9.3**	**0.79**	**339.1**	**1524.2**	**19.2**	**17.8**
P2Y12 platelet receptor inhibitors	1.41	7.6	0.51	1.10	6.6	0.45	147.8	304.7	1.5	36.5
Acetylsalicylic acid alone and in combination	1.43	53.0	0.07	0.01	1.5	0.02	84.6	1171.0	0.4	0.0
Monoclonal antibodies for episodes of acquired TTP	<0.005	<0.05	2.96	0.97	<0.05	119.91	56.9	0.5	82.8	0.3
Other platelet aggregation inhibitors				0.50	<0.05	3402.90	29.3	<0.05	52.6	
Acetylsalicylic acid/clopidogrel	0.22	1.0	0.60	0.11	1.2	0.24	19.5	48.0	0.3	31.2
Glycoprotein IIb/IIIa inhibitors				0.02	<0.05	62.71	1.0	<0.05		
Anti-epileptics	**4.64**	**9.5**	**1.34**	**1.00**	**1.7**	**1.65**	**332.0**	**240.1**	**7.3**	**6.3**
Second-generation antiepileptics	2.55	3.5	1.98	0.17	0.7	0.66	160.0	90.8	1.3	4.0
First-generation antiepileptics	1.53	5.5	0.76	0.10	0.6	0.48	96.1	131.0	2.5	0.0

continued

Table 3.27 - *continued*

ATC 1st level Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Third-generation antiepileptics	0.56	0.5	3.30	0.39	0.3	3.20	55.9	17.2	7.1	23.8
Cannabidiol				0.21	<0.05	48.28	12.4	0.3	85.3	
Other antiepileptics	<0.005	<0.05	12.93	0.13	<0.05	8.84	7.5	0.8	70.3	14.5
Antipsychotics	**1.64**	**3.0**	**1.51**	**3.40**	**7.6**	**1.22**	**296.4**	**227.5**	**32.1**	**9.5**
Atypical and other antipsychotics	1.40	1.8	2.15	3.12	6.3	1.35	266.1	174.2	33.9	7.9
Typical antipsychotics	0.19	1.1	0.45	0.12	1.1	0.32	18.1	47.1	20.2	0.0
Atypical and other antipsychotics - lurasidone	0.03	<0.05	3.15	0.13	0.2	1.99	9.2	4.3	9.9	65.0
Atypical and other antipsychotics - brexpiprazole	0.02	<0.05	4.28	0.03	0.1	1.13	3.0	1.9	10.7	40.6
Medicines for genitourinary disorders	**4.74**	**41.5**	**0.31**	**0.01**	**0.6**	**0.07**	**279.8**	**904.2**	**0.2**	**0.0**
Medicines for benign prostatic hypertrophy (alpha-blockers)	3.04	29.8	0.28	0.01	0.4	0.05	179.5	647.8	0.1	0.0
Medicines for benign prostatic hypertrophy (5-alpha reductase inhibitors)	1.59	11.2	0.39	<0.005	0.2	0.07	93.8	244.0	0.2	0.0
Medicines for incontinence and urinary frequency disorders (anticholinergics)	0.11	0.6	0.52	<0.005	<0.05	0.33	6.3	12.3	1.4	0.0
Other medicines for benign prostatic hypertrophy	<0.005	<0.05	1.45	<0.005	<0.05	0.79	0.1	0.1	16.2	
Medicines for incontinence and urinary frequency disorders (beta-3 adrenergic antagonists)	<0.005	<0.05	2.61	<0.005	<0.05	1.13	0.1	<0.05	37.9	2.7
Medicines for benign prostatic hypertrophy (alpha-blockers in combination)	<0.005	<0.05	1.22	<0.005	<0.05	0.83	<0.05	<0.05	4.3	3.1
Antiparkinson medicines	**2.63**	**5.1**	**1.40**	**0.80**	**0.6**	**3.61**	**201.9**	**123.4**	**16.7**	**5.6**
DOPA-derivatives agonists, alone or in combination	0.73	2.1	0.93	0.54	0.2	6.33	75.1	51.1	40.3	0.8
Dopamine-agonists	0.99	0.9	2.92	0.05	0.1	1.63	61.7	22.0	2.7	1.6
MAO inhibitors	0.79	1.6	1.33	0.02	<0.05	1.07	47.8	36.3	1.2	1.1
COMT inhibitors	0.07	<0.05	6.92	0.17	0.1	3.28	14.6	3.7	7.2	63.3
Anticholinergics	0.04	0.4	0.28	<0.005	0.1	0.14	2.6	10.2	6.9	
Amantadine	<0.005	<0.05	0.98	<0.005	<0.05	0.74	<0.05	<0.05	167.1	2.4

continued

Table 3.27 - *continued*

ATC 1st level / Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
NSAIDs	**2.45**	**17.1**	**0.39**	**0.08**	**1.0**	**0.21**	**148.9**	**389.3**	**0.3**	**0.0**
Traditional NSAIDs	1.67	12.3	0.37	0.08	1.0	0.21	102.6	284.5	0.5	0.0
Coxib	0.72	4.3	0.46	<0.005	<0.05	0.52	42.4	92.8	0.1	0.0
Oxicam	0.06	0.5	0.31	<0.005	<0.05	0.20	3.6	11.7	0.0	
Other non-steroidal anti-inflammatory/ anti-rheumatic pharmaceuticals	<0.005	<0.05	0.67	<0.005	<0.05	0.66	0.2	0.3	0.6	
NSAIDs combined with decongestant	<0.005	<0.05	6.45	<0.005	<0.05	4.02	<0.05	<0.05		
Antifungals for systemic use	**0.84**	**0.5**	**4.47**	**1.62**	**0.1**	**31.17**	**144.7**	**14.1**	**11.3**	**1.9**
Triazole derivatives	0.84	0.5	4.47	0.55	0.1	14.51	81.5	13.2	18.7	3.3
Polyenes				0.85	<0.05	101.55	50.2	0.5	0.6	
Echinocandins				0.21	<0.05	46.77	12.2	0.3	1.1	
Imidazole derivatives	<0.005	<0.05	13.60	0.01	<0.05	9.41	0.8	0.1	81.7	11.0
Contrast media				**1.88**	**0.1**	**53.01**	**110.6**	**2.1**	**0.0**	
Radiological contrast media				1.37	0.1	54.37	80.7	1.5	0.0	
MRI contrast media				0.46	<0.05	48.22	26.8	0.6		
Contrast agents for ultrasound				0.05	<0.05	67.50	3.0	<0.05	0.0	
Thyroid medicines	**1.57**	**24.8**	**0.17**	**0.01**	**0.4**	**0.05**	**93.0**	**542.2**	**0.3**	**0.0**
Thyroid hormones	1.51	23.5	0.18	0.01	0.4	0.05	89.4	512.8	0.2	0.0
Antithyroid preparations	0.06	1.3	0.12	<0.005	0.1	0.07	3.5	29.4	1.7	0.0
Antimigraine medicines	**1.01**	**0.9**	**3.22**	**0.55**	**0.3**	**5.06**	**91.8**	**24.9**	**34.8**	
Triptans	1.01	0.9	3.22	<0.005	<0.05	3.31	59.4	18.5	0.3	
Calcitonin gene-related peptide antagonists (monoclonal antibodies)				0.55	0.3	5.08	32.4	6.4	98.1	
Other antimigraine medicines	<0.005	<0.05	3.99	<0.005	<0.05	2.32	<0.05	<0.05	25.7	

continued

Table 3.27 - *continued*

ATC 1st level / Subgroups	Approved care regime			Direct purchases			Total expenditure (million)	Total DDD (million)	% expenditure DD	% expenditure DPC
	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost	Expenditure *per capita*	DDD/1000 inhab. per day	Average DDD cost				
Radiopharmaceuticals				**1.32**	**<0,05**	**486.90**	**77.8**	**0.2**	**0.6**	
Radiopharmaceuticals for cancer detection				0.53	<0.05	558.38	31.4	0.1		
Other radiopharmaceuticals for therapeutic use				0.26	<0.05	2072.91	15.3	<0.05	3.2	
CNS diagnostic radiopharmaceuticals				0.24	<0.05	752.77	14.1	<0.05		
Thyroid diagnostic radiopharmaceuticals				0.17	<0.05	251.59	10.1	<0.05		
Other diagnostic radiopharmaceuticals				0.05	<0.05	35165.32	2.9	<0.05		
Cardiovascular system diagnostic radiopharmaceuticals				0.04	<0.05	110.53	2.3	<0.05		
Skeletal system diagnostic radiopharmaceuticals				0.01	<0.05	75.89	0.9	<0.05		
Renal system diagnostic radiopharmaceuticals				0.01	<0.05	114.42	0.5	<0.05		
Therapeutic radiopharmaceuticals				<0.005	<0.05	55000.00	0.2	<0.05		
Respiratory system diagnostic radiopharmaceuticals				<0.005	<0.05	150.00	0.1	<0.05		
Radiopharmaceuticals for detection of inflammation and infections				<0.005	<0.05	566.14	0.1	<0.05		
Hepatic and reticuloendothelial system diagnostic radiopharmaceuticals				<0.005	<0.05	458.61	<0.05	<0.05		
Radiopharmaceuticals with analgesic/anti-inflammatory action				<0.005	<0.05	925.50	<0.05	<0.05		
Antidementia medicines	**0.19**	**0.6**	**0.81**	**0.13**	**1.8**	**0.21**	**18.9**	**51.3**	**2.8**	**39.1**
Anticholinesterases	0.13	0.4	0.88	0.10	0.9	0.29	13.1	28.3	3.0	41.2
Other antidementia medicines	0.06	0.2	0.71	0.04	0.8	0.12	5.8	23.0	2.3	34.5

Most frequently prescribed therapeutic classes

For each ATC 1st level, after showing the overall data on expenditure, consumption and exposure, we provide in-depth analyses, mainly for the most prescribed therapeutic categories, reporting the temporal trend of consumption and expenditure along with national and regional data; where possible, indicators of exposure and adherence to drug treatment in the population are analysed. The national data on expenditure and consumption include both drugs supplied under approved care regime, including co-payments and discounts, and drugs purchased directly by public health facilities. The exposure data and the adherence and persistence indicators were processed through the administrative flow of prescriptions for class A-NHS drugs dispensed through local pharmacies, including "on-behalf" distribution (so-called Art. 50 flow/Health Card).
The categories that will be examined in depth are the following:

- **Antineoplastic and immunomodulating agents**
  - Antineoplastic medicines
  - Immunosuppressants and immunomodulating agents
- **Cardiovascular system**
  - Medicines for hypertension and heart failure
  - Lipid-lowering medicines
- **Gastrointestinal system and metabolism**
  - Antidiabetics
  - Medicines for peptic ulcer and GERD
  - Diseases due to altered functionality of cellular metabolism
- **General antimicrobials for systemic use**
  - Antibiotics
  - Anti-HIV antivirals
  - Vaccines
  - Antifungals for systemic use
- **Blood and blood-forming organs**
  - Anticoagulants
  - Coagulation factors
  - Platelet aggregation inhibitors
- **Central Nervous System**
  - Medicines for multiple sclerosis
  - Antidepressants
  - Medicines for pain therapy
  - Anti-epileptics
  - Antipsychotics
  - Antiparkinsonians
  - Antimigraine medicines
  - Antidementia medicines
- **Respiratory system**
  - Medicines for asthma and COPD
  - Medicines for cystic fibrosis
- **Musculo-skeletal system**
  - Medicines for osteoporosis
  - Nonsteroidal anti-inflammatory drugs (NSAIDs)
- **Systemic hormonal preparations, excluding sex hormones and insulins**
  - Thyroid medicines
- **Genito-urinary system and sex hormones**
  - Medicines for genitourinary disorders
- **Sensory organs**
  - Medicines for eye disorders
- **Various**
  - Contrast agents
  - Radiopharmaceuticals-Radiofarmaci
- **Dermatologicals**

For the classification of categories, please refer to Appendix 3.

Figure 3.6 2023-2022 % variation in consumption of the most frequently prescribed therapeutic categories

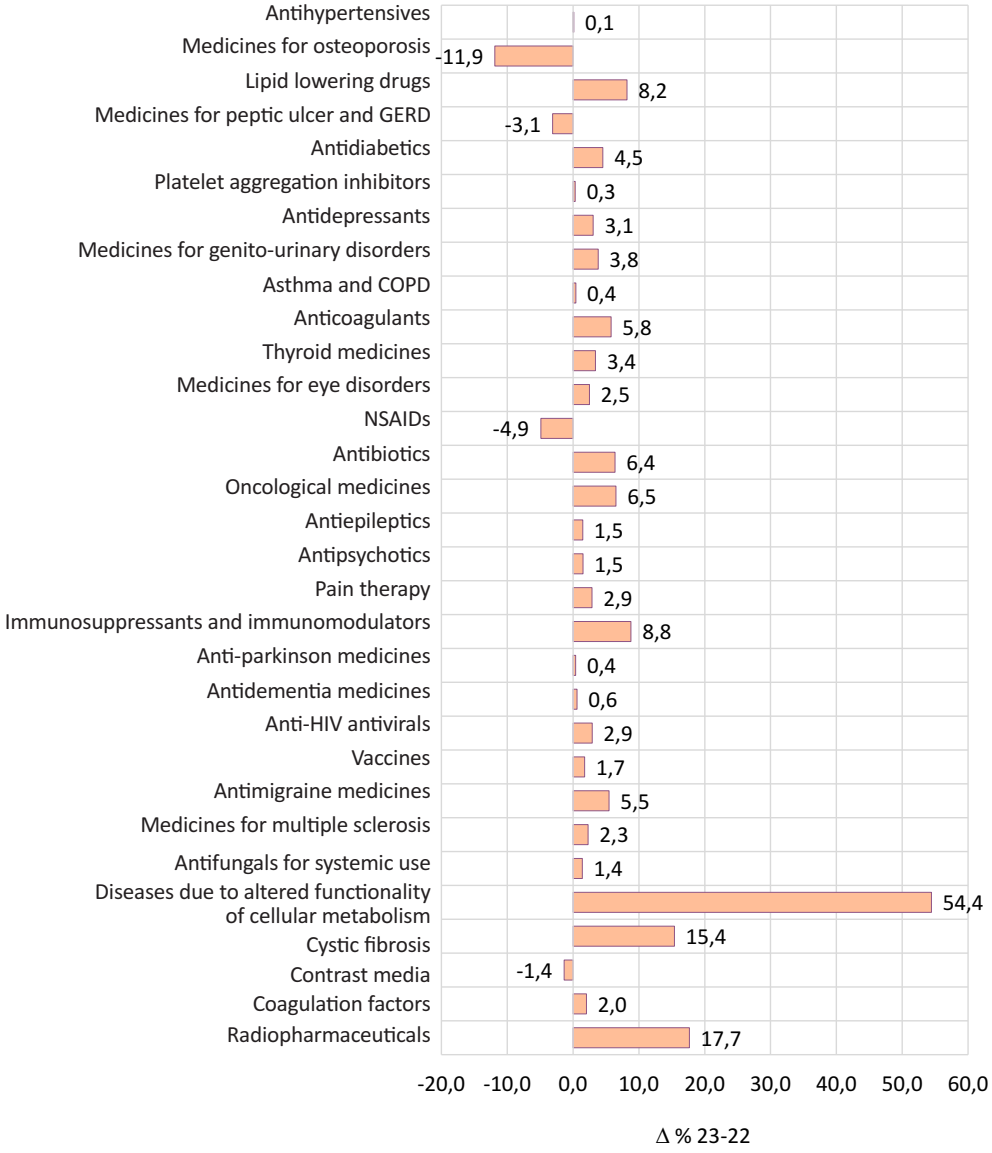


Figure 3.7 2023-2022 % variation in high adherence by therapeutic category

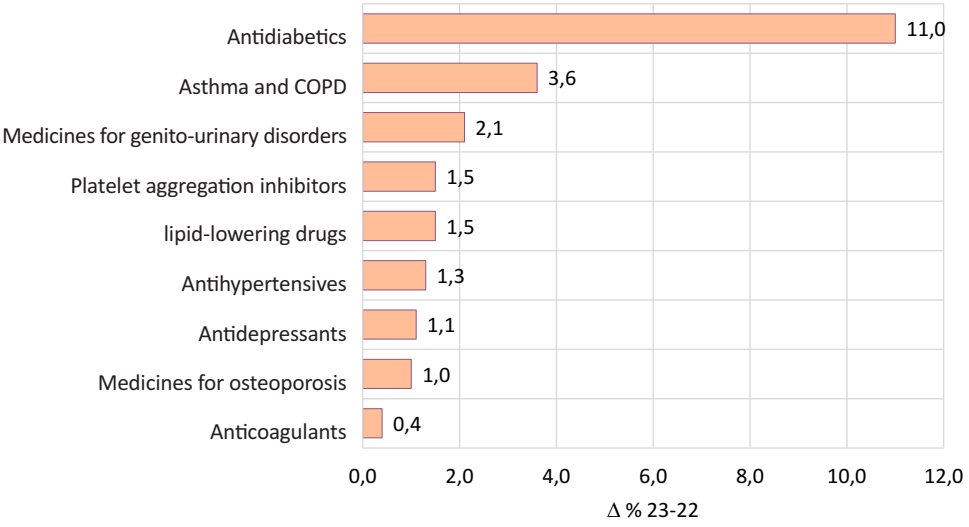
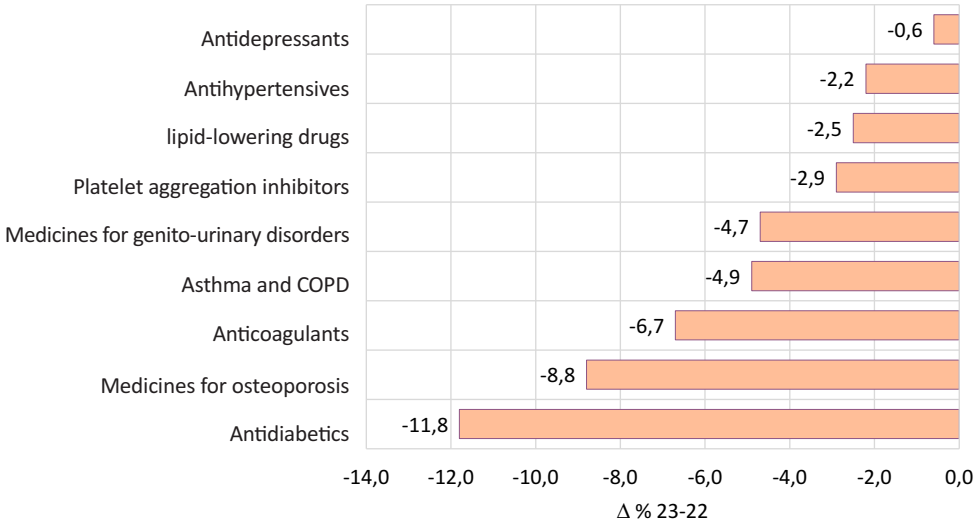


Figure 3.8 2023-2022 % variation in low adherence by therapeutic category



3.1 Antineoplastic and immunomodulating agents

Antineoplastic and immunomodulating agents were the therapeutic category with the highest public expenditure in 2023, amounting to 7,358 million euros (28.3% of overall expenditure), with a 6.4% increase compared to the previous year (Box. Main indices of expenditure, consumption and exposure). The overall per capita expenditure on such medicines was 125.03 euros, mainly due to the purchase by public health facilities (120.47 euros per capita), thus recording an increase compared to the previous year (+6.6%). On the contrary, the share due to the approved care regime was lower (4.55 euros per capita) (Table 3.1). Consumption for this category of drugs was 22.4 DDD/1000 inhabitants per day, a 6.1% increase compared to 2022 (Table 3.2), which confirms the growing trend of the last ten years.

The analysis of the medicine utilisation profile by age group and gender (including approved care regime and "on-behalf" distribution) confirms a higher use with increasing age, with a marked increase in the prevalence of use in women compared to men starting from the age of 35, probably attributable to the prescription of medicines for breast cancer therapy and to the different prevalence of autoimmune diseases. However, a turnaround is recorded in the population aged over 75, with a greater prevalence of use in the male population (5.2% compared to 4.1% in women), probably due to the increase in the incidence of prostate cancer in this population. Per capita expenditure on drugs in this category increases with age up to 74 years, remaining at higher levels in females than in males. Subsequently, starting from 75 years, expenditure reaches higher values in males (26.4 euros per capita compared to 14.8 for females).

Analysing the trends over the last six years (2017-2023) of per capita expenditure, consumption and average cost per DDD of class A medicines and medicines purchased by public facilities (Figures 3.1-3.3), the category of antineoplastics and immunosuppressants ranks first in terms of expenditure and average cost per DDD. In particular, per capita expenditure shows an evident upward trend, driven by both an increase in consumption and in the average cost per DDD.

As regards approved care regime, the regional distribution shows a high variability both in gross per capita expenditure (Table 3.5), with maximum values in Lombardy (6.8 euros) and minimum values in Tuscany (0.6 euros), and in consumption (Table 3.6), with a greater use in Lombardy and Sardinia (8.8 and 8.5 DDD/1000 inhabitants per day) and a lower use in Tuscany (1.4 DDD). As for approved care regime, in 2023 per capita expenditure was 4.6 euros, up 2.2% compared to the previous year. This trend was determined exclusively by an increase in consumption (+1.3%), as there was no shift towards more expensive medicinal products and the average DDD cost remained stable (Table 3.9). Under this supply regime, aromatase inhibitors are the first category both in terms of expenditure (2.43 euros per capita) and consumption (3.3 DDD), followed by other substances with immunosuppressive action and calcineurin inhibitors (belonging to the class of immunosuppressants), with a per capita expenditure respectively of 0.86 euros and 0.51 euros and 1.8 and 0.2 DDD (Table 3.9). Letrozole, an aromatase inhibitor used for the treatment of breast cancer in menopausal women, is the first active ingredient in the category by per capita expenditure (1.57 euros) and by consumption (1.9 DDD/1000 inhabitants per day) (Table 3.10). This is the only antineoplastic and immunosuppressant drug within the first 30 active ingredients for expenditure under approved care regime (Table 3.11), and, along with exemestane, it is among the top thirty active ingredients with the highest average cost DDD with a value equal

to 2.24 euros and 2.21 euros respectively (Table 3.12). Letrozole, together with exemestane and methotrexate, is among the top 30 active ingredients with the greatest increase in expenditure, with a variation of 3.9%, 9.2% and 5.1% respectively (Table 3.14).
As for purchases by public healthcare facilities, the regional distribution (Table 3.7) shows a moderate variability of gross per capita expenditure with maximum values in Campania (145.8 euros) and Sardinia (142.8 euros), and minimum values in Valle d'Aosta (86.6 euros) and in the Province of Trento (92.0 euros). The distribution of consumption shows high values of use in Tuscany (19.2 DDD) and Emilia Romagna (18.0 DDD) and lower values in Valle d'Aosta (9.9 DDD) and Lombardy (10.2 DDD) (Table 3.8). Overall, an increase in expenditure (+6.3%) and consumption (+9.6%) was recorded, as well as a shift towards more expensive medicinal products (mix effect: +1.9%). Compared to 2022 there was a reduction in prices (-4.8%) and in the average DDD cost (-3.0%) (Table 3.17).
PD-1/PDL-1 inhibitors, which include pembrolizumab and nivolumab, are the first category in per capita expenditure (14.96 euros), with a 12.7% increase compared to the previous year. They also record an increase in consumption (+26.0%) and a shift towards more expensive drugs (mix effect: -4.9%), while reporting a reduction in prices (-6.0%) and in the average DDD cost (-10.6%). Half of the per capita expenditure is attributable to pembrolizumab alone.
In second and third place in terms of expenditure are interleukin inhibitors (11.57 euros per capita) and CD38 inhibitors (8.21 euros per capita). For these two categories there were increases both in expenditure (respectively +17.1% and +18.7%) and consumption (respectively +19.5% and +32.8%) compared to the previous year, as well as a reduction of prices (-1.6% and -6.2%) and of the average DDD cost (-2.0% and -10.6%). As for CD38 inhibitors, whose the cost is largely attributable to daratumumab, a monoclonal antibody used in combination with bortezomib, thalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma eligible for autologous stem cell transplantation, there is a shift towards less expensive medicinal products (mix effect: -4.7%). Compared to the previous year, the category "Other monoclonal antibodies and antibody drug conjugates" also shows an increase in both expenditure and consumption by more than 100%. On the other hand, expenditure on the category of other immunosuppressants decreased (-39.6%), mainly driven by the shift towards less expensive medicinal products (mix effect: -35.4%) and by the reduction in the average DDD cost (-41.3%). As observed the previous year, there was a reduction in the expenditure on anti-TNF-alpha inhibitors (-4.2%), despite an increase in consumption (+8.7%), mainly due to a reduction in prices (-5.5%) and the shift towards less expensive medicinal products (-6.8%). The expenditure trend in this category is attributable to the reduction in prices (-5.5%) due to the presence on the market of biosimilars of some molecules. On the contrary, monoclonal antibodies show an increase in expenditure (+17.5%), consumption (+13.7%) and a reduction in prices (-3.1%), but and a shift to more expensive medicines (mix effect +6.7%), also confirmed by an increase in the average DDD cost (+3.4%; Table 3.17).
In 2023, pembrolizumab and daratumumab are the drugs with the highest value of expenditure per capita (7.76 euros and 7.75 euros) and each accounts for 6.4% of expenditure in this category (Table 3.18). For pembrolizumab there was an increase in expenditure (+3.0%) and in consumption of +8.3% and a slight reduction in the average DDD cost (-4.9%). Daratumumab shows a higher increase in both expenditure (+17.2%) and consumption (+32.4%), against a reduction in the average DDD cost (-11.5%). Nivolumab, a PD-1 immune checkpoint inhibitor, ranks third in per capita expenditure (3.78 euros), up 14.5% compared

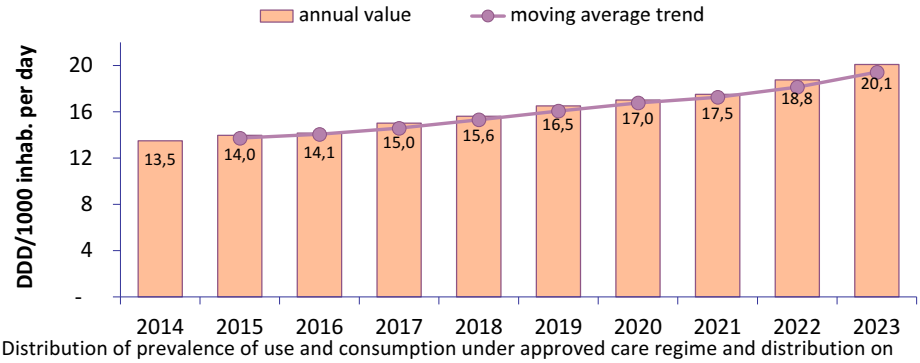
to 2022, showing a 22.5% increase in consumption and a 6.5% reduction in average DDD cost, presumably linked to a renegotiation of the drug. In addition, ibrutinib, an inhibitor of Bruton tyrosine kinase, shows a reduction in the average DDDD cost (-3.5%), although the expenditure is reduced only slightly (-0.8%) due to a 2.8% increase in consumption.
The list of the 30 most expensive medicines purchased by public health facilities (Table 3.19) includes 15 active ingredients belonging to the category of antineoplastics and immunomodulators. Pembrolizumab and daratumumab rank first and second among the most expensive drugs purchased by public health facilities (Table 3.19), even considering the total with approved care expenditure (Table 3.25). On the other hand, 12 active ingredients of the ATC L group are included in the list of the top thirty with the greatest variation in expenditure compared to the previous year (Table 3.20), reporting increases ranging from a minimum of 22% for riboclib to a maximum of 100% and above for ravulizumab, acalabrutinib, axicabtagene ciloleucel, and apalutamide. Fingolimod is the first drug for expenditure reduction among medicines purchased by public health facilities (-29.2% per capita expenditure) (Table 3.21).
Among the top 30 drugs purchased by public health facilities with the highest average cost per DDD, 13 belong to the ATC L group (Table 3.22). In first place is a CAR-T therapy (axicabtagene ciloleucel), with a value of almost 283 thousand euros, up 70.7% compared to the previous year. This variation is due to the change in the methods of accounting for the expenditure of the drug that were subject to conditional reimbursement agreements, payment at result, which provided for the allocation and for the attribution of fractions of the cost of treatment over time following the verification of the maintenance of therapeutic success. Subsequently, the amendment provided for the revision of the negotiating agreement and for accounting for the full cost of the infusion treatment. In second and third place are two drugs indicated in the treatment of adults and children with paroxysmal nocturnal hemoglobinuria (PNH), eculizmab with an average cost per DDD of 710.9 euros and ravulizumab with a cost of 548.3 euros, both decreasing compared to 2022, respectively -2.5% and -9.7%. The other 10 active ingredients have an average cost that varies between a maximum of 293.2 euros for brentuximab vedotin and a minimum of 119.2 euros for ibrutinib. There are 6 active ingredients of ATC L in the list of the top 30 active ingredients with the lowest average cost per DDD purchased by public health facilities (Table 3.23), including triptorelin with an average DDD cost of 2.70 euros, adalimumab with 4.37 euros and tacrolimus (5.88 euros). With the exception of triptorelin, a reduction in the average cost per DDD was observed for all compared to the previous year. Table 3.27 shows the different trend in terms of expenditure, consumption and average DDD cost between the approved care regime and direct purchases for antineoplastic medicines, immunosuppressants and immunomodulating agents.

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

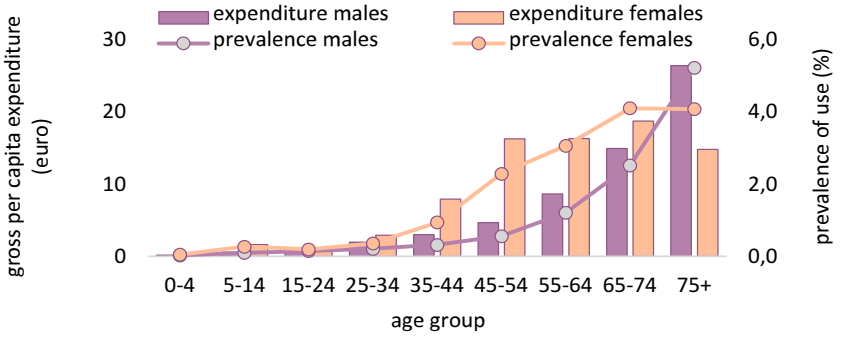
Antineoplastic and immunomodulating agents

Public expenditure* in million euros (% over total)	**7,358.1**	**(28.3)**
Δ % 2023-2022		6.4
Regional range of gross per capita expenditure:	90.3	150.9
DDD/1000 inhabitants per day* (% over total)	**20.1**	**(1.5)**
Δ % 2023-2022		7.1
Regional range DDD/1000 inhabitants per day	15.7	23.2

** includes prescriptions under approved care regime and purchases by public health facilities*



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf by age and gender in 2023 (Figure and Table)



Age group	Gross per capita expenditure			DDD/1000 inhab. per day		
	Males	Females	Total	Males	Females	Total
0-4	0.2	0.2	0.2	0.1	0.1	0.1
5-14	0.6	1.6	1.1	0.4	1.5	0.9
15-24	1.1	1.1	1.1	0.6	0.8	0.7
25-34	2.0	2.9	2.4	0.9	1.7	1.3
35-44	3.0	7.9	5.5	1.5	6.5	4.0
45-54	4.7	16.3	10.5	2.6	17.6	10.2
55-64	8.6	16.3	12.6	5.4	19.4	12.6
65-74	14.9	18.7	16.9	10.7	25.0	18.2
75+	26.4	14.8	19.6	26.1	22.5	24.0

3.1.1 Antineoplastic medicines

In 2023, total public expenditure on antineoplastic drugs amounted to 4,773.9 million euros, up 9.6% compared to 2022, representing 18.4% of total public expenditure (Box Main expenditure and consumption indices). The corresponding total consumption was equal to 11.6 DDD/1000 inhabitants per day, up 6.5% compared to 2022, accounting for 0.9% of the total consumption of drugs covered by the NHS. In the period 2014-2023, expenditure on antineoplastic medicines more than doubled, going from 35.1 euros in 2014 to 81.1 euros in 2023, recording a 9.8% average annual increase. At the same time, the average DDD cost increased by 76%, shifting from 10.9 euros in 2014 to 19.1 euros in 2023. Consumption has also increased over the last 10 years, with an average annual increase of 2.8%. In 2023, the first three categories with the highest expenditure are monoclonal antibodies (Table 3.1.1a); in first place are immune checkpoint inhibitors (15.65 euros per capita), for which a significant increase is observed, compared to 2022, both in expenditure (+13.3%) and consumption (+26.4%), despite a reduction in the average cost per DDD (-10.4%). This category shows the most marked increase in per capita expenditure in the last 10 years (Figure 3.1.1a). The reasons for this trend are due to the numerous extensions of indication of use for these molecules, in combination with other drugs in various solid tumors, all of which have reported results of therapeutic improvement. They are followed by monoclonal antibodies active on specific targets (9.93 euros), which for the second consecutive year have recorded an increase in both expenditure (+16.0%) and consumption (+16.7%) compared to the previous year, and monoclonal antibodies blocking the action of growth factors (5.14 euros), which instead show a reduction in both expenditure (-10.9%) and average cost per DDD (-9.9%) and a slight reduction in consumption (-1.0%), due to the presence of biosimilars for some drugs in this class.

In fourth place for per capita expenditure (4.52 euros) are Bruton tyrosine kinase inhibitors, with an increase of 19.0% compared to 2022, attributable to the increase in consumption (+20.9%) observed for this group of drugs, while the average cost decreased by 1.5%. This category of drugs will probably be affected by further increases in the coming years due to the arrival of new molecules on the market, such as pirtobrutinib and acalabrutinib, for the treatment of some onco-haematological diseases.

Aromatase inhibitors, used as endocrine therapy in some forms of hormone-sensitive carcinomas, are the drugs with the highest consumption in 2023 within the category, equal to 4.0 DDD/1000 inhabitants per day, corresponding to a per capita expenditure of 2.9 euros and an average cost per DDD of 1.99 euros. The 29.7% decrease compared to 2022 can be attributed to the introduction on the market at the end of 2022 of equivalent medicines due to the patent expiry of abiraterone, a drug used in combination with prednisone and prednisolone in the treatment of some forms of prostate cancer. On the other hand, a new hormonal therapy was reported based on elacestrant, a selective inhibitor of the estrogen receptor (ER) in the treatment of advanced or metastatic carcinoma, positive for the estrogen receptor (ER+) and negative for the HER2- receptor, which has developed ESR1 mutations, after at least one line of treatment with endocrine therapy, currently classified in Cnn (C-class, non-negotiated). However, this could have increased the impact of expenditure in this therapeutic setting.

JAK tyrosine kinase inhibitors, which include drugs such as ruxolitinib and fedratinib, both indicated for the treatment of splenomegaly or disease-related symptoms in adult patients

with primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis, are the category that in the period 2014-2023 recorded the highest average annual increase in both expenditure (+68.5%) and consumption (+71.7%), while CAR-Ts showed the highest average cost per DDD (approximately 271.45 thousand euros), up 28.8% compared to 2022 (Table 3.1.1a). Increases in expenditure and consumption are also recorded for the group of antibody-drug conjugates (ADC), respectively +36.7% and +51.7%, which have the characteristic of "combining" the efficacy of molecular-targeted therapies with the cytotoxicity of chemotherapy and for which the impact on expenditure will have to be monitored in the coming years, given the average annual increase recorded for consumption (+34.7%). Finally, marked increases are reported in expenditure and consumption (>100%) compared to the previous year for the combination pertuzumab/trastuzumab indicated in HER2-positive breast cancer, for the RET protein kinase inhibitors (pralsetinib, selpercatinib) indicated in the treatment of some forms of thyroid cancer and advanced RET fusion-positive non-small cell lung cancer (NSCLC), for the bispecific fusion protein ImmTAC (tebentafusp) in the treatment of metastatic uveal melanoma and for the FGFR tyrosine kinase inhibitor (pemigatinib) for the treatment of intrahepatic cholangiocarcinoma. The trend of the individual active ingredients follows the trend of the subgroups; in fact, pembrolizumab (7.76 euros) and daratumumab (7.75 euros) are at the top of the list, both with an increase in expenditure and consumption compared to the previous year. Daratumumab also records an increase in consumption (+32.4%) and in expenditure (+17.2%) and a reduction in the average DDD cost (-11.5%) (Table 3.1.1a). On the other hand, ribociclib is the active ingredient with the lowest cost with 67.98 euros per DDD, a -0.2% reduction compared to the previous year.

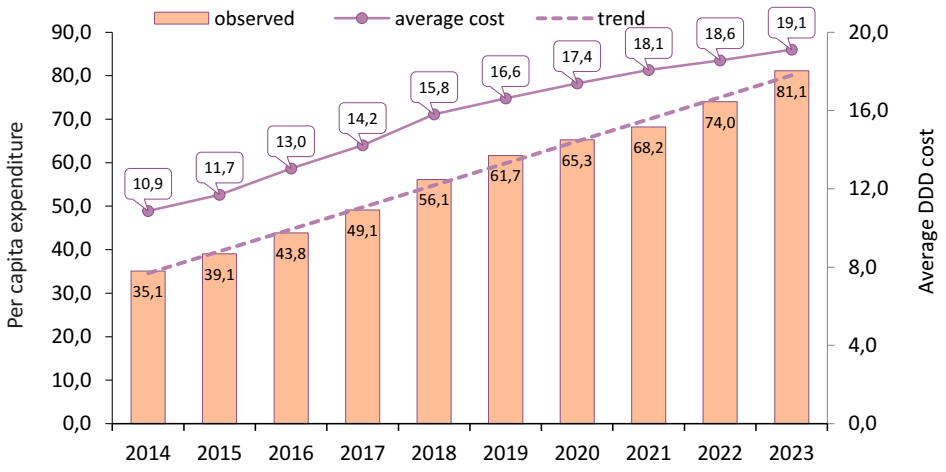
Analysing the regional per capita expenditure (national average value 81.12 euros), the Centre and the South tend to spend more (84.72 and 83.57 euros respectively) than the North (77.86 euros) (Table 3.1.1b). The profound variability is evident from the difference between Friuli Venezia Giulia's highest expenditure value (97.23 euros) and Valle d'Aosta's lowest (55.56 euros). In 2023, all regions recorded increases in both per capita expenditure and consumption compared to the previous year, while only three regions showed a reduction in the average cost per DDD (Molise: -4.4%; Umbria: -1.6%; Veneto: -1.1%). Finally, Valle d'Aosta and Emilia Romagna are the regions where the most significant increase in per capita expenditure (+27.2%) and consumption (+11.0%) is observed, respectively. The possibility of identifying molecular alterations present in a single patient has allowed personalizing oncological treatments, with the development of increasingly targeted therapies with fewer adverse effects than traditional cytotoxic therapies. However, in this new model of mutational oncology, it is necessary to take into account not only the economic impact of pharmacological therapies but also the impact deriving from the diffusion in clinical practice of both genetic sequencing tests (for tumor profiling and identification of specific biomarkers) and of diagnostic drugs used for the detection of specific lesions before the start of treatment.

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE.
Antineoplastic medicines

Public expenditure* in million euros (% over total)	**4,773.9**	**(18.4)**
Δ % 2023-2022		9.6
Regional range of gross per capita expenditure:	55.6	97.2
DDD/1000 inhabitants per day* (% over total)	**11.6**	**(0.9)**
Δ % 2023-2022		6.5
Regional range DDD/1000 inhabitants per day	9.2	12.9

** includes prescriptions under approved care regime and purchases by public health facilities*

Antineoplastic medicines, temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)



National data on consumption and expenditure by subgroup and substance

Table 3.1.1a Antineoplastic medicines, per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and by substance: comparison 2014-2023

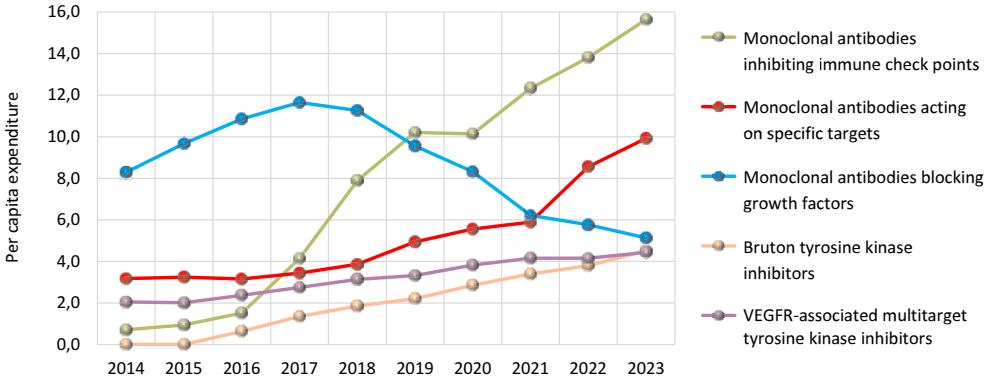
Subgroups and substances	Expenditure per capita	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Monoclonal antibodies inhibiting immune checkpoints	15.65	13.3	36.2	0.5	26.4	64.8	92.02	-10.4
Monoclonal antibodies acting on specific targets	9.93	16.0	12.1	0.8	16.7	6.7	35.52	-0.6
Monoclonal antibodies blocking growth factors	5.14	-10.9	-4.7	0.4	-1.0	3.9	36.88	-9.9
Bruton tyrosine kinase (BTK) inhibitors	4.52	19.0	—	0.1	20.9		122.69	-1.5
VEGFR-associated multitarget tyrosine kinase inhibitors	4.43	6.9	8.0	0.1	11.5	11.4	90.58	-4.2
CDK protein kinase inhibitors 4/6	4.36	14.5	—	0.2	19.9		62.75	-4.5
Endocrine therapy – antiandrogens	3.84	42.0	31.0	0.8	2.0	-3.5	12.96	39.2
Monoclonal antibodies conjugated with drugs	3.80	36.7	28.8	0.1	51.7	34.7	193.83	-9.9
EGFR tyrosine kinase inhibitors	3.01	2.5	11.3	0.1	7.2	6.1	121.86	-4.4
Endocrine therapy - aromatase inhibitors	2.90	-26.7	1.3	4.0	4.3	4.8	1.99	-29.7
BRC-ABL tyrosine kinase inhibitors	2.63	-16.6	-6.0	0.2	0.0	1.4	40.16	-16.5
JAK tyrosine kinase inhibitors	2.49	17.1	68.5	0.1	17.8	71.7	109.30	-0.7
Endocrine therapy - hormones and GnRH analogues	2.27	5.8	1.4	1.4	8.1	3.1	4.48	-2.1
Cytostatic antineoplastics - PARP inhibitors	2.15	14.0	—	<0.05	14.3		135.13	-0.2
Cytostatic antineoplastics - other cytostatics	2.03	11.8	12.9	0.4	4.3	3.4	14.75	7.2
CAR-T	1.81	51.6	—	<0.05	17.7		271450.37	28.8
BRAF tyrosine kinase inhibitors	1.59	6.1	12.2	<0.05	4.9	24.7	113.46	1.2
ALK tyrosine kinase inhibitors	1.49	3.3	—	<0.05	11.1		131.63	-7.0
Cytostatic antineoplastics – antimetabolites	1.21	-10.6	-8.0	0.6	-2.6	-3.5	5.31	-8.1
Cytostatic antineoplastics - proteasome inhibitors	0.89	4.7	-4.9	<0.05	7.7	3.3	58.56	-2.7
MEK tyrosine kinase inhibitors	0.69	-3.4	—	<0.05	1.8		53.52	-5.1
Antineoplastics in combination	0.64	>100	—	<0.05	>100		2765.26	45.8
Other protein kinase inhibitors	0.61	11.9	—	<0.05	11.1		448.61	0.7
Cytotoxic antineoplastics of natural derivation – taxanes	0.42	-5.7	-2.3	0.2	1.3	2.2	6.31	-6.9
Cytostatic antineoplastics - alkylating agents	0.36	4.7	-7.1	0.2	0.7	-3.1	5.58	4.0
Cytotoxic antineoplastics - cytotoxic antibiotics - anthracyclines and related substances	0.36	-18.8	-3.7	0.1	-9.3	-2.9	11.09	-10.5
Hedgehog pathway inhibitors	0.34	13.3	48.6	<0.05	18.0	63.3	113.12	-3.9

continued

Table 3.1.1a – *continued*

Subgroups and substances	Expenditure per capita	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
MTOR protein kinase inhibitors	0.23	-37.6	-14.4	<0.05	-2.6	-3.7	43.05	-36.0
Combination of antineoplastic agents	0.21	40.4	—	<0.05	40.1		3817.23	0.2
Cytotoxic antineoplastics of natural derivation – others	0.20	-43.2	-8.8	0.1	-1.4	-1.1	10.37	-42.4
Endocrine therapy - antiestrogens	0.20	1.0	-9.5	0.9	9.2	-2.6	0.60	-7.5
RET protein kinase inhibitors	0.11	>100	—	<0.05	>100	—	139.66	244.4
NTRK protein kinase inhibitors	0.11	65.1	—	<0.05	64.2	—	181.74	0.6
Bispecific fusion protein (ImmTAC)	0.08	>100	—	<0.05	>100	—	294.60	>100
Cytostatic antineoplastics – platinum compounds	0.07	-3.7	-3.0	0.2	-3.0	-0.2	0.99	-0.7
Cytotoxic antineoplastics – cytotoxic antibiotics - others	0.07	1.4	-3.1	0.2	37.7	11.9	1.09	-26.4
Cytostatic antineoplastics - PI3K inhibitors	0.06	-21.1	—	<0.05	-17.0	—	97.67	-4.9
IL-3 fusion protein and diphtheria toxin (anti-CD123 cytotoxin)	0.05	—	—	<0.05	—	—	1168.63	—
HER2 tyrosine kinase inhibitors	0.04	-45.1	-16.7	<0.05	-45.3	-14.7	70.56	0.3
MET tyrosine kinase inhibitors	0.03	—	—	<0.05	—	—	155.17	—
FGFR tyrosine kinase inhibitors	0.02	>100	—	<0.05	>100	—	197.39	0.0
IgG1 monoclonal antibodies bispecific against EGFR-MET	0.02	—	—	<0.05	—	—	131.14	—
Cytostatic antineoplastics - TOP1 inhibitors	0.02	-16.5	-8.2	<0.05	-4.9	-1.7	2.01	-12.2
KIT and PDGFRA tyrosine kinase inhibitors	0.02	—	—	<0.05	—	—	428.60	—
KRAS G12C selective inhibitors	0.01	—	—	<0.05	—	—	277.09	—
Alkylating agents	<0.005	-36.2	—	<0.05	-29.8	—	79.65	—
Antineoplastic medicines	**81.12**	**9.6**	**9.8**	**11.6**	**6.5**	**2.8**	**19.11**	**2.9**
pembrolizumab	7.76	3.0	—	0.2	8.3	—	87.70	-4.9
daratumumab	7.75	17.2	—	0.3	32.4	—	83.48	-11.5
nivolumab	3.78	14.5	—	0.1	22.5	—	109.12	-6.5
ibrutinib	3.40	-0.8	—	0.1	2.8	—	119.24	-3.5
osimertinib	2.94	3.6	—	0.1	11.6	—	130.71	-7.2
enzalutamide	2.52	25.2	68.9	0.1	32.0	81.3	65.62	-5.2
ruxolitinib	2.36	12.8	67.6	0.1	12.0	70.5	111.23	0.6
pertuzumab	2.32	-11.5	24.6	0.1	-11.5	27.7	105.55	0.0
nintedanib	2.05	28.9	—	0.1	30.1	—	91.01	-0.9
ribociclib	1.71	22.0	—	0.1	22.2	—	67.98	-0.2

Figure 3.1.1a Antineoplastic medicines, temporal trend 2014-2023 of per capita expenditure on most expensive subgroups



Regional data on consumption and expenditure

Table 3.1.1b Antineoplastic medicines, regional trend of per capita expenditure, consumption (DDD/1000 inhab. per day) and average cost per day of therapy: comparison 2014-2022

Region	2022			2023			Δ % 23-22			CAGR % 14-23		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost
Piedmont	65.62	10.8	16.72	74.16	11.5	17.64	13.0	7.1	5.5	8.1	2.9	5.1
Valle d'Aosta	43.67	8.8	13.67	55.56	9.2	16.55	27.2	5.1	21.0	7.8	2.1	5.6
Lombardy	65.53	11.1	16.23	70.54	11.7	16.52	7.6	5.8	1.8	9.2	2.2	6.8
Province of Bolzano	74.76	9.3	21.95	83.78	9.4	24.38	12.1	0.9	11.1	8.4	3.3	4.9
Province of Trento	57.03	10.3	15.21	63.44	10.8	16.07	11.2	5.3	5.7	9.0	3.5	5.3
Veneto	73.29	11.0	18.32	75.46	11.4	18.12	3.0	4.1	-1.1	8.4	2.7	5.6
Friuli V.G.	82.71	10.8	20.93	97.23	11.9	22.42	17.5	9.7	7.1	8.8	1.9	6.8
Liguria	82.69	11.3	20.07	92.01	12.4	20.33	11.3	9.9	1.3	9.9	3.0	6.7
Emilia R.	82.17	11.0	20.49	91.34	12.2	20.52	11.2	11.0	0.1	9.9	3.6	6.2
Tuscany	73.90	11.0	18.39	83.43	12.0	19.09	12.9	8.7	3.8	7.2	3.0	4.0
Umbria	89.76	11.6	21.22	95.97	12.6	20.88	6.9	8.7	-1.6	9.8	3.7	5.8
Marche	87.41	12.6	18.99	93.31	12.9	19.76	6.8	2.6	4.1	8.7	2.9	5.7
Lazio	74.06	11.1	18.33	81.48	11.7	19.14	10.0	5.4	4.4	9.0	2.2	6.7
Abruzzo	80.33	11.7	18.79	90.45	12.4	19.98	12.6	5.9	6.3	7.8	2.7	5.0
Molise	73.24	10.6	18.92	73.95	11.2	18.09	1.0	5.6	-4.4	9.1	3.9	5.0
Campania	85.80	11.3	20.75	95.22	12.0	21.78	11.0	5.7	4.9	8.8	3.5	5.1
Puglia	80.10	11.0	19.99	83.51	11.4	19.99	4.3	4.2	0.0	7.7	2.3	5.3
Basilicata	76.94	10.7	19.63	83.87	11.2	20.45	9.0	4.7	4.1	7.6	3.6	3.8
Calabria	70.52	10.3	18.82	77.17	10.9	19.43	9.4	6.0	3.3	9.2	3.3	5.7
Sicily	64.08	9.5	18.53	71.28	10.2	19.20	11.2	7.4	3.6	9.5	2.7	6.6
Sardinia	73.07	11.1	18.04	84.89	12.1	19.18	16.2	9.3	6.3	8.3	3.4	4.7
Italy	**74.01**	**10.9**	**18.56**	**81.12**	**11.6**	**19.11**	**9.6**	**6.5**	**2.9**	**8.7**	**2.8**	**5.8**
North	71.31	10.9	17.88	77.86	11.7	18.26	9.2	6.9	2.2	9.0	2.7	6.2
Centre	76.92	11.3	18.67	84.72	12.0	19.35	10.1	6.3	3.6	8.4	2.6	5.6
South and Islands	76.08	10.7	19.50	83.57	11.3	20.19	9.8	6.1	3.5	8.6	3.0	5.4

3.1.2 Immunosuppressants and immunomodulating agents

In 2023, total public expenditure on immunosuppressants and immunomodulating agents amounted to 1,817.5 million euros, up 1.0% compared to 2022, representing 7.0% of total public expenditure (Box Main expenditure and consumption indices). The corresponding total consumption was 7.3 DDD/1000 inhabitants per day, up 8.8% compared to the previous year, representing 0.6% of the total consumption of NHS-covered drugs.
In the period 2014-2023, expenditure on immunosuppressants and immunomodulating agents increased by about 39.4%, shifting from 22.1 to 30.9 euros per capita, with an average annual increase of 3.4%. Similarly, the average DDD cost recorded a 30.4% decrease, switching from 16.70 to 11.62 euros, with an average annual decrease of 3.6%, while consumption increases on average by 7.2% each year (Table 3.1.2a).
The category with the greatest per capita expenditure is interleukin inhibitors (11.57 euros), up 17.5% compared to 2022. This is followed by selective immunosuppressive monoclonal antibodies (4.66 euros), whose expenditure values increased by 20.8% compared to the previous year, and TNF-α inhibitors (4.49 euros), whose values instead decreased by 3.9%.
All subgroups belonging to this category of drugs showed increases in consumption in 2023, with JAK tyrosine kinase inhibitors reporting the most significant increase (+23.0% compared to 2022), with the exception of interferons, down 3.6% as regards the number of DDDs consumed per 1000 inhabitants per day (Table 3.1.2a). The subgroup "Other immunosuppressants" recorded the most significant reduction in per capita expenditure (-43.0% compared to 2022), due to the marked reduction in 2023 in the average DDD cost (-45.0%), maybe due to greater use of biosimilar drugs. In fact, these drugs represent the group with the lowest average cost per DDD in the category (3.98 euros). Conversely, the highest average cost per DDD was observed for "other immunomodulators", with 176.63 euros, up 4.7%.
Interleukin inhibitors, selective immunosuppressive monoclonal antibodies and JAK tyrosine kinase inhibitors show a constantly increasing trend in consumption, especially in the last five years (Figure 3.1.2a).
Analyzing the trend of the individual active ingredients, ustekinumab, an interleukin inhibitor indicated in the treatment of adult patients with Crohn's disease and ulcerative colitis, records the highest value of expenditure (2.60 euros) and consumption (0.5 DDD/1000 inhabitants per day) in the category, confirming the growth trend observed in recent years, despite a 2.1% reduction in the average cost per DDD in 2023. High increases in expenditure and consumption are also observed for ixekizumab (+14.5% for expenditure and consumption), canakinumab (+16.2% for expenditure and +21.3% for consumption) and guselkumab (+43.7% for expenditure and consumption), although this last active ingredient has the lowest expenditure and consumption values compared to the others.
Adalimumab and etanercept are the only molecules reporting a reduction in per capita expenditure compared to the previous year, by 6.2% and 8.2% respectively, and a reduction in the average cost per DDD in 2023 equal to over 14% for both molecules, probably due to the presence of biosimilars on the market.
Analysing the regional variability of per capita expenditure, the Southern regions show a higher value (36.57 euros) compared to the national average (30.88 euros), while the Northern regions (28.65 euros) and the Central ones (26.82 euros) show lower values (Table 3.1.2b). The marked regional variability is evident considering the minimum value in Lazio

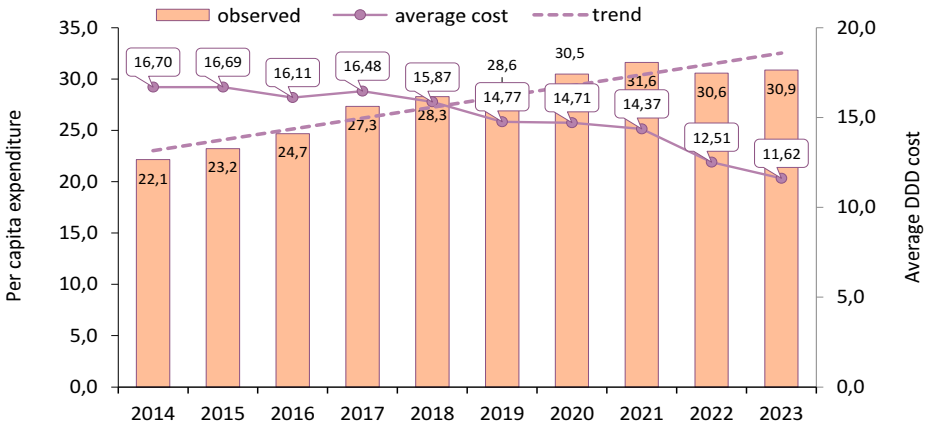
(22.61 euros) and the maximum value in Calabria (45.76 euros). However, this variability appears to be less marked in consumption, with the South showing a value slightly higher (7.8 DDD/1000 inhabitants per day) than the national average (7.3 DDD) and the Centre (6.9 DDD) and the North (7.1 DDD) showing values slightly below the average.
Compared to the previous year, Valle d'Aosta in 2022 shows the greatest increase in per capita expenditure (+13.1%), while Friuli Venezia Giulia records the highest increase in consumption (+13.9%). All Regions show a reduction in the cost per DDD, with values ranging between -3.2% in Sardinia and -15.6% in Umbria.
As regards the average cost for DDD, compared to a national figure of 11.62 euros, the South shows a higher value (12.77 euros), while the North (11.12 euros) and the Centre (10.67 euros) show slightly lower values. Calabria records the highest average DDD cost (17.03 euros) while Lazio shows the lowest (8.54 euros).

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE.
Immunosuppressants and immunomodulating agents

Public expenditure* in million euros (% over total)	**1,817.5**	**(7.0)**
Δ % 2023-2022		1.0
Regional range of gross per capita expenditure:	22.6	45.8
DDD/1000 inhabitants per day* (% over total)	**7.3**	**(0.6)**
Δ % 2023-2022		8.8
Regional range DDD/1000 inhabitants per day	5.6	9.4

** includes prescriptions under approved care regime and purchases by public health facilities*

Immunosuppressants and immunomodulating agents, temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)

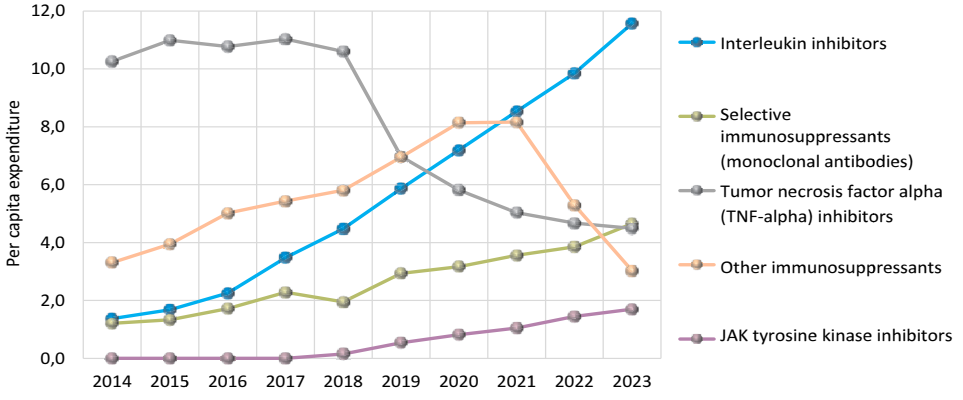


National data on consumption and expenditure by subgroup and substance

Table 3.1.2a Immunosuppressants and immunomodulating agents, per capita expenditure and consumption (DDD/1000 inhab. per day) by therapeutic category and substance: comparison 2014-2023

Subgroups and substances	Expenditure per capita	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Interleukin inhibitors	11.57	17.5	23.7	1.3	19.9	28.4	24.29	-2.0
Selective immunosuppressants (monoclonal antibodies)	4.66	20.8	14.4	0.2	15.1	39.9	69.84	5.0
Tumor necrosis factor alpha inhibitors (TNF-alpha)	4.49	-3.9	-7.9	1.8	9.0	7.2	6.66	-11.9
Other immunosuppressants	3.02	-43.0	-0.9	2.1	3.7	5.4	3.98	-45.0
JAK tyrosine kinase inhibitors	1.70	17.2	—	0.2	23.0	—	20.97	-4.6
Calcineurin inhibitors	1.41	-0.6	-2.1	0.6	1.3	0.4	6.51	-1.9
Selective immunosuppressants	1.29	13.1	8.8	0.7	7.7	5.1	5.39	5.0
Selective T cell co-stimulation modulators	0.94	-21.7	6.1	0.1	11.8	8.7	34.10	-30.0
MTOR protein kinase inhibitors	0.73	3.8	3.5	0.2	4.2	5.4	11.07	-0.4
Growth factors	0.48	-0.3	-10.1	0.1	8.0	2.2	10.46	-7.6
Other immunomodulators	0.45	10.0	8.5	<0.05	5.1	7.2	176.63	4.7
Interferons	0.14	36.7	-18.1	<0.05	-3.6	-23.7	37.04	41.8
Immunosuppressants and immunomodulating agents	**30.88**	**1.0**	**3.4**	**7.3**	**8.8**	**7.2**	**11.62**	**-7.2**
ustekinumab	2.60	13.9	14.5	0.5	16.4	22.4	14.11	-2.1
secukinumab	2.12	4.9	—	0.2	6.4	—	28.95	-1.4
eculizumab	2.01	0.3	5.5	<0.05	2.8	8.4	710.85	-2.5
vedolizumab	1.46	9.1	—	0.1	11.8	—	30.18	-2.4
ixekizumab	1.41	14.5	—	0.1	14.5	—	30.31	0.1
adalimumab	1.36	-6.2	-10.6	0.9	9.6	10.7	4.37	-14.4
canakinumab	1.24	16.2	28.1	<0.05	21.3	32.7	141.56	-4.2
etanercept	1.11	-8.2	-11.0	0.3	7.2	1.8	9.38	-14.3
pomalidomide	1.09	5.9	38.6	<0.05	13.9	41.1	225.52	-7.0
guselkumab	0.99	43.7	—	0.1	43.7	—	24.39	<0.05

Figura 3.1.2a Immunosuppressants and immunomodulating agents, temporal trend 2014-2023 of per capita expenditure on most expensive subgroups



Regional data on consumption and expenditure

Table 3.1.2b Immunosuppressants and immunomodulating agents, regional trend of per capita expenditure, consumption (DDD/1000 inhab. per day) and average cost per day of therapy: comparison 2014-2023

Region	2022			2023			Δ % 23-22			CAGR % 14-23		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost
Piedmont	31.65	6.7	13.01	32.67	7.4	12.03	3.2	11.7	-7.6	5.4	8.5	-2.8
Valle d'Aosta	21.51	5.0	11.80	24.33	5.6	11.83	13.1	12.8	0.2	6.6	5.9	0.7
Lombardy	26.11	6.0	11.85	26.63	6.5	11.25	2.0	7.5	-5.1	3.3	6.1	-2.7
Province of Bolzano	33.95	8.9	10.42	31.61	9.4	9.21	-6.9	5.3	-11.6	2.4	6.8	-4.1
Province of Trento	23.02	7.0	9.03	23.09	7.4	8.54	0.3	6.1	-5.5	3.9	7.1	-2.9
Veneto	28.03	7.0	10.91	26.33	7.1	10.13	-6.0	1.1	-7.1	2.4	6.7	-4.1
Friuli V.G.	32.09	7.9	11.12	34.61	9.0	10.53	7.8	13.9	-5.3	4.5	6.2	-1.7
Liguria	27.66	5.8	13.00	28.67	6.4	12.26	3.7	9.9	-5.7	5.4	7.2	-1.7
Emilia R.	30.38	6.6	12.60	30.42	7.3	11.38	0.1	10.8	-9.7	4.9	7.9	-2.8
Tuscany	27.71	6.6	11.44	28.41	7.5	10.38	2.5	13.0	-9.3	1.2	7.6	-6.0
Umbria	30.15	6.7	12.36	27.30	7.2	10.43	-9.4	7.3	-15.6	2.0	7.0	-4.7
Marche	42.27	7.0	16.62	38.17	7.4	14.10	-9.7	6.4	-15.2	4.5	7.3	-2.6
Lazio	22.76	5.9	10.54	22.61	6.3	9.86	-0.6	6.2	-6.4	0.6	6.9	-6.0
Abruzzo	37.82	7.2	14.48	38.71	7.9	13.39	2.4	10.7	-7.5	5.0	8.6	-3.3
Molise	36.45	6.3	15.94	34.75	6.7	14.22	-4.6	6.9	-10.8	3.0	7.7	-4.4
Campania	40.06	7.3	15.09	42.26	8.1	14.30	5.5	11.3	-5.2	5.5	8.6	-2.9
Puglia	32.90	7.3	12.41	31.05	8.0	10.66	-5.6	9.8	-14.1	0.4	6.8	-6.0
Basilicata	36.25	6.8	14.70	38.06	7.4	14.09	5.0	9.5	-4.1	4.5	7.6	-2.9
Calabria	45.04	6.9	17.76	45.76	7.4	17.03	1.6	5.9	-4.1	5.2	6.7	-1.4
Sicily	28.94	6.8	11.64	30.86	7.5	11.20	6.6	10.8	-3.8	3.9	7.7	-3.5
Sardinia	33.85	7.7	12.00	35.75	8.4	11.62	5.6	9.1	-3.2	2.6	5.4	-2.6
Italy	**30.58**	**6.7**	**12.51**	**30.88**	**7.3**	**11.62**	**1.0**	**8.8**	**-7.2**	**3.4**	**7.2**	**-3.6**
North	28.45	6.5	11.91	28.65	7.1	11.12	0.7	7.9	-6.7	3.9	7.0	-2.9
Centre	27.42	6.3	11.85	26.82	6.9	10.67	-2.2	8.6	-9.9	1.5	7.2	-5.3
South and Islands	35.56	7.1	13.67	36.57	7.8	12.77	2.8	10.1	-6.6	3.7	7.5	-3.5

3.2 Cardiovascular system

Cardiovascular diseases are the main cause of death in the world, with about 18 million deaths every year, accounting for about 30% of the total, 85% of which are due to heart attack and stroke. In 2023, cardiovascular drugs represent the second therapeutic category with the highest public expenditure, accounting for 3,557 million euros and 13.7% of total public expenditure (Box Main indices of expenditure, consumption and exposure). The overall per capita expenditure on these drugs was equal to 60.43 euros (86.4% due to approved care regime), up 4.9% compared to the previous year. The purchase by public health facilities is significantly lower (8.18 euros per capita) but with an increase compared to 2022 (+11.4%) (Table 3.1).

These drugs are confirmed to be the most used (513.91 DDD/1000 inhabitants per day) with 494.98 DDD of the approved care (96.3% of the total) (Table 3.2). The analysis of the drug utilization profile by age group and gender, including approved care regime and distribution on behalf, shows a constant increase in use with increasing age for both genders (maximum prevalence of 90% in the over 75 age group) and this is also reflected in the NHS-covered expenditure, with a maximum value of 197.2 euros per capita in males over 75 years.
As regards approved care regime, the change in expenditure (+3.7%) was due to the shift in prescription towards higher-cost products (mix effect: +2.4%) and to an increase in consumption (+1.3%), while prices remained almost stable (-0.1%) (Table 3.9).

In 2023, HMG-CoA reductase inhibitors (statins) are the active ingredients with the greatest use (82.0 DDD/1000 inhabitants per day) and expenditure per capita (8.09 euros); their indicators remain unchanged compared to the previous year. Selective beta-blockers are the second category with the highest per capita expenditure (5.10 euros), with a 2.1% increase, while consumption stands at 41.9 DDD (+1.3% compared to 2022). Combinations of various lipid modifiers are among the molecules with the greatest variation in expenditure (+39.8%) and consumption (+46.2%) compared to 2022, despite only taking into account 4.9% of total doses. A marked increase is also observed for the category of other cardiac preparations both in expenditure and consumption (>100%), due to the increase in ranolazine, which has been subject to a shift in supply under the approved care regime. Atorvastatin is confirmed as the molecule with the highest per capita expenditure (4.66 euros), while the greatest increases, in addition to ranolazine (>100%), are recorded for the ezetimibe/rosuvastatin combination (+47.4%) (Table 3.10); the latter accounts for 4.4% of the approved care expenditure and 3.2% of consumption. The top thirty active ingredients by expenditure include 13 active ingredients related to the cardiovascular system, with atorvastatin in first place (274.4 million), while only two are on the list of the top 30 active ingredients by average cost: omega 3 (2.27 euros) and ranolazine (2.08 euros), both decreasing compared to the previous year by 2.0% and 8.4% respectively (Table 3.11 and Table 3.12). Analysing the active ingredients with the lowest DDD cost (Table 3.13), 17 belong to the cardiovascular system category, with furosemide having the lowest cost (0.08 euros). Ranolazine ranks first in the list of the top 30 drugs, with the highest increase in expenditure, followed by seven other cardiovascular drugs (Table 3.14). Nine active ingredients in the category are among the first to show the greatest reduction in expenditure, including barnidipine and simvastatin, which record a reduction in expenditure of 8.4% and 7.4%, mainly due to a decrease in consumption (Table 3.15). Ramipril remains the most prescribed active ingredient with 60.7 DDD/1000 inhabitants per day, accounting

for over 12% of total consumption for this category, followed, at a distance, by atorvastatin with 50.6 DDD/1000 inhabitants per day.

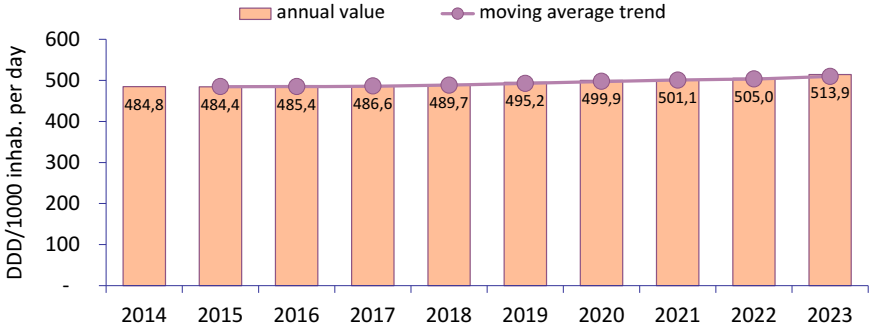
As for drugs purchased by public health facilities, other lipid-modifying substances with 3.67 euros per capita are the subgroup with the highest expenditure; they show an increase of 56.0% compared to 2022, exclusively due to an increase in consumption (+72.6%) compared to a reduction in prices of 3.9%, of the average cost per DDD (-9.7%) and to a shift towards less expensive medicinal products (mix effect: -6.0%) (Table 3.17). Almost 75% of the expenditure by public health facilities for cardiovascular drugs is related to four active ingredients: the combination valsartan/sacubitril, evolocumab, alirocumab and macitentan. However, as regards consumption, these molecules account for only 13.2% of the total, indicating a high average cost per DDD of these active ingredients (Table 3.18). The sacubitril/valsartan combination, used in the treatment of chronic symptomatic heart failure with reduced ejection fraction, is the product with the highest per capita expenditure (1.96 euros; Table 3.18) and is also on the list of the first 30 active ingredients for expenditure of drugs purchased by public facilities (Table 3.19), recording an increase of 27.2% in expenditure and 45.4% in consumption. This is followed by the monoclonal antibody inhibitor of PCSK9, evolocumab, recording a 19.6% increase in expenditure (1.60 euros), due to a significant increase in consumption (+45.5%). Furthermore, these two active ingredients, together with alirocumab, are listed within the first thirty active ingredients with the greatest variation in expenditure among the drugs purchased by public health facilities (Table 3.20). No cardiovascular drug is among the top 30 for cost reduction and among the top 30 for average DDD cost (Table 3.21 and 3.22), while valsartan/sacubitril (3.57 euros), alirocumab (7.18 euros) and evolocumab (11.13 euros) are among the top 30 active ingredients purchased by public health facilities at the lowest cost, all decreasing compared to the previous year (Table 3.23). As for consumption, three active ingredients of the cardiovascular system category are in the list of the first 30 most consumed drugs purchased by public health facilities: furosemide (4.4 DDD), ramipril (1.7 DDD) and the combination valsartan/sacubitril (1.5 DDD; Table 3.24). The list of the top 30 most expensive active ingredients (Table 3.25) for drugs under approved care regime (A-NHS) and purchased by public health facilities includes atorvastatin (274.5 million euros), bisoprolol (172.1 million euros), valsartan/sacubitril (134 million euros) and omega 3 (130.8 million euros). Almost 50% of the top thirty most consumed active ingredients, supplied under approved care regime and purchased by public health facilities in 2023, belong to ATC C (Table 3.26). Table 3.27 shows the different trend of expenditure, consumption and average DDD cost between the approved care regime and direct purchases for drugs for hypertension and heart failure and for lipid-lowering drugs. There is a clear difference in the average DDD cost between the two delivery channels, lower in the direct purchase channel than in the approved care. On average, the cost of a day of therapy for a beta-blocker, and for an angiotensin II receptor antagonist (categories with higher expenditure), is 50% lower in direct purchase than the approved care regime.

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

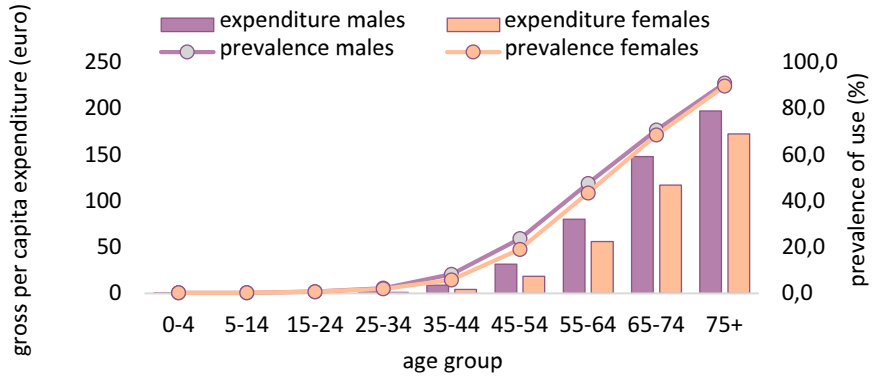
Cardiovascular system

Public expenditure* in million euros (% over total)	**3,557.4**	**(13.7)**
Δ % 2023-2022		4.9
Regional range of gross per capita expenditure:	41.4	77.3
DDD/1000 inhabitants per day* (% over total)	**513.9**	**(38.8)**
Δ % 2023-2022		1.8
Regional range DDD/1000 inhabitants per day	389.5	611.7

** includes prescriptions under approved care regime and purchases by public health facilities*



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf by age and gender in 2023 (Figure and Table)



Age group	Gross per capita expenditure			DDD/1000 inhabitants per day		
	Males	Females	Total	Males	Females	Total
0-4	0.2	0.4	0.3	0.4	0.3	0.4
5-14	0.1	0.1	0.1	0.9	0.7	0.8
15-24	0.5	0.3	0.4	3.8	2.5	3.2
25-34	1.8	1.0	1.4	14.9	8.1	11.6
35-44	8.6	4.2	6.4	74.7	37.7	56.3
45-54	31.5	18.2	24.8	284.2	171.2	227.2
55-64	80.1	55.8	67.7	726.8	510.4	615.9
65-74	147.8	117.0	131.6	1331.6	1054.3	1185.4
75+	197.2	172.3	182.5	1852.8	1639.0	1726.3

3.2.1 Medicines for hypertension and heart failure

In 2023, the category of medicines for hypertension and heart failure recorded a total public expenditure of 2,053.6 million euros, stable compared to the previous year. Consumption has remained stable over the last ten years (CAGR -0.1%), recording a value of 373.6 DDD in 2023, and an average cost per day of therapy of 0.26 euros (Box Main indices of expenditure, consumption and exposure).

The prevalence of use tends to increase with age, remaining higher in the population over 75 years, with values exceeding 80% in both genders. Consumption also records maximum values above 75 years, respectively equal to 1,852 DDD in males and 1,639 DDD in females.

In 2023, per capita expenditure on this category of drugs was 34.90 euros, with a 0.7% average annual reduction over the last ten years (Table 3.2.1a). Beta-blockers are confirmed as the therapeutic category with the highest per capita expenditure (5.78 euros), up 1.7% compared to 2022, with an average cost per day of therapy of 0.33 euros, slightly higher than the value observed for the entire therapeutic class (0.26 euros) and with a 2.4% increase in consumption (47.7 DDD). Both indicators show an annual growth, referable to the period 2014-2023 (expenditure +2.1%; consumption +1.2%) (Table 3.2.1a and Figure 3.2.1a). Beta-blockers remain the category with the highest prevalence of use (11.3%), despite showing a median duration of therapy of only 3.5 months (98 days), presumably linked to their greater use in the treatment of heart failure rather than hypertension (Table 3.2.1b).

ACE inhibitors are the category with the highest consumption (80.5 DDD/1000 inhabitants per day) and with the lowest average cost per DDD (0.12 euros). The per capita expenditure on this class of drugs was instead equal to 3.44 euros, although there was a reduction trend over time of all the values considered (CAGR: expenditure -2.7%; consumption -1.2%)

Ramipril is the most used active ingredient (62.3 DDD), while bisoprolol is the substance with the highest per capita expenditure, with a value of 2.93 euros (+3.3% compared to the previous year). Also in 2023, a significant increase was observed, both in terms of expenditure (+10.8%) and consumption (+32.1%), of the combination sacubitril/valsartan, the only drug belonging to the category of angiotensin II receptor antagonists associated with a neprilysin inhibitor. This also recorded the highest average cost per user in the category (1,002 euros), eight times higher than the average of drugs for hypertension and heart failure (125 euros) (Table 3.2.1b).

Over a quarter of the Italian population (26.8%) used these drugs in 2023, with a higher prevalence in the South and the Islands (28.6%) and in the North (27.4%), compared to the Centre (25.3%) (Table 3.2.1c). Each person uses approximately 485 doses per year and half of the exposed population is treated with a number of DDDs equal to 364, while only 3% of users have a single prescription. There are no major differences in median age, and overall there is a higher prevalence of use in women (Table 3.2.1b).

Umbria is the Region recording the greatest use of these drugs, with a consumption of 482.3 DDD/1000 inhabitants per day, and an average cost per DDD that is the lowest (together with Tuscany and Emilia-Romagna), equal to 0.22 euros, while the PA of Bolzano confirms the lowest value (277.4 DDD/1000 inhabitants per day). Campania, Calabria and Basilicata show the highest average cost per DDD (0.29 and 0.30 euros). Compared to the national average, the North showed a lower consumption (360.5 compared to 373.6 DDD/1000 inhabitants

per day), while the Centre and the South have higher values, equal to 383.5 and 386.3 DDD/1000 inhabitants per day, respectively.

The analyses of adherence and persistence show that the percentage of subjects adhering to the treatment remains rather stable, with low adherence values decreasing by 2% compared to 2022 (Figure 3.2.1b), recording the highest value in subjects over 85 years and especially in women. High adherence is equal to 53.1% of users, with an increasing trend since 2019 (Figure 3.2.1c). Males appear to be more adherent than females, with a difference of almost ten percentage points between the two genders. A similar trend was also observed for treatment persistence data, with higher values in males (58.0%) than females (49.7%). Overall, 53.6% of subjects were found to be persistent to therapy after 12 months, with a higher percentage in the Centre than the North and the South (Figures 3.2.1d and 3.2.1e).

For further information on regional data on exposure and duration of therapy and on indicators of adherence and persistence to treatment stratified by age, gender and geographical area, please refer to the supplementary documents published online.

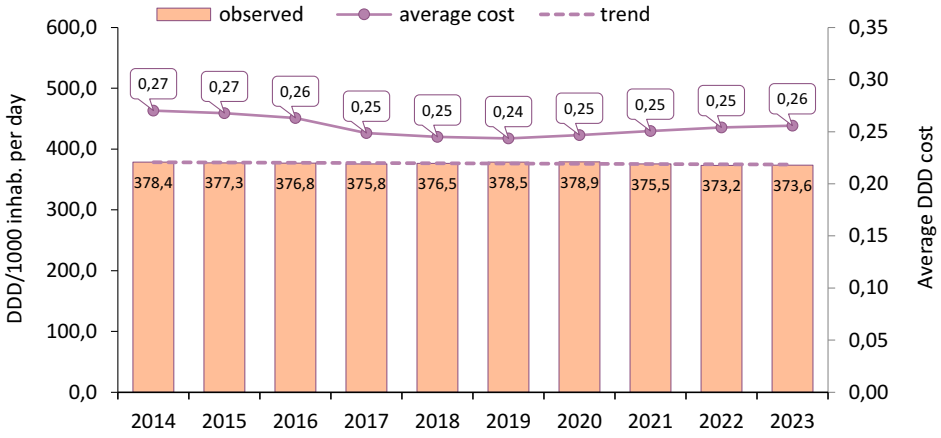
MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

Medicines for hypertension and heart failure

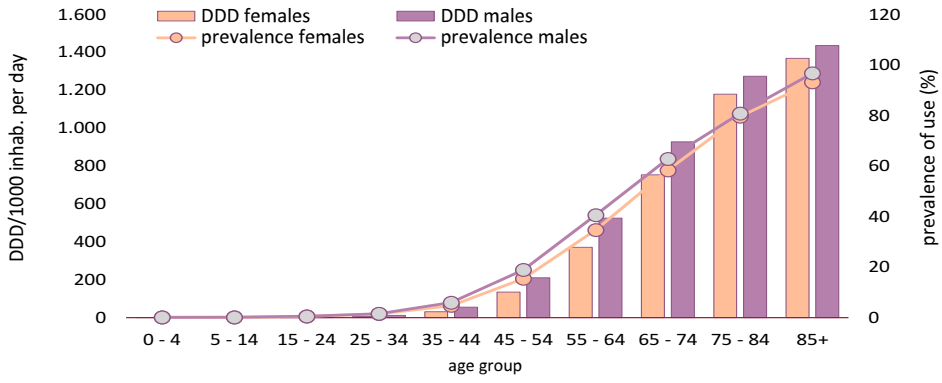
Public expenditure* in million euros (% over total)	**2,053.6**	**(7.9)**
Δ % 2023-2022		0.8
Regional range of gross per capita expenditure:	24.7	42.4
DDD/1000 inhabitants per day* (% over total)	**373.6**	**(28.2)**
Δ % 2023-2022		0.1
Regional range DDD/1000 inhabitants per day	277.4	482.3

** includes prescriptions under approved care regime and purchases by public health facilities*

Temporal trend of consumption and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of medicines for hypertension and heart failure under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.2.1a Medicines for hypertension and heart failure, per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and substance: comparison 2014-2023

Subgroups and substances	Expenditure per capita	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Beta-blockers	5.78	1.7	2.1	47.7	2.4	1.2	0.33	-0.7
Angiotensin II receptor blockers	5.01	2.0	-1.8	59.1	1.1	0.4	0.23	0.9
Calcium channel blockers (dihydropyridines)	3.99	-2.5	-1.7	50.5	-0.1	-0.7	0.22	-2.4
Angiotensin II receptor blockers and diuretics (combinations)	3.72	-1.6	-5.6	31.4	-1.3	-2.4	0.33	-0.3
ACE inhibitors	3.44	-3.5	-2.7	80.5	-2.0	-1.2	0.12	-1.4
Angiotensin II receptor antagonists and niprilysin inhibitor (combinations)	2.28	10.8	—	1.6	32.1	—	3.84	-16.1
ACE inhibitors and diuretics (combinations)	2.25	-4.8	-4.7	17.9	-4.1	-3.4	0.35	-0.7
Angiotensin II receptor blockers and calcium channel blockers (combinations)	1.72	12.9	6.1	11.9	13.5	15.6	0.40	-0.6
ACE inhibitors and calcium channel blockers (combinations)	1.64	-0.1	2.7	12.3	1.2	6.3	0.36	-1.3
Alpha-blockers	1.23	-1.2	-0.3	7.8	0.1	-0.1	0.43	-1.3
High-ceiling diuretics, alone or in combination with potassium-sparing agents	0.96	-3.0	-1.1	28.6	-3.1	-0.4	0.09	0.0
ACE inhibitors, calcium channel blockers and diuretics (triple combination)	0.73	15.1	—	5.3	12.9	—	0.38	2.0
Beta-blockers and diuretics (combinations)	0.70	-0.2	0.6	7.5	-0.4	1.7	0.25	0.2
Potassium-sparing diuretics	0.64	7.2	1.7	3.8	2.3	0.6	0.47	4.8
Calcium channel blockers (not dihydropyridines)	0.24	-8.7	-7.8	1.7	-8.0	-7.4	0.39	-0.7
Thiazides and similars (including combinations)	0.20	-5.3	-3.7	3.4	-5.0	-4.8	0.16	-0.4
Imidazoline receptor agonists	0.18	-5.2	-6.4	1.3	-4.6	-5.2	0.39	-0.6
ACE inhibitors, other combinations	0.14	9.7	—	1.1	9.7	—	0.33	0.0
Aliskiren alone or in combination	0.02	-26.5	-18.6	0.1	-28.7	-18.3	0.88	3.0
Angiotensin II receptor blockers, calcium channel blockers and diuretics (triple combination)	0.02	>100	—	0.2	>100	—	0.32	2.4
Medicines for hypertension and heart failure	**34.90**	**0.8**	**-0.7**	**373.6**	**0.1**	**-0.1**	**0.26**	**0.7**
bisoprolol	2.93	3.3	5.2	13.6	3.5	5.0	0.59	-0.2
valsartan/sacubitril	2.28	10.8	—	1.6	32.1	—	3.84	-16.1
olmesartan	2.07	7.9	-1.0	18.0	7.8	9.4	0.31	0.1
ramipril	1.90	-2.4	-0.9	62.3	-1.1	0.0	0.08	-1.4
olmesartan/amlodipine	1.62	11.2	5.4	11.0	11.4	14.7	0.40	-0.2
amlodipine	1.60	0.0	-0.1	29.5	1.7	0.4	0.15	-1.7
nebivolol	1.59	2.2	2.1	17.4	2.4	2.5	0.25	-0.1
olmesartan/hydrochlorothiazide	1.31	3.5	-4.5	10.8	3.8	5.0	0.33	-0.3
doxazosin	1.22	-1.0	-0.3	7.7	0.1	-0.1	0.43	-1.1
perindopril/amlodipine	0.82	0.5	0.9	5.3	0.9	3.0	0.42	-0.4

Figure 3.2.1a Medicines for hypertension and heart failure, temporal trend (2014-2023) of consumption (DDD/1000 inhabitants per day) and average cost per day of therapy

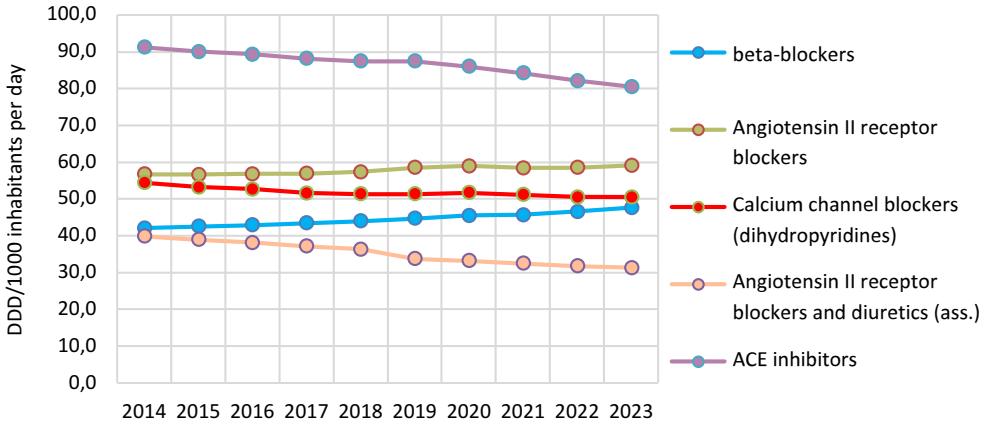


Table 3.2.1b Exposure and duration of therapy with medicines for hypertension and heart failure by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
Beta-blockers	10.5	12.2	11.3	72	49.2	145.0	98.0	4.4
Angiotensin II receptor blockers	5.9	6.2	6.0	71	81.6	348.5	308.0	5.8
Calcium channel blockers (dihydropyridines)	5.7	5.5	5.6	74	69.4	315.8	308.0	8.1
Angiotensin II receptor blockers and diuretics (combinations)	3.6	4.7	4.1	73	88.7	272.4	308.0	4.2
ACE inhibitors	6.5	5.5	6.0	71	56.0	468.4	336.0	6.0
Angiotensin II receptor antagonists and niprilysin inhibitor (combinations)	0.3	0.1	0.2	72	1,002.3	248.7	280.0	3.1
ACE inhibitors and diuretics (combinations)	2.2	2.7	2.5	73	89.1	257.4	280.0	3.9
Angiotensin II receptor blockers and calcium channel blockers (combinations)	1.9	1.4	1.6	67	103.1	259.5	308.0	6.6
ACE inhibitors and calcium channel blockers (combinations)	1.9	1.3	1.6	68	98.8	271.2	300.0	5.5
Alpha-blockers	1.5	1.2	1.4	74	88.0	197.3	180.0	8.5
High-ceiling diuretics, alone or in combination with potassium-sparing agents	4.1	5.2	4.6	80	19.0	186.6	112.5	19.5
ACE inhibitors, calcium channel blockers and diuretics (triple combination)	0.9	0.6	0.7	69	98.6	260.8	300.0	6.8
Beta-blockers and diuretics (combinations)	0.7	1.4	1.1	68	65.0	256.2	280.0	4.7
Potassium-sparing diuretics	1.4	1.4	1.4	78	42.5	88.4	64.0	12.7
Calcium channel blockers (not dihydropyridines)	0.3	0.4	0.3	76	71.5	181.9	168.0	5.0
Thiazides and similars (including combinations)	0.5	1.0	0.8	74	25.6	156.3	120.0	17.3
Imidazoline receptor agonists	0.1	0.2	0.2	76	106.9	271.8	244.4	7.2
ACE inhibitors, other combinations	0.2	0.2	0.2	65	81.3	243.4	240.0	6.5
Aliskiren alone or in combination	<0.05	<0.05	<0.05	72	327.3	372.7	336.0	5.1
Angiotensin II receptor blockers, calcium channel blockers and diuretics (triple combination)	<0.05	<0.05	<0.05	68	46.1	143.8	112.0	20.2
Medicines for hypertension and heart failure	**26.1**	**27.5**	**26.8**	**70**	**125.0**	**485.4**	**364.0**	**2.9**

Regional data on expenditure, consumption and exposure

Table 3.2.1c Medicines for hypertension and heart failure, regional trend of per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use	Cost/user	Median DDD
Piedmont	31.14	370.3	0.23	0.5	1.3	-0.7	-1.2	0.1	-1.3	27.4	114.2	364.0
Valle d'Aosta	29.25	306.6	0.26	2.1	-0.1	2.2	-1.2	-1.2	0.0	23.7	114.5	357.3
Lombardy	32.28	344.0	0.26	1.0	0.6	0.4	-0.6	-0.4	-0.2	24.0	125.7	378.5
Province of Bolzano	24.69	277.4	0.24	2.5	-0.4	2.9	-1.3	-0.8	-0.5	18.4	117.9	364.0
Province of Trento	27.08	326.2	0.23	1.1	0.1	1.0	-1.0	-0.2	-0.8	22.8	111.0	373.5
Veneto	30.72	359.7	0.23	0.2	-0.2	0.4	-1.4	-0.8	-0.6	25.0	120.9	390.0
Friuli V.G.	31.50	370.1	0.23	0.9	-0.7	1.6	-1.3	-0.4	-0.9	26.5	122.4	392.0
Liguria	31.09	325.2	0.26	0.8	-0.2	1.1	-1.4	-0.8	-0.7	27.3	115.3	356.0
Emilia R.	33.58	412.8	0.22	0.8	-0.2	1.0	-0.1	-0.1	0.0	26.5	115.9	392.0
Tuscany	30.75	376.5	0.22	0.8	-0.4	1.2	-0.4	0.1	-0.5	26.7	114.0	392.0
Umbria	39.56	482.3	0.22	0.5	0.1	0.3	0.2	0.3	-0.2	31.2	129.2	420.0
Marche	36.99	380.3	0.27	1.0	0.8	0.3	-0.4	0.2	-0.6	28.4	127.9	378.0
Lazio	36.95	373.5	0.27	0.5	-0.4	1.0	-0.7	-0.3	-0.4	26.9	129.3	387.3
Abruzzo	37.12	364.2	0.28	0.5	-0.5	1.0	-0.2	0.2	-0.4	28.0	119.5	361.3
Molise	38.33	375.0	0.28	1.3	0.4	0.9	-0.8	0.2	-1.0	30.1	122.3	364.0
Campania	42.44	402.8	0.29	1.3	0.2	1.2	-0.1	0.5	-0.7	28.4	132.7	367.0
Puglia	38.87	381.8	0.28	1.1	0.4	0.7	-0.9	-0.2	-0.8	29.3	121.9	364.0
Basilicata	42.33	384.5	0.30	2.4	0.5	1.8	0.6	0.7	-0.2	30.6	130.2	364.0
Calabria	40.34	381.4	0.29	0.6	-0.1	0.8	-0.6	-0.2	-0.4	29.7	122.9	364.0
Sicily	38.93	399.6	0.27	0.6	0.1	0.5	-0.5	0.3	-0.9	28.2	127.9	381.5
Sardinia	31.61	333.2	0.26	0.7	-0.4	1.1	-2.0	-0.7	-1.3	27.0	117.3	364.0
Italy	**34.90**	**373.6**	**0.26**	**0.8**	**0.1**	**0.7**	**-0.7**	**-0.1**	**-0.5**	**26.8**	**123.2**	**378.0**
North	31.68	360.5	0.24	0.8	0.3	0.5	-0.9	-0.4	-0.5	27.4	120.0	378.0
Centre	35.16	383.5	0.25	0.7	-0.2	0.9	-0.5	0.0	-0.4	25.3	124.5	384.0
South and Islands	39.33	386.3	0.28	1.0	0.1	0.9	-0.6	0.1	-0.7	28.6	126.3	364.0

Adherence and persistence to treatment

Table 3.2.1b Indicators of low adherence to treatment with antihypertensive drugs in the population aged ≥45 years stratified by gender, trend 2019-2023 (raw values). Emilia Romagna not included in the calculation

Table 3.2.1c Indicators of high adherence to treatment with antihypertensive drugs in the population aged ≥45 years stratified by gender, trend 2019-2023 (raw values). Emilia Romagna not included in the calculation

*Adherence to treatment was evaluated only for new users with at least 2 prescriptions. Low adherence to treatment was defined as therapeutic coverage (assessed on the basis of DDD) <40% of the observation period while high adherence was defined as therapeutic coverage ≥80% of the observation period (for further details please refer to statistical methods)

Figure 3.2.1d Time (in days) to discontinuation of anticoagulant treatment in the population aged ≥45 years stratified by gender. Curves are adjusted by age (the Cox model was used to estimate persistence curves). The North does not include Emilia Romagna

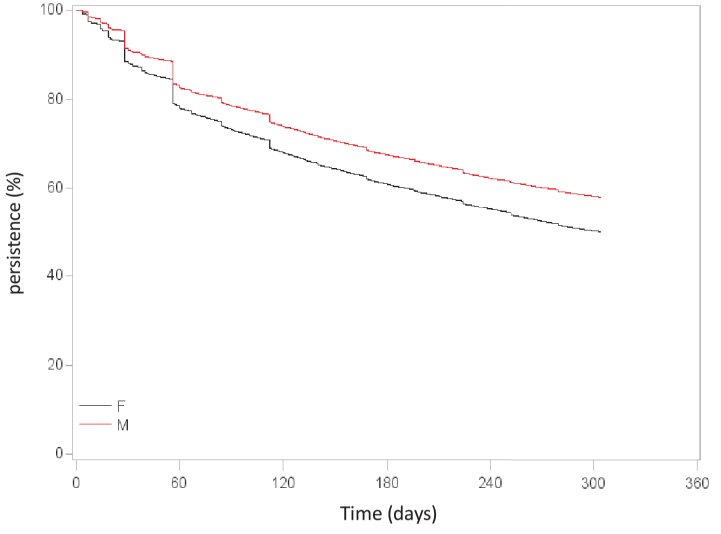
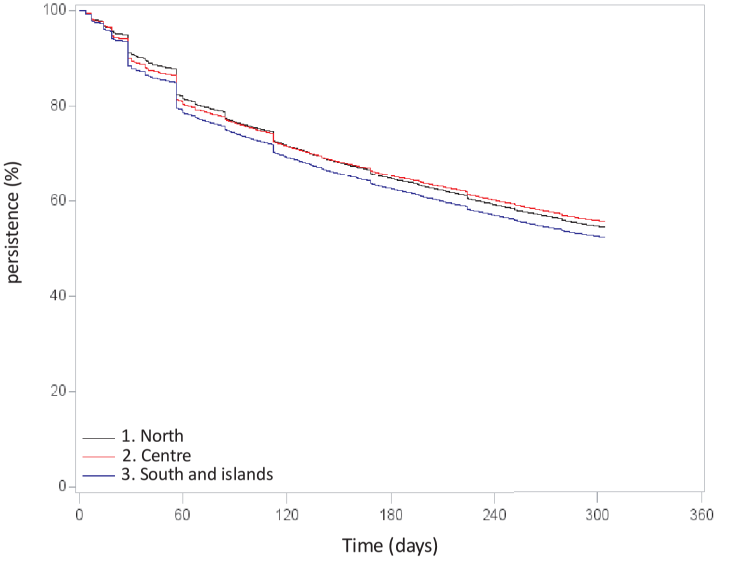


Figure 3.2.1e Time (in days) to discontinuation of anticoagulant treatment in the population aged ≥45 years stratified by geographical area. Curves are adjusted by gender and age (the Cox model was used to estimate persistence curves). The North does not include Emilia Romagna



3.2.2 Lipid-lowering medicines

In 2023, lipid-lowering medicines recorded a total public expenditure of 1,206 million euros, with a 15.7% increase compared to the previous year. Consumption also showed an 8.2% increase, reaching 123.0 DDD (Box Main indices of expenditure, consumption and exposure).

Over the years, the consumption of lipid-lowering medicines has increased by almost 60%, from a value of 77.7 DDD/1000 inhabitants per day in 2014 to 123.0 in 2023 (CAGR +4.7%). However, the average cost per DDD recorded a 22% reduction, going from 0.59 euros in 2014 to 0.46 in 2023. For lipid-lowering drugs, the prevalence of use tends to increase with age, remaining higher in the male population up to 84 years, where it reaches a maximum value of 52.51% and 48.56% in males and females respectively. Consumption also shows an increasing trend with age, with maximum values between 75 and 84 years, respectively equal to 465.46 DDD in males and 355.99 DDD in females (Box Main indices of expenditure, consumption and exposure).

Per capita expenditure on these drugs was 20.50 euros, with a 15.7% increase compared to the previous year and a 2.1% average annual variation in the period 2014-2023 (Table 3.2.2a). The increase in expenditure recorded in 2023 compared to the previous year was due to growth in both consumption (+8.2%) and average cost (+7.0%).

Statins not combined with other molecules are the therapeutic category with the highest per capita expenditure and consumption (8.10 euros and 83.9 DDD), stable compared to 2022, and an average DDD cost lower than the average value of lipid-lowering drugs (0.26 euros). The trend in consumption for this subgroup over the last ten years shows a 2.1% increase (Figure 3.3.2a). On the other hand, ezetimibe in combination with statins is the second category with the highest expenditure, recording a value of 4.02 euros, up 38.3% compared to the previous year. For this category, an equally significant increase was observed in terms of consumption (+46.3%), with 24.5 DDD/1000 inhabitants per day. Particularly interesting is the reduction in the average cost per day of ezetimibe therapy, especially in combination (-5.5%), probably due to patent expiries in recent years. PCSK-9 inhibitors confirm the increasing trend of recent years, both in terms of expenditure (+41.4%) and consumption (+54.9%), placing them in third rank for average cost per DDD (8.82 euros). It is worth noting the recent entry of a new molecule, inclisiran, acting as a small interfering RNA, which in 2023 reached a per capita expenditure of 0.34 euros, with a strong increase compared to 2022 (>100%). Furthermore, in 2023, bempedoic acid, a first-in-class adenosine triphosphate citrate lyase inhibitor, was marketed for the first time, both alone and in combination with ezetimibe, reaching a total expenditure of 0.22 euros per capita in 2023. Drugs for the alteration of lipid metabolism of genetic origin are the therapeutic category with a DDD average cost of 8,190 euros. The category includes the drug volanesorsen, indicated as an adjuvant to diet in adult patients affected by genetically confirmed familial chylomicronemia syndrome (FCS) and at high risk of pancreatitis.

Atorvastatin is the most widely used active ingredient among lipid-lowering drugs (52.1 DDD) and consequently, with the highest expenditure (4.66 euros per capita), rather stable compared to 2022 (-0.3%), with a 4.2% average annual increase in the last ten years. Furthermore, it is confirmed to be the active ingredient with the lowest average cost per DDD for this category, equal to 0.25 euros. The combination ezetimibe/rosuvastatin is the second most expensive active ingredient (2.28 euros per capita), with an increase of almost

50% compared to 2022. Among the other top ten active ingredients by annual expenditure, the monoclonal antibodies evolocumab and alirocumab showed the highest values of average DDD cost, respectively equal to 11.13 and 7.18 euros, both recording significant increases in consumption (respectively +45.5% and +62.4%) and expenditure (+35.3% and +48.8%, respectively; Table 3.2.2a).

The median age of users of lipid-lowering drugs is around 71 years; in particular, a lower median age (63 years) is recorded in subjects treated with PCSK9 inhibitors, reaching 72 years in subjects treated with statins alone (Table 3.2.2b). In 2023, the average cost per user was 106 euros, although there are significant differences in cost based on the category considered, ranging from 45.9 euros for statins in combination, up to 1673.8 euros for PCSK9 inhibitors. Users of these drugs were exposed to 275.6 days of therapy, although even for this indicator it is possible to note differences related to the therapeutic category; users with only one prescription were 3.8%, with the highest values among the groups with the highest prevalence, for ezetimibe alone and in association with statins (9.1% and 6.6%).

Campania was the Region recording the highest value in terms of consumption in 2023, with 139.7 DDD/1000 inhabitants per day, as well as the highest average cost (0.58 euros); Valle d'Aosta was the region with the lowest value, equal to 78.1 DDD (Table 3.2.2c). Compared to the national average value, the South showed a higher consumption (132.2 compared to 123.0 DDD/1000 inhabitants per day), while the North and Centre showed lower consumption, equal to 117.7 and 120.5 DDD/1000 inhabitants per day respectively. The South also recorded the highest increase in expenditure and consumption (respectively +16.6% and +8.6%) compared to the previous year, while the Centre had the smallest variations (+13.6% and +7.4%; Table 3.2.2c).

When analyzing adherence and persistence, the percentage of subjects adhering to treatment remains rather stable, with low adherence values decreasing by 2% compared to 2023 (Figure 3.2.2b), while high adherence is equal to 44.0% of users, following an increasing trend since 2019 (Figure 3.2.2c). A similar trend was also recorded in the data on persistence at 12 months to treatment, with higher values in males (53.6%) than in females (47.9%). Overall, half of the new users were found to be persistent to treatment (50.0%), with a higher percentage in the North and the Centre, compared to the South (Figures 3.2.2d and 3.2.2e).

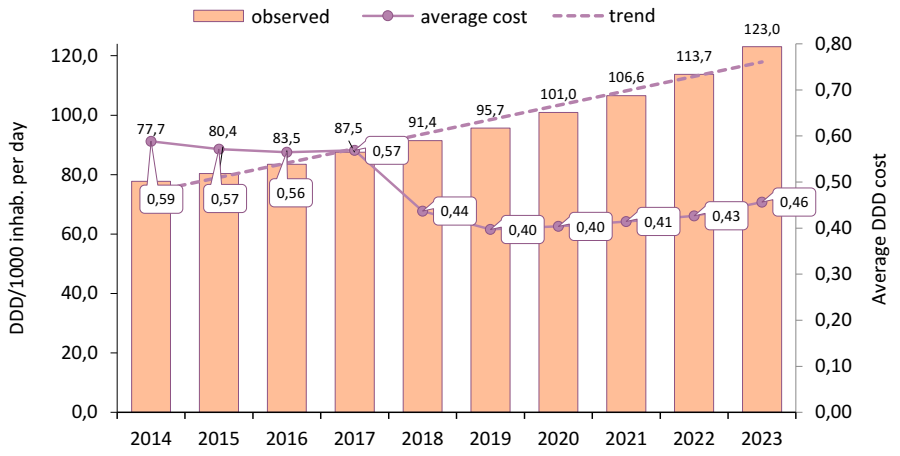
For further information on regional data on exposure and duration of therapy and on indicators of adherence and persistence to treatment stratified by age, gender and geographical area, please refer to the supplementary documents published online.

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Lipid-lowering medicines

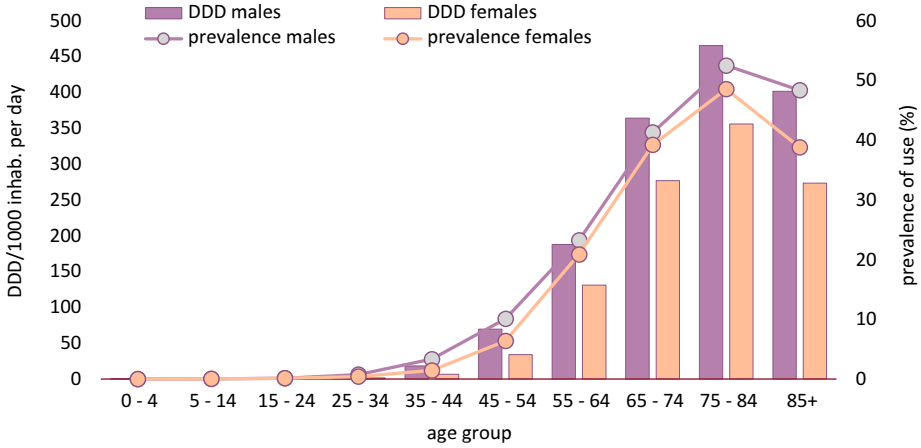
Public expenditure* in million euros (% over total)	**1,206.2**	**(4.6)**
Δ % 2023-2022		15.7
Regional range of gross per capita expenditure:	12.8	29.8
DDD/1000 inhabitants per day* (% over total)	**123.0**	**(9.3)**
Δ % 2023-2022		8.2
Regional range DDD/1000 inhabitants per day	78.1	140.8

** includes prescriptions under approved care regime and purchases by public health facilities*

Lipid-lowering medicines, temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of lipid lowering medicines under approved care regime care and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.2.2a Lipid-lowering medicines, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and substance: comparison 2014-2023

Subgroups and substances	Expenditure per capita	Δ % 23-22	CAGR 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR 14-23	Average DDD cost	Δ % 23-22
Statins, alone	8.10	-0.6	-2.8	83.9	-0.3	2.1	0.26	-0.4
Ezetimibe and statins (combination)	4.02	38.3	4.2	24.5	46.3	21.3	0.45	-5.5
PCSK9 inhibitors (monoclonal antibodies)	3.06	41.4	—	1.0	54.9	—	8.82	-8.7
Omega 3	2.22	2.9	0.8	2.7	5.0	4.2	2.23	-2.0
Ezetimibe	1.86	8.3	7.5	7.1	9.1	17.5	0.72	-0.8
Fibrates	0.41	1.2	1.1	3.0	1.6	1.5	0.38	-0.5
PCSK9 inhibitors (siRNA)	0.34	>100	—	0.1	>100	—	8.84	0.0
MTP inhibitor	0.14	16.4	—	<0.05	-13.7	—	1079.74	34.9
Ezetimibe and bempedoic acid	0.12	—	—	0.2	—	—	2.08	
Adenosine triphosphate citrate lyase (ACL) inhibitors	0.10	—	—	0.1	—	—	2.04	
Drugs for the alteration of lipid metabolism of genetic origin	0.07	46.6	—	<0.05	46.6	—	8190.19	0.0
Statins, calcium channel blockers and ACE inhibitors (triple combination)	0.03	16.3	—	0.2	17.2	—	0.45	-0.7
Statins in combination	0.03	337.6	—	0.3	>100	—	0.24	1.5
Lipid-lowering medicines	**20.50**	**15.7**	**2.1**	**123.0**	**8.2**	**4.7**	**0.46**	**7.0**
atorvastatin	4.66	-0.3	4.2	52.1	-0.4	4.6	0.25	0.1
ezetimibe/rosuvastatin	2.28	47.4	—	15.8	48.7	—	0.39	-0.9
omega-3	2.22	2.9	0.8	2.7	5.0	4.2	2.23	-2.0
ezetimibe	1.86	8.3	7.5	7.1	9.1	17.5	0.72	-0.8
evolocumab	1.60	35.3	—	0.4	45.5	—	11.13	-7.0
rosuvastatin	1.59	6.7	-10.4	16.9	6.6	1.8	0.26	0.1
alirocumab	1.46	48.8	—	0.6	62.4	—	7.18	-8.4
ezetimibe/simvastatin	1.26	2.7	-7.2	5.3	2.8	4.1	0.65	-0.1
simvastatin	1.26	-7.4	-3.8	10.8	-7.1	-3.8	0.32	-0.3
ezetimibe/atorvastatin	0.49	253.1	—	3.4	>100	—	0.39	-0.2

Figure 3.2.2a Lipid-lowering medicines, temporal trend 2014-2023 in consumption (DDD/1000 inhabitants per day) of the highest-expenditure subgroups

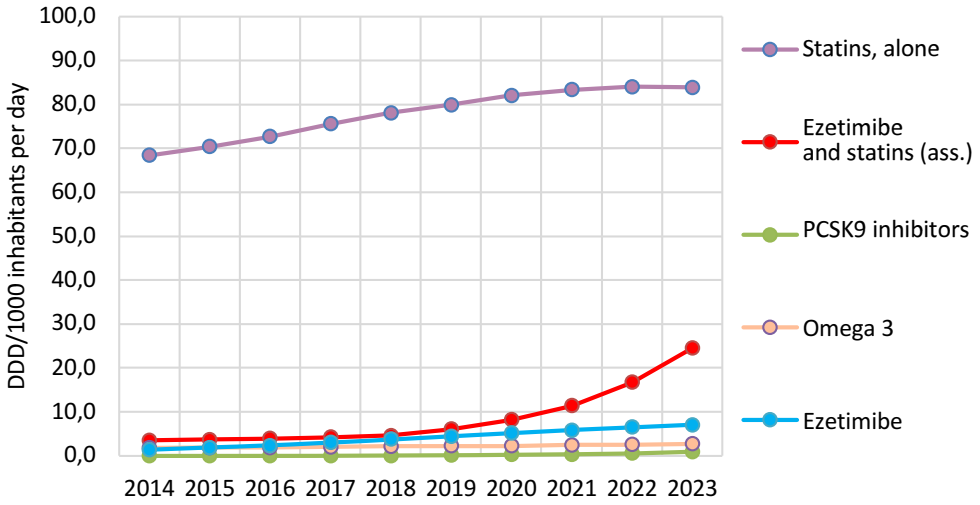


Table 3.2.2b Exposure and duration of therapy with lipid-lowering medicines by subgroup under approved care regime and distribution on-behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
Statins, alone	11.2	11.8	11.5	72	69.4	256.9	196.0	4.3
Ezetimibe and statins (combination)	4.1	3.4	3.8	69	105.2	233.0	240.0	6.6
Omega 3	1.6	0.9	1.2	67	177.0	78.0	70.0	3.9
Ezetimibe	1.2	1.2	1.2	69	158.5	217.7	240.0	9.1
Fibrates	0.8	0.5	0.6	65	64.2	167.8	174.0	7.4
Ezetimibe and bempedoic acid	<0.05	<0.05	<0.05	68	333.7	121.8	112.0	15.3
Adenosine triphosphate-citrate lyase (ACL) inhibitors	<0.05	<0.05	<0.05	69	318.1	116.9	112.0	17.0
Statins, calcium channel blockers and ACE inhibitors (triple combination)	<0.05	<0.05	<0.05	68	116.1	260.7	300.0	6.7
Statins in combination	0.1	0.0	0.1	70	45.9	189.7	168.0	11.6
Lipid-lowering medicines	**15.6**	**15.6**	**15.6**	**71**	**106.0**	**275.6**	**240.0**	**3.8**

Table 3.2.2c Lipid-lowering medicines, regional trend of per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use	Cost/user	Median DDD
Piedmont	18.29	105.6	0.47	19.0	9.7	8.5	2.4	4.9	-2.4	14.1	97.3	224.0
Valle d'Aosta	14.86	78.1	0.52	21.9	9.6	11.3	1.8	3.4	-1.6	10.8	100.2	205.3
Lombardy	17.82	116.4	0.42	16.4	8.5	7.3	1.6	4.9	-3.2	14.0	103.5	240.0
Province of Bolzano	12.83	102.5	0.34	16.5	8.0	7.8	2.0	5.7	-3.5	10.3	98.8	261.3
Province of Trento	15.79	112.8	0.38	13.5	8.7	4.4	1.6	5.9	-4.0	13.1	103.4	240.0
Veneto	17.95	122.9	0.40	14.9	7.9	6.5	1.2	4.7	-3.3	14.4	107.7	242.7
Friuli V.G.	18.64	125.5	0.41	17.4	7.8	8.9	1.3	4.6	-3.2	14.7	108.5	261.3
Liguria	19.73	107.6	0.50	18.2	9.2	8.2	3.0	4.9	-1.8	14.5	101.6	236.0
Emilia R.	18.86	131.8	0.39	12.5	7.0	5.2	3.0	5.0	-1.8	15.7	98.6	224.0
Tuscany	17.41	114.7	0.42	16.5	7.9	7.9	3.2	5.0	-1.7	14.8	95.6	224.0
Umbria	17.51	111.5	0.43	4.7	4.3	0.4	3.0	4.6	-1.5	15.1	105.8	240.0
Marche	23.28	140.8	0.45	18.8	8.6	9.4	2.3	4.9	-2.4	17.9	108.7	240.0
Lazio	21.92	120.3	0.50	11.9	7.1	4.5	0.2	3.1	-2.8	15.8	114.4	232.0
Abruzzo	21.29	118.5	0.49	16.2	8.7	6.9	3.2	5.4	-2.1	15.5	108.0	224.0
Molise	19.42	108.4	0.49	14.6	10.4	3.8	1.0	5.0	-3.7	15.3	106.7	224.0
Campania	29.78	139.7	0.58	18.5	7.9	9.8	4.9	5.4	-0.4	17.6	105.6	224.0
Puglia	22.73	132.5	0.47	16.2	9.6	6.1	1.4	4.7	-3.2	17.6	101.0	224.0
Basilicata	24.01	129.7	0.51	18.1	9.9	7.5	5.0	5.8	-0.8	17.5	98.8	224.0
Calabria	23.36	124.8	0.51	16.5	9.5	6.4	1.5	4.2	-2.5	17.2	102.2	213.3
Sicily	20.95	130.2	0.44	15.4	8.4	6.5	1.9	4.7	-2.6	17.5	101.9	224.0
Sardinia	21.48	137.2	0.43	12.8	7.4	5.0	-0.9	3.8	-4.5	17.0	112.9	242.7
Italy	**20.50**	**123.0**	**0.46**	**15.7**	**8.2**	**7.0**	**2.1**	**4.7**	**-2.5**	**15.6**	**104.1**	**228.0**
North	18.09	117.7	0.42	16.0	8.3	7.1	2.0	4.9	-2.8	15.7	102.4	240.0
Centre	20.32	120.5	0.46	13.6	7.4	5.8	1.5	4.0	-2.5	14.3	107.5	224.0
South and Islands	24.04	132.2	0.50	16.6	8.6	7.4	2.5	4.8	-2.2	17.3	104.1	224.0

Table 3.2.2b Indicators of low adherence to treatment with lipid-lowering drugs in the population aged ≥45 years stratified by gender, trend 2019-2023 (raw values)

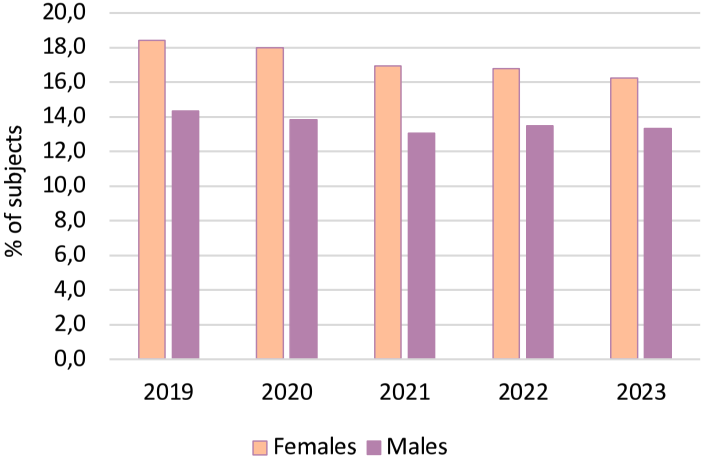
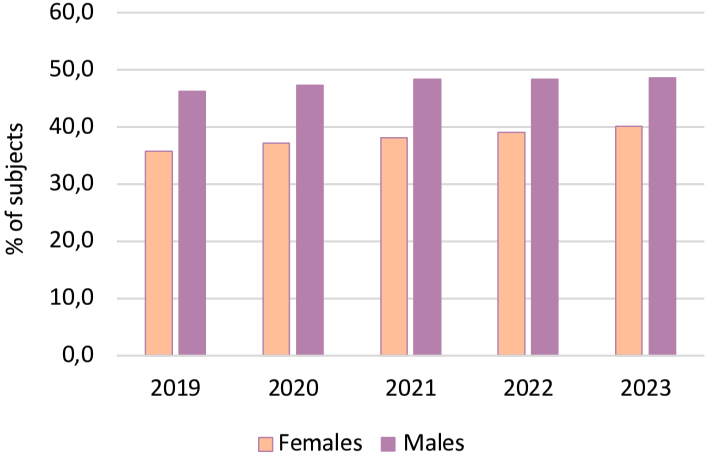


Table 3.2.2c Indicators of high adherence to treatment with lipid-lowering drugs in the population aged ≥45 years stratified by gender, trend 2019-2023 (raw values)



*Adherence to treatment was evaluated only for new users with at least 2 prescriptions. Low adherence to treatment was defined as therapeutic coverage (assessed based on DDD) <40% of the observation period while high adherence was defined as therapeutic coverage ≥80% of the observation period (for further details please refer to statistical methods).

Figure 3.2.2d Time (in days) to discontinuation of treatment with anticoagulants in the population aged ≥45 years stratified by geographical area. Curves are adjusted by gender and age (the Cox model was used to estimate persistence curves).

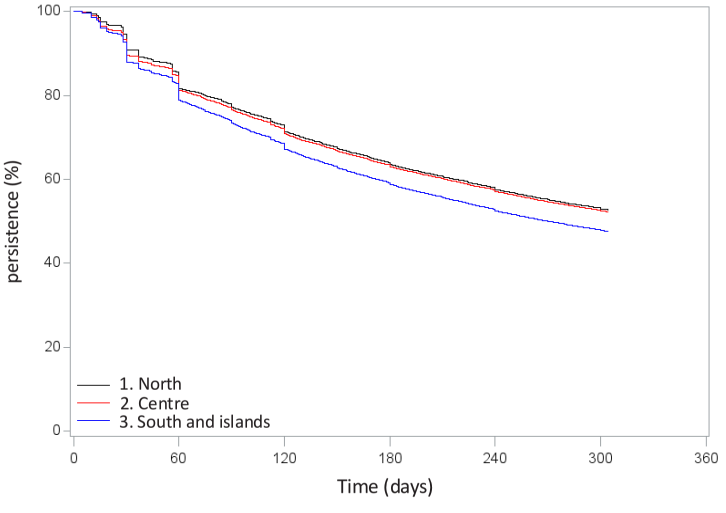
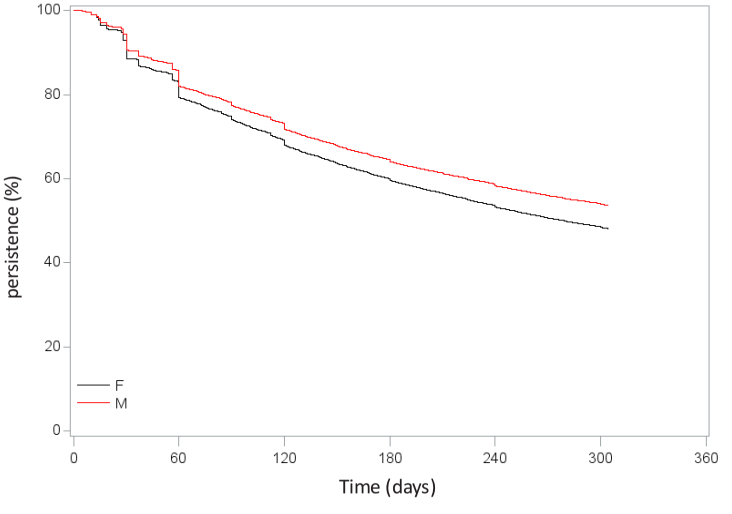


Figure 3.2.2e Time (in days) to discontinuation of treatment with lipid-lowering drugs in the population aged ≥45 years stratified by gender. Curves are adjusted by age (the Cox model was used to estimate persistence curves)



3.3 Gastrointestinal system and metabolism

Medicines for gastrointestinal system and metabolism were the third therapeutic category with the highest public expenditure in 2023, equal to 3.321 million euros and 12.8% of overall public expenditure (Box. Main indices of expenditure, consumption and exposure).

Total per capita expenditure on these pharmaceuticals was 56.39 euros (+2.2% compared to the previous year), mainly due to the approved care regime (30.73 euros per capita; 54.5% of the total). However, it is possible to note a 5.8% reduction in the approved care regime and a concomitant 13.7% increase in expenditure by public health facilities, with a per capita value equal to 25.66 euros (Table 3.1). Analyzing consumption in 2023, an overall value of 298.61 DDD/1000 inhabitants per day is recorded, a significant reduction compared to 2022 (-6.1%; Table 3.2), of which 85.4% can be attributed to the approved care expenditure. Even for consumption, there was a reduction in the approved care regime (-8.7%) and a significant increase in public health facilities (+13.0%). Overall, over the last five years, these drugs have recorded an increase in public expenditure, with the exception of 2020 when there was a decline (Figure 3.1), while consumption showed a reduction in 2020 and in the last year (Figure 3.2).

Per capita expenditure on class A drugs dispensed under the approved care regime shows a high regional variability, with Lombardy recording a value more than double (46.9 euros) compared to the Province of Bolzano (17 euros) and Umbria, Tuscany, Emilia Romagna (around 20 euros; Table 3.5 and Figure). Basilicata showed the highest consumption with 320.6 DDD/1000 inhabitants per day, followed immediately by Sardinia (318.1 DDD/1000 inhabitants per day) and Campania (312.6 DDD/1000 inhabitants per day), almost double than Umbria and Tuscany (166.1 and 175.5 DDD/1000 inhabitants per day, respectively; Table 3.6 and Figure). Campania, Calabria and Puglia are the regions with the highest expenditure by public health facilities, respectively 35, 32.5 and 32.4 euros (Table 3.7 and Figure). Valle d'Aosta, Province of Bolzano and Lombardy have the lowest expenditure (14.8, 15.4 and 17.5 euros, respectively), Emilia R. (67.5 DDD) and Lombardy (25.4 DDD) record the highest and lowest value in terms of consumption (Table 3.8 and Figure).

The analysis of the drug use profile by age group and gender, including approved care regime and distribution on behalf, shows a progressive increase in the use of pharmaceuticals belonging to this category with increasing age for both genders, with a more marked trend in the over 45 age group. At the same time, per capita expenditure also shows a similar trend, reaching a maximum value of 146.5 euros in males over 75 years (Box Main indices of expenditure, consumption and exposure).

In 2023, for this ATC, more expensive medicinal products were used under the approved care regime (mix effect: +5.7%), which is also underlined by the increase in the average DDD cost (+3.2%), despite a reduction in prices (-2.3%) (Figure 3.4 and Table 3.9). In particular, slow-acting injectable insulins and analogues, combinations of oral hypoglycemics and GLP-1 analogues recorded a trend similar to the first ATC level, with values respectively equal to +25.9%, +23.3% and +5.1% for the mix effect and +25.9%, +22.3% and +5.5% for the average DDD cost. On the other hand, prices remain substantially stable, with a decrease for fast-acting insulins and analogues (-11.1%) and for peripheral opioid receptor antagonists (-6.2%). Proton pump inhibitors remain in first place in terms of expenditure (11.09 euros per capita) and in second place in terms of consumption (76.6 DDD/1000 inhabitants per day), recording

a decrease in consumption (-1.4%), expenditure (-3.0%) and use of less expensive products (mix effect: -1.6%). Vitamin D and analogues (4.01 euros) rank second for gross expenditure per capita, with significant reductions in both expenditure (-14.9%) and consumption (-14.6%) in 2023. Similar reductions are also observed for the category of calcium in combination with vitamin D and/or other drugs, with decreases of 5.0% in expenditure and 5.1% in consumption. In the case of gliflozins (SGLT2 co-transporter inhibitors) and DPP-4 inhibitors, an increase in consumption was observed, respectively +23% and >100%, as well as the use of less expensive medicinal products (mix effect: -2.6% and -31.0%). For these categories, a substantial price stability was observed for gliflozins and a 31.0% reduction for DPP-4 inhibitors. However, both show a decrease in the average cost of 2.6% and 32.7%.

Pantoprazole and cholecalciferol are the molecules with the highest per capita expenditure (respectively 4.51 and 3.36 euros) and together they represent the main cost item of the approved care expenditure on drugs for the gastrointestinal system (25.6%) (Table 3.10). These two molecules confirm their top positions, considering the first 30 active ingredients for approved care expenditure (respectively 265.5 and 198.0 million euros), similar to the previous year (Table 3.11), together with esomeprazole (131.1 million), mesalazine (127.1 million), omeprazole (121.3 million), lansoprazole (117.9 million), metformin (98.9 million) and rifaximin (80.1 million).

Semaglutide (9.34 euros), dulaglutide (4.88 euros) and rifamyxin (2.08 euros) are among the drugs with the highest cost per day of therapy under approved care regime (Table 3.12). Instead, cholecalciferol (0.08 euros), metformin (0.20 euros) and omeprazole (0.33 euros) are included in the first 30 active ingredients with the lowest cost per day of therapy (Table 3.13).

Ursodeoxycholic acid is the only active ingredient in this therapeutic category on the list of the top 30 active ingredients with the highest increase under approved care regime compared to the previous year (+5.5%), due to a marked increase in consumption (+5.4%) (Table 3.14). Eight ATC A molecules are ranked among the top thirty active ingredients with the greatest reduction in approved care expenditure compared to 2022: dulaglutide (-19.9%), insulin lispro (-17.6%), cholecalciferol (-16.9%), insulin aspart (-14.0%), magaldrate (-12.1%), semaglutide (-10.5%), lansoprazole (-7.7%) and omeprazole (-4.6%) (Table 3.15).

Six out of thirty most consumed active ingredients under the approved care regime (Table 3.16) belong to the category of medicinal products for gastrointestinal system and metabolism. Cholecalciferol ranks first with 116.7 DDD/1000 inhabitants per day, confirming also in 2023 as the most prescribed active ingredient within the category. It is followed by pantoprazole (29.4 DDD/1000 inhabitants per day) and metformin (23.0 DDD/1000 inhabitants per day). The remaining active substances are the proton pump inhibitors omeprazole (17.1 DDD), esomeprazole (15.9 DDD) and lansoprazole (12.5 DDD).

In terms of purchases by public health facilities, there is an increase in consumption (+12.7%), the use of more expensive medicinal products (mix effect: +7.4%) and a reduction in prices (-6.3%) (Figure 3.5 and Table 3.17), together with a 13.4% increase in expenditure. GLP-1 receptor analogues are the highest-expenditure subgroup with a per capita value of 6.55 euros, up 32.7% compared to 2022. This increase is due to an increase in consumption (+34.8%) and the use of more expensive medicinal products (mix effect: +4.2%). Enzymes follow with 5.78 euros, up 2.7% compared to the previous year, entirely due to an increase in consumption (+14.4%). For this subgroup, in fact, a reduction is recorded in prices and

average DDD costs of 6.1% and 10.2% respectively, attributable to the renegotiation of some active ingredients. The most significant increases in expenditure were recorded for other drugs used in biliary therapy (>100%). This can be attributed to an increase in consumption (>100%) and the use of more expensive medicinal products (mix effect: +14.6%). SGLT2 co-transporter inhibitors also saw a 62.3% increase in expenditure, entirely due to an increase in consumption (+66.5%) and the use of more expensive medicinal products (mix effect: +1.9%), especially if considering the reduction in prices (-4.3%) and the average DDD cost (-2.5%).

Analyzing the active ingredients of this group of drugs, it is evident that semaglutide and dulaglutide account for 24.2% of the expenditure (Table 3.18). On the other hand, a high average DDD cost is highlighted for enzymes such as, for example, alglucosidase alfa, agalsidase alfa, agalsidase beta, imiglucerase, idursulfase, mainly used in the treatment of rare diseases. Insulin glargine alone represents 10.4% of consumption in the category, a figure that is substantially stable compared to the previous year. Semaglutide and dulaglutide are also present in the list of the top 30 active ingredients for expenditure by public health facilities with an absolute value of 185.6 and 179 million respectively (Table 3.19). Compared to 2022, semaglutide shows a shift in rank from twenty-seventh to tenth place and a significant difference in the average DDD cost between approved care (9.3 euros) and public health facilities (3.03 euros). This active ingredient is also among the top 30 with the highest increase in expenditure (Table 3.20), recording an 84.2% increase, entirely attributable to an increase in consumption (+96.7%). Dapagliflozin (+70.1%), empagliflozin (+69.9%), insulin degludec combined with liraglutide (+24.5%) and agalsidase beta (+22.7%) showed a significant increase in expenditure. These increases are mainly due to an increase in consumption. The list of the first 30 active ingredients with the greatest reduction in expenditure on drugs active on the gastrointestinal system and metabolism, includes insulin glargine (-1.1%) and alglucosidase alfa (-0.7%) (Table 3.21). The first 30 active ingredients with the highest average cost per day of therapy, selected from the first 100 with the highest expenditure, for ATC A, include 3 ERTs (enzyme replacement therapy): imiglucerase (1,096.5 euros), indicated in type 1 or 3 Gaucher disease with significant non-neurological clinical manifestations, alglucosidase alfa (960.5 euros), used in patients with Pompe disease, and agalsidase beta (483.6 euros), indicated in Fabry disease (Table 3.22). In the list of molecules with the lowest average DDD cost, six molecules belong to ATC A, specifically insulin glargine (0.89 euros), dapagliflozin (1.18 euros), empagliflozin (1.37 euros), dulaglutide (2.05 euros), semaglutide (3.03 euros), insulin degludec/liraglutide (3.46 euros) (Table 2.23). In total, nine molecules are in the list of the top 30 active ingredients by consumption among those purchased by public health facilities in 2023: insulin glargine (4.5 DDD), dulaglutide (4.1 DDD), dapagliflozin (3.6 DDD), cholecalciferol (3.1 DDD), semaglutide (2.9 DDD), empagliflozin (2.1 DDD), pantoprazole (1.8 DDD), linagliptin (1.6 DDD) and dapagliflozin/metformin (1.5 DDD) (Table 3.24). For these active ingredients, significant increases are recorded compared to 2022. Semaglutide moves from the twenty-seventh to the fourteenth rank and empagliflozin from the thirty-third to the twentieth.

If we consider the overall expenditure values of the approved care regime and public healthcare facilities, pantoprazole (274.1 million), dulaglutide (240.7 million), semaglutide (231.5 million), cholecalciferol (198.6 million) and esomeprazole (131.6 million) are on the list of the first 30 active ingredients with the highest expenditure (Table 3.25). Cholecalciferol

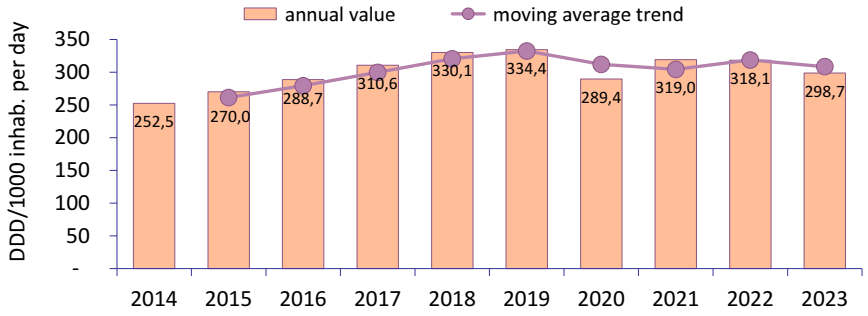
(119.8 DDD), pantoprazole (31.2 DDD), metformin (23.3 DDD), omeprazole (18.1 DDD), esomeprazole (16 DDD) and lansoprazole (13.4 DDD) are instead among the top 30 with the highest consumption (Table 3.26). Finally, Table 3.30 shows different trends in expenditure, consumption and average cost per DDD between approved care regime and direct purchasing for antidiabetics, drugs for peptic ulcer and gastroesophageal reflux disease (GERD).

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

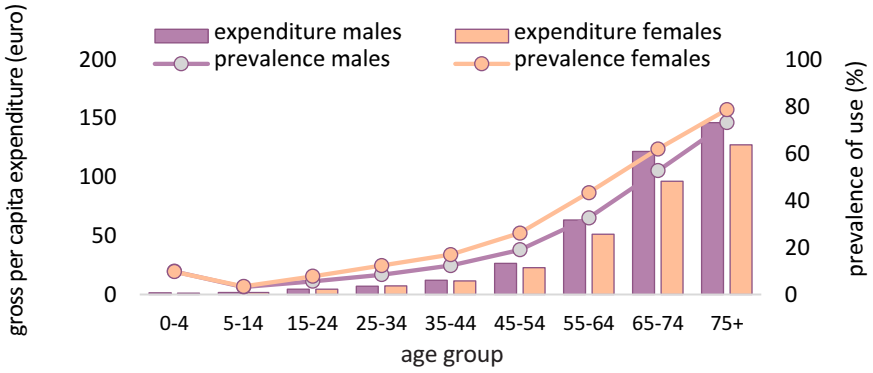
Gastrointestinal system and metabolism

Public expenditure* in million euros (% over total)	**3,320.7**	**(12.8)**
Δ % 2023-2022		2.2
Regional range of gross per capita expenditure:	32.4	72.9
DDD/1000 inhabitants per day* (% over total)	**298.7**	**(22.6)**
Δ % 2023-2022		-6.1
Regional range DDD/1000 inhabitants per day	212.7	361.8

** includes prescriptions under approved care regime and purchases by public health facilities*



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf by age and gender in 2023 (Figure and Table)



Age group	Gross per capita expenditure			DDD/1000 inhabitants per day		
	Males	Females	Total	Males	Females	Total
0-4	1.4	1.3	1.3	61.1	60.3	60.7
5-14	1.8	1.8	1.8	18.4	19.8	19.1
15-24	4.6	4.5	4.6	22.4	30.3	26.2
25-34	7.0	7.3	7.1	31.0	47.2	38.9
35-44	12.1	11.5	11.8	52.7	80.2	66.4
45-54	26.5	23.0	24.7	111.2	176.7	144.2
55-64	63.6	51.5	57.4	257.2	400.9	330.9
65-74	121.8	96.5	108.5	518.8	733.7	632.1
75+	146.5	127.5	135.3	761.2	1023.8	916.6

3.3.1 Antidiabetics

In 2023, the antidiabetic category recorded a total public expenditure of 1,450.7 million euros, equal to 5.6% of pharmaceutical expenditure including the approved care expenditure and purchases by public facilities, up 7.6% compared to the previous year. Consumption also showed a 4.5% increase, reaching a total value of 71.4 DDD/1000 inhabitants per day, approximately 5.4% of total consumption (Box Main indices of expenditure, consumption and exposure).

Analyzing the trend over the last 10 years, it is worth noting that the consumption of these drugs has increased, going from 62.3 to 71.4 DDD per thousand inhabitants per day, with an average annual variation (CAGR) of 1.4%. The cost per day of therapy has increased by an average of 4.8% per year, going from 0.59 euros in 2014 to 0.95 euros in 2023. These trends indicate an increasing use of more recently introduced, high-cost drugs, such as GLP-1 analogues, gliptins and gliflozins.

For antidiabetic drugs, the prevalence of use tends to increase with age, showing a growing gap between females and males starting from the age of 45 (2.54% and 3.75% respectively), up to a maximum value in the over-85 age group of 18.46% and 24.59% respectively. Consumption also shows an increasing trend with age, with maximum values recorded in the 75 to 84 age group (180.03 DDD in females and 265.10 in males), then decreasing slightly in the over-85 age group (146.22 DDD in females and 208.05 DDD in males).

In 2023, per capita expenditure on this category of drugs was 24.65 euros, with an average annual variation, over the last ten years, equal to 6.2% (Table 3.3.1a). The increase in expenditure (+7.6%) last year, however, is linked to both an increase in consumption (+4.5%), and in the average DDD cost (+2.9%).

Analyzing the therapeutic categories, GLP-1 analogues are the drugs with the highest per capita expenditure (8.38 euros), up 17.9% compared to the previous year, exclusively attributable to an increase in consumption (+26.4%). In fact, for this therapeutic category, there was a 6.7% reduction in the average cost. Gliflozins are the second highest expenditure category (3.04 euros), up 60.1% compared to 2022. This category also recorded a 65.6% increase in consumption and a 3.3% reduction in average cost. Combined insulins (long/intermediate with fast), on the other hand, show the greatest reduction in expenditure (-36.1%), attributable to both a reduction in consumption (-31.4%) and in the average cost (-6.9%).

Metformin remains the most widely used drug in the treatment of diabetes (23.3 DDD per 1000 inhabitants per day when used alone, equal to 32.6% of the total), followed by GLP-1 analogues (approximately 8.2 DDD/1000 inhabitants per day, equal to 11.5% of the total) and fast-acting insulins (7.7 DDD/1000 inhabitants per day, equal to 10.8% of the total). Gliflozins alone report a consumption of 6.5 DDD/1000 inhabitants per day. If considered in combination with metformin, this is equal to 9.7 DDD/1000 inhabitants per day, approximately 13.6% of the total. Gliptins, both alone and in combination with metformin, show stable or slightly decreasing consumption compared to the previous year. Although they are no longer recommended by the main national and international guidelines, drugs with secretagogue action (sulfonylureas, alone or in combination, and glinides) are still widely used, with an overall consumption of 6.4 DDD/1000 inhabitants per day, although in constant and strong decline as highlighted by the CAGR. Insulins combined with GLP-1 analogues are the category with the highest average cost per day of therapy with a value of 4.39 euros, followed by GLP-

1 analogues with 2.81 euros. Metformin and sulfonylureas, not associated with other active ingredients, have the lowest value of 0.20 euros. Overall, it is possible to note a reduction in the average DDD cost of the most recently introduced categories both considering medicinal products with a single active ingredient and those in association with others.

Confirming the trend of expenditure and consumption of the therapeutic categories, dulaglutide is the active ingredient with the highest per capita value (4.09 euros), followed by semaglutide (3.93 euros) which shows an increase of 52.3%, compared to the previous year, attributable to an increase in consumption (+75.9%). In fact, this active ingredient shows an average cost reduction of 13.4%. Overall, gliflozins record an increase in consumption of 65.6%, driven by the active ingredients dapagliflozin (+81.1%) and empagliflozin (+60.4%). The highest average DDD cost is recorded for insulin degludec associated with liraglutide (4.44 euros), followed by semaglutide (3.50 euros).

Analyzing the consumption trend over time of the main therapeutic categories, starting from 2021, there has been a slight reduction in the consumption of insulins, both long and fast acting, and a sharp increase in gliflozins and GLP-1 analogues. On the contrary, metformin was confirmed as the most used drug in the treatment of diabetes since 2014, with a stable increasing trend over time (Figure 3.3.1a). The median age of users of antidiabetic drugs is around 71 years, ranging from 79 years of subjects treated with gliptins alone (a choice consistent with the greater tolerability of these drugs even if at the expense of the benefit over chronic complications) to 67 years of those exposed to gliflozins and GLP-1 analogues (Table 3.3.1b). In 2023, the average cost per user was 357.1 euros, although there are significant differences based on the category considered. GLP-1 analogues show the highest cost values both as single-components (809.2 euros) and when combined with insulins (749.4 euros). Metformin, on the other hand, shows the lowest cost both in medicines in which it is present as the only active ingredient (38.3 euros) and in those in which it is found in association with sulfonylureas (49.5 euros). Antidiabetic users were on average treated for 374.8 days, although differences in exposure related to therapeutic category can also be noted. Users of GLP-1 analogues and sulfonylureas showed a higher intensity of use (275.7 and 272.6 DDD respectively), while users of acarbose recorded significantly lower values (108 DDD). In 2023, users with a single prescription for antidiabetics were 3.4%, with particularly high values in the case of insulins, namely 19.0% for intermediate, 16.5% for combined, 14.5% for long-acting, 12.7% for those associated with GLP-1 analogues and 10.9% for fast-acting. On the other hand, the value of subjects who received only one prescription is particularly low in the case of gliptins associated with metformin (3.9%) or with pioglitazone (4.3%).

The prevalence of use is 6.5% overall, higher in the South and the Islands (7.7%) and lower in the North (5.5%) and in the Centre (6.7%) (Table 3.3.1c). At a regional level, it is possible to note an extreme variability, going from a value of 8.8% in Calabria to 3.9% in the Province of Bolzano. The cost per user also shows a percentage difference between the two extreme values of more than 100%, ranging from the minimum value of 234.7 euros in Emilia Romagna to the maximum value of 593.8 euros in Lombardy. Each user was exposed to antidiabetic therapy for 374.8 days.

Analyzing adherence to treatment instead, a low adherence value of 23.9% is highlighted, a reduction of 12.0% compared to 2022 (Figure 3.3.1b). Females show higher rates of low adherence (28.1%) than males (23.9%), although males show the greatest reduction compared to the previous year. High adherence is equal to 34.3% of users following an increasing trend since 2019 (Figure 3.3.1c). Males appear to be more highly adherent than

females and have seen the greatest increase in the last year. As regards treatment persistence, 47.5% of subjects were found to be persistent to therapy after 12 months, with higher values in males and therefore trends similar to those highlighted for adherence (Figure 3.3.1d). Finally, analyzing the trend by geographical area, it is possible to observe higher persistence to treatment in the North than in the Centre and the South and islands (Figure 3.3.1e).

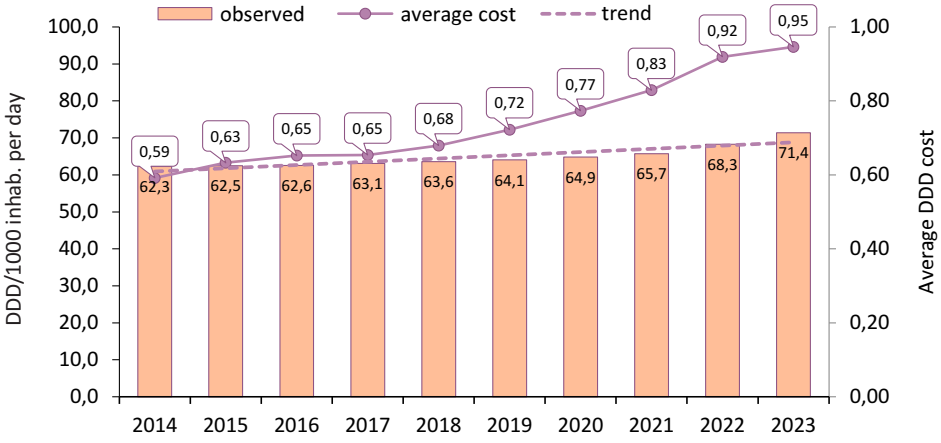
For further information on regional data on exposure and duration of therapy and on indicators of adherence and persistence to treatment stratified by age, gender and geographical area, please refer to the supplementary documents published online.

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Antidiabetics

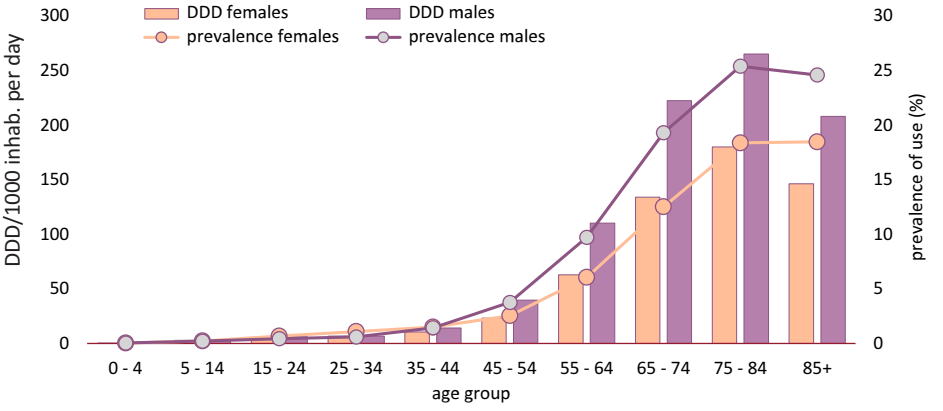
Public expenditure* in million euros (% over total)	**1,450.7**	**(5.6)**
Δ % 2023-2022		7.6
Regional range of gross per capita expenditure:	13.9	33.4
DDD/1000 inhabitants per day* (% over total)	**71.4**	**(5.4)**
Δ % 2023-2022		4.5
Regional range DDD/1000 inhabitants per day	44.6	89.3

** includes prescriptions under approved care regime and purchases by public health facilities*

Antidiabetics, temporal trend of consumption and average cost per day of therapy (2014-2023)



Antidiabetics, distribution of prevalence of use and consumption under approved care and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.3.1a Antidiabetics, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and substance: comparison 2014-2023

Subgroups and substances	Expenditure per capita	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
GLP-1 (glucagon-like one) analogues	8.38	17.9	27.0	8.2	26.4	30.1	2.81	-6.7
Glifozins (SGLT2 inhibitors) alone	3.04	60.1	—	6.5	65.6	—	1.29	-3.3
Fast acting insulins	2.92	-13.8	-2.9	7.7	-3.1	-0.8	1.04	-11.1
Long acting insulins	2.09	-9.7	-1.7	6.1	-3.2	1.6	0.94	-6.7
Metformin	1.69	1.3	2.2	23.3	-0.5	1.3	0.20	1.8
Insulins combined with GLP-1 (glucagon-like one) analogues	1.48	26.5	—	0.9	33.8	—	4.39	-5.4
Gliflozins (SGLT2 inhibitors) in combination with metformin	1.45	14.5	—	3.2	19.6	—	1.23	-4.2
Gliptins (DPP-4 inhibitors) alone	1.18	-19.8	3.7	3.6	2.7	9.8	0.90	-21.9
Gliptins (DPP-4 inhibitors) in combination with glifozins (SGLT2 inhibitors)	0.77	55.4	—	1.2	63.5	—	1.74	-4.9
Gliptins (DPP-4 inhibitors) in combination with metformin	0.58	-34.6	-6.1	2.2	-8.9	0.7	0.74	-28.2
Sulfonylureas alone	0.35	-17.7	-4.8	4.9	-19.3	-8.1	0.20	2.0
Glitazones alone	0.16	12.3	-0.8	0.9	10.0	-0.1	0.49	2.1
Repaglinide	0.14	-22.6	-12.2	1.0	-23.6	-13.0	0.40	1.2
Glitazones in combination with metformin	0.14	-7.6	-11.8	0.6	-4.4	-6.1	0.60	-3.4
Acarbose	0.11	-9.6	-5.4	0.4	-9.7	-4.7	0.72	0.1
Gliptins (DPP-4 inhibitors) in combination with pioglitazone	0.07	-7.2	44.6	0.2	-2.8	49.3	1.12	-4.6
Combined insulins (long/intermediate with fast)	0.04	-36.1	-21.0	0.1	-31.4	-19.9	1.12	-6.9
Sulfonylureas in combination with metformin	0.04	-27.9	-20.0	0.5	-28.1	-20.1	0.21	0.3
Sulfonylureas in combination with pioglitazone	0.01	-22.1	-12.2	<0.05	-22.2	-11.2	1.06	0.2
Intermediate acting insulins	0.00	-19.0	-35.8	0.0	-16.2	-29.5	0.47	-3.4
Antidiabetics	**24.65**	**7.6**	**6.2**	**71.4**	**4.5**	**1.4**	**0.95**	**2.9**
dulaglutide	4.09	1.1	—	4.7	11.8	—	2.41	-9.6
semaglutide	3.93	52.3	—	3.1	75.9	—	3.50	-13.4
metformin	1.69	1.3	2.2	23.3	-0.5	1.3	0.20	1.8
dapagliflozin	1.58	70.0	—	3.7	81.1	—	1.18	-6.1
insulin glargine	1.51	-2.7	-2.5	4.6	-1.2	1.2	0.90	-1.5
insulin degludec/liraglutide	1.34	25.3	—	0.8	32.8	—	4.44	-5.7
insulin lispro	1.22	-18.0	-4.7	3.5	-3.7	-1.3	0.94	-14.9
insulin aspart	1.22	-14.8	-4.1	3.0	-3.6	-2.1	1.11	-11.6
empagliflozin	1.04	68.8	—	2.1	60.4	—	1.37	5.3
linagliptin	0.84	7.1	24.6	1.9	11.0	27.8	1.23	-3.5

Figure 3.3.1a Antidiabetics, 2014-2023 temporal trend in consumption (DDD/1000 inhabitants per day) by highest-expenditure subgroups

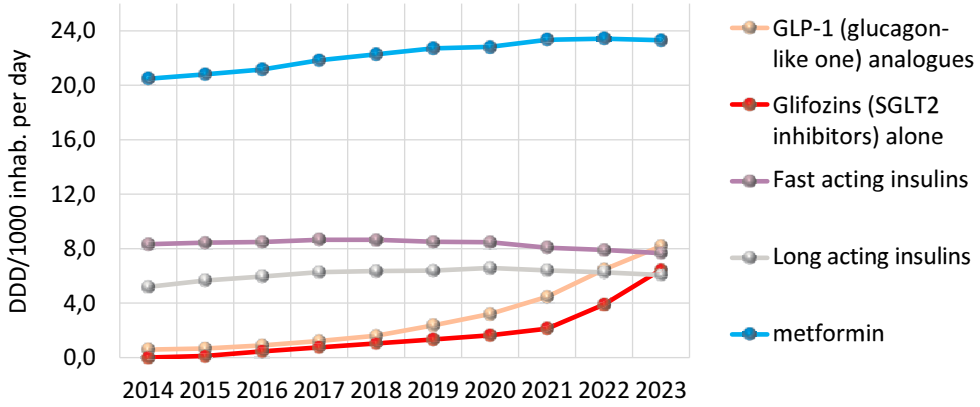


Table 3.3.1b Exposure and duration of therapy with antidiabetics by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Average cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
GLP-1 (glucagon-like one) analogues	1.18	0.78	0.97	67	809.2	275.7	254.5	5.4
Glifozins (SGLT2 inhibitors) alone	1.28	0.67	0.97	71	270.2	205.5	192.0	8.0
Fast acting insulins	1.07	0.9	0.99	70	283.6	259.2	225.0	10.9
Long acting insulins	1.39	1.12	1.25	71	152.7	157.9	135.0	14.5
Metformin	4.71	3.95	4.32	70	38.3	191.0	175.0	4.8
Insulins combined with GLP-1 (glucagon-like one) analogues	0.21	0.16	0.19	71	749.4	164.4	150.0	12.7
Gliflozins (SGLT2 inhibitors) in combination with metformin	0.59	0.28	0.43	67	320.6	254.1	280.0	5.1
Gliptins (DPP-4 inhibitors) alone	0.51	0.51	0.51	79	223.6	242.7	280.0	5.4
Gliptins (DPP-4 inhibitors) in combination with gliflozins (SGLT2 inhibitors)	0.20	0.13	0.16	73	442.4	243.7	270.0	6.4
Gliptins (DPP-4 inhibitors) in combination with metformin	0.31	0.25	0.28	74	209.7	263.1	300.0	3.9
Sulfonylureas alone	0.69	0.58	0.63	75	54.0	272.6	240.0	5.7
Glitazones alone	0.16	0.11	0.13	72	113.9	227.4	196.0	5.4
Repaglinide	0.22	0.20	0.21	78	66.9	164.2	101.3	10.1
Glitazones in combination with metformin	0.12	0.06	0.09	71	149.0	243.1	224.0	4.8
Acarbose	0.14	0.13	0.14	76	77.7	108.0	86.7	6.8
Gliptins (DPP-4 inhibitors) in combination with pioglitazone	0.03	0.02	0.02	73	306.6	267.8	308.0	4.3
Combined insulins (long/intermediate with fast)	0.02	0.02	0.02	76	208.9	182.3	150.0	16.5
Sulfonylureas in combination with metformin	0.08	0.07	0.08	77	49.5	239.9	200.0	4.5
Sulfonylureas in combination with pioglitazone	0.01	<0.005	0.01	73	283.2	264.3	280.0	5.1
Intermediate acting insulins	<0.005	<0.005	<0.005	71	101.4	172.2	150.0	19.0
Antidiabetics	**7.17**	**5.81**	**6.47**	**71**	**357.1**	**374.8**	**305.0**	**3.4**

Table 3.3.1c Antidiabetics, regional trend of per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use	Cost/user	Median DDD
Piedmont	22.36	68.9	0.89	12.1	5.9	5.8	6.1	1.5	4.5	6.2	358.8	336.0
Valle d'Aosta	14.15	62.1	0.62	10.0	2.2	7.6	3.4	0.3	3.1	5.1	284.4	321.4
Lombardy	33.43	65.2	1.41	5.6	4.1	1.4	10.7	1.6	9.0	5.5	593.8	336.0
Province of Bolzano	13.90	44.6	0.85	5.7	6.3	-0.5	3.6	0.3	3.2	3.9	393.9	337.5
Province of Trento	21.18	61.9	0.94	12.8	8.6	3.9	7.5	2.5	4.9	4.9	298.3	280.0
Veneto	19.36	59.9	0.88	3.0	2.3	0.7	5.5	1.3	4.1	5.2	341.8	336.0
Friuli V.G.	21.43	66.8	0.88	12.9	6.1	6.4	6.3	1.5	4.7	6.0	350.5	336.0
Liguria	18.43	57.1	0.88	9.4	5.7	3.4	5.9	1.0	4.9	5.7	303.9	293.3
Emilia R.	17.93	68.1	0.72	10.1	4.3	5.6	6.6	1.6	4.9	5.5	234.7	280.0
Tuscany	18.93	64.2	0.81	10.5	7.5	2.7	4.9	1.0	3.8	6.5	275.1	272.0
Umbria	23.17	67.4	0.94	4.2	4.7	-0.5	5.1	1.6	3.5	6.7	350.9	312.0
Marche	19.83	64.5	0.84	3.2	2.4	0.7	7.1	2.5	4.5	6.1	323.6	330.0
Lazio	22.45	71.5	0.86	5.3	4.6	0.7	5.2	1.0	4.1	7.0	309.5	270.0
Abruzzo	25.21	72.9	0.95	6.0	3.0	2.8	4.5	1.3	3.2	6.9	361.8	308.0
Molise	24.57	73.2	0.92	6.6	1.9	4.6	5.3	1.2	4.1	7.2	281.7	277.3
Campania	27.68	83.2	0.91	8.6	5.4	3.0	5.0	1.9	3.0	7.3	329.7	315.0
Puglia	28.83	84.6	0.93	7.9	4.2	3.5	6.7	1.4	5.3	7.8	365.1	300.0
Basilicata	29.39	86.5	0.93	14.7	4.6	9.7	6.8	2.1	4.6	8.2	353.3	310.5
Calabria	27.58	89.3	0.85	0.0	-1.6	1.7	4.5	1.2	3.3	8.8	308.6	275.0
Sicily	25.97	87.1	0.82	16.7	7.4	8.6	3.6	0.9	2.7	8.0	289.9	295.0
Sardinia	23.69	73.2	0.89	0.6	0.6	0.0	2.6	0.8	1.8	6.8	322.2	322.5
Italy	**24.65**	**71.4**	**0.95**	**7.6**	**4.5**	**2.9**	**6.2**	**1.4**	**4.8**	**6.5**	**357.1**	**305.0**
North	24.57	64.5	1.04	7.3	4.4	2.7	8.0	1.5	6.4	5.5	416.4	327.5
Centre	21.04	67.9	0.85	6.4	5.2	1.1	5.3	1.2	4.0	6.7	303.7	280.0
South and Islands	26.98	83.4	0.89	8.6	4.3	4.1	4.8	1.3	3.4	7.7	325.8	300.0

Adherence and persistence to treatment

Table 3.3.1b Indicators of low adherence to treatment with antidiabetic drugs in the population aged ≥45 years stratified by gender, trend 2019-2023 (raw values). Emilia Romagna not included in the calculation

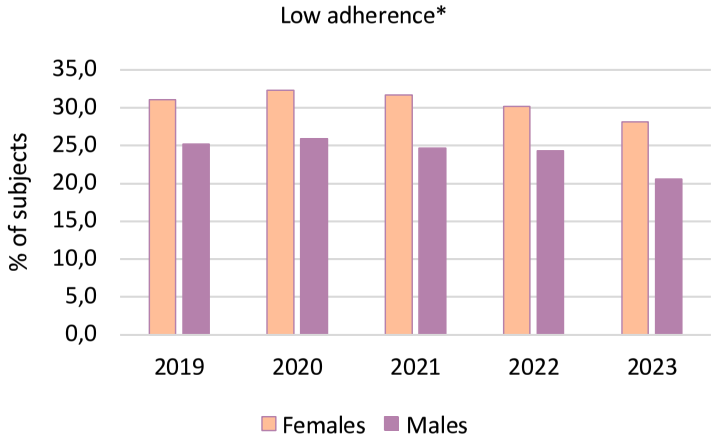
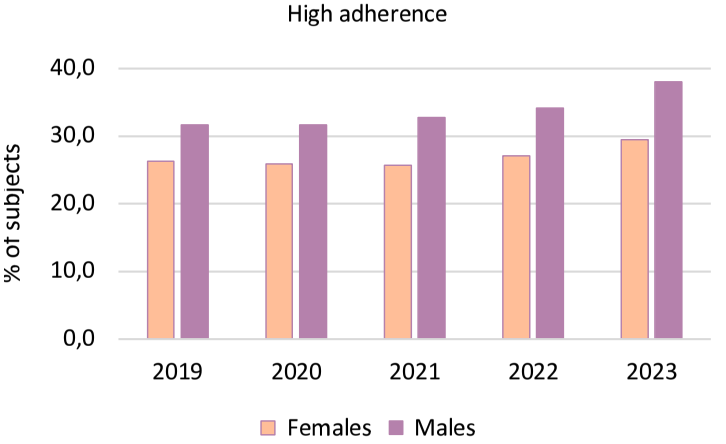


Table 3.3.1c Indicators of high adherence to treatment with antidiabetic drugs in the population aged ≥45 years stratified by gender, trend 2019-2023 (raw values). Emilia Romagna not included in the calculation



*Adherence to treatment was evaluated only for new users with at least 2 prescriptions. Low adherence to treatment was defined as therapeutic coverage (assessed on the basis of DDD) <40% of the observation period while high adherence was defined as therapeutic coverage ≥80% of the observation period (for further details please refer to statistical methods

Figure 3.3.1d Time (in days) to discontinuation of treatment with antidiabetic drugs in the population aged ≥45 years stratified by gender. Curves are adjusted by age (the Cox model was used to estimate persistence curves). The North does not include Emilia Romagna

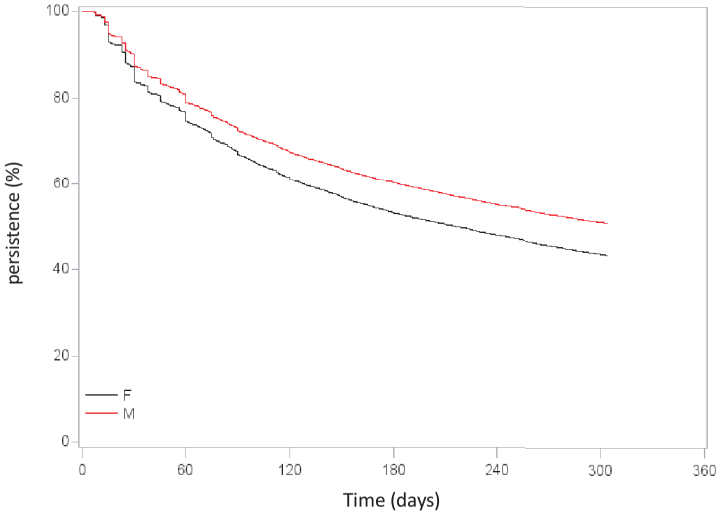
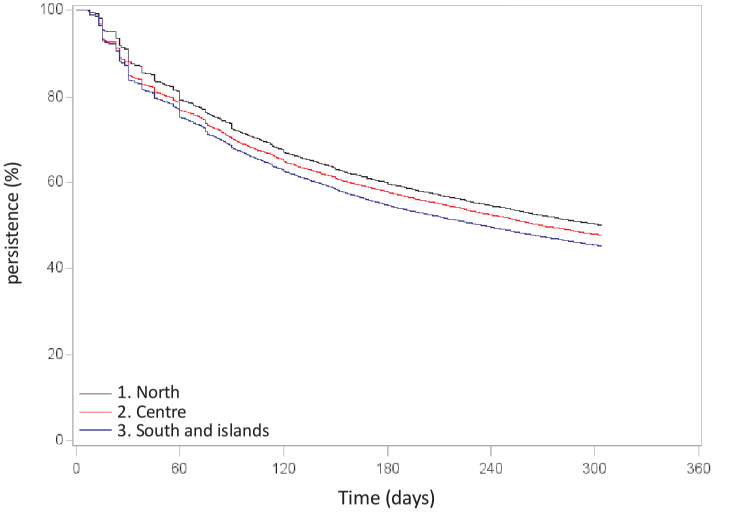


Figure 3.3.1e Time (in days) to discontinuation of treatment with antidiabetic drugs in the population aged ≥45 years stratified by geographical area. Curves are adjusted by gender and age (the Cox model was used to estimate persistence curves). The North does not include Emilia Romagna.



3.3.2 Medicines for peptic ulcer and GERD

In 2023, medicines for peptic ulcer and GERD recorded a total public expenditure of 704.7 million euros, equal to 2.7% of pharmaceutical expenditure including the approved care expenditure and purchases by public facilities, up 5.7% compared to the previous year. Consumption also showed a 3.1% increase, reaching a total value of 83.5 DDD/1000 inhabitants per day, approximately 6.3% of total consumption (Box Main indices of expenditure, consumption and exposure).

Analyzing the trend over the last 10 years, the consumption of these drugs has decreased, going from 89.3 to 83.5 DDD per 1000 inhabitants per day, with an average annual variation (CAGR) of 0.7%. The cost per day of therapy, on the other hand, decreased by an average of 3.1% per year, going from 0.54 euros in 2014 to 0.39 euros in 2023.

As for drugs for peptic ulcer and GERD, the prevalence of use tends to increase with age, remaining slightly higher in the female population up to 84 years, and then reaching a maximum value of 65.29% and 62.20% in females and males respectively in the over-85 age group. Consumption also shows an increasing trend with age, with maximum values recorded in people over 85, respectively 330.18 DDD in females and 344.87 in males.

In 2023, the per capita expenditure on this category of drugs was 11.97 euros, with a -3.8% average annual variation, from 2014 to 2023 (Table 3.3.2a). However, the reduction in expenditure (-5.7%) in the last year is linked to a decrease in both consumption (-3.1%) and in the average DDD cost (-2.7%).

Analyzing the therapeutic categories, proton pump inhibitors are the category with the highest per capita expenditure (11.35 euros), down 2.5% compared to the previous year. This is due to a slight decrease in both consumption (-0.9%), and the average DDD cost (-1.7%). Other drugs for peptic ulcer and gastroesophageal reflux disease (GERD), including alginate, bicarbonate and sucralfate-based medicines, record the greatest reduction in expenditure, mainly due to a reduction in consumption (-88.0%) and only partially to a reduction in the average DDD cost (-11.9%). Prostaglandins are the category with the highest average DDD cost, with a value of 0.96 euros, down 2.2% compared to the previous year, although there was also a reduction in the other indicators considered (expenditure -12.5% and consumption -10.5%). Histamine H2 receptor antagonists are the third most expensive category with a per capita value of 0.06 euros, with a 17.2% increase. This is entirely attributable to an increase in consumption (+20.9%), given the 3.0% reduction in the average DDD cost.

Proton pump inhibitors, pantoprazole (4.66 euros), esomeprazole (2.24 euros), omeprazole (2.13 euros) and lansoprazole (2.03 euros) are the most expensive active ingredients. These drugs recorded an overall reduction in the average DDD cost, ranging from 0.32 euros for omeprazole to 0.42 euros for lansoprazole. Consumption is higher for pantoprazole (31.2 DDD) and increased by 1.9% compared to the previous year, followed by omeprazole (18.1 DDD, -2.2%), esomeprazole (16.0 DDD, +0.8%) and lansoprazole (13.4 DDD, -6.5%)

For the aluminium hydroxide/magnesium hydroxide combination, there was an increase in all the indicators considered (expenditure +114.1%, consumption +14.8%, average DDD cost +86.5%).

By analyzing over time the global trend of consumption of the main therapeutic categories,

the consumption of proton pump inhibitors recorded a reduction between 2016 and 2018, then started growing again in 2022 and decreased in 2023. The other drugs for peptic ulcer and GERD, however, have recorded a reduction starting from 2021 (Figure 3.3.2a).

The median age of patients using drugs for peptic ulcer and GERD is around 69 years, ranging from 64 years of subjects treated with H2 receptor antagonists to 72 years of those exposed to prostaglandins (Table 3.3.2b). In 2023, the average cost per user was 60.85 euros, although there are some differences based on the category considered. In fact, prostaglandins show the highest cost values (62.06 euros), while antacids show the lowest (16.77 euros). Users of these drugs were exposed to 150.8 days of therapy, although even for this indicator thee are differences related to the therapeutic category. In fact, users of proton pump inhibitors showed a greater intensity of use (154.47 DDD), while users of antacids recorded significantly lower values (27.76 DDD). In 2023, users with a single prescription for drugs for peptic ulcer and GERD were 18.08%, with particularly high values in the case of other drugs for peptic ulcer (56.13%). Proton pump inhibitors show the lowest value in the category, equal to 17.44%.

For further information on regional data on exposure and duration of therapy, please refer to the supplementary material published online.

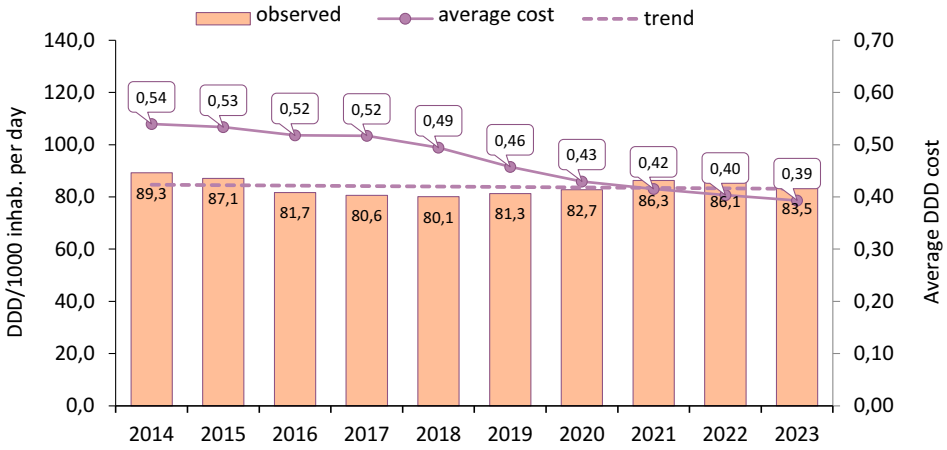
MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

Medicines for peptic ulcer and GERD

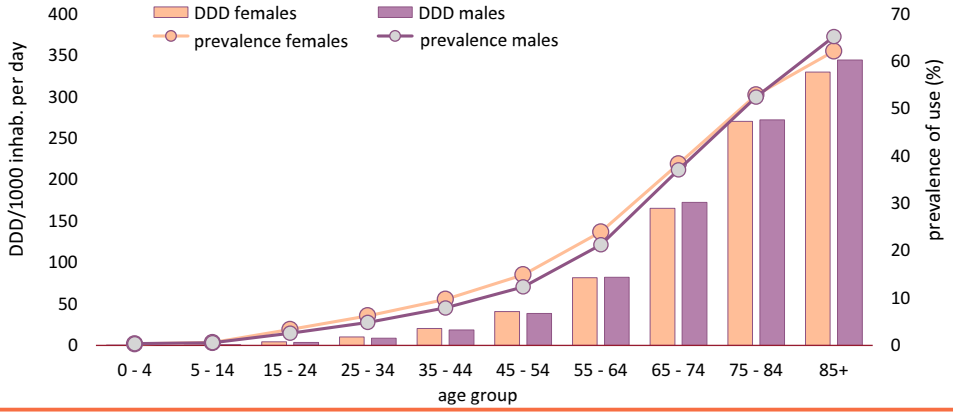
Public expenditure* in million euros (% over total)	**704.7**	**(2.7)**
Δ % 2023-2022		-5.7
Regional range of gross per capita expenditure:	7.0	18.2
DDD/1000 inhabitants per day* (% over total)	**83.5**	**(6.3)**
Δ % 2023-2022		-3.1
Regional range DDD/1000 inhabitants per day	50.7	122.4

** includes prescriptions under approved care regime and purchases by public health facilities*

Temporal trend of consumption and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.3.2a Medicines for peptic ulcer and GERD, per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and substance: comparison 2014-2023

Subgroups and substances	Expenditure per capita	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Proton pump inhibitors	11.35	-2.5	-3.3	80.5	-0.9	0.0	0.39	-1.7
Antacids	0.51	-10.6	2.5	2.4	-10.1	2.0	0.59	-0.6
H2 receptor antagonists	0.06	17.2	-17.0	0.3	20.9	-19.7	0.61	-3.0
Other medicines for peptic ulcer and gastroesophageal reflux disease (GERD)	0.04	-89.4	-25.5	0.2	-88.0	-24.6	0.51	-11.9
Prostaglandins	0.01	-12.5	-11.1	<0.05	-10.5	-10.1	0.96	-2.2
Medicines for peptic ulcer and GERD	**11.97**	**-5.7**	**-3.8**	**83.5**	**-3.1**	**-0.7**	**0.39**	**-2.6**
pantoprazole	4.66	0.3	-0.7	31.2	1.9	3.6	0.41	-1.6
esomeprazole	2.24	-0.6	-2.0	16.0	0.8	1.8	0.38	-1.4
omeprazole	2.13	-4.7	-4.8	18.1	-2.2	-1.3	0.32	-2.6
lansoprazole	2.03	-7.5	-7.0	13.4	-6.5	-4.8	0.42	-1.1
magaldrate	0.50	-11.8	2.4	2.3	-10.0	2.3	0.60	-2.0
rabeprazole	0.29	-8.4	-5.4	1.7	-5.6	-4.3	0.45	-3.0
famotidine	0.06	17.2	32.2	0.3	20.9	35.3	0.61	-3.0
sucralfate	0.04	20.3	-1.0	0.2	19.1	-1.8	0.49	1.0
aluminium hydroxide/ magnesium hydroxide	0.01	>100	7.2	<0.05	14.8	-3.8	1.06	86.5
misoprostole	0.01	-12.5	-11.1	<0.05	-10.5	-10.1	0.96	-2.2

Figure 3.3.2a Medicines for peptic ulcer and GERD, temporal trends 2014-2023 in consumption (DDD/1000 population days) of the highest-expenditure subgroups

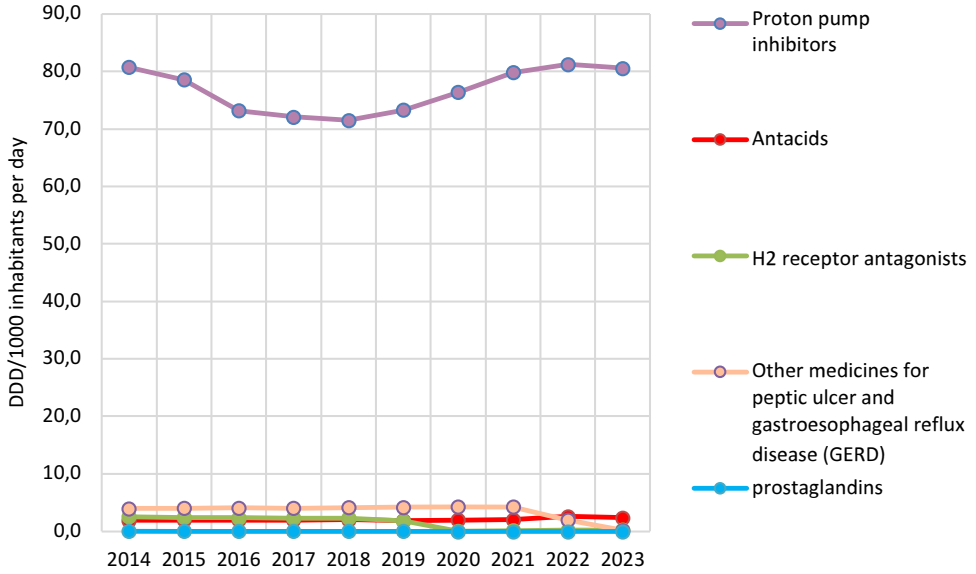


Table 3.3.2b Exposure and duration of therapy with medicines for peptic ulcer and GERD by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Average cost peruser	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
Proton pump inhibitors	16.14	19.45	17.84	69	61.24	154.47	126.0	17.44
Antacids	2.27	3.5	2.90	65	16.77	27.76	20.0	45.98
H2 receptor antagonists	0.08	0.14	0.11	64	55.29	89.57	40.0	34.90
Other medicines for peptic ulcer and gastroesophageal reflux disease (GERD)	0.19	0.26	0.22	66	18.65	35.86	15.0	56.13
Prostaglandins	0.01	0.01	0.01	72	62.06	55.53	37.5	33.84
Medicines for peptic ulcer and GERD	**17.02**	**20.74**	**18.93**	**69**	**60.85**	**150.80**	**112.0**	**18.08**

Regional data on expenditure, consumption and exposure

Table 3.3.2c Medicines for peptic ulcer and GERD, regional trend of per capita expenditure, consumption (DDD/1000 inhab. per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use	Cost/user	Median DDD
Piedmont	9.88	71.2	0.38	-4.5	-2.5	-2.1	-5.0	-1.6	-3.5	17.6	56.3	112.0
Valle d'Aosta	10.68	76.7	0.38	-1.3	1.8	-3.1	-3.3	-0.2	-3.1	16.9	61.5	112.0
Lombardy	11.96	84.9	0.39	-1.6	0.1	-1.7	-1.5	1.8	-3.2	17.0	67.1	140.0
Province of Bolzano	6.98	51.2	0.37	-1.6	2.3	-3.8	-1.2	1.7	-2.9	10.2	60.7	93.3
Province of Trento	12.77	88.8	0.39	-1.1	-0.2	-0.9	-0.8	2.2	-3.0	16.8	71.3	140.0
Veneto	9.29	68.5	0.37	-5.4	-2.1	-3.3	-4.7	-1.7	-3.1	13.2	66.9	136.0
Friuli V.G.	10.27	70.8	0.40	-3.4	-0.9	-2.6	-3.7	-0.6	-3.2	16.4	64.0	112.0
Liguria	13.74	97.4	0.39	-4.6	-2.0	-2.7	-2.8	0.1	-2.9	21.5	66.6	140.0
Emilia R.	9.91	70.6	0.38	-5.3	-3.2	-2.1	-3.3	-0.9	-2.4	15.9	58.6	98.0
Tuscany	7.92	56.7	0.38	-11.6	-8.8	-3.2	-5.4	-2.2	-3.3	14.6	53.6	94.0
Umbria	7.00	50.7	0.38	-25.6	-22.1	-4.4	-8.7	-5.4	-3.5	14.3	48.5	84.0
Marche	9.78	65.3	0.41	-2.7	-1.1	-1.5	-5.4	-2.3	-3.2	16.9	57.3	112.0
Lazio	12.48	84.8	0.40	-9.5	-6.7	-3.0	-5.3	-2.2	-3.2	20.6	58.3	112.0
Abruzzo	13.64	90.9	0.41	-3.6	-1.1	-2.5	-1.9	0.9	-2.8	21.9	57.4	98.0
Molise	14.74	96.3	0.42	3.5	3.1	0.4	-2.2	0.5	-2.7	22.1	62.2	122.0
Campania	18.21	122.4	0.41	-5.0	-2.5	-2.6	-1.3	2.0	-3.2	26.7	62.2	112.0
Puglia	12.74	85.2	0.41	-8.6	-5.9	-2.8	-5.7	-2.5	-3.2	20.3	59.5	112.0
Basilicata	15.21	99.2	0.42	-1.8	1.4	-3.2	-1.2	1.7	-2.8	25.2	58.1	112.0
Calabria	14.59	97.4	0.41	-5.6	-2.6	-3.1	-4.7	-2.0	-2.8	23.7	59.2	112.0
Sicily	13.27	94.8	0.38	-7.7	-3.8	-4.0	-5.0	-1.6	-3.4	21.8	58.0	112.0
Sardinia	13.49	95.0	0.39	-3.2	-0.4	-2.8	-4.3	-1.4	-2.9	22.0	61.8	112.0
Italy	**11.97**	**83.5**	**0.39**	**-5.7**	**-3.1**	**-2.6**	**-3.8**	**-0.7**	**-3.1**	**18.9**	**60.9**	**112.0**
North	10.78	77.0	0.38	-3.5	-1.3	-2.2	-3.1	0.0	-3.0	16.3	63.7	120.0
Centre	10.26	70.7	0.40	-10.2	-7.6	-2.8	-5.5	-2.4	-3.2	17.8	56.4	102.7
South and Islands	14.74	100.5	0.40	-5.8	-3.0	-3.0	-3.6	-0.5	-3.1	23.2	60.1	112.0

3.3.3 Diseases due to altered functionality of cellular metabolism

euros, equal to 2.4% of pharmaceutical expenditure including the approved care expenditure and purchases by public facilities and an 18.2% increase compared to the previous year (Box Main indices of expenditure, consumption and exposure).

Analyzing the trend over the last 10 years, the consumption of these drugs has increased, going from 3.8 to 10.69 DDD per thousand inhabitants per day, with an average annual variation (CAGR) of 10.9% (Table 3.3.3a). However, the cost per day of therapy decreased by an average of 8.0% per year, going from 447.3 euros in 2014 to 194.1 in 2023.

In 2023, the increase in per capita expenditure on these drugs (+18.2%) was mainly due to a consumption increase (+54.4%), which stands at 0.2 DDD (Table 3.3.3a).

Analyzing the therapeutic categories, drugs for the treatment of hereditary transthyretin amyloidosis are the category with the highest per capita expenditure (3.08 euros) and show a 65.8% increase compared to the previous year, exclusively attributable to an increase in consumption (+90.8%). This category shows a 13.1% reduction in the average cost. Enzyme replacement therapy used in Fabry disease is the second highest cost category (1.87 euros), up 9.3% compared to 2022. This category also recorded a 17.5% increase in consumption and a 7.0% reduction in average cost.

Enzyme replacement therapy for the lysosomal storage disease alpha-mannosidosis, on the other hand, shows the greatest expenditure increase (>100%) entirely due to a consumption increase (>100%).

The largest reductions instead concern enzyme replacement therapies for mucopolysaccharidosis types II and VI, with values of 14.5% and 13.6% respectively. These reductions are correlated with a decrease in the average DDD cost by 18.0% and 12.3% respectively. Overall, the average DDD cost has decreased or remained stable for most active ingredients, with the sole exception of chaperone therapy for type 1 Gaucher disease (+9.3%), drugs for Wilson disease (+13.2%) and drugs for lipodystrophy (+5.7%). The category with the highest average DDD cost is related to liposomal storage enzyme replacement therapy (mucopolysaccharidosis IVA – Morquio syndrome), with a value of 2,744.5 euros, down 8.3%. The most expensive active ingredient is alglucosidase alfa, authorised as an ERT in Pompe disease, with a value of 1.41 euros, a reduction of almost one percentage point, despite a 9.9% increase in consumption. This active ingredient shows a 9.6% reduction in the average DDD cost. In second place is agalsidase beta, an ERT used in Fabry disease, with a per capita value of 1.11 euros, up 15.1%, entirely attributable to an increase in consumption (+22.7%). Patisiran also has a per capita value of 0.89 euros, a 33.9% increase exclusively due to a consumption increase (+33.9%).

In 2023, drugs for diseases caused by altered cellular metabolism recorded a total expenditure of 629 million

Analyzing the consumption trend over time of the main therapeutic categories, starting from 2020, there has been a significant increase in per capita expenditure on most drugs used in diseases caused by altered functionality of cellular metabolism. In particular, a strong increase in hereditary transthyretin amyloidosis is evident (Figure 3.3.1b). Analysing the regional variability, a per capita expenditure value higher than the national average of 10.69 euros is recorded in the Centre (11.1 euros) and in the South and the Islands (11.5 euros). Northern Italy, on the other hand, shows a lower value, equal to 9.97 euros. For this category of drugs,

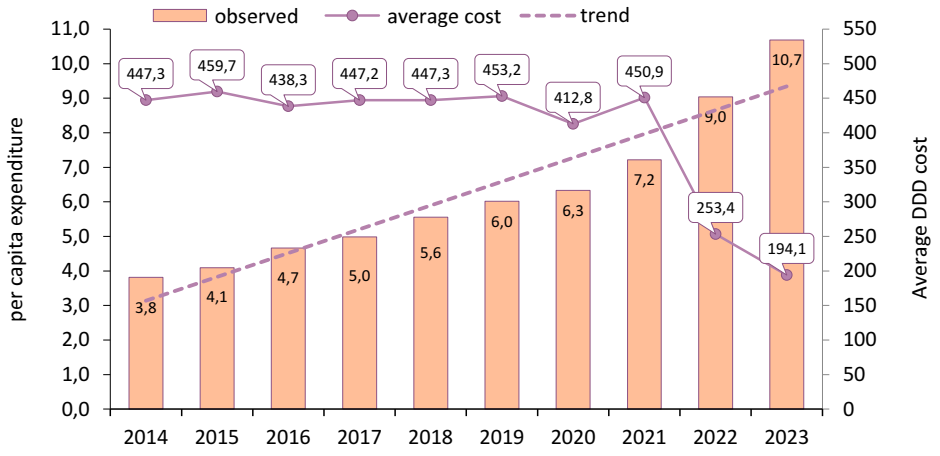
Campania records the highest value (13.72 euros), while the Province of Bolzano records the lowest (5.91 euros). In 2023, Calabria showed the highest average DDD cost value (421.9 euros), while the Province of Bolzano showed the lowest (90.9 euros).

MAIN INDICES OF EXPENDITURE AND CONSUMPTION

Diseases due to altered functionality of cellular metabolism

Public expenditure* in million euros (% over total)	**629.0**	**(2.4)**
Δ % 2023-2022		18.2
Regional range of gross per capita expenditure:	5.9	13.7
DDD/1000 inhabitants per day* (% over total)	**0.2**	**(0.0)**
Δ % 2023-2022		54.4
Regional range DDD/1000 inhabitants per day	0.1	0.2

Temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)



National data on consumption and expenditure by subgroup and substance

Table 3.3.3a Diseases caused by altered functionality of cellular metabolism, per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and substance: comparison 2014-2023

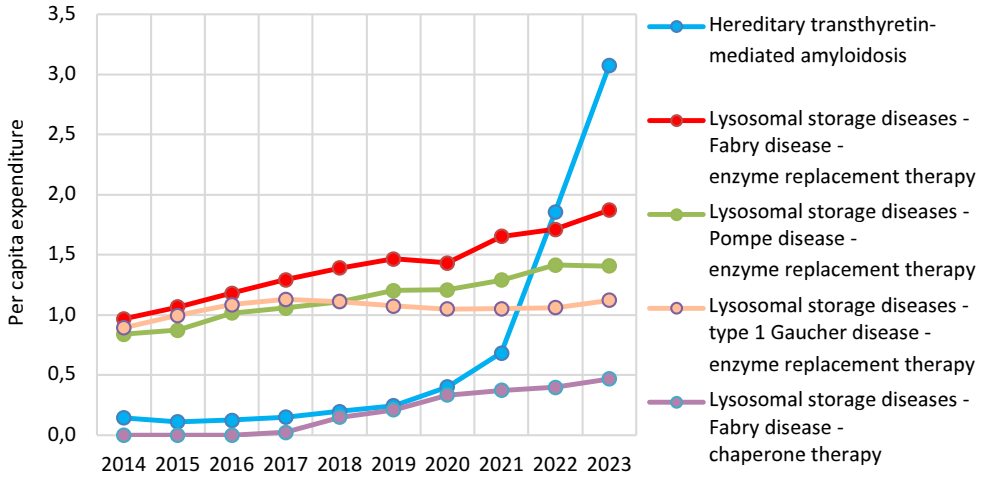
Subgroups and substances	Expenditure per capita	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Hereditary transthyretin-mediated amyloidosis	3.08	65.8	35.7	0.1	90.8	59.5	85.07	-13.1
Lysosomal storage diseases - Fabry disease - enzyme replacement therapy	1.87	9.3	6.8	<0.05	17.5	11.0	676.50	-7.0
Lysosomal storage diseases - Pompe disease - enzyme replacement therapy	1.41	-0.7	5.3	<0.05	9.9	6.8	960.53	-9.6
Lysosomal storage diseases - type 1 Gaucher disease - enzyme replacement therapy	1.12	5.8	2.3	<0.05	5.8	2.1	1096.50	0.0
Lysosomal storage diseases - Fabry disease - chaperone therapy	0.47	17.6	—	<0.05	22.3	—	447.75	-3.8
Lysosomal storage diseases - type 1 Gaucher disease - chaperone therapy	0.43	3.3	14.4	<0.05	-5.5	9.8	362.71	9.3
Lysosomal storage diseases - mucopolysaccharidosis II - enzyme replacement therapy	0.42	-14.5	-0.7	<0.05	4.3	1.5	2264.25	-18.0
Lysosomal storage diseases - mucopolysaccharidosis IV-A (Morquio syndrome) - enzyme replacement therapy	0.29	-1.5	—	<0.05	7.4	—	2744.48	-8.3
Congenital amino-acid transport and metabolism defects - phenylketonuria	0.24	9.9	8.2	<0.05	14.8	9.9	144.10	-4.3
Acute hepatic porphyria	0.21	35.6	—	<0.05	35.6	—	854.52	0.0
Lysosomal storage diseases - mucopolysaccharidosis I - enzyme replacement therapy	0.19	0.4	4.9	<0.05	11.0	6.0	1296.72	-9.6
Juvenile neuronal ceroid lipofuscinosis	0.18	8.8	—	<0.05	57.9	—	473.07	-31.1
Primary hyperoxaluria (siRNA)	0.17	66.2	—	<0.05	66.2	—	1036.83	0.0
Lysosomal storage diseases - mucopolysaccharidosis VI - enzyme replacement therapy	0.12	-13.6	4.7	<0.05	-1.5	5.1	2517.58	-12.3
Wilson disease	0.12	8.6	32.3	<0.05	-4.1	3.7	46.70	13.2
Lysosomal storage diseases - Liposomal acid lipase deficiency - enzyme replacement therapy	0.10	7.2	—	<0.05	7.2	—	1181.17	0.0
Urea cycle disorders	0.08	-3.2	7.6	<0.05	45.7	17.3	34.06	-33.6
Hypophosphatasia-enzyme replacement therapy	0.06	49.4	—	<0.05	62.2	—	2353.42	-7.9
Lipodystrophy	0.05	69.1	—	<0.05	60.0	—	969.88	5.7

continued

Table 3.3.3a – *continued*

Subgroups and substances	Expenditure per capita	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Congenital amino-acid transport and metabolism defects - homocystinuria	0.03	9.4	4.8	<0.05	8.9	5.9	13.27	0.4
Lysosomal storage diseases - alpha-mannosidosis - enzyme replacement therapy	0.02	>100	—	<0.05	118.6	—	664.26	-0.2
Congenital amino-acid transport and metabolism defects - type 1 hereditary tyrosinemia	0.02	-2.1	-5.2	<0.05	24.5	5.3	38.90	-21.4
Congenital defects of amino acid metabolism and transport-manifest nephropathic cystinosis	0.01	-6.8	4.9	<0.05	-1.4	3.0	24.58	-5.5
Medicines for diseases due to altered functionality of cellular metabolism	**10.69**	**18.2**	**10.9**	**0.2**	**54.4**	**20.5**	**194.06**	**-23.4**
agalsidase alfa	1.41	-0.7	5.3	<0.05	9.9	6.8	960.53	-9.6
agalsidase beta	1.11	22.7	15.1	<0.05	22.7	15.1	483.63	0.0
patisiran	0.89	33.9	—	<0.05	33.9	—	516.03	0.0
imiglucerase	0.85	8.4	1.8	<0.05	8.4	1.8	1096.50	0.0
agalsidase alfa	0.76	-5.8	0.9	<0.05	-2.8	1.2	1625.02	-3.1
migalastat	0.47	17.6	—	<0.05	22.3	—	447.75	-3.8
idursulfase	0.42	-14.5	-0.7	<0.05	4.3	1.5	2264.25	-18.0
eliglustat	0.41	7.8	—	<0.05	8.0	—	621.79	-0.1
elosulfase alfa	0.29	-1.5	—	<0.05	7.4	—	2744.48	-8.3
velaglucerase alfa	0.27	-1.9	4.1	<0.05	-1.9	3.3	1096.51	0.0

Figure 3.3.3a Diseases caused by altered functionality of cellular metabolism, temporal trend 2014-2023 in per capita expenditure of most expensive subgroups



Regional data on consumption and expenditure

Table 3.3.3b Diseases caused by altered functionality of cellular metabolism, regional trend of per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2022			2023			Δ % 23-22			CAGR % 14-23		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost
Piedmont	6.59	0.1	253.26	8.22	0.1	176.08	24.7	79.3	-30.5	9.0	22.6	-11.1
Valle d'Aosta	4.55	0.1	150.22	6.05	0.2	110.05	33.0	81.6	-26.7	80.0	37.5	31.0
Lombardy	8.02	0.1	213.91	10.01	0.2	174.57	24.9	53.0	-18.4	11.1	24.2	-10.5
Province of Bolzano	6.75	0.1	151.29	5.91	0.2	90.90	-12.5	45.6	-39.9	10.2	37.3	-19.7
Province of Trento	9.84	0.1	187.59	11.36	0.2	140.93	15.5	53.8	-24.9	9.5	22.9	-10.9
Veneto	8.34	0.1	206.24	9.85	0.2	158.26	18.2	54.1	-23.3	10.9	21.6	-8.8
Friuli V.G.	8.15	0.1	189.20	9.78	0.2	145.62	19.9	55.8	-23.0	14.1	28.3	-11.1
Liguria	5.66	0.1	192.85	7.47	0.1	141.65	32.0	79.7	-26.5	10.8	25.3	-11.6
Emilia R.	11.53	0.1	262.88	13.11	0.2	177.43	13.7	68.5	-32.5	11.5	25.5	-11.2
Tuscany	9.06	0.1	191.19	11.35	0.2	142.10	25.2	68.5	-25.7	13.6	24.8	-9.0
Umbria	8.53	0.1	200.73	11.46	0.2	135.39	34.3	99.2	-32.6	10.7	23.7	-10.5
Marche	8.02	0.2	146.32	9.42	0.2	120.36	17.4	42.8	-17.7	6.9	23.5	-13.5
Lazio	9.63	0.1	287.00	11.33	0.1	224.32	17.7	50.6	-21.8	14.5	22.8	-6.8
Abruzzo	8.00	0.1	210.89	10.44	0.2	144.75	30.5	90.1	-31.4	9.4	22.9	-10.9
Molise	5.98	0.1	224.13	6.76	0.1	210.64	13.2	20.5	-6.0	11.6	17.5	-5.0
Campania	12.12	0.1	387.98	13.72	0.1	310.38	13.2	41.5	-20.0	9.2	15.1	-5.2
Puglia	9.01	0.1	312.33	10.49	0.1	248.55	16.4	46.3	-20.4	12.9	15.0	-1.8
Basilicata	7.93	0.1	368.06	8.95	0.1	268.24	12.9	54.9	-27.1	10.0	15.5	-4.8
Calabria	11.58	0.1	492.18	12.33	0.1	421.88	6.4	24.2	-14.3	8.4	9.1	-0.6
Sicily	10.23	0.1	346.45	11.53	0.1	309.06	12.8	26.4	-10.8	8.9	11.6	-2.5
Sardinia	6.94	0.1	220.63	7.91	0.1	221.73	14.0	13.4	0.5	12.0	10.2	1.6
Italy	**9.04**	**0.1**	**253.44**	**10.69**	**0.2**	**194.06**	**18.2**	**54.4**	**-23.4**	**10.9**	**20.5**	**-8.0**
North	8.27	0.1	221.58	9.97	0.2	166.40	20.5	60.5	-24.9	10.9	24.1	-10.6
Centre	9.16	0.1	221.11	11.10	0.2	168.08	21.3	59.5	-24.0	12.7	23.7	-8.9
South and Islands	10.06	0.1	338.12	11.46	0.1	276.81	13.9	39.1	-18.1	9.8	14.0	-3.6

3.4 General antimicrobials for systemic use

In 2023 general antimicrobials for systemic use were the fourth therapeutic category with the highest public expenditure, equal to 2762.1 million euros and 10.6% of overall public expenditure (Box Main indices of expenditure, consumption and exposure).

The overall per capita expenditure on such medicines was 46.92 euros, mainly due to purchases by public health facilities (35.28 euros per capita). On the contrary, the share of the approved care regime was lower (11.64 euros per capita). As in 2022, in 2023 there was an increase in expenditure in both direct purchase by public health facilities (+5.5%) and approved care regime (+6.1%) (Table 3.1).

Consumption for this pharmaceutical category was equal to 22.4 DDD/1000 inhabitants per day, up 6.1% compared to 2022 (Table 3.2). Contrary to expenditure, approved care accounts for the highest share of consumption, since almost 70% of doses are provided through this distribution channel.

The analysis of the drug use profile by age group and gender, including expenditure under approved care regime and distribution on behalf, indicates that the consumption of antimicrobials for systemic use increases with age, reaching the maximum value after 75 years. It is higher in men (27.6 DDD/1000 inhabitants per day) than in women (24.1 DDD/1000 inhabitants per day). In the intermediate age groups, on the other hand, women show a more frequent use than men. At the same time, NHS per capita expenditure also increases with age, reaching the maximum value of 23.4 euros and 20.6 euros per capita in men and women respectively, in subjects over 75 years.

Analysing the trends of per capita expenditure over the last six years (2018-2023), consumption and average cost per DDD of class A medicines and medicines purchased by public facilities (Figures 3.1-3.3), there is a fluctuating trend in both expenditure and average DDD cost, with maximum values in 2019 slightly declining in the following years. Per capita expenditure slightly increased in 2023, due to a consumption increase.

As regards approved care regime, the regional distribution (Table 3.5) shows a high variability of gross per capita expenditure with maximum values in Campania and Calabria (both with 17.8 euros) and minimum values in the Province of Bolzano (5.9 euros) and Friuli VG (7.2 euros). The distribution of consumption (Table 3.6) shows similar trends. Overall, expenditure in this delivery channel increased by 5.8%, solely due to an increase in consumption (+6.0%). Prices are substantially stable, while there is a slight shift towards lower-cost medicinal products (mix effect: -0.2%); the average DDD cost also remains practically stable (-0.2%) (Table 3.9). Within this delivery channel, penicillin combinations, including beta-lactamase inhibitors, show the highest expenditure (3.19 euros), up 16.9%, exclusively related to an increase in consumption (+16.4%), followed by third-generation cephalosporins with 2.82 euros per capita and an increase in both expenditure and consumption by +14.6% and 15.7%, respectively. Next come macrolides (1.43 euros per capita), down 10.0% and 9.2% in both expenditure and consumption. After the increase recorded in 2022, the consumption of fluoroquinolones slightly decreased both in terms of expenditure (-2.9%) and consumption (-1.1%), compared with a reduction in average DDD cost (-1.7%) and a shift toward less expensive medicinal products (mix effect: -1.6%).

Amoxicillin in combination with clavulanic acid is the first active ingredient in the category by per capita expenditure (3.05 euros) and consumption (6.1 DDD), recording an increase in both indicators, by 17.6% and 16.8% respectively (Table 3.10). In 2023, the active ingredients

most commonly dispensed under approved care regime showed major consumption increases, except for azithromycin (-18.4%) and ciprofloxacin (-1.7%). In particular, after amoxicillin in combination with clavulanic acid, cefixime (+15.0%) and ceftriaxone (+14.2%) recorded the greatest increases.

The amoxicillin/clavulanic acid combination is the only active ingredient in this category on the list of the top 30 molecules highly impacting on approved care regime, with a total expenditure value of 179.7 million (Table 3.11). Ceftriaxone (11.63 euros), fluconazole (5.48 euros) phosphomycin (4.60 euros), ciprofloxacin (2,55 euros), cefixime (2.34 euros) and azithromycin (1.47 euros) are among the top thirty active ingredients with the highest average cost per day of therapy under approved care regime (Table 3.12). No systemic use antimicrobial is on the list of the top 30 active ingredients with the lowest DDD cost (Table 3.13). Amoxicillin in combination with clavulanic acid (+17.6%), cefixime (+15.3%) and ceftriaxone (+11.3%) are included among the top thirty active ingredients with the greatest variation in expenditure compared to the previous year in this delivery channel (Table 3.14). For all active ingredients, the increase in expenditure is associated with a relative increase in consumption, while the average DDD cost remains almost stable, with only a slight decrease for ceftriaxone (-2.5%). Azithromycin (-16.2%), together with ciprofloxacin (-2.2%), are on the list of the first thirty active ingredients with the greatest reduction in expenditure under the approved care regime (Table 3.15). In contrast, no active ingredients are included in the list of those with the highest consumption in this delivery channel (Table 3.16).

As for purchases by public healthcare facilities, the regional distribution (Table 3.7) shows a moderate variability of gross per capita expenditure with maximum values in Lombardy (41.8 euros) and Liguria (40.9 euros), and minimum values in Basilicata (22.3 euros) and Molise (23.1 euros). The distribution of consumption (Table 3.8) highlights the highest usage values in Emilia Romagna (9.2 DDD), Lombardy and Tuscany (7.0 DDD) and the lowest in Molise (3.8 DDD) and Calabria (3.9 DDD). Overall, there was a 5.0% increase in expenditure compared to 2022, linked to an increase in consumption (+5.2%) and a shift towards more expensive medicinal products (mix effect +1.1%; Table 3.17), against a reduction in prices (-1.2%) and substantial stability in the average DDD cost (-0.2%). Antiviral combinations for the treatment of HIV infections are the highest expenditure category (8.66 euros per capita), followed by influenza vaccines (2.56 euros per capita). The latter group recorded a decrease in expenditure (-3.5%) mainly due to a decrease in consumption (-4.1%) and a reduction in prices (-7.4%), although there was a shift toward more expensive medicinal products (mix effect: +8.6%). The category of varicella-zoster vaccines continues to record an increase in expenditure (+46.4%), although less than in 2022, mainly related to the shift towards more expensive medicinal products (mix effect: +38.9%) and to the increase in the average DDD cost (+38.4%), and to a lesser extent to the increase in consumption (+5.8%).

The most expensive active ingredients are the combination emtricitabine/tenofovir alafenamide/bictegravir (2.68 euros per capita), the adjuvanted recombinant varicella zoster vaccine (2.10 euros), the combination dolutegravir/lamivudine (1.98 euros) and the vaccine for human papilloma virus (1.64 euros) (Table 3.18). For all these drugs, there was a sharp increase in expenditure and consumption, in particular for the adjuvanted recombinant varicella zoster vaccine, which records a 66.6% increase in expenditure, 41.0% in consumption and 18.2% in the average DDD cost. Furthermore, the combination emtricitabine/tenofovir alafenamide/bictegravir, the adjuvanted recombinant varicella zoster vaccine and the combination dolutegravir/lamivudine are on the list of the first thirty active ingredients in

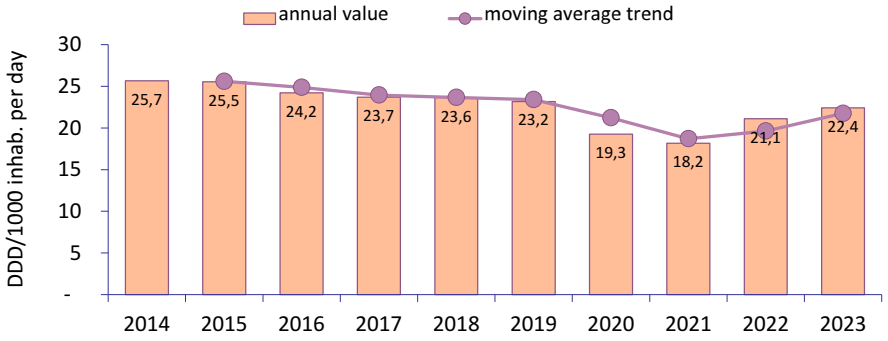
terms of expenditure on drugs purchased by public facilities, with a total value of 157.7 and 123.4 and 116.4 million euros respectively (Table 3.19). The molecules with the greatest variation in expenditure in 2023 include the adjuvanted recombinant varicella zoster vaccine (+66.6%) and normal human immunoglobulin for intravascular administration (+32.3%, Table 3.20). Only the combination emtricitabine/rilpivirine/tenofovir alafenamide (-22.8%) and remdevisir (-22.8%) are among the molecules with the greatest cost reduction (Table 3.21). Human immunoglobulin for extravascular administration (531.0 euros), normal human immunoglobulin for intravascular administration (385.4 euros), remdesivir (357.0 euros) and the adjuvanted recombinant varicella zoster vaccine (321.4 euros) are the antimicrobials that are on the list of the active ingredients with the highest DDD cost (Table 3.22). The active ingredients with the lowest cost (Table 3.23), however, include the tetravalent influenza vaccines, from inactivated virus, surface antigen, adjuvanted (15.00 euros) and the dolutegravir/lamivudine combination (16.60 euros). In contrast, no systemic use antimicrobial is included within the highest consumed antimicrobials (Table 3.24). Overall, considering both approved care regime and direct purchases, the top 30 active ingredients by expenditure include: the combination amoxicillin/clavulanic acid (186.8 million and emtricitabine/tenofovir alafenamide/bictegravir (157.7 million) (Table 3.28). In contrast, no active ingredient of this ATC is on the list of the highest consumed molecules (Table 3.25).

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

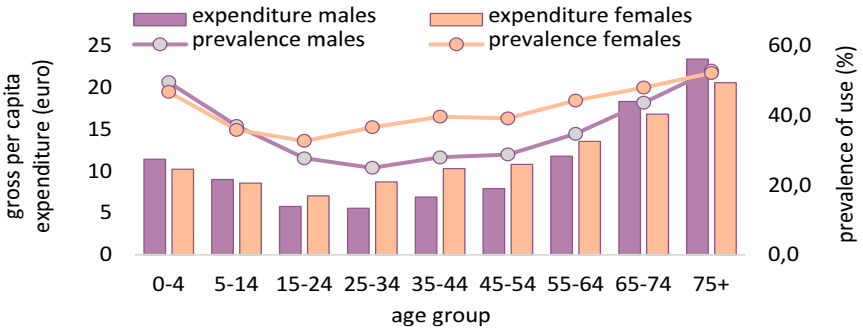
Antimicrobials for systemic use

Public expenditure* in million euros (% over total)	**2,762.1**	**(10.6)**
Δ % 2023-2022		5.5
Regional range of gross per capita expenditure:	35.1	51.9
DDD/1000 inhabitants per day* (% over total)	**22.4**	**(1.7)**
Δ % 2023-2022		6.1
Regional range DDD/1000 inhabitants per day	15.1	26.7

** includes prescriptions under approved care regime and purchases by public health facilities*



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf by age and gender in 2022 (Figure and Table)



Age group	Gross per capita expenditure			DDD/1000 inhabitants per day		
	Males	Females	Total	Males	Females	Total
0-4	11.4	10.2	10.8	16.3	14.6	15.5
5-14	9.0	8.6	8.8	14.0	13.2	13.6
15-24	5.8	7.1	6.4	10.1	11.5	10.8
25-34	5.6	8.7	7.1	9.0	13.5	11.2
35-44	6.9	10.3	8.6	11.0	15.8	13.4
45-54	7.9	10.8	9.4	11.9	15.9	13.9
55-64	11.8	13.6	12.7	15.8	19.2	17.5
65-74	18.3	16.8	17.5	22.5	22.4	22.5
75+	23.4	20.6	21.7	27.6	24.1	25.5

3.4.1 Antibiotics

In 2023, the category of antibiotics recorded a total public expenditure of 822.6 million euros, up 5.8% compared to the previous year. Consumption also showed a 6.4% increase, reaching 17.2 DDD/1000 inhabitants per day (Box Main indices of expenditure, consumption and exposure).
Analyzing the temporal trend, the consumption of these drugs slowly decreased from 2014 to 2019, while in 2020 and 2021 there was a strong reduction, due to the effects of the Covid-19 pandemic. However, consumption has shown an increasing trend in the last two years. The cost per day of therapy remained almost stable (CAGR: +0.0%) with a peak recorded in 2021.
Nearly 4 in 10 people have received at least one prescription for antibiotics, with higher levels of use in children up to 4 years of age and in people over 75 years. There is a higher prevalence in women than men (40.8% vs. 33.7%), with more marked differences between 35 and 54 years, probably caused by the use of antibiotics in the treatment of urinary tract infections in women. Therefore, there is a need to implement "Antimicrobial Stewardship" programs, especially in populations with a high prevalence of use, to optimize consumption and reduce antimicrobial resistance; furthermore, in a vulnerable population, such as the over-75 age group, there is also a greater need for management and prevention of infections.
In 2023, per capita expenditure on this category of drugs was 14.0 euros, up 5.8% compared to 2022, with an average annual reduction of 1.5%, from 2014 to 2023 (Table 3.4.1a). However, the increase in expenditure in 2023 is linked to the increase in consumption (+6.4%), while the average DDD cost has slightly decreased (-0.5%).
Analyzing the therapeutic categories, penicillin combinations, almost entirely represented by amoxicillin/clavulanic acid, remain the category of antibiotics with the highest prescription (6.6 DDD) and expenditure (3.79 euros per capita) and show an increase of 15.9% and 13.3% respectively compared to 2022. Macrolides and lincosamides (3.5 DDD) and third-generation cephalosporins (2.3 DDD) follow in terms of consumption. Third-generation cephalosporins recorded an increase in consumption of 15.1%, while macrolides and lincosamides reported a reduction of 8.2%. Similar to 2022, the second largest category in terms of expenditure is third-generation cephalosporins (3.37 euros per capita).
The subgroup with the greatest increase, both in terms of expenditure and consumption, is beta-lactamase-sensitive penicillins (respectively +27.6% and +28.2%), while the cost for DDD remained stable and is among the highest of the entire category (49.81 euros). The second subgroup for expenditure variation is beta-lactamase-resistant penicillins (+18.4%), which also show an increase in consumption (+14.5%) and in the average cost per DDD (+3.3%). The most significant reductions were recorded in expenditure on fourth-generation cephalosporins (-21.8%), both due to a reduction in consumption (-13.9%) and in the average DDD cost (-9.2%) and for macrolides and lincosamides (-9.3%), associated with a reduction in consumption (-8.2%) and in the average DDD cost (-1.2%).
Amoxicillin+clavulanic acid, a broad-spectrum drug widely used in pediatrics, is confirmed as the most widely used molecule with 6.5 DDD as well as in terms of expenditure (3.17 euros per capita), followed in consumption by clarithromycin and azithromycin. All these molecules, with the exception of azithromycin, have recorded an increase in consumption compared to 2022. Amoxicillin+clavulanic acid and cefixime are the substances that have recorded the greatest increases, among the top 10 antibiotics by expenditure. However, a reduction in expenditure and consumption was recorded for azithromycin (-16.3% and -17.1% respectively) and ciprofloxacin (-1.5% for both expenditure and consumption) compared to

2022. The combination piperacillin/tazobactam and levofloxacin showed an expenditure decrease due to a reduction in the average cost per day of therapy (-10.0% and -2.4% respectively).

Figure 3.4.1a shows the trend in consumption in the period 2014-2023 of the sub-groups with the highest expenditure. Fluoroquinolones have shown a reduction in use since 2019, following the publication in 2018 of restrictive recommendations by EMA and AIFA on this subgroup of drugs, although a slight recovery was recorded in 2022 and then decreased again in 2023. However, for third-generation cephalosporins and combinations of penicillins (including beta-lactamase inhibitors), after the reduction in 2020 and 2021, a strong upturn in consumption is observed, reaching levels even higher than the pre-pandemic period. Macrolides and lincosamides, which recorded a decrease in the years 2020-2021, had a strong increase in 2022 and in 2023 they recorded a marked reduction, attributable to the trend of azithromycin. The category of other antibacterials, which includes antibiotics mainly used in hospitals (e.g. linezolid, tedizolid, daptomycin and fosfomycin), shows a constantly growing trend. Considering that some of these antibiotics are used in the treatment of infections caused by multi-drug resistant microorganisms, these data suggest the need to improve the surveillance of nosocomial infections in healthcare facilities, ensuring a timely and adequate response to infections.

Combinations of penicillins, including beta-lactamase inhibitors and macrolides and lincosamides have the highest exposure in the population, with values of 18.4% and 10.3% respectively (Table 3.4.1b). They are followed by third-generation cephalosporins (9.1%) and fluoroquinolones (5.9%). A wide variability is observed in the median age of antibiotic users, ranging from 38 years for broad-spectrum penicillins to over 70 years for aminoglycosides, glycopeptides and fourth-generation cephalosporins. For the latter two categories, we note low levels of exposure and lower levels of sporadic prescription (7.7% and 3.8% respectively), but high costs per user (595.8 euros and 97.7 euros respectively). With an average of 14.7 DDD per user, there is a wide variability between the different subgroups, with the highest doses per user for tetracyclines (23.9 DDD) and the lowest for fourth-generation cephalosporins (2.9 DDD). There is also a high variability in the cost per user, since broad-spectrum penicillins have the lowest value (5.4 euros) and glycopeptides the highest (595.8 euros).

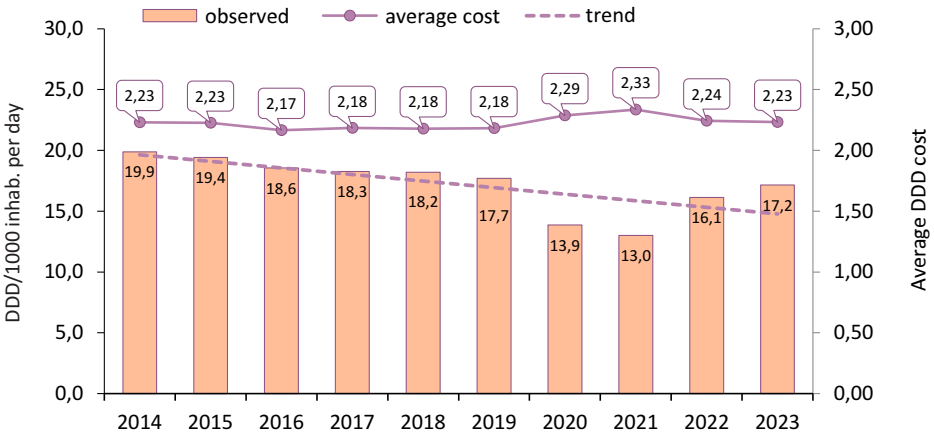
The prevalence of use, equal to 37.3% at a national level, is higher in the South and the Islands (44.8%) and lower in the North (30.9%) and in the Centre (39.9%; Table 3.4.1c). The cost per user found in the South (28.8 euros) is also higher than the North (22.7 euros) and the Centre (26.6 euros), suggesting a greater tendency to prescribe antibiotics at a higher cost.

For further information on regional data on exposure and duration of therapy, please refer to the supplementary material published online.

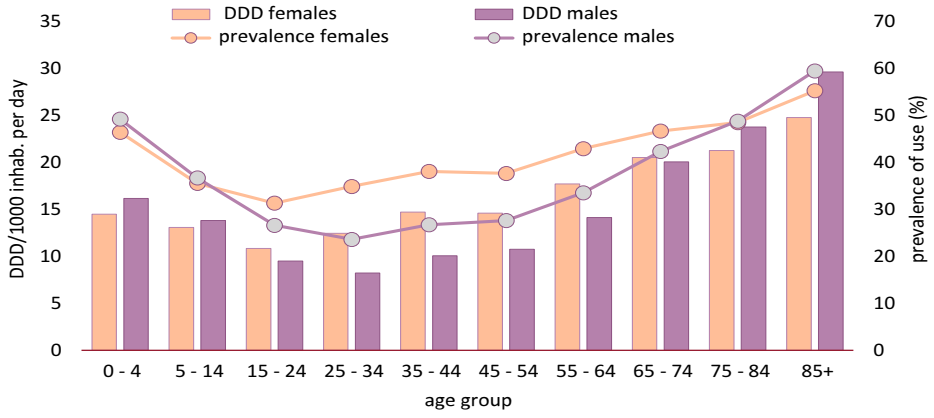
MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Antibiotics

Public expenditure in million euros (% over total)	**822.6**	**(3.2)**
Δ % 2023-2022		5.8
Regional range of gross per capita expenditure:	8.0	20.8
DDD/1000 inhab. per day (% over total)	**17.2**	**(1.3)**
Δ % 2023-2022		6.4
Regional range DDD/1000 inhabitants per day	11.3	22.4

Antibiotics, temporal trend of consumption and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of antibiotics for systemic use under approved care regime and distribution on behalf (year 2023)



National data on expenditure, consumption and exposure by subgroup and substance

Table 3.4.1a Antibiotics, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and by substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Combinations of penicillins (including beta lactamase inhibitors)	3.79	13.3	0.6	6.6	15.9	0.1	1.56	-2.2
Third-generation cephalosporins	3.37	12.6	-0.2	2.3	15.1	1.1	3.97	-2.1
Macrolides and lincosamides	1.50	-9.3	-2.5	3.5	-8.2	-2.0	1.17	-1.2
Fluoroquinolones	1.22	-2.5	-7.3	1.7	-1.0	-7.3	2.01	-1.5
Other antibacterials	1.11	-2.4	-3.3	0.5	-1.0	2.6	6.02	-1.4
Other cephalosporins and penems	0.80	7.5	83.7	0.0	7.3	69.5	220.83	0.2
Carbapenems	0.48	12.0	-0.4	0.1	-9.6	-1.4	21.15	23.8
Glycopeptides	0.36	6.7	-8.1	0.0	-11.7	-4.1	22.05	20.8
Broad-spectrum penicillins	0.27	-0.1	-2.6	1.0	6.9	-4.9	0.76	-6.5
Polymyxin	0.16	-5.9	-2.0	0.0	-10.1	-2.5	38.53	4.6
Tetracyclines	0.16	0.3	-9.9	0.4	3.6	0.9	1.13	-3.2
Aminoglycosides	0.15	9.6	-3.8	0.0	1.6	-5.7	9.27	7.9
First-generation cephalosporins	0.11	0.8	-0.5	0.1	9.5	0.4	2.60	-8.0
Beta-lactamase resistant penicillins	0.09	18.4	18.9	0.0	14.5	8.1	6.87	3.4
Sulphonamides (alone and in combination)	0.09	12.8	2.7	0.4	12.7	2.8	0.53	0.0
Second-generation cephalosporins	0.08	-7.3	-8.4	0.1	-3.0	-7.2	1.68	-4.5
Other combinations	0.08	41.8	—	0.0	41.6	—	6.71	0.1
Nitrofuran derivatives	0.06	9.2	57.6	0.2	8.3	40.2	0.93	0.8
Fourth-generation cephalosporins	0.06	-21.8	-2.8	0.0	-13.9	0.7	18.65	-9.2
Monobactams	0.03	-15.1	-3.9	0.0	-15.1	-3.9	88.12	0.0
Imidazole derivatives	0.02	2.0	-0.1	0.0	1.8	0.9	1.01	0.1
Beta-lactamase sensitive penicillins	0.01	27.6	-1.6	0.0	28.2	-19.3	49.81	-0.5
Amphenicols	0.00	-6.7	-2.5	0.0	-15.8	-2.8	5.82	10.8
Antibiotics	**13.98**	**5.8**	**-1.5**	**17.2**	**6.4**	**-1.5**	**2.23**	**-0.5**
amoxicillin/clavulanic acid	3.17	17.3	0.2	6.5	16.1	0.1	1.35	1.0
cefixime	1.16	15.4	2.7	1.4	15.2	2.9	2.29	0.2
ceftriaxone	1.13	10.9	-3.5	0.5	10.6	-1.1	6.39	0.3
fosfomycin	0.88	3.3	3.9	0.4	1.0	1.1	5.99	2.3
azithromycin	0.80	-16.3	1.1	1.6	-17.1	1.4	1.40	1.0
ciprofloxacin	0.64	-1.5	-5.5	0.7	-1.5	-5.1	2.40	0.0
clarithromycin	0.60	0.6	-4.9	1.8	1.0	-3.8	0.90	-0.4
piperacillin/tazobactam	0.59	-3.9	4.9	0.2	6.7	6.6	9.52	-10.0
levofloxacin	0.47	-1.8	-7.1	0.8	0.5	-8.0	1.55	-2.4
ceftazidime/avibactam	0.40	1.3	—	0.0	1.3	—	190.48	0.0

Figure 3.4.1a Antibiotics, 2014-2023 temporal trend in consumption (DDD/1000 inhabitants per day) by highest-expenditure subgroups

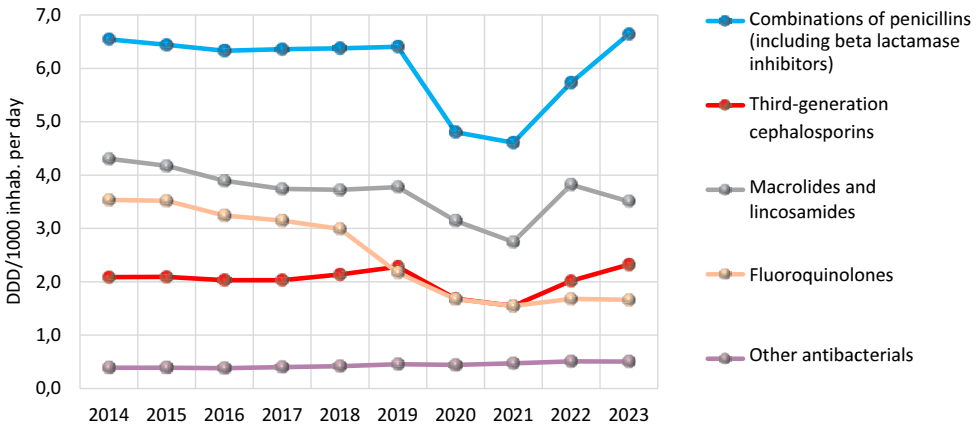


Table 3.4.1b Exposure and duration of therapy with antibiotics by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Average cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
Combinations of penicillins (including beta lactamase inhibitors)	17.4	19.3	18.4	50	17.0	11.9	7.0	55.0
Third-generation cephalosporins	8.4	9.7	9.1	55	30.6	7.9	5.0	47.0
Macrolides and lincosamides	9.2	11.4	10.3	52	13.9	11.6	10.0	62.5
Fluoroquinolones	5.4	6.5	5.9	65	18.4	9.0	6.0	39.1
Other antibacterials	1.4	6.3	3.9	63	16.0	3.5	2.0	65.9
Glycopeptides	<0.05	<0.05	<0.05	71	595.8	9.0	6.0	7.7
Broad-spectrum penicillins	2.8	3.4	3.1	38	5.4	10.7	8.0	58.4
Tetracyclines	0.5	0.6	0.5	43	15.3	23.9	20.0	40.2
Aminoglycosides	0.1	0.1	0.1	71	57.0	6.6	5.1	5.1
First-generation cephalosporins	0.1	0.1	0.1	60	15.2	7.5	4.0	35.9
Beta-lactamase resistant penicillins	<0.05	<0.05	<0.05	58	16.5	9.0	6.0	74.6
Sulphonamides (alone and in combination)	0.9	0.8	0.9	66	7.3	15.6	8.0	67.6
Second-generation cephalosporins	0.4	0.5	0.5	45	15.2	10.0	9.0	41.0
Other combinations	0.1	0.1	0.1	56	71.0	10.5	10.0	96.1
Nitrofuran derivatives	0.2	0.6	0.4	68	13.3	14.2	10.0	71.5
Fourth-generation cephalosporins	<0.05	<0.05	<0.05	76	97.7	2.9	2.8	3.8
Imidazole derivatives	<0.05	<0.05	<0.05	69	54.2	3.2	2.0	19.1
Beta-lactamase sensitive penicillin	<0.05	<0.05	<0.05	36	68.5	0.9	0.6	30.9
Amphenicols	<0.05	<0.05	<0.05	61	31.0	7.4	6.0	57.8
Antibiotics	**33.7**	**40.8**	**37.3**	**52**	**26.0**	**14.7**	**10.0**	**40.0**

Regional data on expenditure, consumption and exposure

Table 3.4.1c Antibiotics, temporal trend of per capita regional expenditure, consumption (DDD/1000 inhab. per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use	Cost/user	Median DDD
Piedmont	11.06	14.5	2.09	2.7	7.0	-4.0	-1.7	-1.2	-0.5	33.0	22.4	10.0
Valle d'Aosta	11.09	14.8	2.05	14.9	15.1	-0.2	-2.0	-1.3	-0.7	29.2	22.0	10.0
Lombardy	10.71	14.5	2.02	6.2	9.8	-3.3	-0.7	-1.1	0.4	30.6	23.8	11.0
Province of Bolzano	8.05	11.3	1.96	12.2	15.2	-2.6	-2.0	-0.9	-1.1	23.3	19.4	10.0
Province of Trento	10.39	15.1	1.89	5.2	7.1	-1.8	-1.9	-0.8	-1.1	31.7	22.1	10.0
Veneto	10.24	13.5	2.08	-2.7	8.3	-10.1	-1.9	-1.6	-0.3	28.6	21.9	10.0
Friuli V.G.	11.47	14.2	2.21	14.2	15.7	-1.3	0.5	-0.5	1.0	28.3	22.9	14.0
Liguria	14.36	14.0	2.80	14.7	9.0	5.2	1.3	-0.3	1.6	32.1	25.0	10.0
Emilia R.	11.37	16.1	1.93	2.4	7.2	-4.5	-1.2	-1.0	-0.2	33.0	21.1	10.0
Tuscany	12.43	16.2	2.11	8.1	8.9	-0.8	-1.9	-1.6	-0.4	35.9	22.3	10.0
Umbria	17.85	20.1	2.43	5.8	11.0	-4.6	-0.4	-1.0	0.6	43.5	24.9	11.0
Marche	16.41	19.3	2.34	8.3	10.1	-1.6	-1.2	-1.0	-0.2	44.1	26.9	10.0
Lazio	16.56	19.0	2.39	8.9	7.5	1.3	-1.1	-1.4	0.3	40.8	29.2	10.0
Abruzzo	20.79	22.4	2.55	11.7	7.0	4.4	1.2	-0.2	1.4	46.2	27.8	11.0
Molise	15.40	19.8	2.13	18.4	13.6	4.2	-2.1	-1.2	-0.9	45.9	28.7	10.0
Campania	19.16	21.7	2.42	1.8	-2.2	4.1	-2.3	-2.3	0.0	45.5	32.2	10.0
Puglia	16.82	20.9	2.20	3.5	6.3	-2.7	-3.1	-2.2	-1.0	47.3	27.6	10.0
Basilicata	17.54	21.5	2.24	11.5	10.3	1.1	-0.6	-0.8	0.2	47.7	27.0	10.0
Calabria	19.51	20.6	2.59	7.7	2.4	5.1	-1.1	-1.7	0.6	44.5	32.7	10.0
Sicily	16.45	19.3	2.34	8.6	2.3	6.1	-1.6	-1.7	0.1	44.0	25.9	10.0
Sardinia	11.66	15.2	2.10	9.0	8.5	0.4	-2.1	-1.8	-0.3	36.4	24.8	10.0
Italy	**13.98**	**17.2**	**2.23**	**5.8**	**6.4**	**-0.5**	**-1.5**	**-1.5**	**0.0**	**37.3**	**26.0**	**10.0**
North	10.99	14.5	2.08	4.4	8.9	-4.1	-1.0	-1.1	0.1	30.9	22.7	10.0
Centre	15.32	18.2	2.31	8.3	8.5	-0.2	-1.3	-1.4	0.1	39.9	26.6	10.0
South and Islands	17.44	20.3	2.35	5.9	2.9	2.9	-1.9	-1.9	0.0	44.8	28.8	10.0

3.4.2 Anti-HIV antivirals

In 2023, the category of anti-HIV antivirals recorded a total public expenditure of 619.2 million euros, stable (+0.9%) compared to the previous year. Consumption showed a 2.9% increase, reaching a total value of 2.2 DDD/1000 inhabitants per day (Box Main indices of expenditure, consumption and exposure).

Per capita expenditure on anti-HIV antiviral drugs, equal to 10.52 euros in 2023, is stable compared to the previous year (+0.9%) and compared to 2014 it recorded a 3.5% reduction and an average annual decrease rate (CAGR) of 0.4%. The average cost for DDD showed a decreasing trend in the period 2018-2020, then it increased again in 2021 and 2022. In 2023, the average cost showed a 2.0% decrease, reaching 12.82 euros compared to 13.1 euros in 2022.

Antivirals in co-formulated regimens with two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) and an integrase inhibitor (INSTI) accounted for 31.3% of expenditure, up 2.9% compared to 2022 and with a CAGR of 53.0% compared to 2014 (Table 3.4.2a and Figure 3.4.2a). Consumption increased by 4.4% compared to 2022, while the average DDD cost decreased by 1.5%. Despite this, it remains among the highest in the entire category (20.21 euros), second only to other anti-HIV antivirals (41.86 euros). Co-formulated regimens (1 NRTI + 1 INSTI), represented exclusively by the dolutegravir/lamivudine combination, have also shown an increasing trend since 2019 and show the highest increase compared to 2022, among all co-formulated regimens, in terms of expenditure and consumption, both equal to 20.6%. Among the highest-expenditure subgroups, the co-formulated regimens (2 NRTIs + 1 NNRTI) are those reporting the greatest decrease in the period 2014-2023, with a 3.8% average annual reduction.

Considering the trend in consumption, nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) recorded the highest value, i.e. 0.5 DDD per 1000 inhabitants per day, stable compared to the previous year (+0.4%). This corresponds to a per capita expenditure of 0.53 euros, down 12.6% from 2022, due to the 14.9% reduction in average cost.

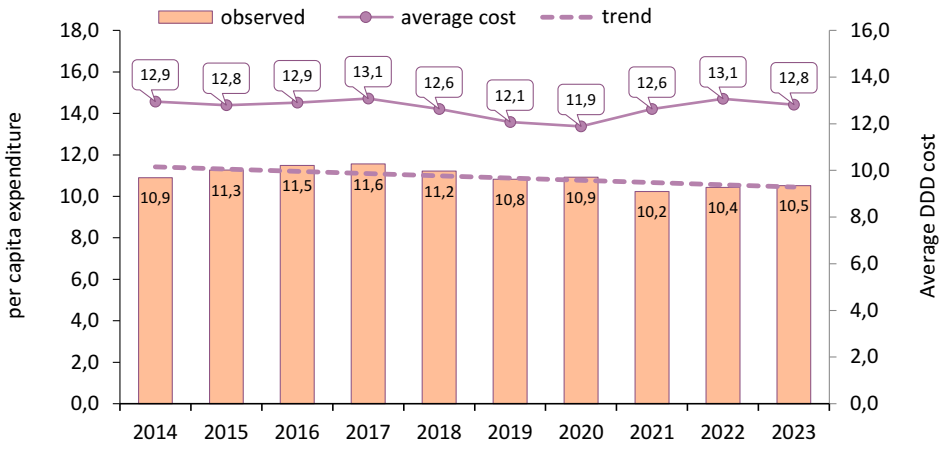
The combination emtricitabine/tenofovir alafenamide/bictegravir, with 2.68 euros per capita, was in first rank among the most expensive active ingredients (Table 3.4.2a). This combination (+17.5%), together with tenofovir disoproxil/lamivudine/doravirine (+32.6%), dolutegravir/lamivudine (+20.6%) and dolutegravir/rilpivirine (+4.9%), were the only ones recording an expenditure increase compared to 2022. All other active ingredients showed reductions ranging between 7.3% and 28.1%.

Regional per capita expenditure (Table 3.4.2.b) showed a wide variability in 2023, with the highest values in the North (12.89 euros per capita) and the Centre (12.05 euros), almost double than the South (6.20 euros). Compared to 2022, expenditure in the North was stable (-0.1%), while Central and Southern Regions recorded a slight increase (+1.9% and +2.7%, respectively).

MAIN INDICES OF EXPENDITURE AND CONSUMPTION
Anti-HIV antivirals

Public expenditure in million euros (% over total)	**619.2**	**(2.4)**
Δ % 2023-2022		0.9
Regional range of gross per capita expenditure:	3.1	17.0
DDD/1000 inhab. per day (% over total)	**2.2**	**(0.2)**
Δ % 2023-2022		2.9
Regional range DDD/1000 inhabitants per day	0.7	3.6

Anti-HIV antivirals, temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)

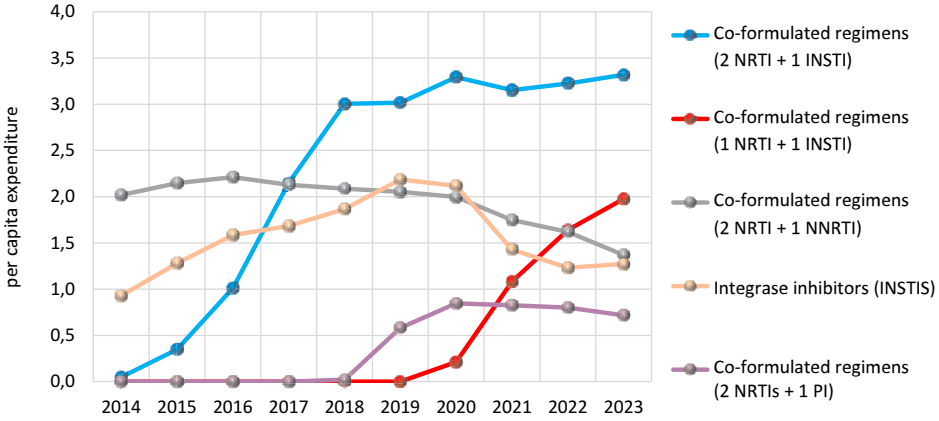


National data on consumption and expenditure by subgroup and substance

Table 3.4.2a Anti-HIV antivirals, per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and by substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Co-formulated regimens - (2 NRTI + 1 INSTI)	3.32	2.9	53.0	0.4	4.4	57.3	20.21	-1.4
Co-formulated regimens (1 NRTI + 1 INSTI)	1.98	20.6	—	0.3	20.6	—	16.60	0.0
Co-formulated regimens - (2 NRTI + 1 NNRTI)	1.37	-15.4	-3.8	0.2	-9.6	-1.2	16.36	-6.4
Integrase inhibitors (INSTIS)	1.27	3.3	3.2	0.3	2.9	4.8	13.30	0.4
Co-formulated regimens - (2 NRTIs + 1 PI)	0.72	-10.3	—	0.1	-10.3	—	21.85	0.0
Co-formulated regimens (1 NNRTI + 1 INSTI)	0.60	4.9	—	0.1	4.9	—	18.30	0.0
Reverse transcriptase inhibitors (NRTIs)	0.53	-12.6	-18.6	0.5	0.4	-6.0	2.65	-12.9
Protease inhibitors (PIs)	0.36	-19.7	-18.8	0.1	-18.8	-15.5	8.80	-1.1
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	0.27	42.6	-7.3	0.1	35.2	-5.7	5.58	5.4
Other anti-HIV antivirals	0.10	9.0	-9.3	0.0	-0.9	-9.1	41.86	10.0
Anti-HIV antivirals	**10.52**	**0.9**	**-0.4**	**2.2**	**2.9**	**-0.3**	**12.82**	**-1.9**
emtricitabine/tenofovir alafenamide/bictegravir	2.68	17.5	—	0.4	17.5	—	19.96	0.0
dolutegravir/lamivudine	1.98	20.6	—	0.3	20.6	—	16.60	0.0
emtricitabine/rilpivirine/ tenofovir alafenamide	1.02	-22.8	—	0.2	-16.5	—	17.96	-7.5
dolutegravir	0.75	-7.3	55.8	0.1	-7.3	55.9	16.42	0.0
emtricitabine/tenofovir alafenamide/darunavir/cobicistat	0.72	-10.3	—	0.1	-10.3	—	21.85	0.0
dolutegravir/rilpivirine	0.60	4.9	—	0.1	4.9	—	18.30	0.0
dolutegravir/abacavir/lamivudine	0.57	-28.1	—	0.1	-28.1	—	21.48	0.0
emtricitabine/tenofovir alafenamide	0.32	-22.3	—	0.1	-22.3	—	11.29	0.0
raltegravir	0.31	-23.2	-10.3	0.1	-23.9	-5.9	9.69	1.0
tenofovir disoproxil/lamivudine/doravirine	0.30	32.6		0.1	32.3		14.41	0.2

Figure 3.4.2a Anti-HIV antivirals, temporal trend 2014-2023 in per capita expenditure of most expensive subgroups



Regional data on consumption and expenditure

Table 3.4.2b Anti-HIV antivirals, regional trend of per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2022			2023			Δ % 23-22			CAGR % 14-23		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost
Piedmont	10.70	2.0	14.33	10.73	2.2	13.56	0.4	6.1	-5.4	0.6	0.6	0.0
Valle d'Aosta	7.72	1.6	13.54	7.98	1.7	12.57	3.3	11.3	-7.2	5.3	5.3	0.0
Lombardy	17.13	3.3	14.33	16.99	3.4	13.85	-0.8	2.6	-3.4	-0.9	-1.3	0.5
Province of Bolzano	6.49	1.3	13.78	7.05	1.5	12.65	8.5	18.2	-8.2	-0.2	-0.7	0.4
Province of Trento	7.96	1.5	14.13	7.76	1.6	13.43	-2.5	2.6	-5.0	0.3	0.3	0.0
Veneto	9.06	2.0	12.26	9.08	2.1	12.12	0.2	1.3	-1.1	-0.5	-1.2	0.7
Friuli V.G.	7.67	1.7	12.25	7.92	1.8	12.11	3.2	4.5	-1.2	1.7	1.7	0.0
Liguria	11.01	1.9	15.70	11.07	2.0	15.09	0.5	4.6	-3.9	-0.1	-0.9	0.8
Emilia R.	13.58	3.6	10.24	13.58	3.6	10.29	0.0	-0.5	0.5	-1.2	0.0	-1.2
Tuscany	11.45	2.2	14.58	12.20	2.4	13.91	6.6	11.7	-4.6	0.5	0.6	0.0
Umbria	9.59	1.8	14.40	10.17	2.0	13.94	6.1	9.6	-3.2	0.5	0.2	0.2
Marche	9.59	1.9	13.57	9.63	1.9	13.60	0.5	0.2	0.2	-0.4	-0.4	0.0
Lazio	13.04	2.7	13.07	12.89	2.7	12.96	-1.1	-0.3	-0.9	-1.1	-0.7	-0.4
Abruzzo	6.74	1.4	13.57	6.74	1.4	13.42	0.0	1.2	-1.2	0.9	1.2	-0.3
Molise	2.97	0.7	11.65	3.24	0.8	11.33	8.9	11.9	-2.7	4.0	5.4	-1.4
Campania	5.75	1.3	11.86	6.12	1.4	11.91	6.5	6.1	0.4	0.9	1.5	-0.5
Puglia	6.39	1.5	11.82	6.70	1.6	11.82	4.8	4.8	0.0	-0.1	0.7	-0.8
Basilicata	3.40	0.8	12.30	3.05	0.7	11.88	-10.3	-7.2	-3.4	-0.5	0.1	-0.6
Calabria	3.29	0.8	11.15	3.31	0.8	11.19	0.6	0.3	0.3	0.4	2.1	-1.6
Sicily	6.35	1.3	12.96	6.42	1.4	12.66	1.0	3.4	-2.3	0.9	1.2	-0.3
Sardinia	9.14	2.1	12.14	9.03	1.9	12.79	-1.3	-6.3	5.3	-2.4	-1.9	-0.5
Italy	**10.43**	**2.2**	**13.07**	**10.52**	**2.2**	**12.82**	**0.9**	**2.9**	**-1.9**	**-0.4**	**-0.3**	**-0.1**
North	12.90	2.7	13.15	12.89	2.8	12.81	-0.1	2.5	-2.6	-0.5	-0.6	0.1
Centre	11.82	2.4	13.64	12.05	2.5	13.38	1.9	3.9	-1.9	-0.4	-0.2	-0.2
South and Islands	6.04	1.4	12.23	6.20	1.4	12.23	2.7	2.7	0.0	0.2	0.8	-0.6

3.4.3 Vaccines

In 2023, the category of vaccines recorded a total public expenditure of 712.2 million euros, with an 11.8% increase compared to the previous year. Consumption showed a slight increase (+1.7%), reaching a total value of 1.2 DDD/1000 inhabitants per day (Box Main indices of expenditure, consumption and exposure).

Expenditure on vaccines more than doubled from 2014 to 2022, going from 4.79 euros to 12.1 euros per capita. Similarly, the average DDD cost, after the reduction in 2020, showed an increasing trend, going from 22.4 euros in 2021 to 27.9 euros in 2023.

The recently marketed adjuvanted recombinant varicella-zoster virus vaccine has become the largest expenditure item in this category, accounting for almost 17% of the total and reaching 2.10 euros per capita in 2023, a 66.6% increase compared to the previous year (Table 3.4.3a). It is also the subgroup with the highest average DDD cost, equal to 321.38 euros and increasing by 18.2% compared to 2022. On the other hand, the live attenuated varicella-zoster vaccine showed much lower expenditure values (0.19 euros) and a sharp decrease compared to the previous year (-28.4%).

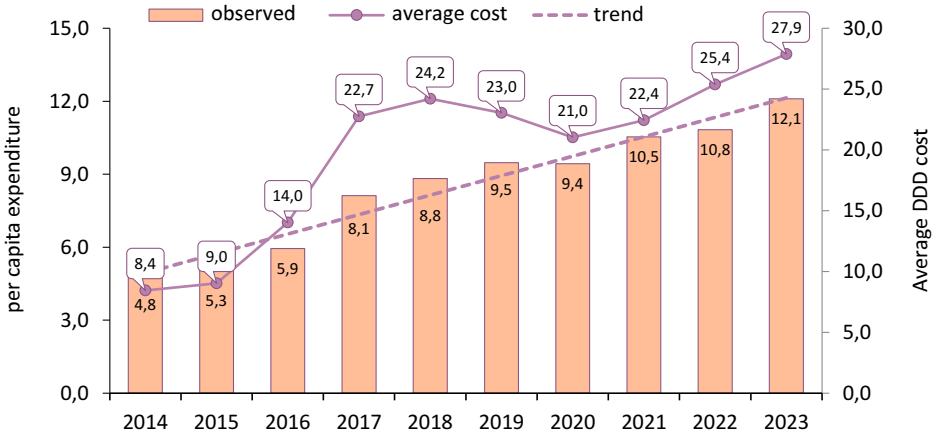
If we consider the three subcategories, the influenza vaccine has the highest overall expenditure (2.56 euros), recording a reduction for the non-adjuvanted formulation (-17.5%), while an increase is reported for the adjuvanted formulation (+4.8%) and for the nasal formulation (+23.7%). The papilloma virus vaccine follows with 1.64 euros, with a 13.6% increase in 2023 compared to the previous year; in the period 2014-2023 it showed a growing trend with an average annual variation of 15.7%. It is immediately followed (with 1.46 euros), by the vaccine for meningococcus B, which showed a strong growth in the period 2014-2017 and has later decreased in the last 6 years (Figure 3.4.3a). In the context of the polysaccharide conjugated pneumococcal vaccine (1.42 euros per capita), the twenty-valent conjugated vaccine with 0.54 euros is the one with the highest value, recording an increase in both expenditure and consumption by over 30%. The thirteen-valent pneumococcal vaccine, on the other hand, recorded a strong reduction in both expenditure and consumption (almost 40%). It should be noted that in 2022, a new fifteen-valent conjugated polysaccharide pneumococcal vaccine was marketed, which can be administered from 6 weeks of age. It recorded a strong growth in expenditure, which in 2023 was equal to 0.42 euros per capita and an average cost per DDD of 45.84 euros.

The North, with 13.07 euros per capita and a 10.5% increase of compared to the previous year, are the geographical area with the highest expenditure, while the South and Centre have fairly similar values (11.62 and 10.65 euros per capita respectively), both growing by 14.4% and 10.9% respectively (Table 3.4.3b).

MAIN INDICES OF EXPENDITURE AND CONSUMPTION
Vaccines

Public expenditure in million euros (% over total)	**712.2**	**(2.7)**
Δ % 2023-2022		11.8
Regional range of gross per capita expenditure:	8.5	17.0
DDD/1000 inhab. per day (% over total)	**1.2**	**(0.1)**
Δ % 2023-2022		1.7
Regional range DDD/1000 inhabitants per day	1.0	1.6

Vaccines, temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)



National data on consumption and expenditure by subgroup and substance

Table 3.4.3a Vaccines, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Adjuvanted recombinant varicella zoster vaccine	2.10	66.6	—	<0.05	41.0	—	321.38	18.2
Human papillomavirus (HPV) vaccine	1.64	13.6	15.7	0.1	13.5	10.2	69.37	0.1
Meningococcal B vaccine	1.46	8.7	35.1	0.1	7.8	35.1	62.66	0.8
Pneumococcal polysaccharide conjugate vaccine (adsorbed)	1.42	22.4	0.3	0.1	22.3	0.1	47.58	0.1
Influenza vaccine - tetravalent adjuvanted	1.40	4.8	—	0.3	3.9	—	15.03	0.9
Influenza vaccine - tetravalent non-adjuvanted	0.98	-17.5	70.3	0.3	-11.0	72.3	7.79	-7.3
MMRV vaccine (measles/mumps/rubella/varicella)	0.66	7.7	13.6	<0.05	6.8	14.8	48.02	0.9
Hexavalent vaccine (diphtheria/ tetanus/pertussis/haemophilus Influenzae B/poliomyelitis/ hepatitis B)	0.50	-4.6	-8.7	0.1	-0.8	-1.6	25.51	-3.8
Tetravalent meningococcal conjugate vaccine	0.37	-3.5	20.9	<0.05	4.1	25.7	25.16	-7.3
Tetravalent vaccine (diphtheria/tetanus/pertussis/ poliomyelitis)	0.33	5.2	8.0	0.1	6.9	8.3	17.75	-1.5
Live attenuated rotavirus vaccine	0.25	-0.1	16.5	<0.05	6.2	24.5	18.97	-6.0
Live attenuated varicella zoster vaccine	0.19	-28.4	97.8	<0.05	-28.4	95.9	96.20	0.0
Intranasal tetravalent influenza vaccine	0.18	23.7	—	<0.05	22.9	—	19.77	0.6
DTP vaccine (diphtheria/tetanus/pertussis)	0.15	14.1	4.1	<0.05	18.2	6.2	11.43	-3.5
Pneumococcal polysaccharide 23 vaccine	0.10	-33.1	19.2	<0.05	-29.7	15.9	21.29	-4.8
Tick-borne encephalitis vaccine	0.08	29.0	30.8	<0.05	27.3	30.4	35.34	1.4
Hepatitis A vaccine	0.06	45.0	1.6	<0.05	43.1	3.2	17.36	1.3
Live attenuated varicella vaccine	0.06	-21.9	-6.4	<0.05	-21.3	-4.9	30.88	-0.7
Hepatitis B vaccine	0.06	35.6	2.4	<0.05	36.5	2.0	16.99	-0.7
MMR vaccine (measles/mumps/rubella)	0.02	-30.1	-18.3	<0.05	-28.8	-17.3	8.90	-1.9
Meningococcal C conjugate vaccine	0.02	-29.9	-16.4	<0.05	-30.1	-17.9	11.96	0.3
Yellow fever vaccine	0.01	41.4	5.4	<0.05	37.0	0.5	20.89	3.2
DT vaccine (diphtheria/tetanus)	0.01	148.1	-2.0	<0.05	135.6	-8.6	4.96	5.3
Live attenuated typhus vaccine	0.01	85.3	5.5	<0.05	76.7	-7.6	11.10	4.9
Hepatitis A and B vaccine	0.01	59.5	1.4	<0.05	55.4	14.1	31.59	2.6
Cholera vaccine	0.01	422.7	0.5	<0.05	428.9	-2.5	27.16	-1.2
Tetanus vaccine	0.01	12.7	-6.2	<0.05	6.5	-12.6	4.71	5.8
Polysaccharide typhus vaccine	0.01	53.7	8.0	<0.05	51.1	4.2	12.05	1.7

continued

Table 3.4.3a – *continued*

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Haemophilus influenzae B conjugate vaccine	0.01	69.3	18.3	<0.05	68.8	17.6	13.08	0.3
Inactivated polio vaccine (IPV)	<0.005	89.4	-0.3	<0.05	92.5	-2.4	7.54	-1.6
Japanese encephalitis vaccine	<0.005	610.3	9.1	<0.05	230.8	-0.8	170.18	114.7
Haemophilus influenzae B vaccine	<0.005	22.7	11.2	<0.05	22.5	7.4	15.85	0.1
Rabies vaccine	<0.005	-86.9	-11.2	<0.05	-87.0	-17.0	50.32	0.3
Vaccines	**12.10**	**11.8**	**9.6**	**1.2**	**1.7**	**-2.7**	**27.88**	**9.8**
adjuvanted recombinant varicella zoster virus vaccine	2.10	66.6	—	<0.05	41.0	—	321.38	18.2
human papillomavirus vaccine (human types 6, 11, 16, 18, 31, 33, 45, 52, 58)	1.64	13.6	168.1	0.1	13.5	193.6	69.37	0.1
Meningococcal group B (MenB) vaccine	1.46	8.7	35.1	0.1	7.8	35.1	62.66	0.8
tetravalent influenza vaccine (surface antigen, inactivated, adjuvanted)	1.40	4.8	—	0.3	3.9	—	15.03	0.9
inactivated, split virus tetravalent influenza vaccine	0.77	-25.0	66.0	0.2	-32.1	64.6	9.55	10.4
Measles/mumps/rubella/varicella live attenuated vaccine	0.66	7.7	13.6	<0.05	6.8	14.8	48.02	0.9
20-valent pneumococcal vaccine	0.54	35.9	—	<0.05	34.3	—	49.02	1.2
diphtheria/ recombinant hepatitis b/ Haemophilus influenzae B conjugate and adjuvanted/ acellular pertussis/inactivated poliomyelitis/tetanus vaccine	0.50	-4.6	-8.7	0.1	-0.8	-1.6	25.51	-3.8
13-valent pneumococcal vaccine	0.44	-38.5	-10.8	<0.05	-38.6	-11.2	48.84	0.2
15-valent pneumococcal vaccine	0.42	>100	—	<0.05	>100	—	45.84	0.0

Figure 3.4.3a Vaccines, temporal trend 2014-2023 of per capita expenditure of the highest-expenditure subgroups

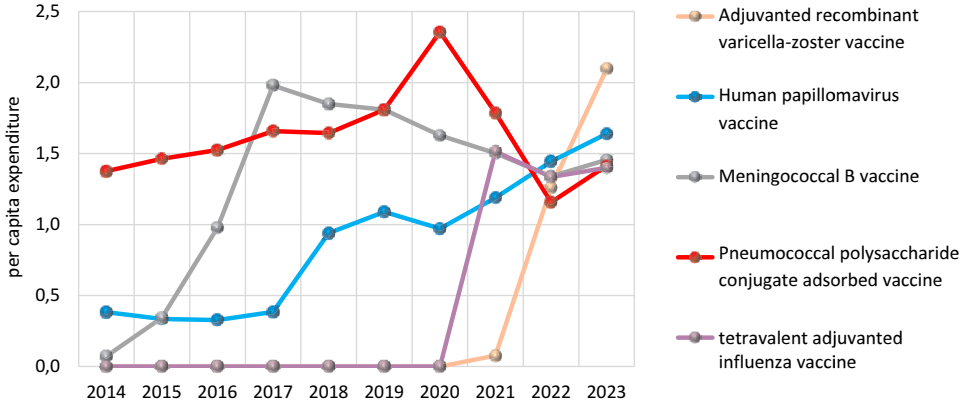


Table 3.4.3b Vaccines, regional trend of per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2022			2023			Δ % 23-22			CAGR % 14-23		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost
Piedmont	9.89	1.0	27.09	11.46	1.1	29.51	16.0	6.3	8.9	11.8	3.8	7.7
Valle d'Aosta	8.04	0.9	23.62	9.21	1.0	25.03	14.7	8.2	6.0	8.2	3.1	5.0
Lombardy	11.62	1.3	25.22	13.01	1.2	28.74	12.0	-1.7	14.0	12.2	-8.2	22.2
Province of Bolzano	12.60	1.2	29.10	16.99	1.3	35.51	34.9	10.5	22.0	12.3	-6.8	20.5
Province of Trento	15.27	1.4	28.94	17.04	1.4	32.61	11.5	-1.0	12.7	12.6	5.3	6.9
Veneto	14.21	1.2	32.96	15.00	1.2	34.06	5.5	2.1	3.3	11.1	-1.4	12.6
Friuli V.G.	10.69	1.1	25.50	13.53	1.2	30.02	26.6	7.5	17.7	9.5	-2.4	12.1
Liguria	10.40	1.0	27.15	12.33	1.1	31.24	18.6	3.1	15.1	11.6	2.3	9.1
Emilia R.	12.07	1.3	25.50	12.01	1.3	25.62	-0.5	-1.0	0.5	10.1	-2.8	13.2
Tuscany	9.90	1.2	22.19	10.65	1.3	22.33	7.5	6.8	0.6	12.6	-4.8	18.3
Umbria	9.82	1.4	19.92	9.94	1.1	24.59	1.2	-18.0	23.5	8.1	1.9	6.1
Marche	8.89	1.1	22.76	9.25	1.1	23.39	4.0	1.2	2.8	8.5	2.9	5.5
Lazio	9.55	1.1	23.94	11.13	1.1	26.97	16.6	3.5	12.7	9.4	0.9	8.4
Abruzzo	9.01	1.1	23.01	10.45	1.1	26.51	16.0	0.7	15.2	9.3	1.9	7.3
Molise	10.45	1.3	22.02	15.78	1.6	26.91	51.0	23.6	22.2	11.9	5.1	6.5
Campania	10.00	1.1	24.02	11.47	1.2	26.40	14.6	4.3	9.9	9.1	0.2	9.0
Puglia	10.90	1.3	23.57	11.95	1.3	25.59	9.6	0.9	8.6	4.5	-0.7	5.3
Basilicata	11.12	1.2	25.43	8.49	1.0	22.70	-23.6	-14.4	-10.7	3.9	-1.7	5.7
Calabria	10.16	1.1	24.91	12.51	1.2	29.37	23.1	4.4	17.9	10.1	-0.7	10.9
Sicily	10.69	1.2	25.40	12.08	1.1	28.84	13.0	-0.5	13.6	5.7	-3.1	9.1
Sardinia	7.90	0.9	24.85	10.22	1.0	29.43	29.3	9.2	18.4	9.0	-0.5	9.6
Italy	**10.83**	**1.2**	**25.38**	**12.10**	**1.2**	**27.88**	**11.8**	**1.7**	**9.8**	**9.6**	**-2.7**	**12.7**
North	11.83	1.2	27.13	13.07	1.2	29.64	10.5	1.1	9.3	11.4	-4.2	16.3
Centre	9.60	1.2	22.85	10.65	1.2	24.73	10.9	2.5	8.3	10.1	-1.4	11.7
South and Islands	10.16	1.1	24.33	11.62	1.2	27.21	14.4	2.3	11.8	7.1	-0.9	8.1

3.4.4 Antifungals for systemic use

In 2023, the category of antifungals for systemic use recorded a total public expenditure of 144.7 million euros, down 1.2% compared to the previous year. On the contrary, consumption (equal to 0.7 DDD) showed a 1.4% increase (Box Main indices of expenditure, consumption and exposure).

Over the last ten years, there has been an average annual decrease (CAGR 3.2%) in expenditure on antifungals, with values shifting from 3.4 euros in 2014 to 2.5 euros per capita in 2023. The average DDD cost showed variations in the different years considered, with an increase until 2017, followed by a subsequent reduction and a slight increase from 2019 to 2022. In 2023 the average DDD cost recorded a slight reduction compared to 2022, going from 10.6 euros to 10.3 euros.

Triazole derivatives, mainly represented by fluconazole, are the category with the highest consumption (0.6 DDD) and the highest expenditure, recording a value of 1.38 euros per capita in 2023, a 1.6% increase compared to the previous year (Table 3.4.4a and Figure 3.4.4a), with a 2.9% average annual reduction from 2014 to 2023. Polyenes follow (0.85 euros per capita), represented exclusively by amphotericin B, confirming the growth trend with a 3.2% increase compared to 2022 and a 6.3% average annual variation from 2014 to 2023. Echinocandins, after the growth in expenditure recorded in the period 2014-2017, have shown a strong reduction in the last 6 years, resulting in a 15.0% average annual reduction. However, the subgroup with the greatest reduction in expenditure and consumption in 2022 compared to the previous year is imidazole derivatives (-44.6% and -44.6% respectively).

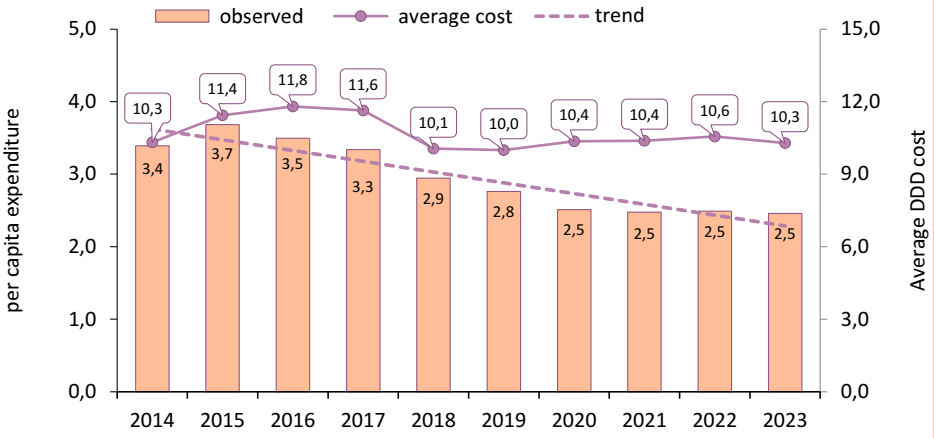
Fluconazole is the highest consumed drug (0.4 DDD), followed by itraconazole (0.2 DDD) with a change compared to 2022 of 1.1% and 2.6%, respectively. Four triazole derivatives, namely fluconazole, isavuconazole, itraconazole and posaconazole, are at the top of the list in terms of expenditure after amphotericin B; all show an increase compared to 2022 except posaconazole (-15.8%) (Table 3.4.4a). Micafungin, an echinocandin, is the substance with the highest average cost per DDD (216.79 euros), although it has decreased compared to 2022 (-9.2%).

In the South there is a higher expenditure (2.61 euros per capita) compared to the North (2.37 euros) and the Centre (2.42 euros); the latter has increased by 3% compared to 2022, while in the South it remained stable and in the North it decreased by 3.8% (Table 3.4.4b).

MAIN INDICES OF EXPENDITURE AND CONSUMPTION
Antifungals

Public expenditure* in million euros (% over total)	**144.7**	**(0.6)**
Δ % 2023-2022		-1.2
Regional range of gross per capita expenditure:	1.0	4.2
DDD/1000 inhabitants per day* (% over total)	**0.7**	**(0.0)**
Δ % 2023-2022		1.4
Regional range DDD/1000 inhabitants per day	0.3	1.1

Antifungals for systemic use, temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)

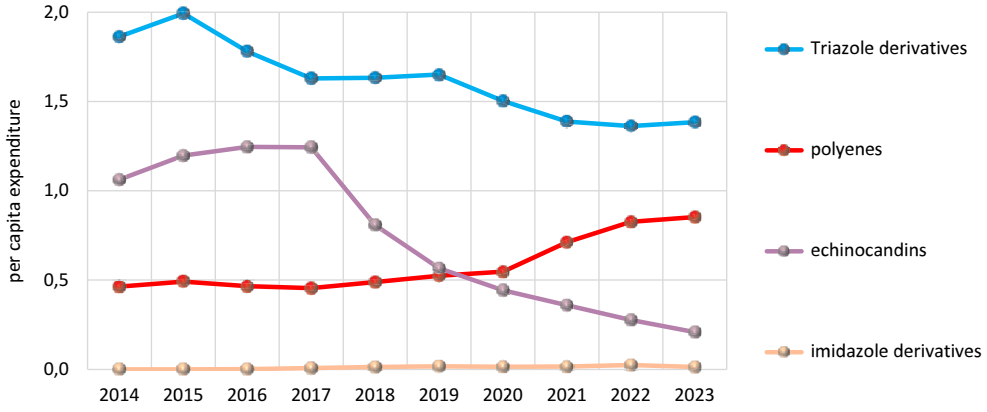


National data on consumption and expenditure by subgroup and substance

Table 3.4.4a Antifungals for systemic use, per capita expenditure and consumption (DDD/1000 inhab. per day) by therapeutic category and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Triazole derivatives	1.38	1.6	-2.9	0.6	2.2	-3.5	6.16	-0.6
Polyenes	0.85	3.2	6.3	<0.05	3.3	5.0	101.55	0.0
Echinocandins	0.21	-24.8	-15.0	<0.05	-13.1	4.8	46.77	-13.5
Imidazole derivatives	0.01	-44.6	49.9	<0.05	-44.6	36.3	9.44	-0.1
Antifungals	**2.46**	**-1.2**	**-3.2**	**0.7**	**1.4**	**-3.1**	**10.28**	**-2.6**
amphotericin B	0.85	3.2	6.3	<0.05	3.3	5.0	101.55	0.0
fluconazole	0.68	0.3	-3.5	0.4	1.1	-3.0	4.78	-0.8
isavuconazole	0.37	13.5	—	<0.05	19.3	—	100.30	-4.9
itraconazole	0.17	2.6	-5.7	0.2	2.6	-5.6	2.55	-0.1
posaconazole	0.14	-15.8	-3.6	<0.05	14.6	4.6	17.49	-26.6
caspofungin	0.10	-24.3	-17.3	<0.05	-14.3	7.0	30.17	-11.7
micafungin	0.08	-25.2	-5.8	<0.05	-17.6	-0.9	216.79	-9.2
voriconazole	0.03	-9.0	-23.5	<0.05	-0.2	1.1	7.14	-8.8
anidulafungin	0.03	-26.0	-19.5	<0.05	-3.0	0.2	39.45	-23.6
ketoconazole	0.01	-44.6	—	<0.05	-44.6	—	9.44	-0.1

Figure 3.4.4a Antifungals, temporal trend 2014-2023 of per capita expenditure of the highest-expenditure subgroups



Regional data on consumption and expenditure

Table 3.4.4b Antifungals for systemic use, regional trend of per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2022			2023			Δ % 23-22			CAGR % 14-23		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/ 1000 inhab. per day	Average DDD cost
Piedmont	2.30	0.6	10.25	1.91	0.6	8.46	-17.1	0.3	-17.4	-5.1	-1.9	-3.3
Valle d'Aosta	1.18	0.5	7.02	1.02	0.5	5.97	-13.7	1.4	-14.9	-3.2	-2.3	-0.9
Lombardy	2.22	0.5	12.41	2.30	0.5	12.67	3.7	1.6	2.1	-1.4	-2.8	1.4
Province of Bolzano	1.01	0.3	10.09	1.38	0.3	12.77	36.9	8.2	26.5	-6.7	-2.9	-4.0
Province of Trento	1.40	0.5	6.99	1.15	0.5	5.91	-18.0	-3.1	-15.4	-6.2	-2.2	-4.1
Veneto	2.91	0.5	14.58	2.69	0.5	13.51	-7.5	-0.1	-7.4	-2.6	-3.5	1.0
Friuli V.G.	2.20	0.6	10.64	2.67	0.6	12.41	21.1	3.8	16.7	-1.3	-2.7	1.4
Liguria	3.17	0.6	13.65	3.53	0.7	14.40	11.6	5.9	5.4	-2.1	-2.1	0.0
Emilia R.	2.81	0.6	13.11	2.41	0.6	11.45	-14.4	-2.0	-12.6	-1.7	-2.7	1.1
Tuscany	2.06	0.5	10.81	2.15	0.5	10.93	4.4	3.2	1.2	-4.0	-3.2	-0.9
Umbria	2.83	0.6	13.03	3.31	0.6	14.63	16.7	4.0	12.3	-5.1	-3.7	-1.5
Marche	2.41	0.7	9.14	2.36	0.8	8.49	-2.1	5.5	-7.2	-2.1	-2.5	0.5
Lazio	2.45	0.6	10.67	2.47	0.7	10.34	1.1	4.3	-3.1	-4.2	-4.2	0.0
Abruzzo	3.00	0.7	11.19	3.22	0.8	11.39	7.3	5.4	1.8	0.8	-2.0	2.9
Molise	1.15	0.5	5.77	1.11	0.6	5.28	-4.1	4.9	-8.5	-9.1	-4.4	-5.0
Campania	2.65	0.8	8.99	2.66	0.8	8.98	0.3	0.4	-0.1	-3.1	-2.5	-0.6
Puglia	2.35	0.7	8.68	2.06	0.8	7.37	-12.2	3.4	-15.1	-6.8	-3.7	-3.2
Basilicata	1.59	0.6	6.82	1.73	0.7	7.12	8.6	4.1	4.3	-5.8	-2.8	-3.1
Calabria	4.05	1.1	10.25	4.22	1.1	10.68	4.2	0.1	4.2	-0.4	-2.4	2.1
Sicily	2.38	0.8	7.68	2.33	0.8	7.70	-2.0	-2.3	0.2	-4.4	-4.3	0.0
Sardinia	2.49	0.8	8.59	2.86	0.8	9.65	14.7	2.2	12.3	-2.4	-3.4	1.0
Italy	**2.49**	**0.6**	**10.56**	**2.46**	**0.7**	**10.28**	**-1.2**	**1.4**	**-2.6**	**-3.2**	**-3.1**	**0.0**
North	2.46	0.5	12.38	2.37	0.5	11.81	-3.8	0.8	-4.6	-2.5	-2.7	0.2
Centre	2.35	0.6	10.65	2.42	0.6	10.53	3.0	4.2	-1.1	-4.0	-3.6	-0.4
South and Islands	2.61	0.8	8.78	2.61	0.8	8.70	-0.1	0.8	-0.9	-3.5	-3.3	-0.3

3.5 Blood and blood-forming organs

Medicines for blood and blood-forming organs were the fifth therapeutic category with the highest public expenditure in 2023 (2.587 million euros), accounting for 10% of total public expenditure (Box Main indices of expenditure, consumption and exposure). Overall, per capita expenditure on these medicines was 43.95 euros, mainly due to purchase by public health facilities (36.76 euros per capita), up 7.6% compared to the previous year. The share due to approved care regime, on the contrary, is smaller (7.19 euros per capita), a 3.2% decrease compared to the previous year (Table 3.1). In terms of consumption, overall there are values of 144.5 DDDs per 1,000 inhabitants per day, with a 0.7% percentage increase compared to the previous year.

The analysis of the drug use profile by age group and gender, including pharmaceutical expenditure under approved care regime and distribution on behalf, shows a progressive increase in the use of these medicines with increasing age. A more marked increase is found in men aged 55-64 years, probably due to the different prevalence of cardio-cerebrovascular diseases. The highest prevalence is reached in patients over 75, with values of 58.8% and 67.3% for females and males, respectively. In the younger age groups, prevalence is higher in women than in men, probably due to a greater use of anti-anaemic preparations. At the same time, per capita NHS expenditure shows a similar trend, reaching the maximum value of 101.5 euros per capita in the +75 age group (116.0 euros in men and 91.4 euros in women).

Concerning the approved care regime, expenditure recorded a reduction in 2023 compared to the previous year (-3.5%), together with a decrease in consumption (-1.2%), with a shift in prescription towards less expensive products (mix effect: -2.6%), and a reduction of the average DDD cost (-2.3%) (Table 3.9). The therapeutic categories with the greatest impact on expenditure are platelet aggregation inhibitors (3.07 euros per capita) and heparins (1.92 euros per capita). Compared to the previous year, inhibitors of coagulation factor Xa (tenth activated), including apixaban, an active ingredient accounting for 4.2% of approved care expenditure, recorded an increase in the same indicator (+8.8%) and in consumption (+9.2%) (Tables 3.9 and 3.10). In 2023, vitamin K antagonists (AVK) showed a 17.2% price increase due to the effect of the warfarin renegotiation (Resolution no. 299 of 21 April 2022, G.U. 101 of 2 May 2022) but with a reduction in consumption (-13.9%). Enoxaparin (1.76 euros), clopidogrel (1.28 euros) and acetylsalicylic acid (1.20 euros) are the molecules with the highest per capita expenditure, representing the main cost item of the approved care regime relating to drugs for blood and haematopoietic organs (59.8%) (Table 3.10). In 2023, there was an increase in consumption of all active ingredients, with the only exceptions of enoxaparin (-12.1%) and human albumin (-2.6%). Overall, the average DDD cost has decreased compared to the previous year, with the sole exception of this last active ingredient, which recorded a 2.3% increase.

Clopidogrel, accounting for 17.8% of expenditure of the entire category, is the only molecule included in the list of the first 30 active ingredients with the greatest impact on approved care regime (Table 3.11) and with the greatest expenditure increase (Table 3.14). Acetylsalicylic acid and folic acid, on the other hand, are on the list of drugs with the lowest average cost per day of therapy, with values of 0.07 and 0.21 euros, respectively (Table 3.13). Clopidogrel is among the top 30 active ingredients with the highest increase in expenditure (+5.5%) compared to 2022 (Table 3.14). Enoxaparin is among the active ingredients with the greatest expenditure reduction (-13.8%) (Table 3.15), although it is among the top 30 for

expenditure under the approved care regime (Table 1 3.11). Finally, acetylsalicylic acid and cyanocobalamin are on the list of the highest consumed drugs, with values of 46.0 and 11.3 DDD/1000 inhabitants per day, respectively (Table 3.16).

As regards purchases by public health facilities, compared to 2022, there was an increase in both expenditure (+7.3%) and consumption (+3.2%) and a shift towards more expensive products (mix effect +3.7%) (Table 3.17). The therapeutic category with the highest impact on expenditure is factor Xa inhibitors, with a per capita expenditure of 9.95 euros, followed by coagulation factors (7.46 euros) and by other systemic hemostatics for systemic use (3.60 euros). The most frequently used therapeutic categories include direct factor Xa inhibitors (16.3 DDD), followed by platelet aggregation inhibitors, excluding heparin (9.3 DDD). Apixaban is the active ingredient ranking first in terms of per capita expenditure (3.80 euros), with a 21.5% increase in expenditure and 21.8% in consumption compared to the previous year (Table 3.18). This is followed by rivaroxaban (3.47 euros), edoxaban (2.68 euros) and enoxaparin (1.91 euros). These active ingredients, together with emicizumab, also rank among the top 30 highest-expenditure active ingredients among drugs purchased by healthcare facilities (Table 3.19).

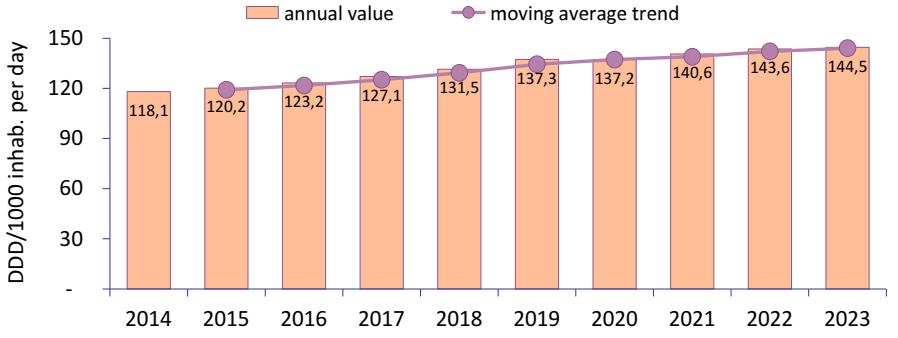
Octocog alfa, ticagrelor, darbepoetin alfa, dabigatran and efmoroctocog alfa are among the molecules purchased by public healthcare facilities with the greatest cost reduction compared to the previous year (Table 3.21), while albutrepenonacog alfa, emicizumab, efmoroctocog alfa and octocog alfa are among the first thirty active ingredients with the highest average cost per DDD (Table 3.22). On the other hand, nine active ingredients in this category are among the top thirty with the lowest average cost per DDD (Table 3.23) and nine are among the top 30 molecules by consumption (Table 3.24). Overall, apixaban, enoxaparin, rivaroxaban and edoxaban are among the active ingredients with the highest overall expenditure (contracted and public health facilities), going from 241.1 million to 159.7 million euros (Table 3.25). Finally, acetylsalicylic acid, cyanocobalamin, clopidogrel and enoxaparin are among the substances with the highest consumption, going from 8.4 DDD of enoxaparin to 47.3 of acetylsalicylic acid (Table 3.26)

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

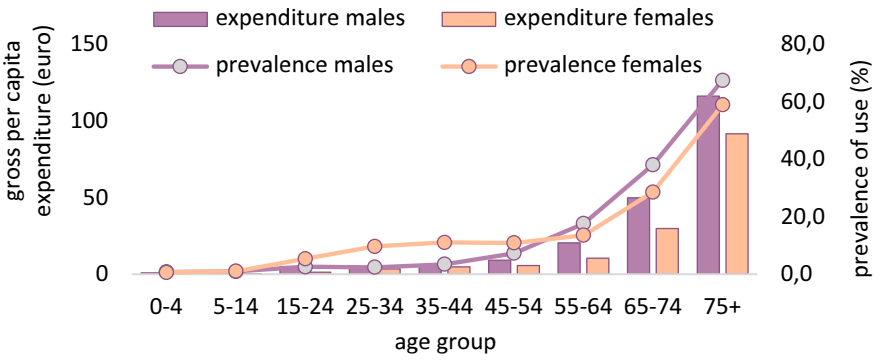
Blood and blood-forming organs

Public expenditure* in million euros (% over total)	**2,587.0**	**(10.0)**
Δ % 2023-2022		5.7
Regional range of gross per capita expenditure:	32.4	72.9
DDD/1000 inhabitants per day* (% over total)	**144.5**	**(10.9)**
Δ % 2023-2022		0.6
Regional range DDD/1000 inhabitants per day	95.4	190.2

** includes prescriptions under approved care regime and purchases by public health facilities*



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf by age and gender in 2023 (Figure and Table)



Age group	Gross per capita expenditure			DDD/1000 inhabitants per day		
	Males	Females	Total	Males	Females	Total
0-4	0.9	0.1	0.5	2.1	1.7	1.9
5-14	2.2	0.3	1.3	1.3	1.3	1.3
15-24	5.0	1.4	3.3	4.4	9.3	6.8
25-34	4.9	3.6	4.3	5.7	23.4	14.4
35-44	5.4	4.7	5.0	12.1	29.5	20.8
45-54	9.1	5.7	7.4	38.8	34.9	36.8
55-64	20.5	10.5	15.4	120.9	70.7	95.1
65-74	49.7	29.8	39.2	307.1	197.3	249.2
75+	116.0	91.4	101.5	577.4	461.5	508.9

3.5.1 Anticoagulants

In 2023, total public expenditure on anticoagulants was 973.8 million euros, up 7.4% compared to 2022, representing 3.7% of total public expenditure (Box Main expenditure and consumption indices). The corresponding total consumption was 30.8 DDD/1000 inhabitants per day, a 5.8% increase compared to 2022, representing 2.3% of the total consumption of drugs covered by the NHS.

In the past ten years, Italy has seen a significant increase in the consumption of anticoagulants (CAGR: +5.0%), reaching 30.8 DDD/1000 inhabitants per day in 2023 and increasing by 5.8% compared to the previous year. At the same time, per capita expenditure has shown an increase since 2014 (CAGR: +7.0%), settling at 16.55 euros in 2023, up 7.4% compared to the previous year (Box Main indices of expenditure, consumption and exposure and Table 3.5.1a). The average cost per DDD reached 1.47 euros in 2023, confirming the upward trend of the past five years (Figure 3.5.1a). Exposure to anticoagulants in the general population tends to increase with the age of patients for both genders, reaching a prevalence of use of 36% in men over 85, with greater use in men than in women for all age groups, except for patients aged between 25 and 44 years (Figure 3.5.1b).

In 2023, the NOACs category recorded the highest consumption (19.0 DDD/1000 inhabitants per day), with a 12.9% increase compared to 2022 and a 28.0% average annual increase in the period 2014-2023 (Table 3.5.1a and Figure 3.5.1a). On the contrary, vitamin K antagonists (AVK) recorded a consumption of 2.3 DDD/1000 inhabitants per day, showing a 13.9% reduction in consumption compared to the previous year and a 10.1% average annual decrease in the period 2014-2023 (Table 3.5.1a and Figure 3.5.1a). NOACs are reportedly preferred in clinical use compared to AVKs, as they do not require periodic monitoring of the blood-coagulation status and have a lower risk of haemorrhage, especially cerebral haemorrhage. Compared to the previous year, the category of direct thrombin inhibitors shows the most significant increase in terms of both expenditure and consumption (+32.4% and +41.1%, respectively), while fondaparinux records the greatest reductions (-21.7% for expenditure and -23.7% for consumption) (Table 3.5.1a). Among NOACs, compared to 2022, a more marked increase in consumption was recorded for edoxaban (+23.4%) and apixaban (+21.5%). Apixaban was introduced more recently than rivaroxaban, which recorded a more modest increase (+5.0%). However, dabigatran shows a slight decrease in consumption (-1.6%) (Table 3.5.1a). Compared to 2022, edoxaban (+21.5%) and apixaban (+20.8%) recorded the most significant increase in per capita expenditure, apixaban being the active ingredient with the highest per capita expenditure (4.10 euros). Compared to the previous year, nadroparin shows the greatest reduction both in expenditure and consumption (-25.7% and -28.7%, respectively), confirming the downward trend recorded in the last ten years (CAGR per capita expenditure: -15.5% and CAGR consumption: -14.5%) as reported in Table 3.5.1a.

In 2023, the prevalence of use of anticoagulants was 5.8%, with substantially overlapping values between males and females for all drug subgroups, while the median age of patients is higher for AVK and NOAC than for LMWH, heparin/heparinoids and fondaparinux (Table 3.5.1b). Considering the entire category, the median age of users is 75 years and each user receives on average approximately 153.5 DDD of drug per year with a cost per user of 235.2 euros. Half of the exposed population was treated with 108.0 DDD (equivalent to more than 3 months of therapy), while 16.5% of users received only one prescription in the year. This percentage varies from 3.3% of NOACs to 35.4% of heparin and heparinoids. These data are

in line with the clinical indications and treatment duration of the different categories of anticoagulants.

In 2023, the difference between the region with the highest consumption (Umbria with 38.3 DDD) and the region with the lowest consumption (Sicily with 24.8 DDD) was equal to 13.5 DDD/1000 inhabitants per day (Table 3.5.1c), although the prevalence of use recorded more or less overlapping values in the North (5.7%), the Centre (6.6%) and the South and Islands (5.5%). Compared to the previous year, the Province of Bolzano recorded the highest increase in consumption (+19.7%), while Veneto had the highest increase in per capita expenditure (+26.0%), with a 7.8% increase in the average cost per DDD.

Analyses of adherence and persistence to treatment with anticoagulant drugs were conducted on a cohort of 74,992 new users (>45 years) of anticoagulant drugs (median age 76 years), followed for one year. The percentage of subjects with high and low adherence to treatment was 51.8% and 9.7%, respectively (Figures 3.5.1b and 3.5.1c), higher in males than in females. Comparing 2023 and 2022 data, at the national level the percentage of users with low adherence decreased by 7%, while the percentage of users with high adherence remained unchanged. Examining the data relating to the last five years on adherence to treatment with anticoagulant drugs in the population aged ≥45 years stratified by gender, the percentage of subjects with high adherence is constantly higher in males than in females while males showed lower adherence only in the last two years. These data reflect the reduced compliance to treatment of anticoagulant users, which generally tends to worsen with age, due to the deterioration of cognitive functions, the likely worsening of health status and changes in socio-economic conditions.

Taking into account persistence to anticoagulant treatment, 67.0% of new users were still on treatment 12 months after starting therapy. This means that one year after the start of treatment, 33% of subjects experience an interruption of at least 60 days. No differences were found by gender in the entire study population, while minimal and non-significant differences were found by gender when differentiating by geographical macro-area (Figures 3.5.1d and 3.5.1e).

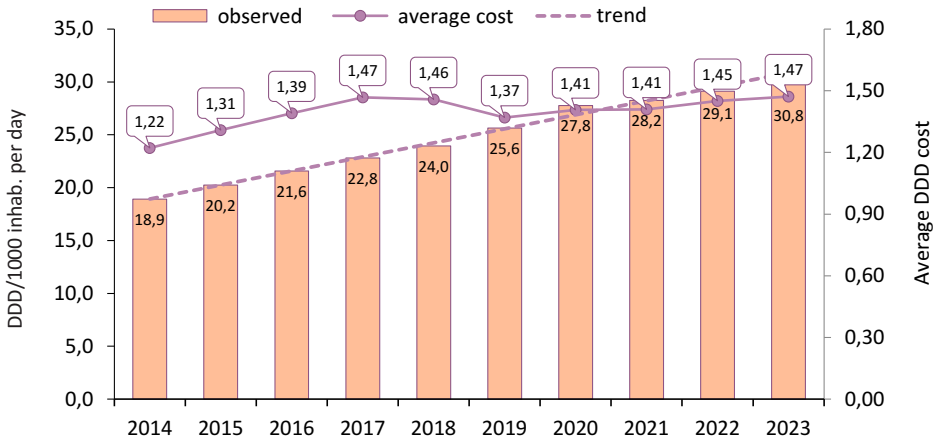
In general, comparing the persistence data between 2023 and 2022, substantial stability is observed in the percentage of subjects persisting at 12 months with more accentuated increases in the North and Centre among individuals in the age group equal to or over 85 years. These variations, although modest in most cases, suggest a general overall improvement in the persistence indicator especially in older subjects. As in the previous year, in the North (64.5%) there was a slightly lower percentage of individuals persisting at 12 months compared to the Centre (71.7%) and the South and Islands (67.4%).

For further information on regional data on exposure and duration of therapy and on indicators of adherence and persistence to treatment stratified by age, gender and geographical area, please refer to the supplementary documents published online.

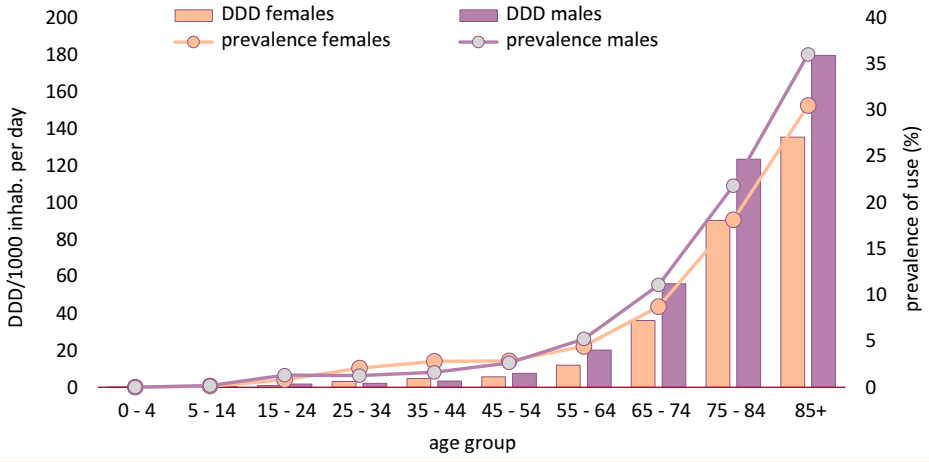
MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Anticoagulants

Public expenditure* in million euros (% over total)	**973.8**	**(3.7)**
Δ % 2023-2022		7.4
Regional range of gross per capita expenditure:	13.7	20.4
DDD/1000 inhabitants per day* (% over total)	**30.8**	**(2.3)**
Δ % 2023-2022		5.8
Regional range DDD/1000 inhabitants per day	24.8	38.3

Anticoagulants, temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of anticoagulants under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.5.1a Anticoagulants, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
NOACs	11.55	13.5	22.6	19.0	12.9	28.0	1.67	0.5
LMWH	3.98	-5.7	-3.5	8.8	-0.3	-1.1	1.24	-5.5
Heparin and heparinoids	0.25	4.6	-4.9	0.4	3.6	-4.5	1.78	0.9
Antithrombotic enzymes	0.24	14.9	0.1	0.0	-2.3	-0.1	924.96	17.6
Fondaparinux	0.23	-21.7	-1.2	0.4	-23.7	1.7	1.66	2.6
Vitamin K antagonists	0.16	1.5	-5.2	2.3	-13.9	-10.1	0.19	17.8
Other antithrombotics	0.13	21.7	—	<0.05	21.5	—	4099.74	0.1
Antithrombotics - direct thrombin inhibitors	0.01	32.4	-12.4	<0.05	41.1	-9.1	203.41	-6.2
Anticoagulants	**16.55**	**7.4**	**7.0**	**30.8**	**5.8**	**5.0**	**1.47**	**1.5**
apixaban	4.10	20.8	33.6	6.4	21.5	40.5	1.75	-0.5
enoxaparin	3.67	-4.5	-0.8	8.4	1.5	1.1	1.20	-5.9
rivaroxaban	3.50	6.7	20.5	6.0	5.0	25.4	1.60	1.6
edoxaban	2.71	21.5	—	4.2	23.4	—	1.77	-1.5
dabigatran	1.24	-2.7	5.3	2.4	-1.6	12.0	1.42	-1.1
fondaparinux	0.23	-21.7	-1.2	0.4	-23.7	1.7	1.66	2.6
nadroparin	0.22	-25.7	-15.5	0.3	-28.7	-14.5	1.97	4.3
heparin	0.20	9.7	-3.0	0.4	3.8	-4.5	1.46	5.7
alteplase	0.16	1.0	7.4	<0.05	0.3	7.2	834.02	0.7
warfarin	0.15	3.2	-4.2	2.1	-13.9	-9.9	0.19	19.8

Figure 3.5.1a Anticoagulants, 2014-2023 temporal trend in consumption (DDD/1000 inhabitants per day) by highest-expenditure subgroups

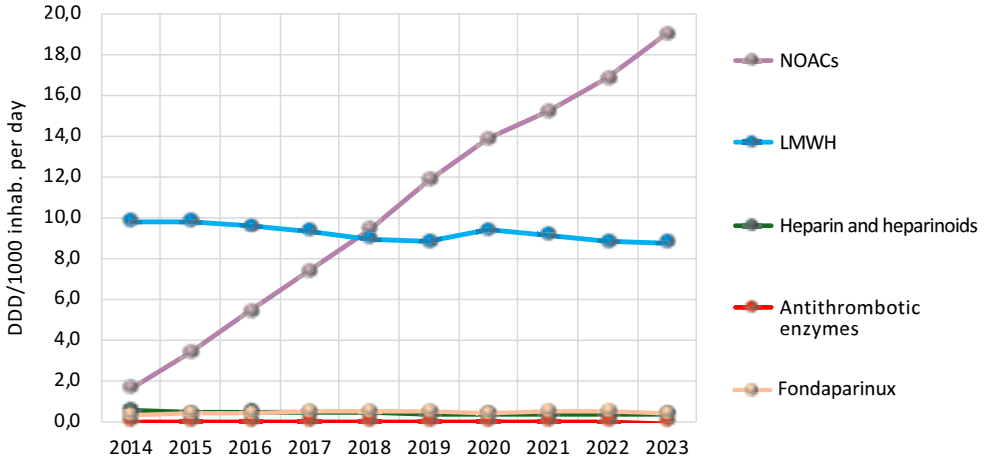


Table 3.5.1b Exposure and duration of anticoagulant therapy by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Average cost per user	DDD per user	DDD age	Users with 1 prescription (%)
	males	females	total					
NOACs	2.8	2.5	2.7	80	397.4	233.8	242.0	3.3
LMWH	2.6	3.3	2.9	66	94.0	61.9	36.0	34.0
Fondaparinux	0.1	0.2	0.1	71	117.3	66.1	30.0	28.0
Heparin and heparinoids	0.0	0.0	0.0	77	101.3	39.5	15.0	35.4
Vitamin K antagonists	0.6	0.5	0.6	78	27.4	139.6	120.0	4.9
Anticoagulants	**5.6**	**6.0**	**5.8**	**75**	**235.2**	**153.5**	**108.0**	**16.5**

Regional data on expenditure, consumption and exposure

Table 3.5.1c Anticoagulants, regional trend of per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use	Cost/user	Median DDD
Piedmont	15.31	29.9	1.40	10.4	3.6	6.5	8.5	5.9	2.5	5.5	228.7	132.0
Valle d'Aosta	16.11	29.7	1.48	7.9	1.6	6.2	12.0	4.7	6.9	5.6	247.8	120.0
Lombardy	18.27	29.8	1.68	5.4	5.8	-0.3	8.1	5.7	2.3	5.8	278.5	100.0
Province of Bolzano	16.51	30.1	1.50	24.6	19.7	4.1	8.5	3.9	4.4	5.4	239.6	120.0
Province of Trento	17.17	34.9	1.35	-1.5	-5.3	4.0	12.4	4.3	7.7	5.9	190.0	90.0
Veneto	17.75	35.3	1.38	26.0	16.9	7.8	8.4	4.1	4.1	5.0	256.9	168.0
Friuli V.G.	20.45	36.9	1.52	14.5	8.5	5.5	9.1	4.9	4.0	5.9	286.6	176.0
Liguria	16.89	32.9	1.41	10.8	14.5	-3.3	7.7	3.7	3.8	7.0	209.6	94.5
Emilia R.	17.65	37.3	1.29	5.9	3.4	2.4	11.1	4.4	6.4	5.7	220.0	128.0
Tuscany	17.06	34.4	1.36	9.7	6.9	2.7	7.7	3.5	4.1	7.2	194.7	84.0
Umbria	19.50	38.3	1.39	8.7	6.4	2.2	10.8	4.9	5.6	7.4	232.4	122.0
Marche	17.12	35.7	1.31	2.9	0.5	2.5	13.6	8.3	4.8	7.7	203.6	100.0
Lazio	16.88	28.9	1.60	3.4	2.6	0.8	5.3	5.2	0.1	5.8	246.8	96.0
Abruzzo	16.03	31.5	1.39	-1.1	3.5	-4.5	6.7	6.1	0.6	6.9	195.6	80.0
Molise	13.69	28.6	1.31	0.7	2.1	-1.4	7.9	5.8	2.0	5.5	190.5	80.0
Campania	14.02	25.6	1.50	1.0	2.5	-1.5	2.9	5.8	-2.7	5.4	207.9	80.0
Puglia	15.92	29.6	1.47	4.4	4.8	-0.4	4.7	5.2	-0.4	5.5	269.9	120.0
Basilicata	15.97	30.3	1.44	1.3	3.1	-1.8	6.6	5.2	1.3	6.7	210.1	88.0
Calabria	14.01	25.6	1.50	0.1	-1.4	1.5	1.4	3.5	-2.0	5.7	198.6	64.0
Sicily	14.04	24.8	1.55	9.5	9.8	-0.3	5.1	5.4	-0.2	5.0	227.6	80.0
Sardinia	15.54	32.0	1.33	5.0	2.1	2.9	6.7	4.3	2.3	6.0	209.9	110.0
Italy	**16.55**	**30.8**	**1.47**	**7.4**	**5.8**	**1.5**	**7.0**	**5.0**	**1.9**	**5.8**	**235.2**	**108.0**
North	17.56	32.6	1.48	10.3	7.5	2.6	8.8	4.9	3.7	5.7	251.0	120.0
Centre	17.17	32.3	1.46	5.7	4.0	1.7	7.3	4.9	2.3	6.6	221.5	92.0
South and Islands	14.72	27.3	1.48	3.7	4.2	-0.5	4.3	5.2	-0.8	5.5	222.5	84.0

Figure 3.5.1b Indicators of low adherence to treatment with anticoagulants in the population aged ≥45 years stratified by gender, trend 2019-2023 (raw values). Valle d'Aosta not included in the calculation

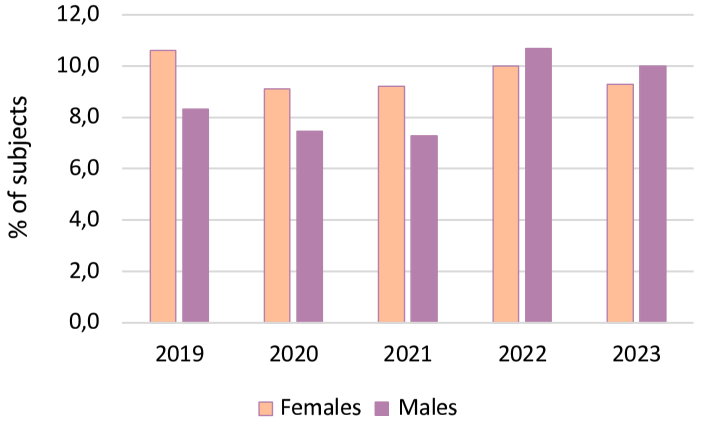


Figure 3.5.1c Indicators of high adherence to treatment with anticoagulants in the population aged ≥45 years stratified by gender, trend 2019-2023 (raw values). Valle d'Aosta not included in the calculation

*Adherence to treatment was evaluated only for new users with at least 2 prescriptions. Low adherence to treatment was defined as therapeutic coverage (assessed by DDD) <40% of the observation period while high adherence was defined as therapeutic coverage ≥80% of the observation period (see statistical methods for further details).

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Figure 3.5.1d Time (in days) to discontinuation of treatment with anticoagulants in the population aged ≥45 years stratified by geographical area. Curves are adjusted by gender and age (the Cox model was used to estimate persistence curves). The North does not include Valle d'Aosta

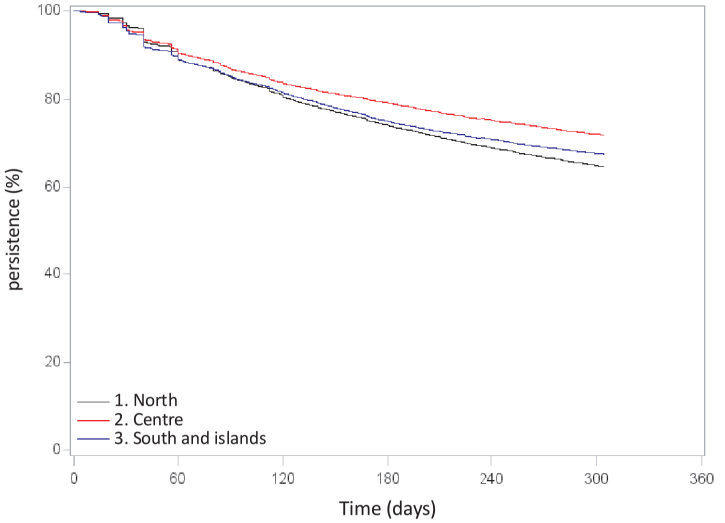
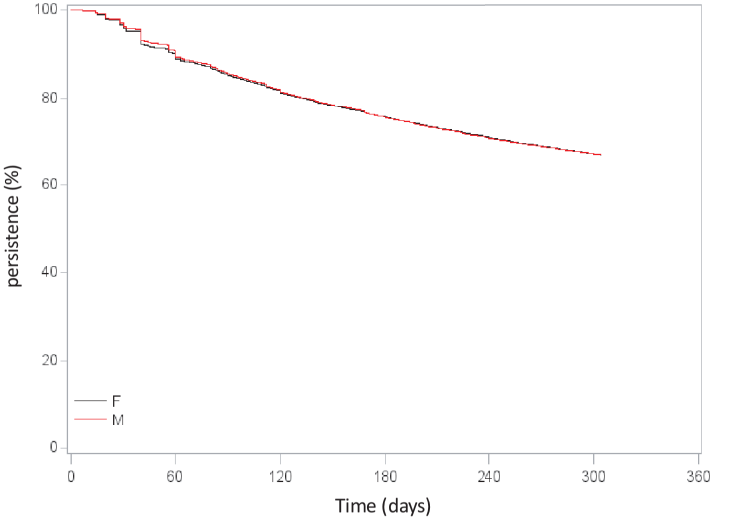


Figure 3.5.1e Time (in days) to discontinuation of treatment with anticoagulants in the population aged ≥45 years stratified by gender. Curves are adjusted by age (the Cox model was used to estimate persistence curves)



3.5.2 Coagulation factors

In 2023, total public expenditure on coagulation factors amounted to 553.4 million euros, a 1.7% increase compared to 2022, representing 2.1% of total public expenditure (Box. Main expenditure and consumption indices). The corresponding total consumption was equal to 0.1 DDD/1000 inhabitants per day, a 2.0% increase compared to 2022.

In 2023, coagulation factors recorded an increase in overall per capita expenditure (+1.7%), corresponding to an increase in consumption (+2.0%). Per capita expenditure has shown an increasing trend since 2014 (CAGR: +2.4%), with 9.4 euros in 2023. Conversely, the average DDD cost has continued to decrease over the last five years, reaching 404.2 euros in 2023 (Figure 3.5.2a).

Short-acting recombinant drugs for the treatment of haemophilia A showed a reduction in consumption also in 2023 (-18.0%); on the other hand, long-acting recombinant factors recorded an increase in use equal to 14.0% and are confirmed as the category with the highest per capita expenditure of 2.84 euros (Table 3.5.2a).

In the field of recombinant drugs, long-acting factors allow for a lengthening of the interval between infusions, greater safety margins with respect to haemorrhagic episodes, improved adherence to prophylaxis and the quality of life of patients. These aspects have caused an ever-increasing use in recent years of active ingredients with a longer half-life, as also demonstrated by the increasing expenditure trend of long-acting compared to short-acting products (Figure 3.5.2a).

In the treatment of haemophilia A, the monoclonal antibody emicizumab showed an increase in consumption in 2023 (+20.6%) compared to the previous year and is the active ingredient with the highest per capita expenditure (1.91 euros) (Table 3.5.2a).

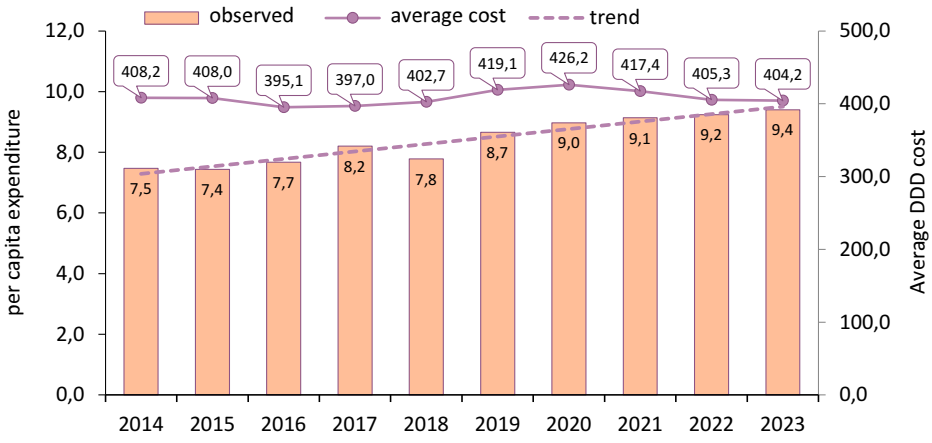
In line with the epidemiological and clinical data, the analysis shows that among the top ten active ingredients for per capita expenditure there are nine factors used in the treatment of haemophilia A and one factor used in the treatment of haemophilia B, i.e. eftrenonacog alfa with a value of 0.32 euros (Table 3.5.2a).

Short-acting recombinant drugs for the treatment of haemophilia B show a reduction in consumption (-18.0%) while long-acting recombinant factors have recorded a simultaneous increase in consumption (+21.2%). They are confirmed as the category with the highest per capita expenditure (1.35 euros) for the treatment of Factor IX deficiency (Table 3.5.2a). As in the previous year, there is a wide regional variability with a North-South gradient both in terms of per capita expenditure (North 8.72 euros - Centre 9.52 euros - South and Islands 10.31 euros) and in terms of the average cost per DDD (North 428.87 euros - Centre 390.70 euros - South and Islands 384.93 euros) (Table 3.5.2b).

MAIN INDICES OF EXPENDITURE AND CONSUMPTION
Coagulation factors

Public expenditure* in million euros (% over total)	**553.4**	**(2.1)**
Δ % 2023-2022		1.7
Regional range of gross per capita expenditure:	5.3	13.9
DDD/1000 inhabitants per day* (% over total)	**0.1**	**(0.0)**
Δ % 2023-2022		2.0
Regional range DDD/1000 inhabitants per day	<0.05	0.1

Coagulation factors, temporal trend in per capita expenditure and average cost per day of therapy (2014-2023)

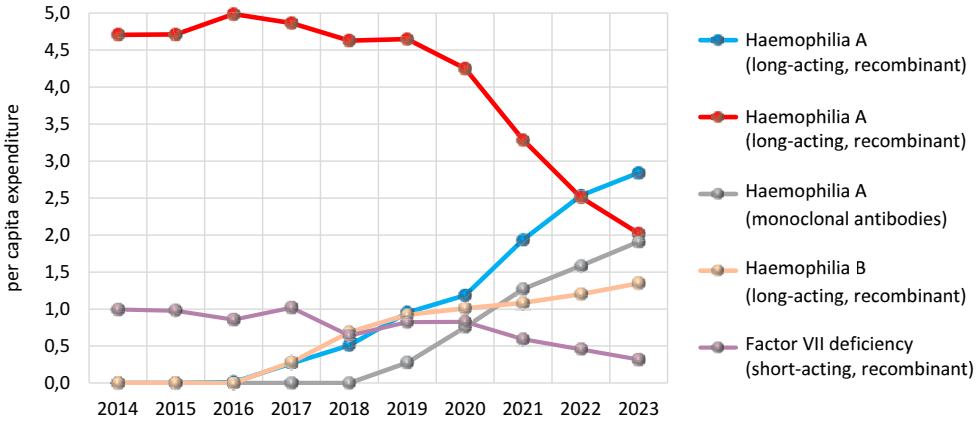


National data on consumption and expenditure by subgroup and substance

Table 3.5.2a Coagulation factors, per capita expenditure and consumption (DDD/1000 inhab. per day) by therapeutic category and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Haemophilia A (long-acting recombinant)	2.84	12.2	—	<0.05	14.0	—	315.46	-1.5
Haemophilia A (long-acting recombinant)	2.02	-19.5	-8.1	<0.05	-18.0	-7.3	330.60	-1.8
Haemophilia A (monoclonal antibodies)	1.91	20.7	—	<0.05	20.6	—	683.67	0.1
Haemophilia B (long-acting recombinant factors)	1.35	12.2	—	<0.05	21.2	—	855.43	-7.4
Factor VII deficiency (short-acting recombinant factors)	0.32	-30.7	-10.8	<0.05	-27.2	-9.5	3855.66	-4.8
Haemophilia A (plasma derivatives)	0.31	-2.7	-6.2	<0.05	-3.9	-5.7	252.46	1.2
Haemophilia B (short-acting recombinant factors)	0.20	-17.7	-10.6	<0.05	-18.0	-10.7	378.91	0.4
Activated human antihemophilic prothrombin complex	0.16	33.8	-9.4	<0.05	31.9	-10.3	8496.29	1.5
Combination of coagulation factors (plasma derivatives)	0.08	7.4	11.3	<0.05	10.1	11.4	102.00	-2.4
Factor VII deficiency (plasma derivatives)	0.08	0.2	5.7	<0.05	-1.1	5.6	366.29	1.3
Von Willebrand disease (plasma derivatives)	0.06	14.2	2.2	<0.05	14.3	2.3	71.65	-0.1
Other deficiencies of coagulation factors (long-acting recombinant factors)	0.06	16.5	27.8	<0.05	16.5	25.6	15524.20	0.0
Other deficiencies of coagulation factors (plasma derivatives)	0.02	57.1	—	<0.05	39.8	—	6169.18	12.4
Haemophilia B (plasma derivatives)	0.01	-49.8	-9.8	<0.05	-52.3	-11.3	227.46	5.3
Coagulation factors	**9.40**	**1.7**	**2.3**	**0.1**	**2.0**	**2.4**	**404.20**	**-0.3**
emicizumab	1.91	20.7	—	<0.05	20.6	—	683.67	0.1
efmoroctocog alfa	1.05	-1.5	—	<0.05	-1.6	—	357.40	0.1
albutrepenonacog alfa	0.93	3.4	—	<0.05	11.8	—	979.96	-7.5
octocog alfa	0.88	-24.4	-13.3	<0.05	-22.9	-12.3	320.66	-1.8
damoctocog alfa pegol	0.79	19.8	—	<0.05	20.0	—	329.77	-0.1
pegylated turoctocog alfa	0.62	28.2	—	<0.05	30.3	—	254.47	-1.6
lonoctogoc alfa	0.37	-1.6	—	<0.05	-0.6	—	314.45	-1.0
rurioctocog alfa pegol	0.37	18.2	—	<0.05	17.8	—	307.97	0.3
moroctocog alfa	0.36	-18.8	-10.0	<0.05	-19.3	-9.0	327.04	0.6
eftrenonacog alfa	0.32	8.6	—	<0.05	8.8	—	668.14	-0.2

Figure 3.5.2a Coagulation factors, temporal trend 2014-2023 in per capita expenditure of most expensive subgroups



Regional data on consumption and expenditure

Table 3.5.2b Coagulation factors, regional trend in per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2022			2023			Δ % 23-22			CAGR % 14-23		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost
Piedmont	9.10	0.1	463.12	8.81	0.1	438.99	-3.2	2.1	-5.2	1.1	0.4	0.7
Valle d'Aosta	10.71	<0.05	662.27	7.07	<0.05	400.36	-33.9	9.3	-39.5	8.0	8.1	0.0
Lombardy	8.44	0.1	418.72	9.18	0.1	450.79	8.8	1.0	7.7	5.1	4.0	1.1
Province of Bolzano	6.21	0.1	334.97	7.26	0.1	335.29	17.0	16.9	0.1	2.3	2.3	0.0
Province of Trento	5.52	<0.05	346.49	6.17	<0.05	346.65	11.8	11.7	<0.05	3.3	3.7	-0.4
Veneto	8.16	0.1	396.34	7.94	0.1	402.57	-2.7	-4.2	1.6	5.3	4.0	1.2
Friuli V.G.	5.42	<0.05	587.14	5.35	<0.05	612.55	-1.3	-5.4	4.3	-5.1	-4.4	-0.8
Liguria	8.53	0.1	462.80	8.35	<0.05	461.20	-2.1	-1.8	-0.3	5.4	3.2	2.1
Emilia R.	10.72	0.1	422.94	10.09	0.1	394.77	-5.9	0.9	-6.7	5.2	6.4	-1.1
Tuscany	9.02	0.1	485.74	9.05	0.1	472.88	0.4	3.1	-2.6	2.3	3.1	-0.7
Umbria	6.94	<0.05	395.36	8.58	0.1	397.38	23.6	23.0	0.5	9.2	9.3	-0.1
Marche	7.46	<0.05	419.15	7.29	<0.05	417.84	-2.3	-2.0	-0.3	1.1	3.2	-2.0
Lazio	10.81	0.1	347.66	10.58	0.1	350.65	-2.2	-3.0	0.9	0.9	1.4	-0.5
Abruzzo	14.29	0.1	429.81	13.88	0.1	410.73	-2.8	1.7	-4.4	5.5	5.2	0.3
Molise	6.73	<0.05	378.05	8.63	0.1	364.89	28.2	32.9	-3.5	4.3	4.1	0.2
Campania	11.43	0.1	387.59	11.84	0.1	379.69	3.5	5.7	-2.0	0.2	1.5	-1.2
Puglia	9.71	0.1	391.48	10.03	0.1	393.88	3.2	2.6	0.6	0.2	0.4	-0.2
Basilicata	6.03	<0.05	400.69	6.09	<0.05	372.49	1.1	8.7	-7.0	-0.1	-0.8	0.8
Calabria	11.42	0.1	432.02	11.53	0.1	415.45	1.0	5.0	-3.8	2.3	1.7	0.6
Sicily	8.91	0.1	371.44	9.42	0.1	372.14	5.7	5.5	0.2	1.0	1.9	-0.8
Sardinia	5.36	<0.05	324.41	6.17	<0.05	352.75	14.9	5.7	8.7	0.8	-0.4	1.2
Italy	**9.24**	**0.1**	**405.26**	**9.40**	**0.1**	**404.20**	**1.7**	**2.0**	**-0.3**	**2.3**	**2.4**	**-0.1**
North	8.65	0.1	426.80	8.72	0.1	428.87	0.9	0.4	0.5	3.8	3.4	0.4
Centre	9.51	0.1	390.78	9.52	0.1	390.70	0.1	0.1	0.0	1.8	2.4	-0.6
South and Islands	9.93	0.1	389.30	10.31	0.1	384.93	3.8	5.0	-1.1	1.1	1.5	-0.5

3.5.3 Platelet aggregation inhibitors

In 2023, total public expenditure on platelet aggregation inhibitors was 339.1 million euros, down 1.6% compared to 2022, accounting for 1.3% of total public expenditure (Box Main indices of expenditure, consumption and exposure). The corresponding total consumption was 71.0 DDD/1000 inhabitants per day, 5.4% of the total consumption covered by the NHS, substantially stable in the period 2014-2023 (CAGR: +0.3%). Exposure to platelet aggregation inhibitors in the general population tends to increase with age for patients of both genders, reaching a higher prevalence of use in males aged 85 years or older (48.4%). In all age groups except those aged 15 to 44, males also consume more doses than females.

Over the last decade, consumption of the main categories with the highest expenditure has been substantially stable (Table 3.5.3a and Figure 3.5.3a). In particular, in 2023, acetylsalicylic acid alone or in combination remained stable both for per capita expenditure and for consumption (-0.2% and +0.3% respectively compared to 2022). Similarly, expenditure and consumption of platelet P2Y12 receptor inhibitors are stable compared to the previous year (+0.3% and +0.5%, respectively). As in the previous year, the category of glycoprotein IIb/IIIa inhibitors shows the greatest decrease in per capita expenditure and consumption (-18.5% and -16.2%, respectively).

Ticagrelor is the active ingredient with the greatest increase in the last ten years in terms of DDD/1000 inhabitants per day (CAGR: +7.8%), followed by clopidogrel and acetylsalicylic acid (CAGR: +5.6%). As regards the change in per capita expenditure compared to 2022, ticagrelor recorded a 4.9% decrease while clopidogrel a 4.5% increase (Table 3.5.3a). Treprostinil used in the treatment of chronic thromboembolic pulmonary hypertension showed the greatest reduction in per capita expenditure compared to 2022 (-16.8%) and substantial stability in consumption (+0.9%). Monoclonal antibodies for the treatment of episodes of acquired Thrombotic Thrombocytopenic Purpura (TTP), represented by caplacizumab, recorded a 9.2% reduction in per capita expenditure compared to the previous year, with an average cost per DDD among the highest in the category of 3402.90 euros. In line with previous years, the analysis on the consumption of platelet aggregation inhibitors confirms a preferential use of monotherapy or concomitant therapy based on clopidogrel and acetylsalicylic acid, compared to the fixed combination.

The prevalence of use of platelet aggregation inhibitors at national level is 9.1%, slightly higher in males (9.7%) than in females (8.5%),with a lower value in the North (7.4%) than in the Centre (10.3%) and in the South and Islands (10.8%). Nationally, 3.8% of users received only one prescription in the year, with a percentage ranging from 4.5% for acetylsalicylic acid alone and in combination to 31.5% for other platelet aggregation inhibitors. The median age of users is 75 years and each individual receives an average of 270.7 doses of the drug during the year with an average cost per user of 44.5 euros. Half of the population exposed at a national level is treated for at least 10 months in a year (Table 3.5.3b and Table 3.5.3c).

In 2023, the Region with the highest consumption recorded a value double than the one with the lowest consumption (Molise: 94.8 DDD vs. Province of Bolzano: 43.5 DDD/1000 inhabitants per day). Similarly, the Region with the highest expenditure recorded a value three times higher than the one with the lowest expenditure (Basilicata: 9.90 euros vs. Veneto: 3.20 euros). Compared to the previous year, the variations in consumption at the regional level are limited, and substantially stable. As regards per capita expenditure, Valle d'Aosta recorded the greatest increase (+21.4%) and a 21.6% increase in the average cost

per DDD while Umbria recorded the greatest decrease (-26.6%) and a 26.2% reduction in the average cost per DDD (Table 3.5.3c).

With regard to the adherence and persistence analyses, the data refer to a cohort of 162,843 new users (median age 72 years), 51.0% of whom were male, followed for one year (Figures 3.5.3b and 3.5.3c). In 2023, the percentage of subjects with high and low adherence to platelet aggregation inhibitors treatment was 62.0% and 6.8%, respectively. Low adherence is higher in females than males (7.3% vs 6.3%), while high adherence is greater in males than females (64.8% vs 59.1%). From a 2023-2022 comparison of the adherence data, general stability is observed (with some cases of slight increase) in the percentage of subjects with high adherence. Examining the last five years' data on adherence to treatment with platelet aggregation inhibitors in the population aged ≥45 years stratified by gender, the percentage of subjects with high adherence is consistently greater in males than females, contrary to subjects with low adherence, which is consistently higher in females.

Analysing the persistence to treatment (Figure 3.5.3d and 3.5.3e), more than half of the new users are persistent to treatment after one year (54.2%), with slightly lower percentages for the South (56.3%) compared to the Centre and the North (56.2% and 56.3%, respectively). Males show slightly higher rates of persistence than females (57.0% and 51.2%, respectively). The South (51.0%) shows a slightly lower percentage of individuals persisting at 12 months compared to the Centre (56.2%) and the North (56.3%).

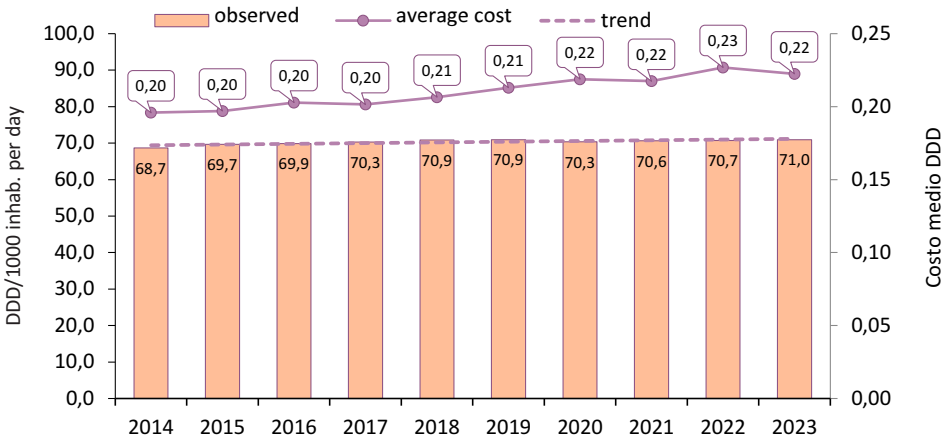
In general, both adherence and persistence to treatment with platelet aggregation inhibitors are suboptimal in the population with cardiovascular risk and further efforts should be supported to improve use in cardiovascular prevention.

For further information on regional data on exposure and duration of therapy and on indicators of adherence and persistence to treatment stratified by age, gender and geographical area, please refer to the supplementary documents published online.

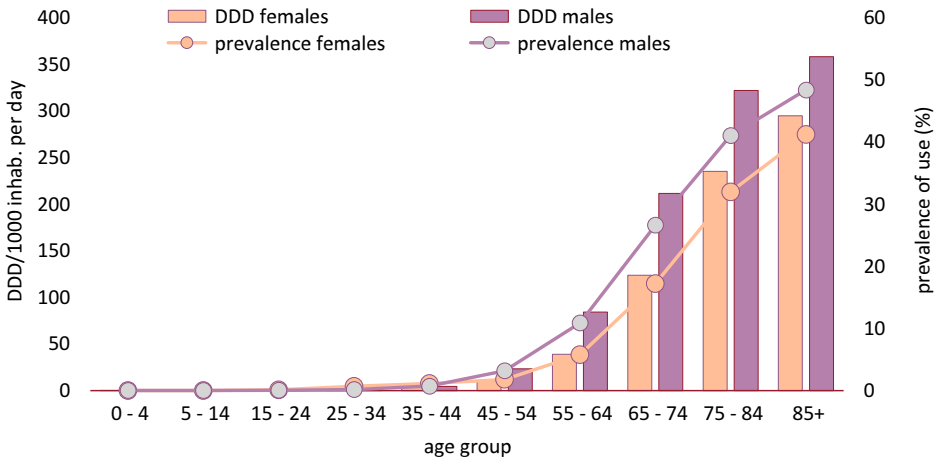
MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Platelet aggregation inhibitors

Public expenditure* in million euros (% over total)	**339.1**	**(1.3)**
Δ % 2023-2022		-1.6
Regional range of gross per capita expenditure:	3.2	9.9
DDD/1000 inhabitants per day* (% over total)	**71.0**	**(5.4)**
Δ % 2023-2022		0.3
Regional range DDD/1000 inhabitants per day	43.5	94.8

Platelet aggregation inhibitors, temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of platelet aggregation inhibitors under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.5.3a Platelet aggregation inhibitors, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
P2Y12 platelet receptor inhibitors	2.51	0.3	1.7	14.2	0.5	1.2	0.48	-0.1
Acetylsalicylic acid alone and in combination	1.44	-0.2	-0.5	54.5	0.3	<0.05	0.07	-0.4
Other platelet aggregation inhibitors	0.97	-6.1	1.7	<0.05	4.9	1.2	114.51	-10.5
Monoclonal antibodies for episodes of acquired TTP	0.50	-9.2	—	<0.05	-9.4	—	3402.90	0.2
Acetylsalicylic acid/clopidogrel	0.33	5.3	0.8	2.2	0.7	5.6	0.41	4.6
Glycoprotein IIb/IIIa inhibitors	0.02	-18.5	-20.0	<0.05	-16.2	-5.5	62.71	-2.8
Platelet aggregation inhibitors	**5.76**	**-1.6**	**1.6**	**71.0**	**0.3**	**0.3**	**0.22**	**-1.9**
clopidogrel	1.38	4.5	3.2	11.8	3.0	5.2	0.32	1.5
acetylsalicylic acid	1.21	0.7	1.1	47.3	0.9	0.8	0.07	-0.2
ticagrelor	0.92	-4.9	5.9	1.1	-2.8	7.8	2.29	-2.2
caplacizumab	0.50	-9.2	—	<0.05	-9.4	—	3402.90	0.2
treprostinil	0.46	-16.8	-0.5	<0.05	0.9	4.0	400.06	-17.6
selexipag	0.34	15.2	—	<0.05	17.7	—	107.39	-2.1
clopidogrel/acetylsalicylic acid	0.33	5.3	0.8	2.2	0.7	5.6	0.41	4.6
lysine acetylsalicylate	0.19	-2.5	-3.0	6.2	-1.8	-2.5	0.08	-0.7
iloprost	0.13	-8.1	-6.8	<0.05	10.5	-1.8	62.60	-16.8
ticlopidine	0.10	-16.6	-13.2	1.1	-16.6	-13.4	0.25	0.0

Figure 3.5.3a Platelet aggregation inhibitors, 2014-2023 temporal trend in consumption (DDD/1000 inhabitants per day) of highest-expenditure subgroups

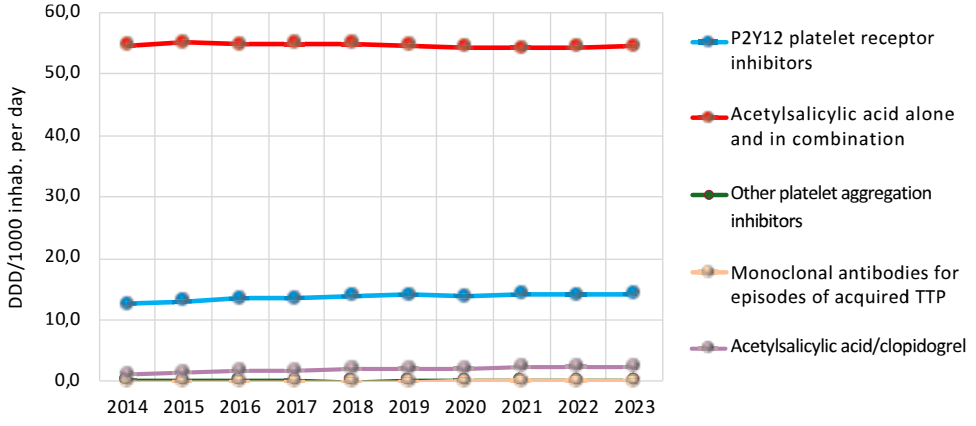


Table 3.5.3b Exposure and duration of therapy with platelet aggregation inhibitors by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Average cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
P2Y12 platelet receptor inhibitors	2.3	1.7	2.0	76	115.9	240.5	280.0	5.1
Acetylsalicylic acid alone and in combination	8.0	7.0	7.5	75	18.7	253.3	300.0	4.5
Other platelet aggregation inhibitors	0.0	0.0	0.0	76	1,023.0	104.4	60.0	31.5
Acetylsalicylic acid/clopidogrel	0.5	0.2	0.3	73	103.9	250.7	280.0	6.3
Platelet aggregation inhibitors	**9.7**	**8.5**	**9.1**	**75**	**44.5**	**270.7**	**300.0**	**3.8**

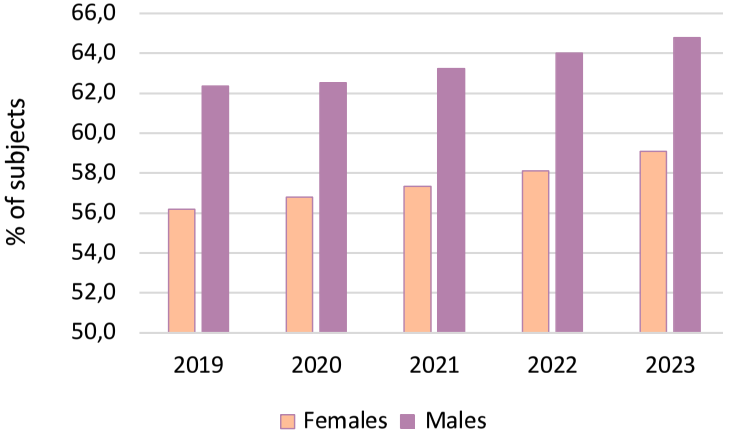
Table 3.5.3c Platelet aggregation inhibitors, regional trend in per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use	Cost/user	Median DDD
Piedmont	4.60	73.0	0.17	-2.4	0.9	-3.3	0.6	0.0	0.6	9.4	31.6	300.0
Valle d'Aosta	5.58	62.1	0.25	21.4	-0.1	21.6	3.4	-2.0	5.5	7.7	30.5	300.0
Lombardy	4.83	48.5	0.27	-6.0	-0.2	-5.9	1.4	-0.1	1.5	6.1	62.4	300.0
Province of Bolzano	3.52	43.5	0.22	-17.7	-1.3	-16.7	2.3	-1.5	3.8	5.0	44.5	300.0
Province of Trento	4.42	73.7	0.16	3.7	-1.5	5.2	-0.3	-0.3	-0.1	8.6	40.8	300.0
Veneto	3.20	46.6	0.19	1.5	0.0	1.5	-0.1	0.6	-0.6	5.5	39.6	300.0
Friuli V.G.	3.74	68.4	0.15	-3.6	-0.5	-3.1	-0.8	-1.2	0.5	8.8	29.9	300.0
Liguria	3.98	53.7	0.20	-9.2	-5.0	-4.4	0.5	-1.4	1.9	7.9	33.8	270.0
Emilia R.	4.50	83.2	0.15	-0.7	-0.6	-0.1	0.6	-0.5	1.1	9.9	26.3	300.0
Tuscany	6.45	76.3	0.23	18.3	0.0	18.3	3.3	-0.4	3.8	10.0	52.8	300.0
Umbria	4.57	74.2	0.17	-26.6	-0.5	-26.2	-0.4	-0.4	0.0	9.6	31.7	300.0
Marche	4.87	84.2	0.16	-1.3	-1.2	-0.2	2.6	0.6	2.0	11.0	33.5	300.0
Lazio	8.00	80.7	0.27	-3.9	0.4	-4.3	1.4	0.7	0.7	10.4	58.9	300.0
Abruzzo	8.84	91.9	0.26	-3.6	-0.3	-3.3	3.1	0.7	2.4	11.7	54.0	300.0
Molise	5.68	94.8	0.16	21.2	0.3	20.8	-1.2	0.7	-1.9	12.3	27.7	300.0
Campania	7.37	76.9	0.26	-2.6	1.1	-3.6	1.9	2.2	-0.3	10.2	42.9	270.0
Puglia	8.57	88.5	0.27	-0.9	1.2	-2.0	2.9	0.8	2.0	11.2	52.9	300.0
Basilicata	9.90	93.0	0.29	-0.4	2.1	-2.4	4.7	1.8	2.8	12.4	58.6	300.0
Calabria	9.12	88.0	0.28	-0.9	-1.0	0.1	6.2	0.7	5.5	12.0	57.3	300.0
Sicily	4.60	80.9	0.16	-0.3	4.0	-4.1	-1.3	1.1	-2.4	10.5	29.6	300.0
Sardinia	6.31	71.1	0.24	1.9	-1.1	3.0	3.4	-1.0	4.4	9.3	32.0	300.0
Italy	**5.76**	**71.0**	**0.22**	**-1.61**	**0.33**	**-1.9**	**1.6**	**0.3**	**1.3**	**9.1**	**44.5**	**300.0**
North	4.32	59.4	0.20	-3.59	-0.39	-3.2	0.8	-0.3	1.0	7.4	41.2	300.0
Centre	6.84	79.2	0.24	0.53	0.01	0.5	2.0	0.2	1.8	10.3	51.7	300.0
South and Islands	7.16	82.5	0.24	-1.04	1.31	-2.3	2.2	1.1	1.1	10.8	43.6	300.0

Adherence and persistence to treatment

Table 3.5.3b Indicators of low adherence to treatment with platelet aggregation inhibitors in the population aged ≥45 years stratified by gender, trend 2019-2023 (raw values)

Table 3.5.3c Indicators of high adherence to treatment with platelet aggregation inhibitors in the population aged ≥45 years stratified by gender, trend 2019-2023 (raw values).



*Adherence to treatment was evaluated only for new users with at least 2 prescriptions. Low adherence to treatment was defined as therapeutic coverage (assessed on the basis of DDD) <40% of the observation period while high adherence was defined as therapeutic coverage ≥80% of the observation period (for further details please refer to statistical methods)

Figure 3.5.3d Time (in days) to discontinuation of treatment with platelet aggregation inhibitors in the population aged ≥45 years stratified by geographical area; curves are adjusted by gender and age (the Cox model was used to estimate persistence curves)

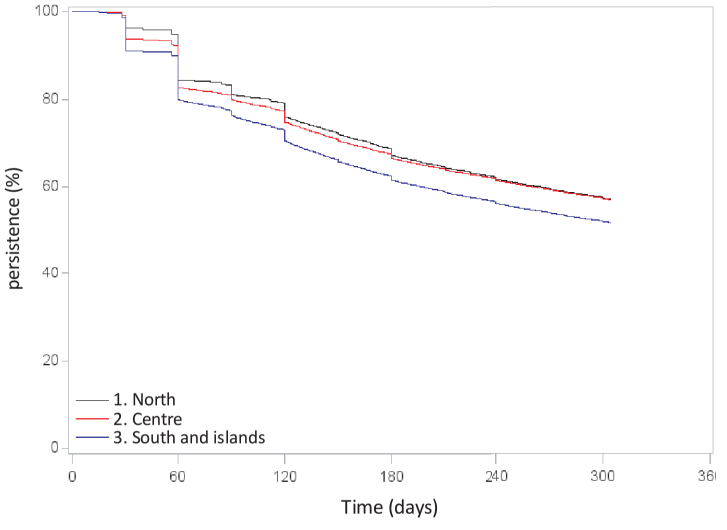
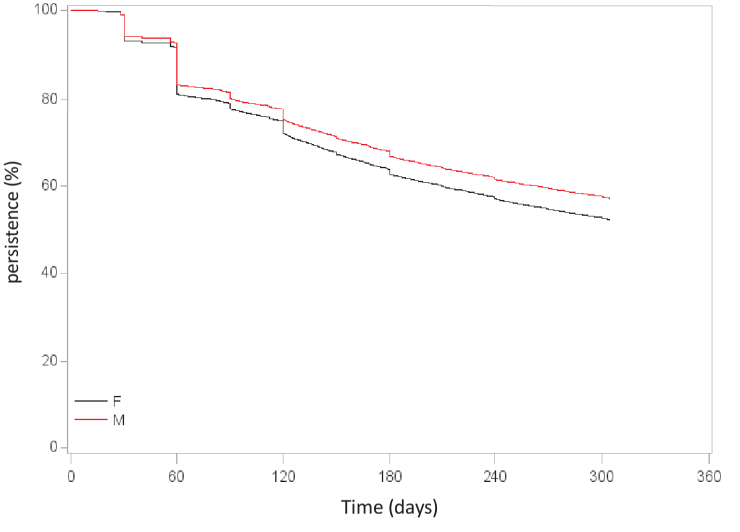


Figure 3.5.3e Time (in days) to discontinuation of treatment with platelet aggregation inhibitors in the population aged ≥45 years stratified by gender. Curves are adjusted by age (the Cox model was used to estimate persistence curves)



3.6 Central Nervous System

In 2023, medicines acting on the central nervous system (CNS) rank sixth among the categories with the highest public expenditure, with 2,061 million euros, equal to 7.9% of total public expenditure (Box Main indices of expenditure, consumption and exposure). Total per capita expenditure was 34.88 euros, up 3.9% compared to the previous year and mainly related to approved care regime (23.65 euros per capita), slightly down compared to 2022 (-0.6%). Expenditure by public health facilities was lower (11.23 euros per capita), but showed a more significant increase (+15.0%) compared to the previous year (Table 3.1).

As regards consumption covered by the NHS, this category of drugs confirms its fourth place with 97.79 DDD/1000 inhabitants per day, stable compared to 2022. Also in this case the highest consumption is recorded in the context of approved care regime with 71.80 DDD/1000 inhabitants per day, while purchase by public health facilities accounts for approximately a third of the total (25.99 DDD) (Table 3.2).

The analysis of the drug use profile by age group and gender in the context of community assistance (including approved care regime and distribution on behalf) confirms the constant increase in the use of central nervous system medicines with increasing age, for both genders, with a higher prevalence of use in women from 15 years of age, consistent with epidemiological data on the frequency of neurological and psychiatric diseases. The highest level of prevalence was reached in the over-75 age group, for both genders (44.14% for females and 32.35% for males) and expenditure (74.4 for females and 57.9 euros per capita for males). In the 5-14 years age group, in one year about one in 100 children received at least one prescription of central nervous system medicines, mainly antidepressants, antipsychotics, and antiepileptics.

As regards the approved care regime, per capita expenditure on central nervous system drugs was 23.65 euros. The change in expenditure compared to 2022 (-0.9%) was exclusively due to a reduction in prices (-2.9%), also confirmed by the 2.8% decrease in the average cost per day of therapy, while the consumption of these drugs increased by 1.9%, with a mix effect (+0.1%) that remained stable in 2023 (Table 3.9). Analysing the individual sub-categories, “other antidepressants”, “selective serotonin reuptake inhibitors (SSRIs)” and “other antiepileptics” have the greatest impact on expenditure, with 3.61 euros, 3.41 euros and 3.03 euros, respectively. SSRIs also have the highest levels of consumption with 31.1 DDD/1000 inhabitants per day, representing about half of the entire category (Table 3.9). All three subgroups show increases compared to 2022 in terms of consumption while in terms of expenditure, “other antiepileptics” showed a 5.9% decrease, due to a reduction in prices (-7.8%) which is also reflected in the decrease in the average cost per day of therapy (-8.1%).

Levetiracetam, pregabalin, fentanyl and tapentadol are the molecules with the greatest impact on expenditure in the category with values of 1.69 euros, 1.48 euros and 1.16 and 1.04 euros per capita respectively, an increase compared to the previous year for the first two (+1.1% and +8.8%) and a decrease for the other two (-9.6% and -1.1%) (Table 3.10). Levetiracetam and pregabalin are among the top thirty active ingredients in approved care expenditure in 2023, ranking eighteenth (99.6 million euros) and twenty-fifth (87.2 million euros) respectively (Table 3.11). As many as seven molecules (rotigotine, fentanyl, tapentadol, naloxone/oxycodone, quetiapine, levetiracetam and pregabalin) are among the active ingredients with the highest cost per day of therapy (Table 3.12), with values

ranging from a maximum of 5.17 euros per DDD for rotigotine to a minimum of 1.51 euros per DDD for pregabalin. Sertraline is the only active ingredient in the category that ranks fourteenth among the top thirty with the lowest average cost per day of therapy, with 0.25 euros (Table 3.13).

Quetiapine, vortioxetine, pregabalin and sertraline are instead the active ingredients belonging to the category with the greatest increase in approved care regime compared to 2022 (from +5.7% to +13.8%) (Table 3.14), while naloxone/oxycodone, fentanyl, rotigotine and paroxetine are among those with the greatest reduction in approved care expenditure (Table 3.15). Sertraline had the highest consumption in the category with 9.7 DDD/1000 inhabitants per day. It is also the only molecule to be included in the top thirty active ingredients with the highest consumption in the approved care regime (25th place in 2023) (Table 3.16).

As regards purchases by public health facilities, there was an increase in expenditure (+14.7%) but a reduction in consumption (-5.2%), with a greater propensity to use more expensive drugs (mix effect: +22.4%) and average cost per DDD +20.9%), although prices have decreased by 1.2% compared to the previous year (Table 3.17). The subgroup of "other nervous system drugs" records the highest expenditure value (3.26 euros per capita), up 62.4% compared to 2022, while "diazepines, oxazepines, thiazepines and oxepines" and "other antipsychotics" are the categories showing the highest consumption (3.5 and 3.0 DDD/1000 inhabitants per day), and a trend to use less expensive drugs (mix effect: -7.1% and -3.6% respectively). Tafamidis (18.6% of the category expenditure), aripiprazole and paliperidone were the molecules with the highest per capita expenditure in 2023 (2.09, 1.26 and 1.22 euros), the first two increasing by 85% and 8.8% compared to the previous year, while paliperidone recorded a 23.2% reduction (Table 3.18).

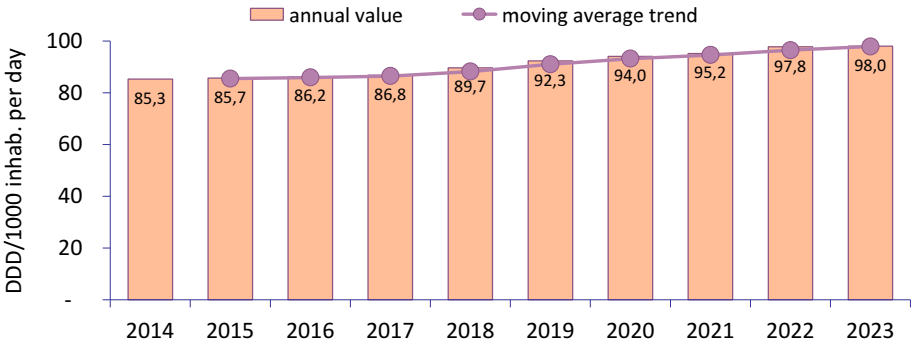
Tafamidis, indicated for the treatment of transthyretin amyloidosis in adult patients with stage 1 symptomatic polyneuropathy, to delay peripheral neurological impairment, is among the most expensive active ingredients purchased by public health facilities (123.2 million euros) and an average cost per day of therapy of 61.20 euros, accounting for 0.8% of total expenditure by public facilities (Table 3.19). Tafamidis and patisiran are the only drugs among the top 30 with the highest expenditure increase in 2023 (+85.0% and +33.9%) (Table 3.20). Paliperidone is on the list of the top 30 active ingredients with the greatest cost reduction (Table 3.21) and patisiran among the top 30 with the highest average cost per day of therapy (Table 3.22). Paracetamol, methadone, olanzapine, lidocaine and quetiapine are instead among the 30 most consumed molecules purchased by public health facilities (Table 3.24), with consumption ranging from 2.4 DDD for paracetamol to 1.5 DDD for quetiapine.

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

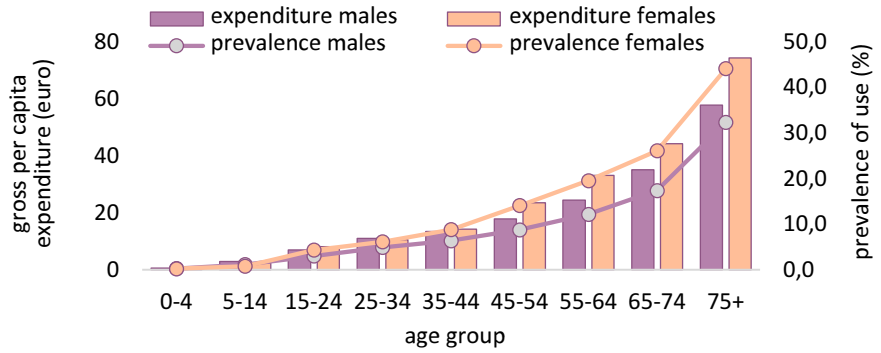
Central Nervous System

Public expenditure* in million euros (% over total)	**2,061.0**	**(7.9)**
Δ % 2023-2022		3.9
Regional range of gross per capita expenditure:	31.4	43.4
DDD/1000 inhabitants per day* (% over total)	**98.0**	**(7.4)**
Δ % 2023-2022		0.2
Regional range DDD/1000 inhabitants per day	84.5	123.0

** includes prescriptions under approved care regime and purchases by public health facilities*



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf by age and gender in 2023 (Figure and Table)



Age group	Gross per capita expenditure			DDD/1000 inhabitants per day		
	Males	Females	Total	Males	Females	Total
0-4	0.6	0.5	0.6	0.7	0.5	0.6
5-14	3.0	2.3	2.6	4.9	3.5	4.2
15-24	6.9	8.1	7.5	19.3	25.9	22.5
25-34	11.0	10.5	10.8	33.8	33.6	33.7
35-44	13.4	14.3	13.9	42.0	46.6	44.3
45-54	17.9	23.6	20.7	56.5	77.8	67.3
55-64	24.4	33.2	28.9	73.2	116.4	95.3
65-74	35.1	44.2	39.9	97.8	152.2	126.5
75+	57.9	74.4	67.6	165.1	238.3	208.4

3.6.1 Medicines for multiple sclerosis

Multiple sclerosis drugs recorded an expenditure of over 763 million euros in 2023, equal to approximately 3% of the total, with a slight but constant increase in consumption over time (CAGR: 1.4%), reaching 1.2 DDD in 2023, a 2.3% increase compared to 2022 (Box Main indices of expenditure, consumption and exposure).

Analyzing the expenditure and prevalence of use of drugs by gender and age group, it is confirmed, in line with epidemiological data, that these indicators increase with advancing age, with higher values in females than in males starting from the age of 45, until reaching a prevalence of use of 44.14% among women over seventy-five (32.35% in males) and a per capita expenditure of 74.39 euros (57.87 euros in males).

Over the last ten years, the average cost per day of therapy in the category has progressively increased to reach 30.7 euros in 2023, probably due to the marketing of new monoclonal antibodies which in 2023 accounted for 25% of the consumption of the entire category (0.3 DDD/1000 inhabitants per day) and recorded the highest average cost per DDD in the category (51.69 euros), impacting on total expenditure by over a third (5.16 out of 12.97 euros) (Table 3.6.1a) and recording the most significant increase in the period 2014-2023 (Figure 3.6.1b). Immunosuppressants also had a significant impact on per capita expenditure (2.93 euros) (albeit down 12.7% with respect to 2022), compared to reduced consumption levels (0.3 DDD/1000 inhabitants per day), up 2.3% compared to 2022. The categories that recorded expenditure reductions compared to 2022 are monoclonal antibodies (+20.4%), pyrimidine synthesis inhibitors (+19.8%) and other S1P receptor modulators (+95.6%), which however had the lowest consumption in the category (0.1 DDD).

Ocrelizumab is the most widely used drug (0.2 DDD) and has the greatest impact on per capita expenditure (2.68 euros) due to the average cost per day of therapy (44.72 euros), although the highest value is observed for ofatumumab, another monoclonal antibody recently introduced on the market, with an average cost per DDD of 1240.44 euros. However, the consumption levels of this active ingredient were negligible in 2023 (Table 3.6.1a).

In the South and Islands, consumption of drugs for multiple sclerosis is higher than the national average (1.4 vs 1.2 DDD), stable compared to 2022, while in the North and Centre they are similar but increasing (+2.7% and +6.8% respectively) (Table 3.6.1b).

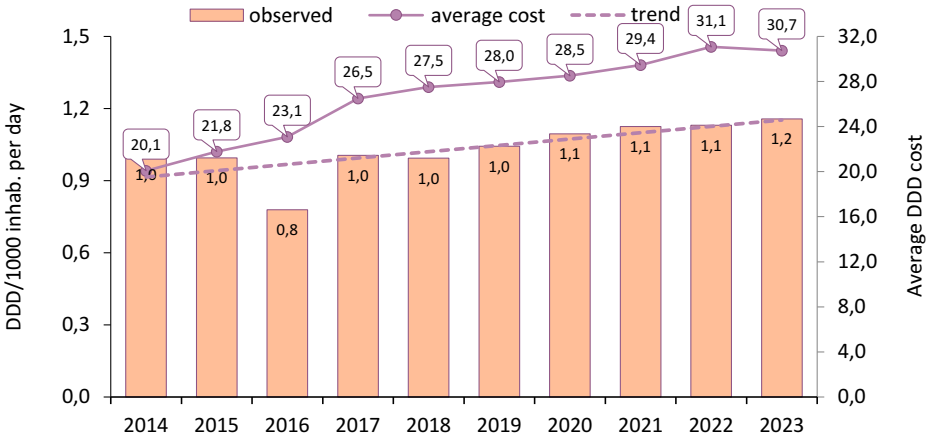
At the regional level, in line with the literature evidence on the prevalence of the pathology, the highest consumption was observed in Sardinia (2.6 DDD), up 2.6% compared to the previous year. Lombardy and Valle d'Aosta recorded the lowest consumption (0.8 DDD), less than half compared to Sardinia, but increasing compared to 2022 and with the most significant average annual increase (CAGR: +2.5%) after Piedmont (CAGR: +2.6%). Molise is the Region with the highest per capita expenditure (26.41 euros) after Sardinia (27.56 euros), due to both consumption levels higher than the national average (1.9 DDD/1000 inhabitants per day) and to the highest regional average cost (37.33 euros).

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

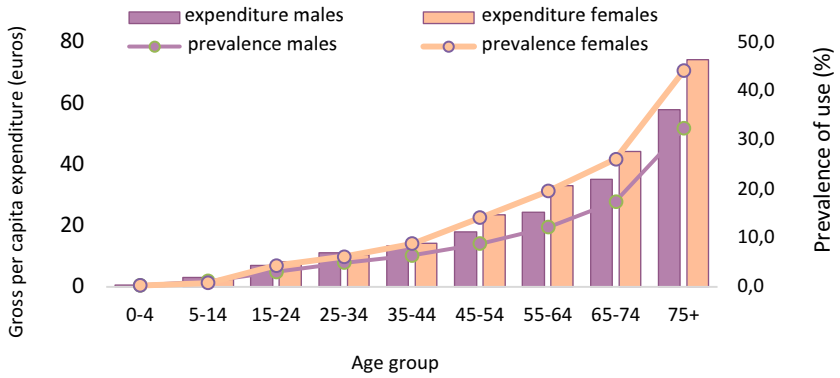
Medicines for multiple sclerosis

Public expenditure* in million euros (% over total)	**763.4**	**(2.9)**
Δ % 2023-2022		1.2
Regional range of gross per capita expenditure:	9.1	27.6
DDD/1000 inhabitants per day* (% over total)	**1.2**	**(0.1)**
Δ % 2023-2022		2.3
Regional range DDD/1000 inhabitants per day	0.8	2.6

Medicines for multiple sclerosis, temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of medicines for multiple sclerosis under approved care regime and distribution on behalf (year 2023)

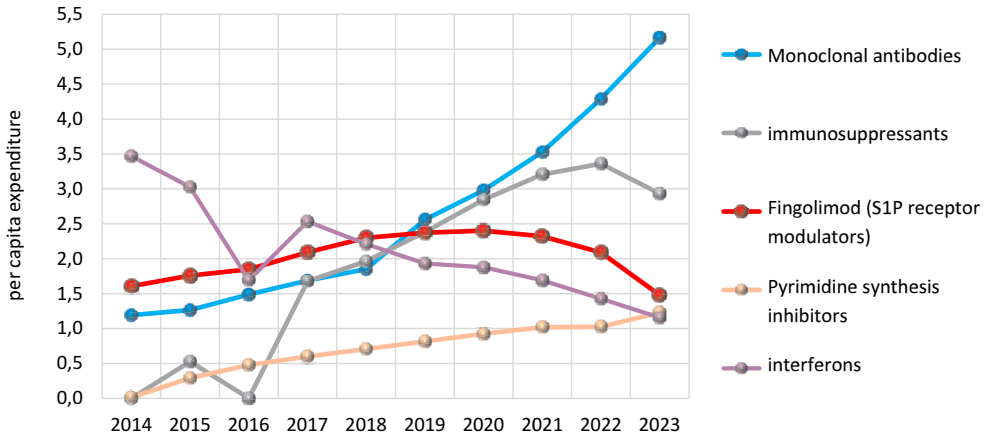


National data on consumption and expenditure by subgroup and substance

Table 3.6.1a Medicines for multiple sclerosis, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and by substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Monoclonal antibodies	5.16	20.4	15.8	0.3	14.3	17.0	51.69	5.3
Immunosuppressants	2.93	-12.7	—	0.3	2.3	—	29.65	-14.7
Fingolimod (S1P receptor modulators)	1.48	-29.2	-0.8	0.1	-12.3	2.7	43.23	-19.3
Pyrimidine synthesis inhibitors	1.23	19.8	54.8	0.1	27.2	56.7	24.72	-5.8
Interferons	1.16	-18.8	-10.4	0.3	-17.2	-10.5	12.65	-1.9
Other S1P receptor modulators	0.87	95.6	—	0.1	83.8	—	35.88	6.4
Glatiramer (AA copolymers)	0.14	-22.7	-18.5	0.1	-12.1	-5.6	6.06	-12.0
Medicines for multiple sclerosis	**12.97**	**1.2**	**5.8**	**1.2**	**2.3**	**1.4**	**30.74**	**-1.0**
ocrelizumab	2.68	19.7	—	0.2	21.0	—	44.72	-1.2
dimethyl fumarate	2.10	-18.0	—	0.2	2.0	—	25.88	-19.6
natalizumab	1.81	-4.4	4.3	0.1	4.4	6.6	45.83	-8.4
fingolimod	1.48	-29.2	-0.8	0.1	-12.3	2.7	43.23	-19.3
teriflunomide	1.23	19.8	54.8	0.1	27.2	56.7	24.72	-5.8
cladribine	0.83	4.0	—	<0.05	3.9	—	46.85	0.1
interferon beta 1a	0.80	-19.5	-12.6	0.2	-18.3	-11.4	10.60	-1.6
ofatumumab	0.63	>100	—	<0.05	>100	—	1240.44	1.1
siponimod	0.44	44.4	—	<0.05	40.9	—	31.76	2.4
ozanimod	0.34	>100	—	<0.05	>100	—	40.57	-3.3

Figure 3.6.1a Medicines for multiple sclerosis, temporal trend 2014-2023 of per capita expenditure of highest-expenditure subgroups



Regional data on expenditure, consumption and exposure

Table 3.6.1b Medicines for multiple sclerosis, regional trend in per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2022			2023			Δ % 23-22			CAGR % 14-23		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost
Piedmont	13.55	1.2	31.91	13.86	1.2	31.49	2.3	3.7	-1.3	6.7	2.6	4.0
Valle d'Aosta	10.54	0.8	34.98	10.28	0.8	33.16	-2.4	3.0	-5.2	4.7	2.5	2.2
Lombardy	9.23	0.8	32.62	9.11	0.8	31.78	-1.3	1.3	-2.6	6.4	2.5	3.8
Province of Bolzano	13.36	1.1	31.94	13.53	1.2	31.83	1.3	1.6	-0.4	5.5	2.0	3.4
Province of Trento	11.51	1.0	32.31	10.37	0.9	30.77	-9.9	-5.4	-4.8	5.6	1.4	4.2
Veneto	13.21	1.1	34.19	13.22	1.1	34.33	<0.05	-0.4	0.4	7.9	2.7	5.0
Friuli V.G.	12.61	1.2	28.96	13.53	1.3	29.36	7.2	5.8	1.4	5.4	1.2	4.1
Liguria	13.97	1.1	35.93	13.89	1.1	36.10	-0.6	-1.1	0.5	7.1	1.5	5.6
Emilia R.	12.08	1.1	30.50	12.88	1.2	29.90	6.6	8.7	-2.0	8.3	4.8	3.4
Tuscany	10.74	1.0	30.65	10.78	1.1	25.77	0.4	19.4	-15.9	4.2	1.1	3.1
Umbria	12.43	1.2	29.32	12.60	1.2	28.01	1.3	6.1	-4.5	5.7	0.8	4.9
Marche	12.75	1.2	28.47	12.42	1.2	29.17	-2.6	-5.0	2.5	5.0	0.8	4.2
Lazio	12.19	1.1	30.41	12.31	1.1	29.76	1.0	3.2	-2.1	4.4	<0.05	4.4
Abruzzo	17.53	1.4	33.67	17.63	1.4	33.39	0.6	1.4	-0.8	5.8	1.3	4.4
Molise	30.76	2.2	38.46	26.41	1.9	37.33	-14.1	-11.5	-2.9	13.1	5.8	6.9
Campania	13.01	1.1	32.00	13.37	1.1	33.71	2.8	-2.4	5.3	5.5	-0.6	6.2
Puglia	14.12	1.3	28.91	14.12	1.3	29.59	0.0	-2.3	2.4	4.5	-0.4	4.9
Basilicata	12.78	1.4	25.56	13.44	1.4	26.54	5.2	1.3	3.8	5.6	1.4	4.1
Calabria	12.78	1.1	31.02	13.19	1.1	32.60	3.2	-1.8	5.1	7.3	1.2	5.9
Sicily	13.33	1.3	28.00	13.93	1.3	28.60	4.5	2.3	2.2	5.0	1.3	3.7
Sardinia	27.57	2.5	29.72	27.56	2.6	28.96	<0.05	2.6	-2.6	3.9	1.2	2.8
Italy	**12.82**	**1.1**	**31.06**	**12.97**	**1.2**	**30.74**	**1.2**	**2.3**	**-1.0**	**5.8**	**1.4**	**4.4**
North	11.65	1.0	32.40	11.80	1.0	31.96	1.3	2.7	-1.4	7.0	2.7	4.1
Centre	11.81	1.1	30.10	11.85	1.1	28.27	0.3	6.8	-6.1	4.5	0.5	4.0
South and Islands	15.11	1.4	30.14	15.34	1.4	30.72	1.6	-0.3	1.9	5.3	0.6	4.6

3.6.2 Antidepressants

In 2023, antidepressants recorded a public expenditure of over 432 million euros (1.7% of the total) and consumption equal to 47.1 DDD/1000 inhabitants per day, a 3.1% increase compared to the previous year, while the average cost per DDD has remained stable since 2016 (Box Main indices of expenditure, consumption and exposure). In line with literature evidence, the consumption of these drugs in females is higher than in males with a gap increasing with age up to a difference of 65% in the +85 age group (157.44 vs 95.35 DDD). The prevalence of use also increases with age in both genders, reaching the highest values in the +85 age group, with values exceeding 28% in females and almost 20% in males.

In 2023, per capita expenditure was 7.35 euros, a 4.4% increase compared to 2022 (Table 3.6.2a). SSRIs account for approximately 69% (32.4 DDD) of consumption (an increase of 3.1% compared to 2022 and 1.8% since 2014) and 46.5% (3.42 euros per capita) of expenditure on the entire category (Table 3.6.2a and Figure 3.6.2a). Higher increases in consumption and expenditure were found for SNRIs (+2.6% and +3.7%), other antidepressants (+4.8% and +4.4%) and vortioxetine (+13.7% and +13.8%), a drug with an average cost per DDD almost three times higher than the average for the entire category (1.13 vs 0.43 euros). However, it is esketamine, an active ingredient introduced on the market in May 2022, a hospital-use medicine indicated in antidepressant therapy in association with an SSRI or SNRI, which records the highest average cost per DDD in the category (19.23 euros).

Paroxetine, with 0.97 euros per capita, down 2.4% compared to 2022, is confirmed as the molecule with the highest expenditure and in second place for consumption (8.2 DDD), preceded only by sertraline (10.3 DDD), recording a 5.8% increase compared to 2022. Bupropion is the molecule with the highest average cost per DDD (1.67 euros) despite limited levels of consumption and per capita expenditure (this drug is also indicated for the treatment of smoking cessation).

Among the categories, the prevalence of use stands at 4.4% for SSRIs in females, with a value more than double compared to males (5.9% vs 2.7%). This is followed by SNRIs and other antidepressants with 1.2% and 1.3% (Table 3.6.2b). Half of the users are older than 67 years. The average days of treatment per user range from a minimum of 63.4 for first-generation antidepressants (alone or in combination) to 256.2 for SSRIs. Half of SNRI users is treated for less than 6 months, rising to 7.3 months for SSRIs, and approximately one patient in five receives only one prescription for vortioxetine or “other antidepressants” in a year. This indicates that these drugs are often prescribed for clinical conditions not related to depression, which could be treated with non-pharmacological approaches.

The Centre has a level of use (52.7 DDD) that is 5% higher than the North (50.1 DDD) and 33% higher than the South (39.5 DDD) (Table 3.6.2c). Confirming this, Tuscany is the Italian region with the highest use and prevalence of use of antidepressant drugs, reaching 69.3 DDD/1000 inhabitants per day and 10.2% in 2023, values almost double than Basilicata (36.5 DDD) and Campania (5.4%). All Regions recorded increases in expenditure, consumption and average cost for DDD compared to the previous year, in particular Valle d’Aosta and Lombardy.

Adherence and persistence analyses of chronic treatments were evaluated considering a cohort of 128,934 new users (67% women) of antidepressant drugs aged at least 45 years and with a one-year follow-up. The results show that women have the most marked levels of low adherence compared to men (27.7% vs 27.1%), with values slightly decreasing

compared to 2022. On the contrary, men are apparently more adherent than women (Figure 3.6.2b and Figure 3.6.2c), and in this case the percentage increased compared to 2022.

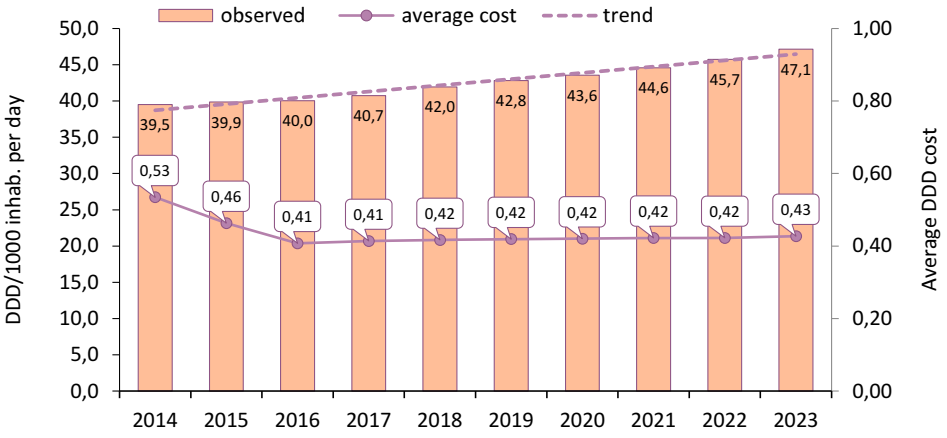
Analyzing treatment persistence at 12 months, only one subject out of three (34.0%) remained persistent, without marked differences between gender and geographical areas. Considering the median time to discontinuation of treatment, a probability of interrupting treatment equal to 50% is reached at approximately 143 days, similar to the data observed in 2022 (148 days) and with values between geographical areas ranging from 148 days for the North, to 145 days for the Centre and to 135 days for the South and Islands (Figure 3.6.2e). Men are slightly more persistent (148 days) than women (140 days) (Figure 3.6.2d). These data highlight the gap between the recommendations on the use of specific guidelines and current clinical practice. A specific public health training activity to improve treatment adherence should be defined and implemented.

For further information on regional data on exposure and duration of therapy and on indicators of adherence and persistence to treatment stratified by age, gender and geographical area, please refer to the supplementary material published online.

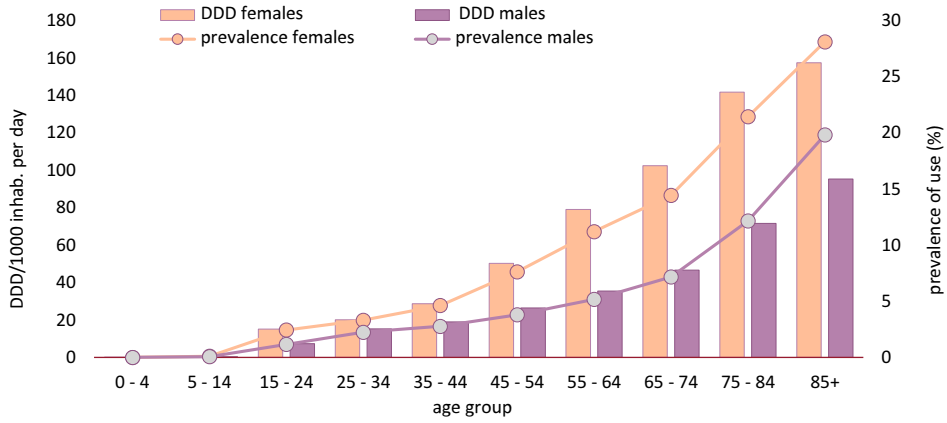
MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Antidepressants

Public expenditure* in million euros (% over total)	**432.7**	**(1.7)**
Δ % 2023-2022		4.4
Regional range of gross per capita expenditure:	5.9	9.9
DDD/1000 inhabitants per day* (% over total)	**47.1**	**(3.6)**
Δ % 2023-2022		3.1
Regional range DDD/1000 inhabitants per day	36.5	69.3

Antidepressants, temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of antidepressants under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.6.2a Antidepressants, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
SSRI antidepressants	3.42	0.6	-1.9	32.4	2.1	1.0	0.29	-1.5
SNRI antidepressants	1.68	2.6	-4.1	7.6	3.7	2.1	0.61	-1.0
Other antidepressants	1.05	4.8	2.6	3.8	4.4	3.2	0.76	0.4
Vortioxetine	0.94	13.7	—	2.3	13.8	—	1.13	0.0
First-generation antidepressants alone or in combination	0.16	0.3	-1.6	1.1	1.8	-0.9	0.41	-1.5
Esketamine	0.09	>100	—	<0.05	>100	—	19.23	51.9
Antidepressants	**7.35**	**4.4**	**-0.5**	**47.1**	**3.1**	**1.8**	**0.43**	**1.3**
paroxetine	0.97	-2.4	-2.3	8.2	<0.05	0.1	0.33	-2.4
escitalopram	0.97	0.1	-4.6	7.8	0.9	0.7	0.34	-0.8
vortioxetine	0.94	13.7	—	2.3	13.8	—	1.13	0.0
sertraline	0.87	5.5	3.0	10.3	5.8	3.6	0.23	-0.2
duloxetine	0.85	3.1	-7.3	3.6	3.9	2.9	0.65	-0.8
venlafaxine	0.84	2.2	0.9	4.0	3.5	1.5	0.57	-1.3
trazodone	0.48	5.5	5.0	1.4	6.0	5.6	0.91	-0.5
citalopram	0.39	-1.3	-2.1	4.1	-0.9	-1.7	0.26	-0.4
mirtazapine	0.37	3.2	1.9	2.0	2.9	2.4	0.50	0.3
bupropione	0.20	7.4	0.6	0.3	8.7	2.2	1.67	-1.2

Figure 3.6.2a Antidepressants, 2014-2023 temporal trend in consumption (DDD/1000 inhabitants per day) of highest-expenditure subgroups

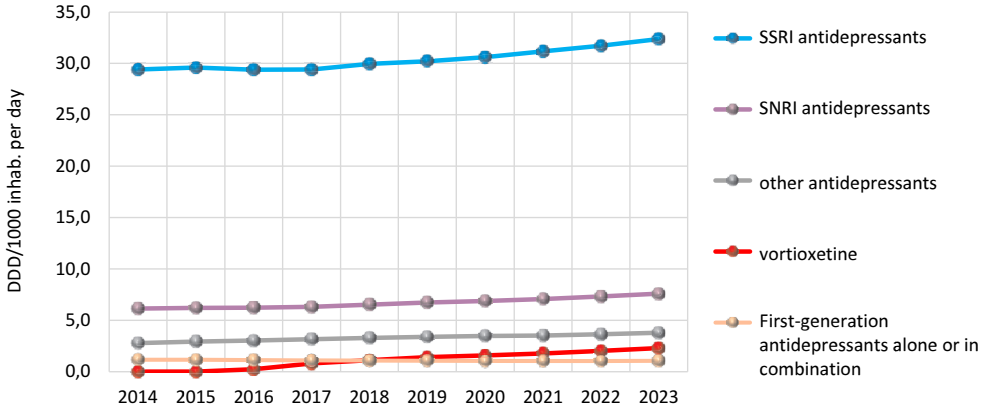


Table 3.6.2b Exposure and duration of therapy with antidepressants by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Average cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
SSRI antidepressants	2.7	5.9	4.4	66	76.9	256.2	224.0	10.4
SNRI antidepressants	0.7	1.7	1.2	66	136.0	216.8	182.0	8.4
Other antidepressants	1.0	1.6	1.3	77	77.4	94.1	54.0	19.9
Vortioxetine	0.3	0.5	0.4	71	212.3	186.4	126.0	19.0
1st generation antidepressants, alone or in combination	0.3	0.8	0.6	61	26.9	63.4	30.0	31.1
Antidepressants	**4.4**	**9.1**	**6.8**	**67**	**103.6**	**237.1**	**186.0**	**11.5**

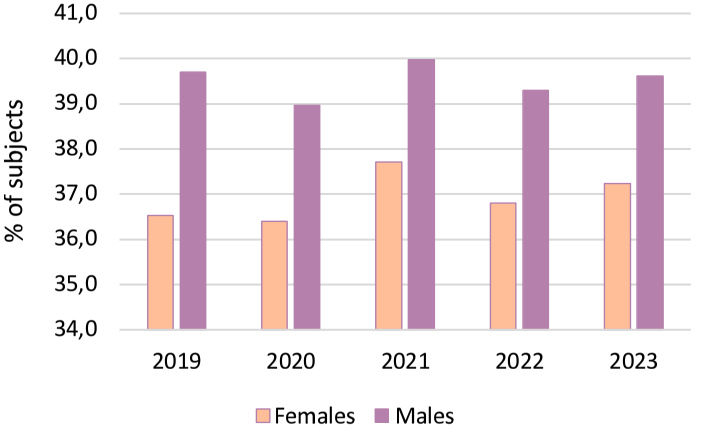
Regional data on expenditure, consumption and exposure

Table 3.6.2c Antidepressants, regional trend in per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use	Cost/user	Median DDD
Piedmont	7.93	54.5	0.40	4.8	3.9	0.9	-1.2	2.1	-3.2	8.1	98.0	196.0
Valle d'Aosta	8.22	47.0	0.48	17.0	4.6	11.9	0.3	1.9	-1.6	6.7	106.0	180.0
Lombardy	6.93	45.6	0.42	6.0	4.3	1.6	-0.3	2.2	-2.4	6.3	103.6	210.0
Province of Bolzano	9.32	60.3	0.42	3.3	1.8	1.5	-1.1	1.5	-2.5	6.9	119.5	224.0
Province of Trento	7.21	47.3	0.42	4.0	2.8	1.2	0.3	2.2	-1.9	6.4	105.9	182.0
Veneto	6.93	45.7	0.41	4.1	3.0	1.1	-0.4	2.0	-2.4	6.3	105.0	192.0
Friuli V.G.	5.88	40.2	0.40	4.4	2.6	1.8	-1.2	1.6	-2.8	6.1	98.8	180.0
Liguria	9.54	61.7	0.42	3.5	2.5	1.0	-0.7	1.4	-2.0	9.8	99.4	180.0
Emilia R.	7.89	58.1	0.37	3.1	1.7	1.4	-0.3	1.5	-1.7	7.7	97.9	196.0
Tuscany	9.86	69.3	0.39	2.8	2.5	0.4	-0.3	1.3	-1.6	10.2	96.2	196.0
Umbria	8.37	59.6	0.39	1.0	3.1	-2.0	-1.0	1.6	-2.5	8.6	97.2	196.0
Marche	7.96	48.9	0.45	3.7	3.0	0.7	-0.2	1.7	-1.9	7.5	106.9	196.0
Lazio	6.94	41.4	0.46	3.6	2.5	1.0	-0.9	1.6	-2.5	6.3	106.5	180.0
Abruzzo	8.29	46.4	0.49	6.3	3.2	3.0	1.0	2.3	-1.3	6.7	113.3	182.0
Molise	6.73	39.3	0.47	6.1	3.3	2.6	-0.6	1.7	-2.3	5.9	109.7	188.0
Campania	6.51	36.7	0.49	5.9	2.9	2.9	0.4	2.2	-1.7	5.4	108.7	180.0
Puglia	6.39	37.9	0.46	5.1	4.2	0.9	-0.3	2.1	-2.4	5.8	106.2	180.0
Basilicata	6.15	36.5	0.46	2.1	2.0	<0.05	0.0	1.7	-1.7	5.9	103.6	180.0
Calabria	7.16	42.7	0.46	3.2	2.6	0.6	-0.7	1.4	-2.1	6.7	103.8	180.0
Sicily	6.48	37.3	0.48	4.3	3.0	1.2	-0.4	1.8	-2.2	5.8	106.2	180.0
Sardinia	8.30	50.5	0.45	3.8	2.7	1.1	-1.1	1.4	-2.5	7.2	117.5	224.0
Italy	**7.35**	**47.1**	**0.43**	**4.4**	**3.1**	**1.3**	**-0.5**	**1.8**	**-2.2**	**6.8**	**103.6**	**186.0**
North	7.41	50.1	0.41	4.6	3.2	1.4	-0.6	1.9	-2.4	7.0	101.7	196.0
Centre	8.11	52.7	0.42	3.1	2.5	0.5	-0.6	1.4	-2.0	7.8	101.6	195.0
South and Islands	6.81	39.5	0.47	4.8	3.1	1.7	-0.2	1.9	-2.0	5.9	108.2	180.0

Figure 3.6.2b Indicators of low adherence to treatment with antidepressants in the population aged ≥45 years stratified by gender, trend 2019-2023

Figure 3.6.2c Indicators of high adherence to treatment with antidepressants in the population aged ≥45 years stratified by gender, trend 2019-2023



*Adherence to treatment was evaluated only for new users with at least 2 prescriptions. Low adherence to treatment was defined as therapeutic coverage (assessed by DDD) <40% of the observation period while high adherence was defined as therapeutic coverage ≥80% of the observation period (see statistical methods for further details).

Figure 3.6.2d Time (in days) to discontinuation of treatment with antidepressants in the population aged ≥45 years stratified by gender. Curves are adjusted by age (the Cox model was used to estimate persistence curves)

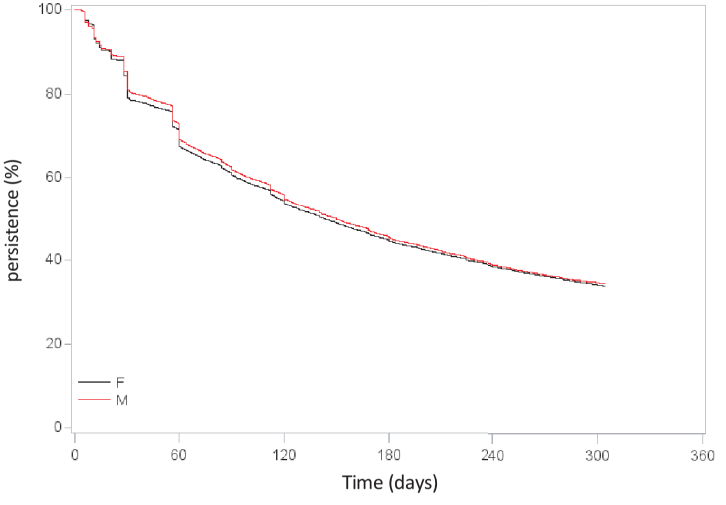
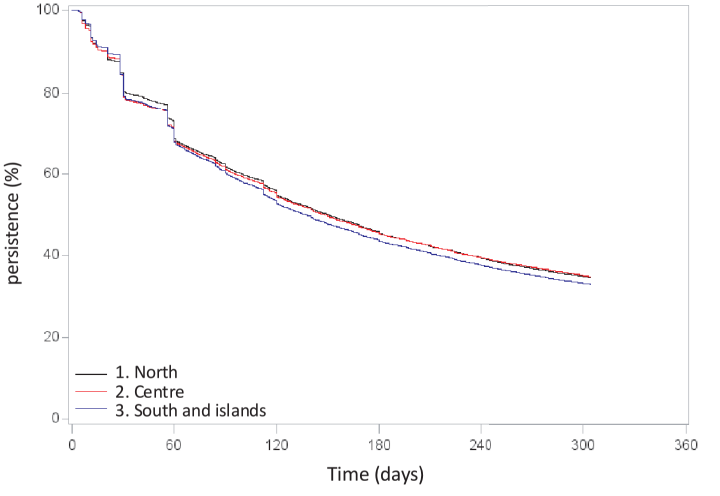


Figure 3.6.2e Time (in days) to discontinuation of treatment with antidepressants in the population aged ≥45 years stratified by geographical area. Curves are adjusted by gender and age (the Cox model was used to estimate persistence curves)



3.6.3 Medicines for pain therapy

(Includes pregabalin and gabapentin prescription for all authorized indications)

Medicines for pain therapy, with 359.8 million euros of public expenditure, account for 1.4% of total pharmaceutical expenditure. While this indicator shows a 2.6% reduction compared to 2022, consumption remains almost stable, equal to 8.1 DDD/1000 inhabitants per day in 2023 (Box Main indices of expenditure, consumption and exposure). With an average annual variation (CAGR) of +1.6%, the use of drugs for pain therapy has increased over the years from 6.9 DDD/1000 inhabitants per day in 2014 to 8.1 DDD in 2023 (Table 3.6.3a). The average cost per day of therapy decreased in 2018 and remained stable until 2021, and decreased to 2.07 euros in 2023 (-5.3% compared to 2022). As expected, these drugs showed an increase in consumption and prevalence of use with increasing age, with maximum values of these indicators in females over 85 years (35 DDD and 24.02%) compared to males of the same age (22.99 DDD and 18.23%).

Major opioids alone or in combination (consisting of oral, parenteral, transdermal and nasal opioids) represent approximately 40% of the expenditure on the entire category, with 2.43 euros per capita. Transdermal drug consumption increased by 17.4%, while oral and parenteral drugs remained stable or slightly increased (+0.4% and +1.4%, respectively) (Table 3.6.2a). Oral, nasal and transdermal fentanyl-based medicines show the highest average cost per day of therapy and reductions compared to 2022 ranging between 6.3% of transdermal and nasal preparations and 22.1% of oral ones. Confirming the high average cost per DDD (4.33 euros), the active ingredient fentanyl is in second place in terms of per capita expenditure (1.21 euros), after pregabalin (1.49 euros - per capita expenditure and 1.36 euros - average cost per DDD). Consumption of pregabalin (3.0 DDD) accounts for almost a third of the entire category. This active ingredient belongs to the group of drugs for neuropathic pain with the greatest consumption increase from 2014 to date (Figure 3.6.3a). Tapentadol has the highest average cost per day of therapy (4.86 euros), making it the third most expensive active ingredient per capita (1.05 euros). Finally, the increase in consumption of buprenorphine continues (+11.3%). Buprenorphine is also used as maintenance treatment within the scope of drug addiction services (Table 3.6.3a).

The prevalence of use of drugs used for pain therapy in the general population reached 5.4% in 2023, with a higher level in females (6.6%) than in males (4.1%), a difference that is maintained in all subgroups (Table 3.6.3b). For example, in the case of minor opioid drugs alone or in combination, this gap exceeds 60% (3.4% in females vs 2.1% in males). The median age of major oral opioids users is 73 years and is quite similar for all subgroups except transdermal preparations, which have a median age of 78 years. Fentanyl nasal preparations have the highest average cost per user, almost 20 times higher than the average for the entire category (1,938.9 vs. 107.9 euros). In most cases, with the exception of drugs for neuropathic pain (25.7 DDD) and transdermal fentanyl (22.5 DDD), half of users are treated for about a week. Partially confirming this is the high percentage of users with only one prescription in the year (33.1%). This data requires a clinical study on appropriateness to distinguish the treatment of oncological pain, shared and accepted in the long term, from non-oncological and/or neuropathic treatment.

At the regional level, the highest values of consumption are recorded in the North (9.3 DDD) rather than the Centre (8.2), similar to the national average, and in the South (6.3 DDD), all increasing compared to 2022 (Table 3.6.3c). In terms of prevalence of use, there are marked

regional differences, with values ranging from 7.0% in Piedmont to 3.7% in the Province of Bolzano. On average, each user was treated for 13.3 days, with the North reaching 14.0 days and the South 10.7 days. The average cost per user is similar in the Centre and the South, with values just under 100 euros, while in the North it reaches around 120 euros. The regional variability is even more evident, ranging from 80.4 euros in Tuscany to 150.2 euros in Friuli Venezia Giulia.

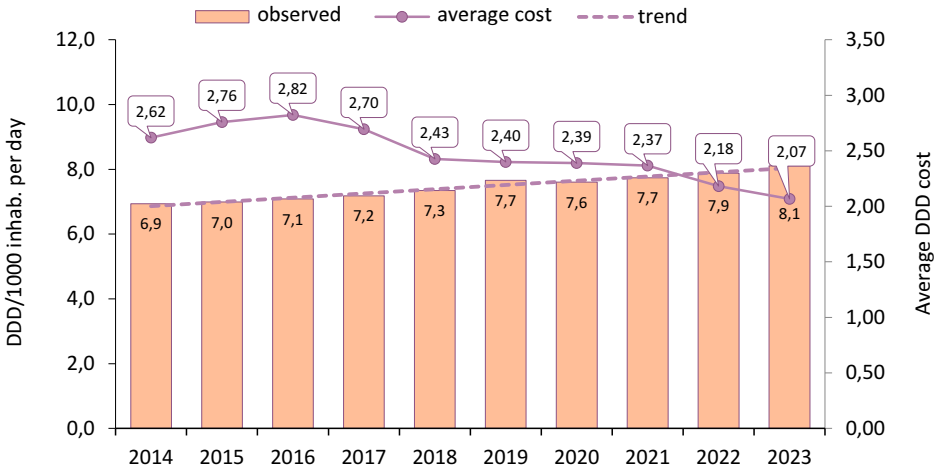
For further information on regional data on exposure and duration of therapy, please refer to the supplementary material published online.

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

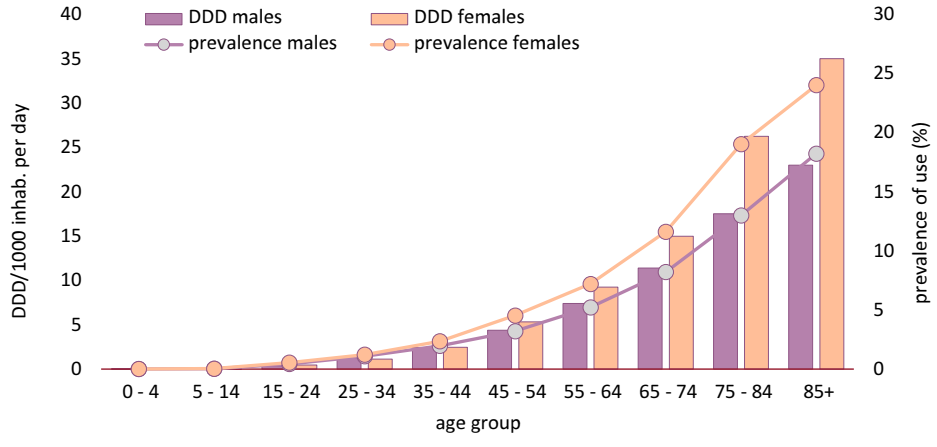
Pain therapy

Public expenditure* in million euros (% over total)	**359.8**	**(1.4)**
Δ % 2023-2022		-2.6
Regional range of gross per capita expenditure:	4.6	8.3
DDD/1000 inhabitants per day* (% over total)	**8.1**	**(0.6)**
Δ % 2023-2022		2.9
Regional range DDD/1000 inhabitants per day	5.6	11.0

Pain therapy, temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of medicines for pain therapy under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.6.3a Pain therapy, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Major opioids alone or in combination - oral	2.04	-8.7	0.2	1.6	0.4	2.6	3.57	-9.0
Medications for neuropathic pain	1.87	8.0	-3.0	3.6	9.5	5.0	1.42	-1.4
Minor opioids alone or in combination	0.60	-5.0	-3.9	1.8	-6.7	-3.4	0.92	1.9
Fentanyl - transdermal	0.53	-5.2	0.5	0.6	0.8	1.1	2.22	-5.9
Fentanyl - oral	0.37	-20.8	-0.9	0.1	-3.3	0.3	12.15	-18.1
Major opioids alone or in combination - transdermal	0.34	20.1	29.2	0.2	17.4	21.1	5.29	2.3
Fentanyl - nasal	0.31	-2.4	2.9	<0.05	3.7	3.5	25.45	-5.9
Major opioids alone or in combination - parenteral	0.05	-1.5	1.1	0.2	1.4	-3.4	0.64	-2.8
Pain therapy	**6.11**	**-2.6**	**-0.8**	**8.1**	**2.9**	**1.6**	**2.07**	**-5.3**
pregabalin	1.49	8.8	-3.8	3.0	10.6	5.8	1.36	-1.6
fentanyl	1.21	-10.0	0.6	0.8	0.4	1.1	4.33	-10.3
tapentadol	1.05	-1.6	6.1	0.6	3.4	8.8	4.86	-4.9
naloxone/oxycodone	0.53	-17.2	-2.9	0.4	-0.9	3.7	3.70	-16.5
buprenorphine	0.40	16.8	10.7	0.2	11.3	5.5	4.68	4.9
gabapentin	0.38	4.7	1.6	0.6	4.7	1.9	1.72	0.0
paracetamol/codeine	0.30	-1.1	-4.3	1.1	-1.6	-3.6	0.73	0.5
paracetamol/oxycodone	0.25	1.8	0.1	0.3	2.0	0.7	2.02	-0.2
tramadol	0.21	-12.1	-5.0	0.5	-16.7	-4.5	1.14	5.5
morphine	0.10	-1.9	-0.3	0.3	0.9	-3.1	1.05	-2.7

Figure 3.6.3a Pain therapy, 2014-2023 temporal trend in consumption (DDD/1000 inhabitants per day) of highest-expenditure subgroups

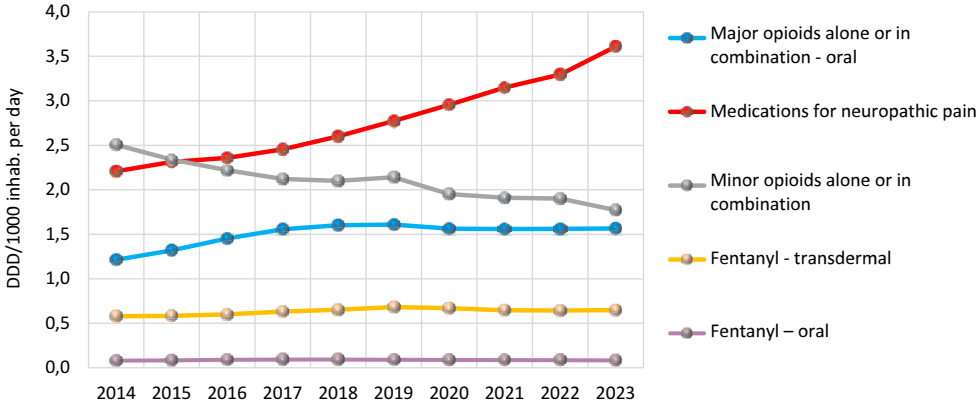


Table 3.6.3b Exposure and duration of therapy with medicines for pain therapy by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
Major opioids alone or in combination - oral	1.1	1.8	1.4	73	134.9	36.5	7.5	38.5
Medications for neuropathic pain	1.5	2.4	2.0	70	93.5	61.4	25.7	19.5
Minor opioids, alone or in combination	2.1	3.4	2.8	71	20.5	21.1	8.7	49.2
Fentanyl - transdermal	0.2	0.3	0.2	77	226.9	84.7	22.5	22.2
Fentanyl - oral	<0.05	<0.05	<0.05	69	840.3	62.4	7.3	33.2
Major opioids, alone or in combination - transdermal	0.2	0.4	0.3	78	115.5	21.5	8.4	38.1
Fentanyl - nasal	<0.05	<0.05	<0.05	71	1,938.9	74.7	5.3	44.6
Pain therapy	**4.1**	**6.6**	**5.4**	**71**	**107.9**	**48.2**	**13.3**	**33.1**

Regional data on expenditure, consumption and exposure

Table 3.6.3c Pain therapy, regional trend in per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use (%)	Cost/user	Median DDD
Piedmont	6.87	10.0	1.87	-2.1	3.3	-5.2	-1.4	1.7	-3.0	7.0	98.4	11.2
Valle d'Aosta	7.43	11.0	1.86	-2.6	6.9	-9.0	-2.6	1.5	-4.0	5.6	127.4	16.0
Lombardy	7.56	9.5	2.19	-3.5	2.9	-6.2	-0.5	2.0	-2.4	5.2	137.1	16.0
Province of Bolzano	5.69	8.4	1.86	-6.6	4.2	-10.4	-1.3	1.5	-2.7	3.7	129.1	14.9
Province of Trento	7.05	8.8	2.20	-1.4	2.0	-3.3	1.9	2.0	-0.1	5.5	120.0	10.7
Veneto	5.87	8.0	2.01	-2.8	1.5	-4.3	-0.6	1.4	-2.0	4.0	135.0	16.0
Friuli V.G.	8.31	9.8	2.32	-4.9	1.8	-6.5	-0.2	0.6	-0.8	5.6	150.2	15.0
Liguria	6.66	9.7	1.88	-6.6	0.0	-6.5	-1.2	1.4	-2.6	6.7	100.9	13.9
Emilia R.	5.87	9.5	1.70	4.6	6.6	-1.9	-0.5	1.0	-1.4	6.0	90.5	10.9
Tuscany	5.44	9.2	1.62	-6.2	1.1	-7.2	-2.7	0.0	-2.7	6.4	80.4	11.1
Umbria	5.34	7.9	1.85	-6.2	-0.1	-6.1	-2.0	1.8	-3.7	5.3	102.0	11.7
Marche	5.19	6.8	2.08	0.3	2.8	-2.5	-1.3	0.6	-1.9	5.1	99.1	11.2
Lazio	6.02	7.9	2.09	-3.4	2.3	-5.6	-1.3	2.0	-3.2	5.2	110.8	14.4
Abruzzo	5.83	6.7	2.37	-5.7	3.4	-8.9	0.8	2.2	-1.3	4.8	111.7	11.0
Molise	5.19	5.7	2.51	-9.5	0.9	-10.2	0.1	1.6	-1.5	4.7	109.9	10.7
Campania	4.59	5.7	2.20	-1.6	3.3	-4.7	-1.0	2.5	-3.4	4.9	86.7	10.7
Puglia	6.08	7.0	2.39	-0.6	3.5	-3.9	0.4	2.2	-1.7	6.2	93.9	10.7
Basilicata	5.03	7.1	1.93	1.4	3.5	-2.0	0.8	3.5	-2.6	6.1	80.6	10.7
Calabria	4.72	5.6	2.32	-3.0	2.9	-5.6	-0.8	1.5	-2.3	4.8	92.6	10.7
Sicily	5.20	6.0	2.38	-2.1	3.0	-4.9	-0.8	1.6	-2.4	4.8	105.0	11.2
Sardinia	7.24	8.3	2.39	-2.9	2.7	-5.4	0.2	2.0	-1.8	5.4	137.8	14.0
Italy	**6.11**	**8.1**	**2.07**	**-2.6**	**2.9**	**-5.3**	**-0.8**	**1.6**	**-2.3**	**5.4**	**107.9**	**13.3**
North	6.81	9.3	2.01	-2.4	3.1	-5.3	-0.7	1.5	-2.2	5.5	118.6	14.0
Centre	5.68	8.2	1.90	-4.1	1.7	-5.7	-1.8	1.0	-2.8	5.6	97.9	13.7
South and Islands	5.38	6.3	2.32	-2.1	3.1	-5.1	-0.3	2.1	-2.4	5.2	98.8	10.7

3.6.4 Anti-epileptics

(does not include pregabalin and gabapentin prescription)

In 2023, public expenditure on antiepileptic drugs was 332 million euros (1.3% of total expenditure), slightly decreasing compared to the previous year (-0.3%). As for consumption, on the other hand, increases were recorded (+1.5%) with values equal to 11.2 DDD in 2023, stable in the years starting from 2014 (Box Main indices of expenditure, consumption and exposure). As expected based on the epidemiology of the condition, exposure increases with age until reaching a 4.8% prevalence of use in people over 85 years with no gender differences. Slight gender difference is found in consumption, which is always higher in males than in females, with the gap reaching 20 DDD in the 25-34 age group. Second-generation antiepileptics, with 2.72 euros per capita, are the category with the highest expenditure, up 1.8% compared to 2022. They account for 48% of the entire category (Table 3.6.4a). This category, together with third-generation antiepileptics, has recorded the greatest increases in consumption since 2014, with an average annual variation (CAGR) of +3.9% and +18.1% (Figure 3.6.4b). The most widely used category is instead first-generation antiepileptics (6.1 DDD), even if they are down 1.4% compared to 2022 and have an average annual variation of -1.4%. Cannabidiol used in two forms of drug-resistant epilepsy (Dravet Syndrome and Lennox-Gastaut Syndrome) in combination with clobazam in patients aged 2 years and over, despite having the highest average cost per DDD (48.28 euros) in the category, is the drug that also records significant increases in expenditure (+66.5%) and consumption (+64%). Levetiracetam and valproic acid are confirmed, also in 2023, as the drugs with the highest expenditure (1.83 and 1.07 euros respectively) and consumption (2.8 and 2.7 DDD respectively) and increasing compared to 2022. In general, all the active ingredients in the category show consumption increases, except for topiramate and oxcarbazepine, which remain stable, and carbamazepine (-3.0%). The average cost of all drugs shows more or less marked reductions, going from -0.2% of lamotrigine to -41.4% of lacosamide, in the latter case due to the patent expiry of the molecule in September 2022 and to the marketing of equivalent medicines (Table 3.6.4a).

In 2023, 2.0% of the population was treated with antiepileptics, mainly first-generation ones. The median age of the users was 60 years and each subject was treated for 6 months on average, at a cost of 245.7 euros. Approximately one in ten users received only one prescription in a year and half of the users were treated for only 3.8 months. This probably indicates a prescription not in line with the main national and international guidelines on the treatment of epilepsy (Table 3.6.4b), which should always be pharmacologically controlled. There is a greater use of antiepileptics in the central-southern areas. In fact, the regions with the highest consumption are Tuscany (13.0 DDD) and Calabria (12.6 DDD), while the two with the lowest are Lombardy and Valle d'Aosta (just over 9 DDD) (Table 3.6.4c). Lazio and Tuscany record 93 and 90 days of median treatment against 168 days in Friuli Venezia Giulia. Compared to 2014, all Regions (with the exception of Valle d'Aosta) showed an average annual increase in both expenditure and consumption.

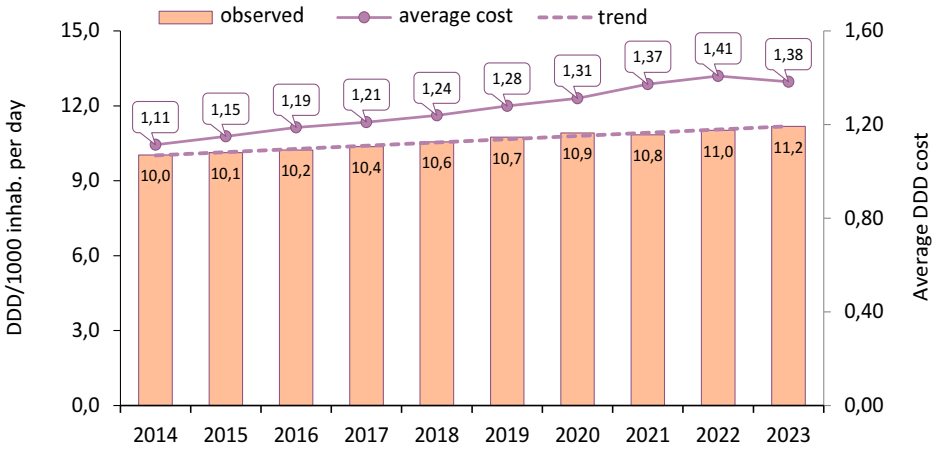
For further information on regional data on exposure and duration of therapy, please refer to the supplementary material published online.

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

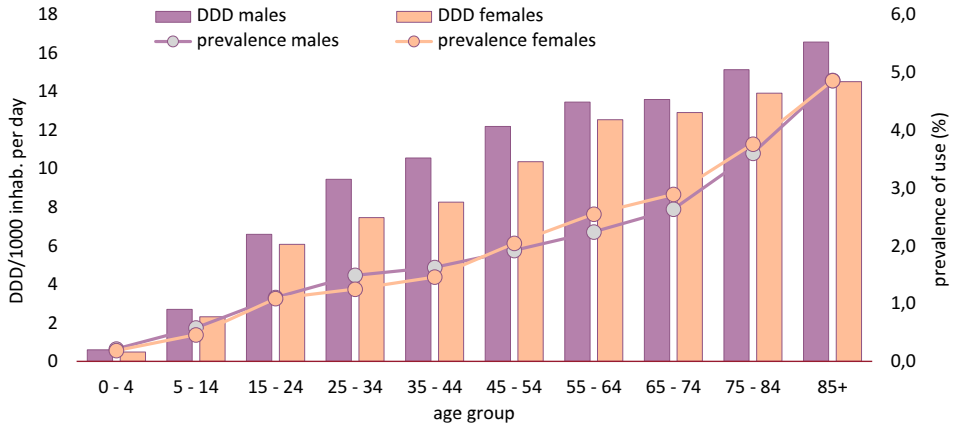
Anti-epileptics

Public expenditure* in million euros (% over total)	**332.0**	**(1.3)**
Δ % 2023-2022		-0.3
Regional range of gross per capita expenditure:	3.8	7.4
DDD/1000 inhabitants per day* (% over total)	**11.2**	**(0.8)**
Δ % 2023-2022		1.5
Regional range DDD/1000 inhabitants per day	9.1	13.0

Antiepileptics, temporal trend of consumption and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of antiepileptics under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.6.4a Antiepileptics, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Costo medio DDD	Average DDD cost
Second-generation antiepileptics	2.72	1.8	2.3	4.2	3.2	3.9	1.76	-1.3
First-generation antiepileptics	1.63	1.1	0.4	6.1	-1.4	-1.4	0.73	2.5
Third-generation antiepileptics	0.95	-22.8	10.9	0.8	10.6	18.1	3.26	-30.2
Cannabidiol	0.21	66.5	—	0.0	64.0	—	48.28	1.5
Other antiepileptics	0.13	726.0	—	<0.05	677.1	—	8.85	6.3
Anti-epileptics	**5.64**	**-0.3**	**3.3**	**11.2**	**1.5**	**1.1**	**1.38**	**-1.8**
levetiracetam	1.83	1.8	3.1	2.8	3.2	4.7	1.79	-1.4
valproic acid	1.07	3.6	1.7	2.7	3.5	1.3	1.09	0.1
lacosamide	0.55	-36.4	7.1	0.5	8.5	14.9	2.85	-41.4
lamotrigine	0.50	5.0	3.5	0.9	5.2	4.4	1.50	-0.2
topiramate	0.29	-1.8	-1.0	0.4	-0.1	-0.5	2.22	-1.7
carbamazepine	0.23	-5.1	-1.5	1.2	-3.0	-1.7	0.53	-2.1
cannabidiol	0.21	66.5	—	<0.05	64.0	—	48.28	1.5
oxcarbazepine	0.18	-1.8	-2.9	0.6	-0.4	-1.7	0.81	-1.4
perampanel	0.17	12.3	—	0.1	14.0	—	5.19	-1.5
brivaracetam	0.14	17.9	—	0.1	19.4	—	2.88	-1.2

Figure 3.6.4a Anti-epileptics, 2014-2023 temporal trend in consumption (DDD/1000 inhabitants per day) of highest-expenditure subgroups

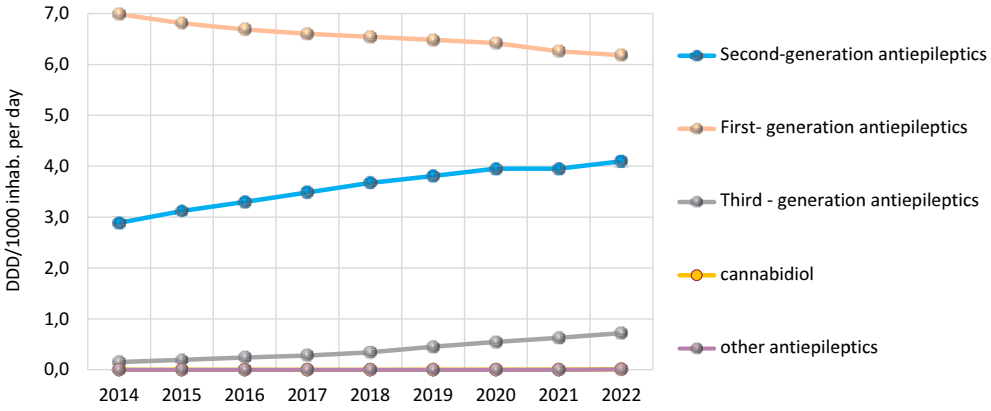


Table 3.6.4b Exposure and duration of therapy with anti-epileptics by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
Second-generation anti-epileptics	0.6	0.9	0.7	58	358.7	194.3	140.0	8.1
First-generation anti-epileptics	1.4	1.4	1.4	59	108.9	143.4	90.0	9.6
Third-generation anti-epileptics	0.1	0.1	0.1	57	790.3	263.1	224.0	5.2
Other antiepileptics	<0.05	<0.05	<0.05	42	1,013.0	204.5	169.3	4.4
Anti-epileptics	**1.9**	**2.1**	**2.0**	**60**	**245.7**	**183.4**	**114.0**	**8.8**

Table 3.6.4c Anti-epileptics, regional trend in per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use (%)	Cost/user	Median DDD
Piedmont	5.39	11.0	1.35	-2.8	0.8	-3.5	3.1	1.2	1.8	1.8	269.0	130.0
Valle d'Aosta	4.40	9.2	1.32	0.9	0.2	0.7	3.2	-0.2	3.4	1.4	274.0	140.0
Lombardy	5.18	9.1	1.57	-0.1	1.5	-1.5	3.8	1.1	2.7	1.5	301.5	128.0
Province of Bolzano	6.04	10.5	1.57	1.4	0.5	0.9	2.3	1.2	1.1	1.3	354.8	149.3
Province of Trento	5.44	10.5	1.41	-3.1	-1.0	-2.1	3.1	-0.1	3.2	1.8	261.1	120.0
Veneto	5.48	10.3	1.46	1.7	2.4	-0.6	4.2	1.1	3.1	1.4	330.7	160.0
Friuli V.G.	5.23	10.3	1.39	-2.5	0.4	-2.8	3.8	0.9	2.9	1.4	338.6	168.0
Liguria	5.79	11.6	1.37	2.2	1.8	0.4	3.5	1.0	2.5	2.3	221.8	100.0
Emilia R.	3.79	10.9	0.96	-2.5	2.8	-5.2	2.0	1.0	1.0	1.7	145.3	96.9
Tuscany	4.00	13.0	0.84	-10.3	2.6	-12.5	2.3	1.6	0.7	2.6	122.6	90.0
Umbria	5.70	12.6	1.24	-1.7	1.5	-3.2	4.1	0.9	3.1	2.0	258.8	121.3
Marche	6.89	12.4	1.53	1.7	1.5	0.2	4.1	0.8	3.2	2.2	274.8	120.0
Lazio	6.45	11.7	1.50	1.7	0.9	0.8	3.4	1.0	2.4	2.4	229.4	93.3
Abruzzo	7.37	12.5	1.62	4.8	0.6	4.1	3.3	0.8	2.5	2.2	268.2	110.0
Molise	5.35	11.4	1.28	-3.7	-0.8	-2.9	2.8	0.8	2.0	2.2	227.2	106.0
Campania	6.67	12.1	1.52	1.3	1.4	-0.1	3.5	1.1	2.4	2.1	275.1	120.0
Puglia	6.11	11.6	1.44	0.6	2.0	-1.4	2.8	1.2	1.6	2.1	255.6	118.8
Basilicata	6.26	12.4	1.38	-1.6	0.5	-2.1	2.8	1.0	1.7	2.4	238.3	116.0
Calabria	6.89	12.6	1.50	-0.6	0.5	-1.1	3.5	1.2	2.3	2.5	243.7	100.0
Sicily	6.19	11.8	1.44	-0.2	1.9	-2.1	3.1	1.5	1.6	2.3	240.1	102.0
Sardinia	5.73	11.8	1.33	-0.5	-0.6	0.1	2.3	0.5	1.8	2.6	213.2	100.0
Italy	**5.64**	**11.2**	**1.38**	**-0.3**	**1.5**	**-1.8**	**3.3**	**1.1**	**2.2**	**2.0**	**245.7**	**114.0**
North	5.10	10.1	1.38	-0.5	1.6	-2.1	3.4	1.0	2.4	1.6	268.6	121.9
Centre	5.67	12.3	1.26	-1.5	1.6	-3.0	3.3	1.2	2.2	2.4	200.4	100.0
South and Islands	6.40	12.0	1.46	0.6	1.2	-0.7	3.1	1.1	2.0	2.3	251.6	110.0

3.6.5 Antipsychotics

In 2023, public expenditure on antipsychotic drugs was just over 296 million euros (1.1% of total expenditure), down 2.8% compared to the previous year (Box Main indices of expenditure, consumption and exposure). From 2014 to 2023, consumption of antipsychotic drugs increased on average by 2.3% each year, going from 8.4 to 10.6 DDD (+1.5% compared to 2022). In line with the epidemiology of the clinical conditions in which antipsychotics are used, the prevalence of use increases with age, reaching 11.1% in females and 8.9% in males in the age group over 85 years. However, when analyzing consumption by gender, levels are higher in males than in females, but only up to the age of 64, after which the trend reverses, reaching a peak in females over 85 (13.41 vs 9.17 DDD).

"Atypical and other antipsychotics" remain the category with the highest expenditure (4.52 euros per capita, equal to 83% of the total) and the highest consumption (8.1 DDD, 76% of the total), with an increase (+1.4%) compared to 2022 only for this last indicator (Table 3.6.5a). This subgroup is the only one recording a consumption increase over the years (Figure 3.6.5b). "Atypical antipsychotics and others - lurasidone" have the highest cost per day of therapy and are five times higher than the cost of typical antipsychotics (2.14 vs 0.37 euros) (Table 3.6.5a).

Also in 2023, aripiprazole and paliperidone are in the first two places in terms of expenditure (1.39 and 1.26 euros respectively), with an increase compared to the previous year of 7.9% for the former and a significant reduction of 22.7% for the latter. Despite a reduced consumption in terms of prescribed doses, 1.5 and 0.9 DDD, the cost of both is due to a high average cost per day of therapy (2.58 and 3.69 euros, respectively).

In 2023, the prevalence of use of antipsychotic drugs in Italy was 1.9%, with the highest value for atypical and other antipsychotics, particularly in females (Table 3.6.5b). The median age of the population using antipsychotic drugs is 66 years and on average, each user is treated for just over 4 months (129.6 days), while half of the users are treated for only 56 days. 11.5% of the users receive a single prescription, with a higher percentage in those receiving typical antipsychotics (17.5%). These data are consistent with clinical context information on the widespread inappropriate and off-label use of these drugs in people with dementia. Furthermore, these data indicate that a non-negligible proportion of patients may experience significant side effects, particularly related to ideation and extrapyramidal disorders (e.g. dystonia, tremor, tardive dyskinesia), or that patients with schizophrenia do not respond to conventional antipsychotics.

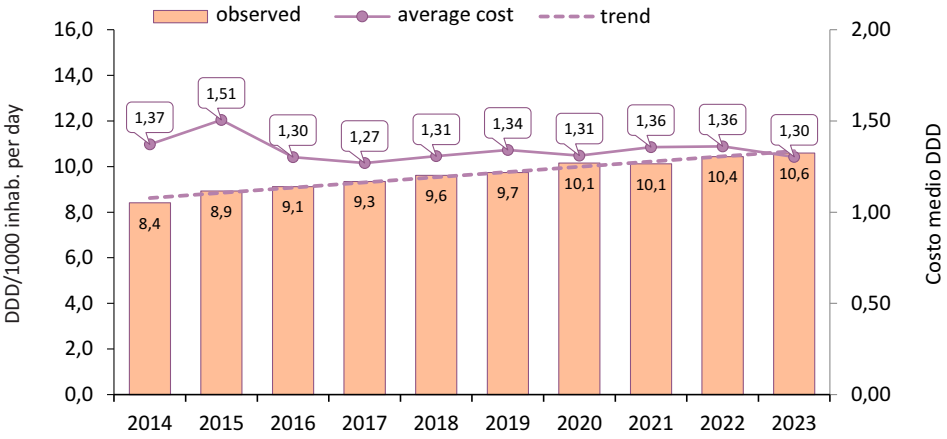
The average annual cost for each user is 110.4 euros, with large differences between geographical areas; indeed, the Centre records a lower cost (77.7 euros) compared to the South (106.4 euros) and the North (132.7 euros). In detail, Lombardy has a cost per user that is almost six times higher than Liguria (232.2 vs 40.6 euros). Half of the users in Liguria are treated for only one month while the longest duration is found in Puglia and Basilicata (median DDD 70 days) (Table 3.6.5c).

For further information on regional data on exposure and duration of therapy, please refer to the supplementary documents published online.

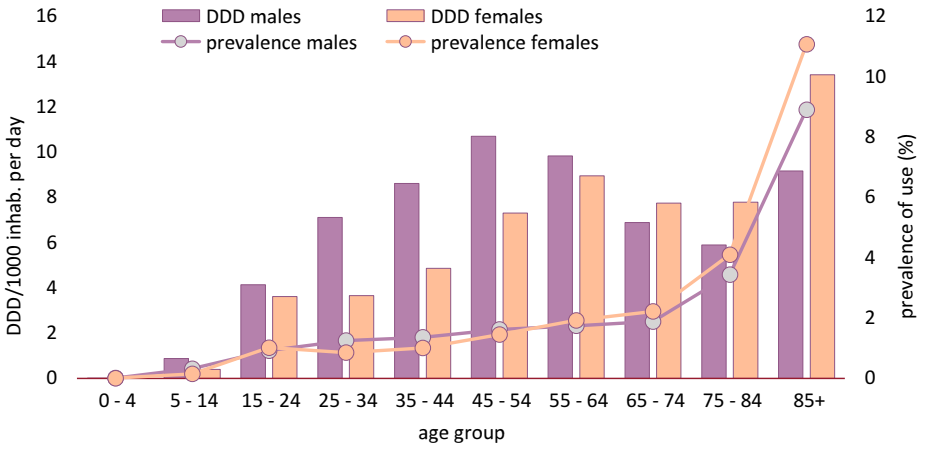
MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Antipsychotics

Public expenditure* in million euros (% over total)	**296.4**	**(1.1)**
Δ % 2023-2022		-2.8
Regional range of gross per capita expenditure:	3.1	7.9
DDD/1000 inhabitants per day* (% over total)	**10.6**	**(0.8)**
Δ % 2023-2022		1.5
Regional range DDD/1000 inhabitants per day	8.8	14.8

Antipsychotics, temporal trend of consumption and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of antipsychotics under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.6.5a Antipsychotics, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Atypical and other antipsychotics	4.52	-4.0	1.5	8.1	1.4	3.5	1.53	-5.3
Typical antipsychotics	0.31	2.4	-0.2	2.2	-0.7	-1.9	0.39	3.1
Atypical and other antipsychotics - lurasidone	0.16	14.8	—	0.2	19.7	—	2.14	-4.1
Atypical and other antipsychotics - brexpiprazole	0.05	51.8	—	0.1	52.4	—	1.55	-0.4
Antipsychotics	**5.04**	**-2.8**	**1.8**	**10.6**	**1.5**	**2.3**	**1.30**	**-4.2**
aripiprazole	1.39	7.9	10.2	1.5	2.6	18.4	2.58	5.2
paliperidone	1.26	-22.7	4.6	0.9	3.8	8.5	3.69	-25.5
quetiapine	0.84	12.5	-1.9	2.0	1.2	1.7	1.15	11.1
olanzapine	0.40	4.8	0.0	2.2	0.4	1.5	0.50	4.4
risperidon	0.34	-5.8	-6.6	0.9	0.1	-0.2	1.10	-5.8
clozapine	0.16	0.3	1.2	0.5	2.7	1.6	0.95	-2.3
lurasidone	0.16	14.8	—	0.2	19.7	—	2.14	-4.1
lithium	0.08	12.7	1.8	0.4	2.6	0.6	0.59	9.9
haloperidol	0.08	-1.1	-0.3	1.1	-0.5	-0.3	0.19	-0.6
amisulpride	0.06	-1.8	-2.6	0.1	-1.2	-2.4	1.62	-0.7

Figure 3.6.5a Antipsychotics, 2014-2023 temporal trend in consumption (DDD/1000 inhabitants per day) of highest-expenditure subgroups

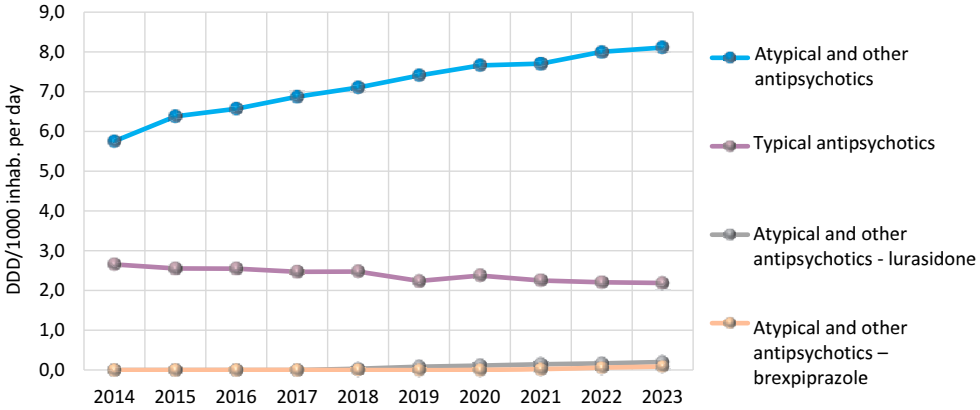


Table 3.6.5b Exposure and duration of therapy with antipsychotics by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
Atypical and other antipsychotics - others	1.4	1.7	1.6	67	106.9	120.5	52.5	11.3
Typical antipsychotics	0.4	0.5	0.4	61	41.3	92.6	45.0	17.5
Atypical and other antipsychotics - lurasidone	<0.05	<0.05	<0.05	47	428.4	194.3	112.2	15.4
Atypical and other antipsychotics - brexpiprazole	<0.05	<0.05	<0.05	45	218.9	126.1	74.7	12.8
Antipsychotics	**1.7**	**2.0**	**1.9**	**66**	**110.4**	**129.6**	**56.0**	**11.5**

Regional data on expenditure, consumption and exposure

Table 3.6.5c Antipsychotics, regional trend in per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use	Cost/user	Median DDD
Piedmont	3.13	10.6	0.80	-13.9	3.3	-16.6	-1.5	2.1	-3.5	1.7	49.5	48.8
Valle d'Aosta	3.44	9.7	0.97	-13.7	7.8	-19.9	3.0	4.2	-1.1	1.5	48.2	56.0
Lombardy	6.89	8.8	2.14	-0.6	2.9	-3.4	4.8	3.0	1.8	1.8	232.2	56.0
Province of Bolzano	5.47	10.5	1.43	-0.2	6.5	-6.3	3.5	1.9	1.6	1.4	102.7	45.0
Province of Trento	3.72	10.1	1.01	10.9	2.1	8.7	5.0	3.8	1.2	1.6	96.0	54.4
Veneto	3.86	10.2	1.04	-4.8	1.6	-6.4	0.1	1.3	-1.2	1.3	88.5	60.0
Friuli V.G.	3.50	10.2	0.94	7.2	2.9	4.2	1.5	1.5	-0.1	1.4	60.8	31.9
Liguria	4.32	10.9	1.08	4.9	5.0	-0.1	0.3	3.1	-2.7	2.1	40.6	38.8
Emilia R.	3.83	11.0	0.95	0.6	1.2	-0.6	-0.1	1.6	-1.7	1.3	54.1	48.0
Tuscany	4.33	11.0	1.08	-8.4	3.8	-11.8	4.9	3.1	1.8	2.1	84.4	45.0
Umbria	4.05	11.4	0.97	-8.9	-2.1	-6.9	1.4	3.2	-1.7	1.8	44.7	37.5
Marche	6.05	11.6	1.43	-0.9	-1.2	0.3	2.4	3.7	-1.2	2.1	63.2	57.9
Lazio	4.81	10.7	1.24	1.9	-1.5	3.5	2.2	2.9	-0.6	2.2	81.0	56.0
Abruzzo	7.85	10.6	2.02	-1.0	-0.6	-0.3	0.4	1.5	-1.2	2.3	176.2	56.0
Molise	3.60	10.3	0.96	-14.1	0.6	-14.6	-4.2	1.0	-5.2	2.1	66.3	50.6
Campania	4.95	9.9	1.36	-7.0	3.2	-9.9	1.9	2.1	-0.1	1.7	94.5	60.0
Puglia	6.79	12.2	1.52	-11.5	1.9	-13.1	3.5	2.9	0.6	2.0	149.1	70.0
Basilicata	6.86	11.6	1.62	-5.4	-2.6	-2.8	3.2	2.7	0.4	2.2	157.0	70.0
Calabria	4.77	10.8	1.21	2.3	-4.5	7.1	-1.0	1.7	-2.7	2.0	83.8	66.7
Sicily	3.95	11.1	0.97	-5.1	-0.4	-4.8	-2.2	1.5	-3.7	2.1	62.3	67.5
Sardinia	7.12	14.8	1.32	23.6	4.3	18.5	1.2	2.7	-1.4	3.0	118.4	57.5
Italy	**5.04**	**10.6**	**1.30**	**-2.8**	**1.5**	**-4.2**	**1.8**	**2.3**	**-0.5**	**1.9**	**110.4**	**56.0**
North	4.85	10.0	1.33	-1.9	2.6	-4.4	2.2	2.2	<0.05	1.6	132.7	50.0
Centre	4.76	10.9	1.19	-2.5	0.1	-2.6	2.9	3.1	-0.1	2.1	77.7	50.6
South and Islands	5.47	11.3	1.33	-4.0	1.0	-4.9	0.8	2.1	-1.2	2.0	106.4	61.9

3.6.6 Anti-Parkinson medicines

In 2023, the consumption of anti-Parkinson drugs reached 5.7 DDD/1000 inhabitants per day, stable (+0.4%) compared to 2022 and with an average annual increase of 0.6% between 2014 and 2023 (Box Main expenditure, consumption, exposure indices). Public expenditure on these drugs, which account for 0.8% of the total, is 201.9 million euros, up 0.5% compared to 2022.

Epidemiological data on Parkinson's disease indicate that, in general, the disease occurs after the age of 60, although about 10% of patients are around 40 years. Parkinson's disease is neurodegenerative and progressive. The prevalence data of drug use and consumption show a clear increase with age, reaching 5.4% in men over 85 years compared to women of the same age (4.1%). Men show greater use in the age groups starting from 45 years with differences in consumption compared to women ranging between 60% and 80% (31.7 DDD vs 19.6 DDD in the extreme age groups).

As regards the categories, dopa-derived agonists, alone or in combination, were again the most widely used in 2023, with 2.4 DDD (42% of all antiparkinsonians) and 1.28 euros of per capita expenditure (+1.0% and +1.9%, respectively, compared to 2022), followed by dopamine agonists, down 4.2% in terms of doses and 4.8% in terms of expenditure. COMT inhibitors, despite representing a small share of consumption (0.2 DDD), continue to increase significantly (+13.8% of consumption and +13.0% of expenditure) and for both indicators the average annual increase between 2014 and 2023 records values just under 20% (Table 3.6.6a). MAO inhibitors had a 4.0% average annual increase in doses compared to 2014 (going from 1.1 to 1.7 DDD), while dopamine agonists in the same period showed a 3.6% increase (Figure 3.6.6b). On average, each day of therapy costs 1.64 euros (-0.9% compared to 2014), with values ranging from 0.26 euros for anticholinergics to 3.90 euros for COMTs (Table 3.6.6a).

The most commonly consumed active ingredients are levodopa and benserazide in combination (1.1 DDD), selegiline and the levodopa/carbidopa combination, both with 1.0 DDD. As already observed in 2022, the increase in opicapone consumption continues (+15.0%). This substance was the latest molecule to be marketed in the COMT inhibitor class and, due to its prolonged action, it allows for single daily administration. The molecules with the highest cost per day of therapy (still covered by patent) are rotigotine (5.05 euros, available as a transdermal patch), safinamide (4.11 euros) and opicapone (3.88 euros) (Table 3.6.6a).

The total prevalence of use of anti-Parkinson drugs in the Italian population in 2023 is 0.8%. Dopa-derivatives alone or in combination have a 0.5% prevalence of use, while dopamine agonists have a 0.3% prevalence. For these two categories there is a difference of 4 years in the median age of users (80 vs 76), just over a month in days of treatment (6 months vs 4.5), of 224 euros in the average cost per user (160.3 vs 384.4 euros) and 3.7% for users with only one prescription (5.5% vs 9.2%). Approximately one in 100 people was treated with anti-Parkinson drugs in 2023 (0.8%). Half of the users are over 77 years old and, on average, each subject has been in treatment for just over 8 months, with an expenditure per user of 361.6 euros (Table 3.6.6b).

The Centre (6.2 DDD) and the South (6.1 DDD) show higher consumption than the North (5.4 DDD). The Centre also has a higher average cost per DDD and per capita expenditure (1.74

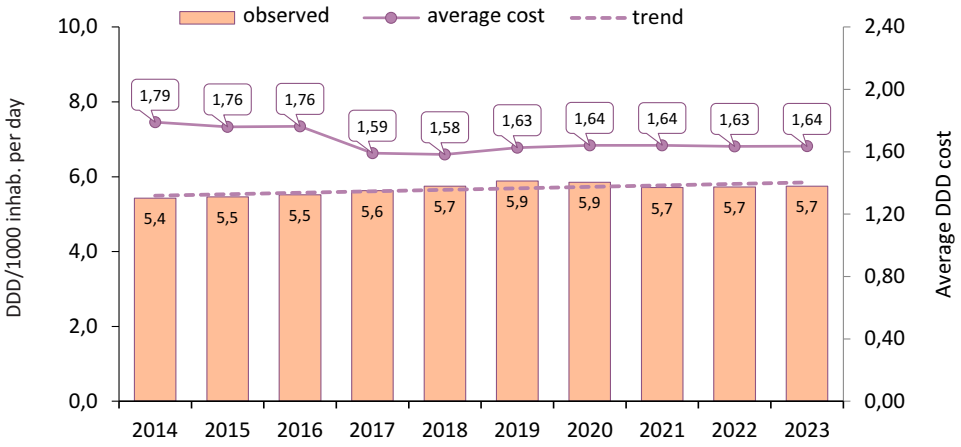
euros and 3.94 euros respectively) than the South (1.60 euros and 3.57 euros respectively) and the North (1.60 euros and 3.13 euros respectively) (Table 3.6.6c). The regional variability, in terms of consumption, ranges from 4.0 DDD in the Province of Bolzano to a maximum of 6.9 DDD in Abruzzo. Molise is the only region that recorded an consumption increase by more than 2% compared to the previous year, while the Province of Bolzano recorded reductions of just under 3%. Sardinia has an average cost per DDD that is almost double than Emilia Romagna (1.91 vs 1.11 euros). A wide regional variability is also found in the cost per user, which in Emilia-Romagna has values approximately 60% lower than Valle d'Aosta (197.4 vs 480 euros). This difference may depend on both the distribution channel (direct purchase vs approved care regime) and the effect of different competitive biddings, when the distribution channel is the same. It should also be underlined that half of the subjects were treated for less than 4 months and 8.2% received only one prescription in the year with large regional differences.

For further information on regional data on exposure and duration of therapy, please refer to the supplementary material published online.

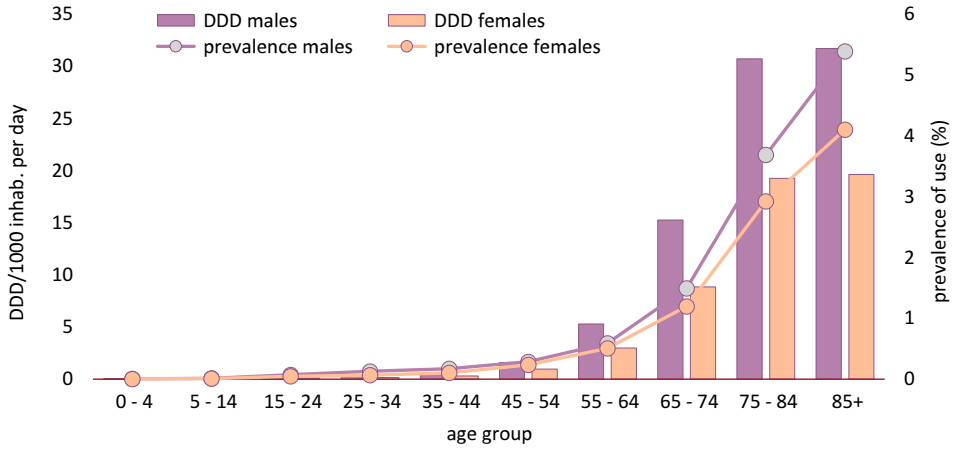
MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Antiparkinson medicines

Public expenditure* in million euros (% over total)	**201.9**	**(0.8)**
Δ % 2023-2022		0.5
Regional range of gross per capita expenditure:	2.1	4.8
DDD/1000 inhabitants per day* (% over total)	**5.7**	**(0.4)**
Δ % 2023-2022		0.4
Regional range DDD/1000 inhabitants per day	4.0	6.9

Anti-Parkinson medicines, temporal trend of consumption and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of anti-Parkinson medicines under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.6.6a Anti-Parkinson medicines, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
DOPA-derived agonists alone or in combination	1.28	1.9	0.5	2.4	1.0	0.6	1.47	0.9
Dopamine-agonists	1.05	-4.8	-2.7	1.0	-4.2	-3.6	2.81	-0.6
MAO inhibitors	0.81	2.0	-0.5	1.7	1.2	4.0	1.32	0.8
COMT inhibitors	0.25	13.0	18.1	0.2	13.8	19.8	3.90	-0.7
Anticholinergics	0.04	0.5	-1.2	0.5	0.5	-1.1	0.26	-0.1
Amantadine	<0.005	-16.7	-4.6	<0.05	-19.7	-10.7	0.77	3.7
Anti-Parkinson medicines	**3.43**	**0.5**	**-0.3**	**5.7**	**0.4**	**0.6**	**1.64**	**0.1**
levodopa/carbidopa	0.72	3.3	3.8	1.0	2.9	1.3	2.03	0.4
rotigotine	0.57	-9.1	-1.3	0.3	-6.6	-0.8	5.05	-2.6
safinamide	0.43	3.3	—	0.3	5.7	—	4.11	-2.2
levodopa/benserazide	0.38	3.9	2.8	1.1	2.3	2.2	0.93	1.6
pramipexole	0.37	-0.7	-3.2	0.5	-1.9	-2.5	2.19	1.2
rasagiline	0.27	0.9	-9.9	0.4	1.0	-1.7	2.03	0.0
opicapone	0.24	14.3	—	0.2	15.0	—	3.88	-0.6
melevodopa/carbidopa	0.15	-4.0	0.8	0.2	-4.2	<0.05	1.83	0.2
selegiline	0.12	-0.2	2.7	1.0	0.1	4.0	0.31	-0.3
ropinirole	0.08	-6.4	-8.0	0.2	-6.2	-7.5	0.96	-0.2

Figure 3.6.6a Anti-Parkinson medicines, 2014-2023 temporal trend in consumption (DDD/1000 inhabitants per day) by highest-expenditure subgroups

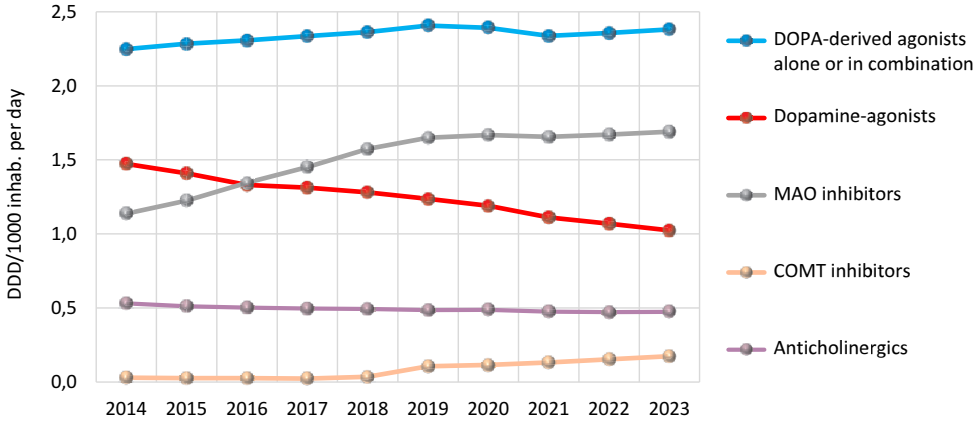


Table 3.6.6b Exposure and duration of therapy with anti-Parkinson medicines by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
DOPA-derived agonists alone or in combination	0.5	0.4	0.5	80	160.3	173.5	136.7	5.5
Dopamine-agonists	0.2	0.3	0.3	76	384.4	136.1	57.0	9.2
MAO inhibitors	0.2	0.1	0.2	77	479.3	361.8	336.0	7.2
COMT inhibitors	<0.05	<0.05	<0.05	73	968.9	239.2	270.0	8.3
Anticholinergics	0.1	0.1	0.1	58	29.2	103.3	84.0	14.5
Amantadine	<0.05	<0.05	<0.05	72	152.0	155.1	120.0	25.7
Antiparkinson medicines	**0.8**	**0.8**	**0.8**	**77**	**361.6**	**252.1**	**126.7**	**8.2**

Regional data on expenditure, consumption and exposure

Table 3.6.6c Anti-Parkinson medicines, regional trend in per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use	Cost/user	Median DDD
Piedmont	3.57	6.1	1.60	0.6	0.2	0.4	-1.7	0.4	-2.0	0.8	352.7	120.0
Valle d'Aosta	3.53	6.2	1.57	-2.8	-0.8	-2.0	2.2	2.0	0.2	0.7	480.0	136.6
Lombardy	3.22	4.8	1.83	0.8	0.8	0.0	0.4	0.7	-0.3	0.6	472.3	140.0
Province of Bolzano	2.09	4.0	1.45	5.3	-2.9	8.5	-0.3	-1.1	0.8	0.6	255.1	80.0
Province of Trento	3.20	4.7	1.86	6.5	-0.6	7.1	-0.1	-0.6	0.5	0.5	392.3	140.0
Veneto	3.49	5.7	1.67	0.5	-0.6	1.0	0.2	0.3	-0.1	0.7	379.3	133.3
Friuli V.G.	2.88	5.3	1.49	1.6	0.0	1.6	-0.6	0.5	-1.1	0.6	388.8	133.3
Liguria	3.47	6.7	1.42	1.5	1.5	-0.1	0.1	0.5	-0.4	1.0	320.4	120.0
Emilia R.	2.10	5.2	1.11	5.6	0.5	5.1	-2.0	-0.3	-1.7	0.7	197.4	110.0
Tuscany	3.44	5.7	1.66	0.4	-0.4	0.8	-0.1	0.0	-0.1	0.8	345.7	115.0
Umbria	4.18	6.5	1.77	-4.9	-0.9	-4.1	-0.8	0.7	-1.5	0.9	367.6	125.0
Marche	3.74	6.8	1.50	-1.2	1.4	-2.6	-1.1	0.3	-1.4	1.0	366.6	125.0
Lazio	4.29	6.4	1.84	-0.9	-0.4	-0.5	0.1	0.9	-0.8	0.8	444.0	141.7
Abruzzo	4.76	6.9	1.88	1.2	0.6	0.6	-0.5	1.7	-2.1	0.9	389.0	120.0
Molise	3.42	5.9	1.58	-3.5	2.3	-5.6	-1.9	0.9	-2.8	0.8	326.3	141.7
Campania	3.04	5.6	1.49	-0.9	0.4	-1.3	-1.1	1.2	-2.3	0.8	330.8	125.0
Puglia	4.06	6.0	1.84	3.0	1.9	1.1	0.4	0.4	0.0	0.9	365.3	121.3
Basilicata	3.77	6.2	1.68	-3.7	0.5	-4.1	0.3	1.2	-0.9	0.9	331.8	132.0
Calabria	3.53	5.9	1.64	1.4	1.1	0.3	1.3	0.5	0.8	0.8	305.6	120.0
Sicily	3.32	6.4	1.41	0.3	1.1	-0.7	-0.3	1.1	-1.4	0.9	297.2	130.7
Sardinia	3.68	5.3	1.91	-3.6	-0.7	-2.9	-1.4	0.6	-2.0	0.8	354.7	140.0
Italy	**3.43**	**5.7**	**1.64**	**0.5**	**0.4**	**0.1**	**-0.3**	**0.6**	**-0.9**	**0.8**	**361.6**	**126.7**
North	3.13	5.4	1.60	1.4	0.3	1.1	-0.4	0.3	-0.7	0.7	369.7	128.7
Centre	3.94	6.2	1.74	-0.9	-0.2	-0.7	-0.2	0.6	-0.7	0.8	396.3	130.0
South and Islands	3.57	6.1	1.60	0.6	0.2	0.4	-1.7	0.4	-2.0	0.8	332.4	125.0

3.6.7 Antimigraine medicines

In 2023, the consumption of drugs for the treatment of migraine was 1.2 DDD/1000 inhabitants per day, recording slight average annual increases in the last ten years (CAGR: +3.1%) and a 5.5% increase in 2023 (Box Main indices of expenditure, consumption and exposure). In the same period, total per capita expenditure remained almost stable (CAGR +1.5%), although in the last year it increased by 6.1%, reaching a value of approximately 92 million euros, i.e. 0.4% of total expenditure.

The average cost per day of therapy in 2023 was 3.69 euros. It has gradually increased starting from 2020 (Figure 3.6.7a), due to the introduction on the market of monoclonal antibodies, which record the highest average cost per day of therapy in the category (5.08 euros, down 3.2% compared to 2022) (Table 3.6.7a).

In 2023, the prevalence of use of antimigraine drugs in the general population was 0.6%, with significant gender differences. Starting from the 15-24 age group, a progressive increase begins to be recorded in the prevalence of use in women, reaching approximately 2% between the ages of 45 and 54, and then decreasing after the age of 65. Consumption levels also follow the same trend with a maximum value of 3 DDD in the same age group. A similar, but significantly less pronounced trend is reported in men, with higher prevalence (0.46%) and consumption (0.7 DDD) values in the 45-54 age group.

Triptans account for almost all expenditure (65%; 1.01 out of 1.56 euros per capita) and consumption (75%), with 0.9 over 1.2 DDD/1000 inhabitants per day for the entire category. They remained stable between 2014 and 2023 (CAGR: +0.5%) (Figure 3.6.7a). Monoclonal antibodies record the most significant increases in both expenditure and consumption compared to 2022 (respectively +16.9% and 20.6%), contributing to the increase in total expenditure in the category (+6.1%) (Table 3.6.7a). For these drugs, it is crucial in terms of public health to acquire data on efficacy and safety in current clinical practice to best characterize the external validity of RCTs.

The individual active ingredients, despite having low consumption values, show a significant increase in expenditure compared to 2022: galcanezumab (+15.4%) and fremanezumab (+52.4%), with the exception of erenumab (-5.3%). Consequently, when interpreting indicators of expenditure and consumption in the different subgroups, particularly monoclonal antibodies and triptans, the different modes of use for prophylaxis and acute treatment must be taken into account. Among triptans, eletriptan has the highest levels of consumption (+4.4%). This triptan is among those with the lowest consumption value (0.2 DDD). Among monoclonal antibodies, fremanezumab is the molecule with the highest average cost per day of therapy (7.01 euros), followed by galcanezumab (5.33 euros).

In 2023, the prevalence of use of antimigraine drugs was 0.6%, with a median age of 51 years (Table 3.6.7b). In line with the prevalence data relating to migraine disorders available in the literature, gender differences affect consumption levels. Each user received, on average, at least one dose of the drug for approximately 50 days during the year, at a cost of 155 euros. The results show that the median duration of treatment at national level drops to 24 days. Users of monoclonal antibodies are younger than average (49 years old) with an average cost per user of 200 euros, the highest among antimigraine drugs.

At a regional level, there are variations in both consumption and expenditure (Table 3.6.7c).

The region with the highest expenditure is Sardinia (2.21 euros), a value almost double than Umbria (1.15 euros); this difference is due to a greater use (1.5 vs 0.8 DDD) while the average cost per DDD is rather similar. Regions show variations in consumption ranging from -2.5% in Valle d'Aosta to +8.4% in Tuscany and Molise, while expenditure variation goes from -7.2% in Valle d'Aosta to +15.2% in Sardinia. The cost per DDD varies between 128 euros in Calabria and 199 euros in Sardinia.

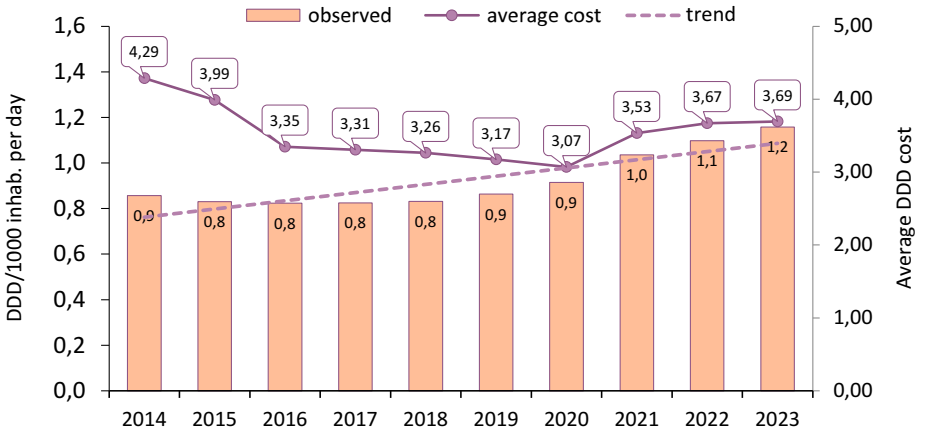
For further information on regional data on exposure and duration of therapy, please refer to the supplementary material published online.

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

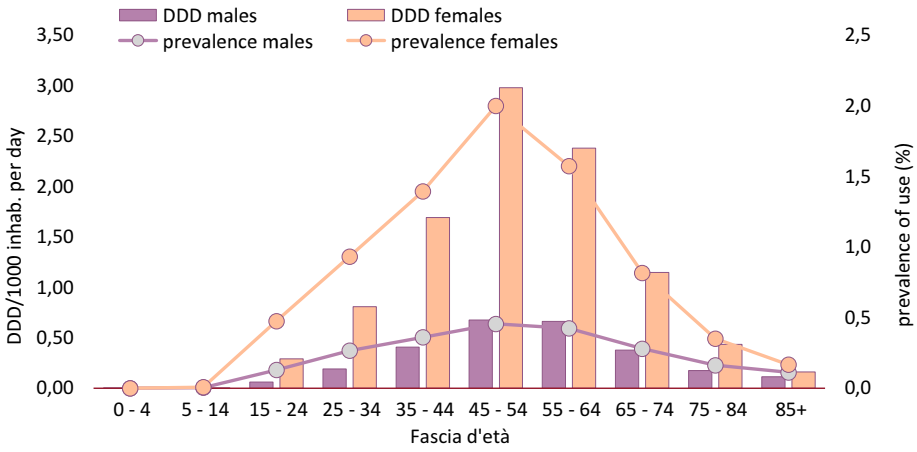
Antimigraine medicines

Public expenditure* in million euros (% over total)	**91.8**	**(0.4)**
Δ % 2023-2022		6.1
Regional range of gross per capita expenditure:	1.1	2.2
DDD/1000 inhabitants per day* (% over total)	**1.2**	**(0.1)**
Δ % 2023-2022		5.5
Regional range DDD/1000 inhabitants per day	0.8	1.5

Antimigraine medicines, temporal trend of consumption and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of antimigraine medicines under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.6.7a Antimigraine medicines, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Triptans	1.01	1.1	-2.8	0.9	1.1	0.5	3.22	<0.05
Calcitonin gene-related peptide antagonists (monoclonal antibodies)	0.55	16.9	—	0.3	20.6	—	5.08	-3.1
Other antimigraine medicines	<0.005	3.3	-18.1	<0.05	-1.1	-34.4	3.22	4.4
Ergot alkaloids	<0.005	-54.5	-40.7	<0.05	-79.5	-43.8	0.54	122.2
Antimigraine medicines	**1.56**	**6.1**	**1.5**	**1.2**	**5.5**	**3.1**	**3.69**	**0.6**
rizatriptan	0.25	2.3	1.6	0.2	2.8	2.2	2.85	-0.5
sumatriptan	0.22	-1.7	-1.5	0.2	-2.5	-1.1	3.69	0.8
galcanezumab	0.20	15.4	—	0.1	47.6	—	5.33	-21.8
almotriptan	0.20	-0.2	-4.7	0.2	-0.1	0.7	3.20	-0.2
eletriptan	0.19	4.0	-1.5	0.2	4.4	4.2	3.48	-0.4
fremanezumab	0.18	52.4	—	0.1	52.5	—	7.01	0.0
erenumab	0.17	-5.3	—	0.1	-5.8	—	3.79	0.5
frovatriptan	0.09	1.7	-10.5	0.1	0.1	-5.3	3.11	1.6
zolmitriptan	0.07	1.0	-0.4	0.1	1.2	0.7	2.92	-0.2
eptinezumab	<0.005	—	—	<0.05	—	—	2.41	—

Figure 3.6.7a Antimigraine medicines, 2014-2023 temporal trend in consumption (DDD/1000 inhabitants per day) by highest-expenditure subgroups

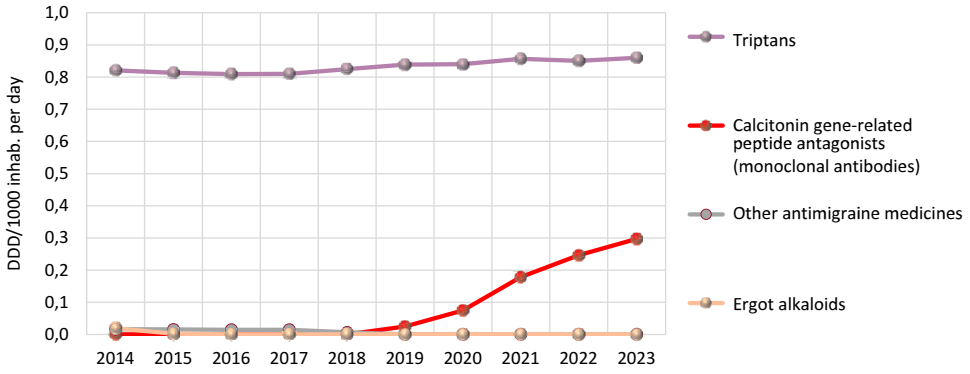


Table 3.6.7b Exposure and duration of therapy with antimigraine medicines by subgroup under approved care regime and distribution on behalf (year 2023))

Subgroup	Prevalence of use (%)			Median age	Cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
Triptans	0.3	1.0	0.6	51	154.6	48.1	24.0	22.2
Calcitonin gene-related peptide antagonists (monoclonal antibodies)	—	<0.05	<0.05	49	199.1	12.0	12.0	—
Other antimigraine medicines	<0.05	<0.05	<0.05	59	101.7	26.0	6.0	49.5
Ergot alkaloids	<0.05	<0.05	<0.05	84	41.6	46.4	7.5	72.7
Antimigraine medicines	**0.3**	**1.0**	**0.6**	**51**	**154.6**	**48.1**	**24.0**	**22.2**

Regional data on expenditure, consumption and exposure

Table 3.6.7c Antimigraine medicines, regional trend in per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use (%)	Cost/user	Median DDD
Piedmont	1.64	1.3	3.50	4.6	4.2	0.4	0.4	2.2	-1.8	0.8	154.0	24.0
Valle d'Aosta	1.55	1.3	3.37	-7.9	-2.5	-5.6	-1.4	0.7	-2.2	0.6	162.9	32.0
Lombardy	1.36	1.1	3.52	3.2	4.0	-0.8	-0.3	2.0	-2.2	0.6	156.3	24.0
Province of Bolzano	1.65	1.2	3.74	2.8	6.2	-3.2	3.1	3.8	-0.7	0.6	131.1	24.0
Province of Trento	1.65	1.3	3.52	11.1	8.1	2.7	0.7	1.9	-1.1	0.7	152.5	24.0
Veneto	1.84	1.4	3.74	7.5	5.6	1.8	1.3	2.9	-1.5	0.7	162.1	24.0
Friuli V.G.	1.98	1.4	3.87	7.5	5.9	1.4	1.6	3.2	-1.5	0.8	166.9	24.0
Liguria	1.45	1.1	3.66	3.2	3.3	-0.1	1.8	3.0	-1.2	0.6	150.0	24.0
Emilia R.	2.05	1.5	3.65	7.7	7.9	-0.2	2.7	4.0	-1.3	0.8	167.0	24.0
Tuscany	1.36	1.0	3.77	9.3	8.4	0.8	2.8	3.5	-0.7	0.5	145.2	24.0
Umbria	1.15	0.8	3.85	9.1	8.2	0.8	2.7	3.8	-1.0	0.5	153.1	24.0
Marche	1.49	1.1	3.62	1.1	3.0	-1.8	1.7	3.5	-1.8	0.7	141.9	24.0
Lazio	1.73	1.2	3.83	4.7	4.2	0.4	2.4	3.9	-1.5	0.6	160.1	24.0
Abruzzo	1.74	1.2	3.85	3.8	1.7	2.1	4.0	4.7	-0.6	0.5	149.4	24.0
Molise	1.32	0.9	3.91	6.9	8.4	-1.3	2.7	4.5	-1.7	0.5	149.0	20.0
Campania	1.29	0.9	3.85	7.4	7.7	-0.3	3.7	4.6	-0.8	0.5	136.1	18.0
Puglia	1.56	1.2	3.69	6.2	5.0	1.2	1.7	3.1	-1.4	0.7	155.0	24.0
Basilicata	1.08	0.8	3.69	4.8	4.2	0.6	2.3	2.6	-0.3	0.5	130.3	18.0
Calabria	1.38	1.0	3.80	7.3	6.8	0.4	2.0	3.5	-1.4	0.6	128.7	16.0
Sicily	1.27	1.0	3.57	6.2	4.8	1.3	-0.1	1.9	-1.9	0.6	147.4	21.0
Sardinia	2.21	1.5	4.06	15.2	8.0	6.7	1.6	2.8	-1.2	0.7	198.8	32.0
Italy	**1.56**	**1.2**	**3.69**	**6.1**	**5.5**	**0.6**	**1.5**	**3.1**	**-1.5**	**0.6**	**154.6**	**24.0**
North	1.65	1.2	3.61	5.5	5.2	0.2	0.9	2.7	-1.7	0.7	158.6	24.0
Centre	1.54	1.1	3.79	5.8	5.5	0.3	2.5	3.8	-1.3	0.6	152.9	24.0
South and Islands	1.45	1.1	3.77	7.5	5.8	1.5	1.9	3.3	-1.3	0.6	149.3	22.0

3.6.8 Antidementia medicines

In 2023 antidementia medicines showed a slight increase in consumption (+0.6%), i.e. 2.4 DDD/1000 inhabitants per day, with a +0.4% average annual variation in the period 2014-2023. Expenditure continues to decrease (-8.3%) compared to 2022, with 0.32 euros per capita (Box Main indices of expenditure, consumption and exposure). In the same period, the average cost per day of therapy decreased by 70% (from 1.19 to 0.37 euros) due to the patent expiry of all molecules belonging to the category. Exposure data of antidementia medicines are in line with data on the prevalence of the disease, which occurs mainly in the +75 age group. In detail, the prevalence of use of these medicines goes from 0.4% in the 65-74 age group to 3% in the +85 age group. Women have a higher level of exposure and consumption in all age groups, particularly in the +85 age group (2.9% vs 2.5% and 18.9 DDD vs 16.2 DDD).

In detail, all drugs recorded expenditure reductions (from -0.5% for galantamine to -14.4% for rivastigmine) compared to 2022 (Table 3.6.8a). Rivastigmine is the active ingredient accounting for half of the expenditure on the entire category with 0.14 euros per capita, and with the highest average cost per day of therapy (0.85 euros), 3.5 times higher than donepezil (0.24). Galantamine is the molecule having the lowest impact on expenditure with 0.01 euros per capita, due to low consumption. Memantine accounts for approximately half of the consumption (1.1 DDD/1000 inhabitants per day) with a 0.7% increase compared to 2022; from 2014 to 2023, it recorded a 3.2% average annual increase (Figure 3.6.8a).

The prevalence of use in the general population is 0.3% and is similar to the level of individual categories (0.2%), while the cost per user of anticholinesterases is twice other antidementia drugs (111 vs 55 euros), just as the DDD per user is 10% higher (224 vs 203 days) (Table 3.6.8b). Overall, half of the users remained on treatment for less than 7 months and 8.1% received only one prescription during the year. At the regional level, the Centre has higher consumption levels (2.9 DDD) with a 4.3% reduction compared to 2022, as opposed to the North and the South (2.3 and 2.2 DDD respectively).

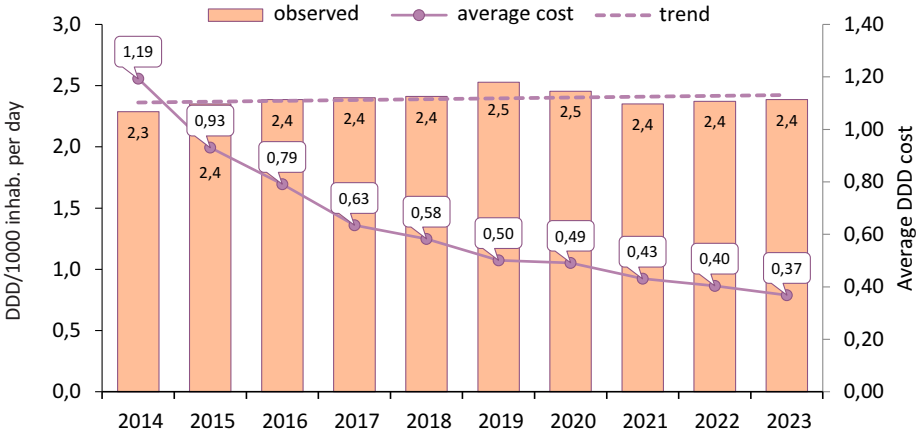
Despite the low consumption levels, the North registers the highest per capita expenditure (0.39 euros) due to an increased use of medicines with a higher average cost per DDD (0.47 euros) (Table 3.6.8c). At a regional level, there is a minimum expenditure of 0.08 euros in Sicily and a maximum of 0.71 euros in Lombardy. This difference is determined not only by a higher consumption (2.1 DDD vs 1.3 DDD), but also by a higher average cost per DDD in Lombardy (0.91 vs 0.17), probably due to the different delivery channel. There is wide regional variability in all indicators compared to 2022. The expenditure variation goes from -62.7% in Umbria to +23.8% in Sardinia, the consumption variation goes from -22.2% in Valle d'Aosta to +22.0% in Liguria; the average cost ranges between -54.5% in Umbria and +33.7% in Valle d'Aosta with a prevalence of use that goes from 0.1% in the Province of Trento to 0.6% in Abruzzo.
The cost per user in Lombardy is approximately 6 times higher than Piedmont (232.7 euros vs 40.2 euros).

For further information on regional data on exposure and duration of therapy, please refer to the supplementary documents published online.

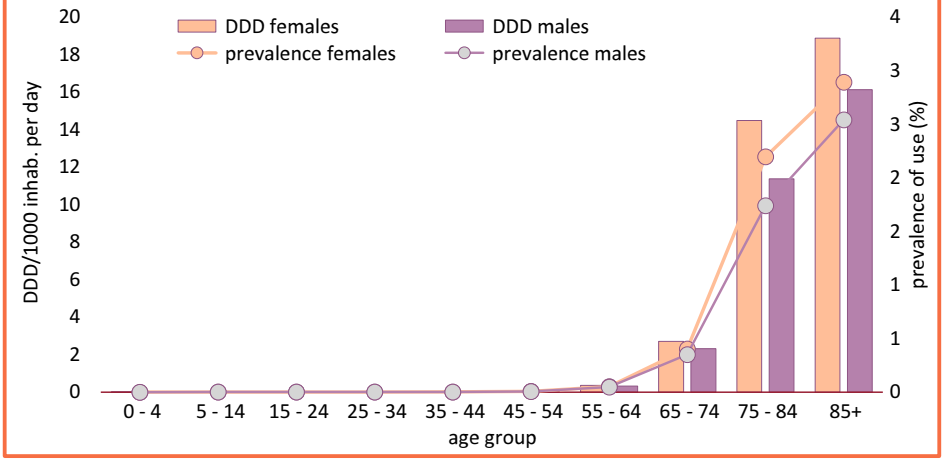
MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Antidementia medicines

Public expenditure* in million euros (% over total)	**18.9**	**(0.1)**
Δ % 2023-2022		-8.3
Regional range of gross per capita expenditure:	0.1	0.7
DDD/1000 inhabitants per day* (% over total)	**2.4**	**(0.2)**
Δ % 2023-2022		0.6
Regional range DDD/1000 inhabitants per day	1.1	4.5

Antidementia medicines, temporal trend of consumption and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of antidementia medicines under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.6.8a Antidementia medicines, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Anticholinesterases	0.22	-6.0	-10.7	1.3	0.5	-1.3	0.46	-6.4
Other antidementia medicines	0.10	-13.1	-10.6	1.1	0.7	3.2	0.25	-13.8
Antidementia medicines	**0.32**	**-8.3**	**-10.7**	**2.4**	**0.6**	**0.4**	**0.37**	**-8.8**
rivastigmine	0.14	-14.4	-13.3	0.4	-5.8	-3.9	0.85	-9.1
memantine	0.10	-13.1	-10.6	1.1	0.7	3.2	0.25	-13.8
donepezil	0.08	13.6	-2.0	0.8	4.4	1.0	0.24	8.9
galantamine	0.01	-0.5	-9.8	<0.05	-7.4	-9.8	1.00	7.5

Figure 3.6.8a Antidementia medicines, 2014-2023 temporal trend in consumption (DDD/1000 inhabitants per day) of the highest-expenditure subgroups

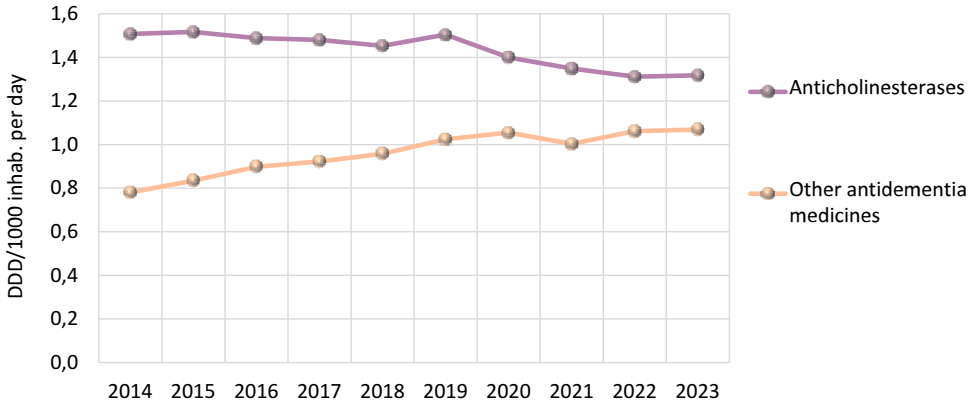


Table 3.6.8b Exposure and duration of therapy with antidementia medicines by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
Anticholinesterases	0.1	0.2	0.2	81	111.0	223.8	196.0	7.6
Other antidementia medicines	0.1	0.2	0.2	82	54.8	202.6	196.0	10.3
Antidementia medicines	**0.2**	**0.4**	**0.3**	**82**	**94.0**	**239.1**	**210.0**	**8.1**

Regional data on expenditure, consumption and exposure

Table 3.6.8c Antidementia medicines, regional trend in per capita expenditure, consumption (DDD/1000 inhabitants per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use (%)	Cost/user	Median DDD
Piedmont	0.14	2.2	0.17	22.8	10.7	10.9	-15.8	-0.1	-15.7	0.3	40.2	210.0
Valle d'Aosta	0.31	1.7	0.49	4.0	-22.2	33.7	-9.3	-1.6	-7.8	0.3	99.8	174.3
Lombardy	0.71	2.1	0.91	-2.2	0.9	-3.0	-4.3	0.4	-4.7	0.3	232.7	224.0
Province of Bolzano	0.70	4.2	0.46	3.3	5.3	-1.8	-5.8	1.8	-7.5	0.3	167.3	298.7
Province of Trento	0.11	1.1	0.26	-23.6	4.8	-27.1	-14.5	-1.5	-13.3	0.1	70.0	224.0
Veneto	0.16	2.1	0.21	-22.1	-13.7	-9.7	-16.2	-1.4	-14.9	0.3	60.5	224.0
Friuli V.G.	0.44	2.1	0.57	2.5	4.1	-1.5	-7.5	0.7	-8.2	0.3	152.9	224.0
Liguria	0.39	4.5	0.24	17.6	23.0	-4.4	-10.9	2.1	-12.7	0.5	63.1	205.3
Emilia R.	0.18	2.1	0.24	4.9	4.3	0.5	-11.2	0.9	-12.0	0.2	59.2	196.0
Tuscany	0.30	3.2	0.25	2.7	-1.9	4.7	-13.9	0.5	-14.3	0.4	63.8	224.0
Umbria	0.25	3.5	0.20	-62.7	-18.1	-54.5	-17.7	0.4	-18.1	0.5	50.6	224.0
Marche	0.24	2.4	0.28	-11.4	-1.1	-10.4	-13.1	-0.7	-12.5	0.4	66.5	224.0
Lazio	0.29	2.7	0.28	1.6	-3.5	5.2	-12.3	1.3	-13.4	0.4	70.3	196.0
Abruzzo	0.54	4.0	0.37	-6.8	2.5	-9.1	-13.3	0.9	-14.1	0.6	89.5	204.3
Molise	0.24	2.9	0.23	6.2	7.1	-0.8	-9.6	5.4	-14.2	0.4	58.3	168.0
Campania	0.22	2.7	0.22	-0.9	12.1	-11.5	-11.5	2.8	-13.9	0.4	53.5	205.3
Puglia	0.32	2.2	0.41	-44.5	-4.3	-41.9	-10.0	0.5	-10.5	0.4	104.2	196.0
Basilicata	0.67	2.6	0.71	8.4	6.0	2.2	-2.1	4.0	-5.9	0.4	177.8	238.1
Calabria	0.27	1.9	0.39	-5.6	-4.1	-1.6	-14.8	-1.5	-13.5	0.3	88.0	168.0
Sicily	0.08	1.3	0.17	-38.0	-3.2	-35.9	-19.1	-3.1	-16.5	0.2	45.9	224.0
Sardinia	0.21	2.1	0.27	23.8	-4.5	29.7	-16.7	-0.9	-15.9	0.3	63.9	186.7
Italy	**0.32**	**2.4**	**0.37**	**-8.3**	**0.6**	**-8.8**	**-10.7**	**0.4**	**-11.1**	**0.3**	**94.0**	**210.0**
North	0.39	2.3	0.47	-1.0	2.3	-3.3	-8.3	0.3	-8.5	0.4	126.1	224.0
Centre	0.28	2.9	0.26	-10.1	-4.3	-6.2	-13.4	0.7	-14.0	0.3	66.1	205.3
South and Islands	0.25	2.2	0.30	-20.4	2.2	-22.1	-12.9	0.4	-13.3	0.3	75.0	196.0

3.7 Respiratory system

Respiratory drugs were confirmed in 2023 as the seventh therapeutic category with the highest public expenditure, equal to 1,655.2 million euros, i.e. 6.4% of total public expenditure, up 7.2% compared to 2022 (Box Main indices of expenditure, consumption and exposure). The total per capita expenditure on these drugs is 28.12 euros. More than half is due to the approved care regime (15.56 euros per capita), which shows a slight reduction compared to the previous year (-1.9%), while the share due to purchases by public health facilities, 12.55 euros per capita, has grown compared to 2022 (+21.1%) (Table 3.1).

Consumption for this category of drugs, 43.2 DDD/1000 inhabitants per day (stable compared to last year, +0.2%), is mainly due to doses dispensed through the approved care regime (40.72 DDD/1000 inhabitants per day), while the share delivered through public health facilities is minimal (2.46 DDD/1000 inhabitants per day), despite growing by 8.9% compared to 2022 (Table 3.2).

Analysis of the drug use profile by age and gender, including approved care regime and distribution on behalf, shows that children under the age of 5 and subjects over 75 years have the highest prevalence of use. The consumption analysis highlights an increase in DDD with increasing age and a maximum value reached in the over-75 age group (94.8 DDD/1000 inhabitants per day), likely due to the treatment of chronic obstructive pulmonary disease (COPD). With regard to gender differences, a higher prevalence of use is found in males up to 14 years and after 75 years. At the same time, the per capita expenditure covered by the NHS also varies with patient age, reaching a maximum value of 44.9 euros per capita in the age group over 75, with a different gender value (57.4 euros for males and 36.2 euros for females).

As regards the approved care regime, per capita expenditure was 15.56 euros, a 2.2% decrease compared to 2022. This trend is determined by a reduction in prices (-3.5%), consumption (-0.5%) and the average cost per DDD (-1.7%), although more expensive products are used (mix effect: +1.9%) (Table 3.9). Within this category, adrenergics in association with corticosteroids or other drugs, excluding anticholinergics, represent the drugs with the highest expenditure and consumption, with 6.6 euros per capita and 12.3 DDD/1000 inhabitants per day, respectively. Analysing the expenditure, consumption and average cost per day of therapy of the most prescribed active ingredients of the category (Table 3.10), the combinations formoterol/beclomethasone, vilanterol/fluticasone furoate and formoterol/budesonide show the highest per capita expenditure and consumption values, representing overall more than a third of the expenditure of the category (incidence on expenditure of 14.4%, 13.6% and 7.7% respectively). These active ingredients belong to the group of LABA+ICS (long-acting beta2-agonists and inhaled corticosteroids) used for the treatment of asthma and COPD and the first two are among the top 30 active ingredients by expenditure, recording values of 131.9 and 124.6 million euros respectively (Table 3.11).

Eight drugs of this category are on the list of the first 30 active ingredients with the highest average cost per day of therapy: vilanterol/umeclidinium/fluticasone furoate, formoterol/glycopyrronium/beclomethasone, vilanterol/umeclidinium, formoterol/budesonide, budesonide, vilanterol/fluticasone furoate, umeclidinium and formoterol/beclomethasone with an average cost per DDD of 2.72 euros, 2.65 euros, 1.91 euros, 1.65 euros, 1.61 euros, 1.57 euros, 1.51 euros and 1.49 euros respectively (Table 3.12).

The combinations vilanterol/umeclidinium, formoterol/glycopyrronium/beclomethasone and vilanterol/umeclidinium/fluticasone furoate show the most significant changes in expenditure and consumption, being included in the list of the top 30 active ingredients with the highest increase in the approved care expenditure compared to 2022. These drugs reported an increase in expenditure of +58.8%, +20.5% and +17.9% respectively, as well as an increase in consumption of +64.3%, +37.1% and +18.4% respectively (Table 3.14). The same list also includes budesonide, an inhaled cortisone that shows a +14.1% variation in expenditure, determined both by an increase in consumption (+10.5%) and by a slight increase in the average DDD cost (+3.2%) (Table 3.14). The list of the first 30 active ingredients with the greatest expenditure reduction includes tiotropium (-17.3%), salmeterol/fluticasone (-12.1%), formoterol/beclomethasone (-11.3%), formeterol/budesonide (-10.3%) and umeclidinium (-1.8%) (Table 3.15).

In terms of purchases by public health facilities, compared to 2022, there was an increase in expenditure (+20.7%) and consumption (+8.5%), against a slight reduction in prices (-2.2%), and a shift towards the purchase of more expensive drugs (mix effect: +13.7%) (Table 3.17). The medicines with the greatest impact on expenditure on this category are the combination elexacaftor/tezacaftor/ivacaftor (38.4%) and ivacaftor (29.7%), used to treat cystic fibrosis, followed by omalizumab (9.5%), used in allergic asthma due to IgE hyperproduction (Table 3.18). Furthermore, the combination elexacaftor/tezacaftor/ivacaftor is included in the list of the top 30 active ingredients for expenditure on drugs purchased by public health facilities with a total value of 284 million euros, followed by ivacaftor with 219.4 million euros (Table 3.19). Both are also included in the first 30 active ingredients with the highest increase in per capita expenditure on drugs purchased by public health facilities, compared to 2022. The combination elexacaftor/tezacaftor/ivacftor shows a 38.1% increase, while ivacaftor a 22.7% increase; mepolizumab also increased by +32.3% (Table 3.20). The first two are among the top 30 active ingredients by average cost per day of therapy among drugs purchased by public facilities: ivacaftor with an average cost per DDD of 431.9 euros, up 0.7% compared to 2022, and a per capita expenditure of 3.73 euros, while the combination elexacaftor/tezacaftor/ivacaftor has an average cost per DDD of 289.3 euros, stable compared to last year, and a per capita expenditure of 4.83 euros (Table 3.22). Among the top 30 active ingredients with the highest expenditure on drugs in approved care and purchased by public health facilities, ivacaftor/elexacaftor/tezacaftor recorded an expenditure of 284 million euros and an impact on total expenditure equal to 1.1%; ivacaftor had an expenditure of 219.4 million euros, accounting for 0.8% of total expenditure; formoterol/beclomethasone recorded an expenditure of 133.9 million euros and a 0.5% impact on expenditure (Table 3.25). As regards expenditure and consumption by group and subgroup, medicines for asthma and COPD and for cystic fibrosis are the most significant in the category (Table 3.27). The former have a total expenditure of 1,052.6 million euros, and a consumption of 688.4 DDD. They are mainly dispensed under approved care regime, where they register a per capita expenditure of 14.43 euros and a consumption of 30.3 DDD/1000 inhabitants per day. The share of asthma and COPD medicines dispensed under the direct purchasing channel is minimal, with a per capita expenditure of 3.41 euros and 1.7 DDD/1000 inhabitants. The subgroup of monoclonal antibodies for asthma therapy (3.19 euros per capita) is the most relevant. The therapeutic subgroups with the highest expenditure are LABA+ICS (388.7 million euros), followed by monoclonal antibodies (188.6 million euros), LAMA (129.9 million euros) and inhaled cortisones (ICS, 108.6 million euros) (Table 3.27). Medicines for cystic fibrosis show a total expenditure of 527.2 million euros, and 2.1 million daily doses delivered. They are dispensed

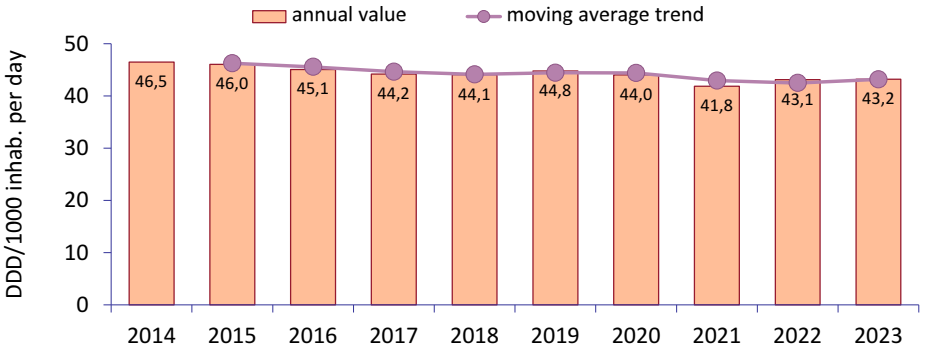
exclusively through the direct distribution channel, with a per capita expenditure of 8.93 euros. CFTR modulators (515.1 million euros in expenditure and 1.5 million DDD) are the subgroups with the highest expenditure and consumption.

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

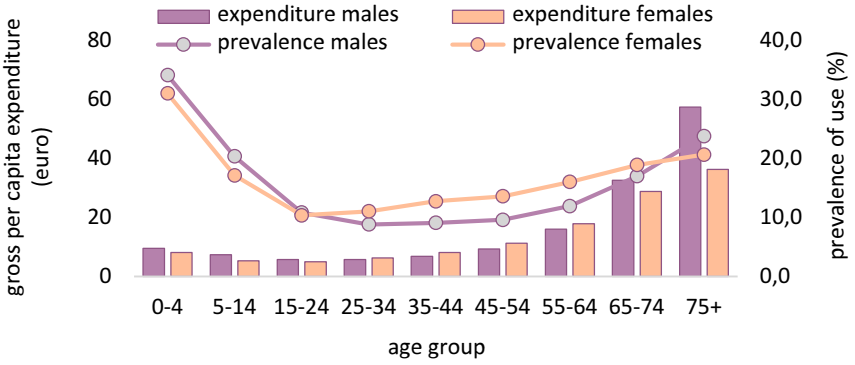
Respiratory system

Public expenditure* in million euros (% over total)	**1,655.2**	**(6.4)**
Δ % 2023-2022		7.2
Regional range of gross per capita expenditure:	22.2	38.7
DDD/1000 inhabitants per day* (% over total)	**43.2**	**(3.3)**
Δ % 2023-2022		0.2
Regional range DDD/1000 inhabitants per day	30.6	61.4

** includes prescriptions under approved care regime and purchases by public health facilities*



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf by age and gender in 2023 (Figure and Table)



Age group	Gross per capita expenditure			DDD/1000 inhabitants per day		
	Males	Females	Total	Males	Females	Total
0-4	9.6	8.1	8.8	27.4	22.5	25.0
5-14	7.3	5.3	6.3	25.6	17.9	21.9
15-24	5.8	4.9	5.4	22.1	18.8	20.5
25-34	5.7	6.2	6.0	20.1	21.1	20.6
35-44	6.8	8.1	7.4	20.8	25.5	23.1
45-54	9.3	11.2	10.2	25.4	33.2	29.4
55-64	16.1	17.8	17.0	37.8	45.6	41.8
65-74	32.6	28.8	30.6	66.4	65.3	65.8
75+	57.4	36.2	44.9	113.7	81.7	94.8

3.7.1 Medicines for asthma and COPD

In 2023, medicines for asthma and COPD recorded a total public expenditure of 1,052.6 million euros, up 1.5% compared to the previous year. Consumption is substantially stable, with 32.0 DDD/1000 inhabitants per day (+0.4% compared to 2022) (Box Main indices of expenditure, consumption and exposure).

Analyzing the temporal trend of average DDD consumption and costs, the consumption of these drugs has decreased over time, going from 34.9 in 2014 to 32.0 DDD per thousand inhabitants per day in 2023, with a -0.9% average annual variation (CAGR). The average cost per day of therapy, on the other hand, has increased, showing a 1.5% average annual variation (CAGR), going from 1.31 euros in 2014 to 1.53 euros in 2023. These trends indicate an increasing use of high-cost and more recently introduced drugs in therapy, such as monoclonal antibodies for asthma therapy and fixed combination therapies for COPD (triple and dual) (Table 3.7.1a)

Prevalence, similarly to consumption, presents higher levels in the extreme age groups, especially in the paediatric population (0-4 years), probably associated with acute infectious episodes affecting the upper respiratory tract. The differences between males and females are more marked with regard to consumption, especially in the population aged 75 and over. Males aged over 85 years reach 123 DDD, while females 71 DDD; this is probably associated with the chronic treatment of COPD, a clinical condition more prevalent in males over 65.

In 2023, per capita expenditure on this category of drugs was 17.89 euros, a 1.5% increase compared to the previous year, with a 0.7% average annual variation from 2014 to 2023 (Table 3.7.1a). The increase in expenditure over the last year reflects both the low increase in consumption (+0.4%) and the average DDD cost (+1.0%).

Analyzing the therapeutic categories, the LABA-ICS association was the category with the highest per capita expenditure (6.60 euros) and consumption (12.3 DDD per 1000 inhabitants per day). Both indicators have decreased, respectively by 7.7% and 1.1% compared to 2022. The same applies to the average DDD cost (-6.7%). LABA-ICS are followed by monoclonal antibodies, which instead recorded a 20.6% expenditure increase (3.21 euros per capita) and a 27.1% consumption increase (0.3 DDD/1000 inhabitants per day), compared to a 5.1% reduction in the average DDD cost compared to last year.

Among the subgroups with the greatest variation in expenditure and consumption, the LABA-LAMA-ICS and LABA-LAMA associations recorded an expenditure increase of 27.6% and 23.4% respectively and a consumption increase of 36.5% and 24.9% respectively. On the other hand, long-acting beta-adrenergic agonists (LABAs) showed the greatest reduction in expenditure (-24.5%), attributable to a reduction in both consumption (-21.6%) and in the average cost (-3.7%).

The combination formoterol/beclomethasone is confirmed as the most used drug in the category (4.2 DDD per 1000 inhabitants per day), followed by the combinations vilanterol/fluticasone (3.7 DDD/1000 inhabitants per day) and formoterol/budesonide (2.0 DDD/1000 inhabitants per day). The monoclonal antibodies omalizumab, mepolizumab and benralizumab are the drugs with the highest average cost per day of therapy with a value of 24.82 euros, 26.01 euros and 29.00 euros respectively (Table 3.7.1a).

Observing the 2014-2023 consumption trend of the highest-expenditure subgroups, the LABA+ICS association increased in the period 2014-2020, and then has decreased in the last 3 years, due to both a reduction in consumption and in the average DDD cost. The triple

association (LABA-LAMA-ICS) shows a constant growth starting from 2018, while the single drugs (LAMA and ICS) show a decreasing trend (Figure 3.7.1a).

The median age of asthma and COPD drug users is around 52 years, ranging from 75 years of subjects treated with long-acting bronchodilators alone or in combination (LAMA, LABA+LAMA and LABA+LAMA+ICS), to 30 years of those exposed to SABA (Table 3.7.1b). In 2023, the average cost per user was 132.1 euros, although there are significant category differences. In fact, monoclonal antibodies show the highest cost value with 5,705.3 euros per user, while SABA have the lowest value (7.8 euros). Users of medicines for asthma and COPD were exposed for 95.4 days of therapy, although there are differences in exposure by therapeutic category. In fact, users of monoclonal antibodies showed a greater intensity of use, with 217.2 DDD per user, while users of SABA+SAMA recorded the lowest value (17.1 DDD). In 2023, users with a single prescription for asthma and COPD drugs were 43.3%, with the highest value reported in patients treated with the SABA+SAMA combination (83.7%), while as regards treatment with monoclonal antibodies only 3.1% of patients received a single prescription (Table 3.7.1b).

The prevalence of use is overall 11.5%, higher in the South and the Islands (13.2%) and lower in the North (10.2%), while the Centre is in line with the national average (11.7%) (Table 3.7.1c). At the regional level, the lowest prevalence of use is in the Province of Bolzano with 8.3%, while the highest is in Campania with 16.3%. Even the cost per user shows geographical differences compared to the national average (132.1 euros), with lower values in the South and Islands (124.6 euros) and higher values in the North and Centre (136.7 euros and 136.9 euros respectively). At a regional level, the lowest expenditure is in Emilia Romagna, with 103.8 euros per user, while the highest value is in Piedmont with 185.5 euros per user. The median DDD was 30: Tuscany showed the highest value of 42.7 DDD and the Province of Trento had the lowest value of 26.7 DDD.

51% of users showed low adherence to therapies, while only 20.2% were high-adherent (Figures 3.7.1b and 3.7.1c) In general, women show a higher percentage of low-adherent subjects (53.0% women vs 48.1% men) (Figure 3.7.1b), vice versa, men have a higher percentage of high-adherent subjects than women (22.0% vs 18.9%) (Figure 3.7.1c). A 50% probability of interrupting treatment is reached at 40 days; the risk of discontinuation increases in the South and Islands compared to the North (38 vs 43 days) and in females (35 vs 48 days) (Figures 3.7.1d and 3.7.1e).

For further information on regional data on exposure and duration of therapy and on indicators of adherence and persistence to treatment stratified by age, gender and geographical area, please refer to the supplementary documents published online.

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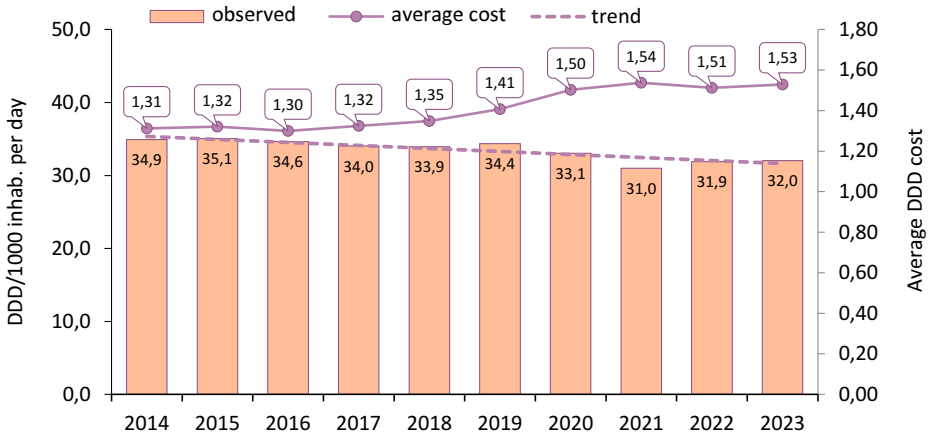
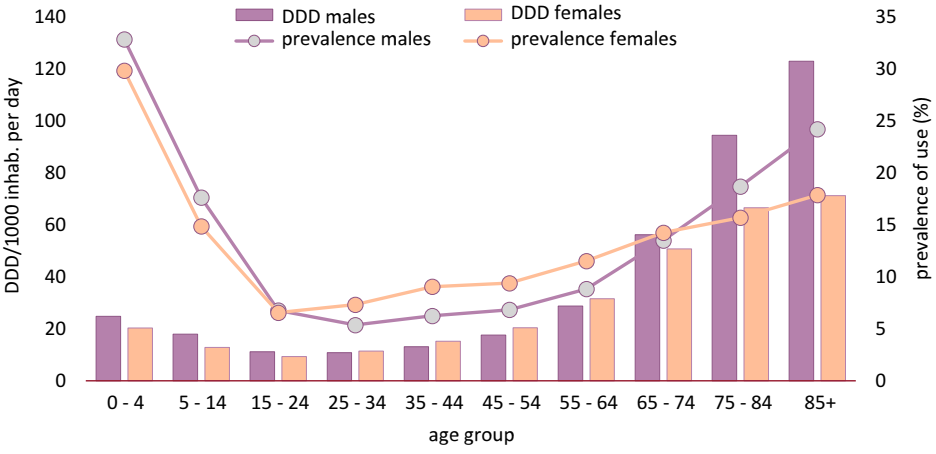
MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Medicines for asthma and COPD

Public expenditure in million euros (% over total)	**1,052.6**	**(4.0)**
Δ % 2023-2022		1.5
Regional range of gross per capita expenditure:	13.0	22.8
DDD/1000 inhab. per day (% over total)	**32.0**	**(2.4)**
Δ % 2023-2022		0.4
Regional range DDD/1000 inhabitants per day	23.7	42.0

Medicines for asthma and COPD, temporal trend of consumption and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of medicines for asthma and COPD under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.7.1a Medicines for asthma and COPD, per capita expenditure and consumption (DDD/1000 inhab. per day) by therapeutic category and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
LABAs+ICS	6.60	-7.7	-1.8	12.3	-1.1	1.5	1.48	-6.7
Monoclonal antibodies	3.21	20.6	24.6	0.3	27.1	27.2	26.26	-5.1
LAMAs	2.21	-12.8	-4.1	4.1	-11.9	-3.1	1.47	-1.1
ICSs	1.85	5.2	-3.6	5.0	4.8	-3.7	1.01	0.4
LABAs+LAMAs+ICS	1.64	27.6	—	1.7	36.5	—	2.64	-6.5
LABAs+LAMAs	1.18	23.4	183.7	1.7	24.9	115.3	1.92	-1.1
Antileukotrienics (LTRA)	0.46	0.2	-1.6	2.0	0.0	-0.5	0.62	0.2
LABAs	0.21	-24.5	-13.9	0.6	-21.6	-13.3	0.95	-3.7
SABAs	0.20	3.5	-3.6	2.6	-1.7	-3.2	0.22	5.3
SABAs+SAMAs	0.14	-6.4	-4.1	0.6	-4.7	-4.1	0.64	-1.8
SABAs+ICSs	0.10	-8.1	-6.1	0.2	-7.5	-5.9	1.20	-0.6
SAMAs	0.05	-2.5	-8.1	0.6	4.0	-2.7	0.22	-6.2
Theophylline-based ronchodilators	0.04	-4.9	-8.4	0.3	-9.1	-10.4	0.37	4.6
PDE-4 inhibitors	<0.005	-13.8	-12.8	<0.05	-13.6	-12.4	1.53	-0.2
Medicines for asthma and COPD	**17.89**	**1.5**	**0.7**	**32.0**	**0.4**	**-0.9**	**1.53**	**1.0**
formoterol/beclomethasone	2.28	-11.4	2.4	4.2	2.3	4.3	1.47	-13.4
vilanterol/fluticasone furoate	2.13	0.2	—	3.7	2.4	—	1.56	-2.2
formoterol/budesonide	1.19	-10.3	0.0	2.0	-2.2	2.8	1.63	-8.3
omalizumab	1.19	10.2	12.8	0.1	12.6	15.8	24.82	-2.1
mepolizumab	1.17	32.3	—	0.1	52.4	—	26.01	-13.2
benralizumab	0.85	22.0	—	0.1	22.0	—	29.00	0.0
tiotropium	0.83	-17.3	-10.5	1.6	-14.8	-9.1	1.42	-2.9
formoterol/glycopyrronium/ beclomethasone	0.82	20.2	—	0.9	36.4	—	2.61	-11.9
salmeterol/fluticasone	0.79	-12.2	-16.5	1.9	-11.2	-11.0	1.16	-1.2
umeclidinium	0.70	-1.8	—	1.3	-1.8	—	1.51	0.0

Figure 3.7.1a Medicines for asthma and COPD, temporal trend of consumption (DDD/1000 inhab. per day) of most expensive subgroups (2014-2023)

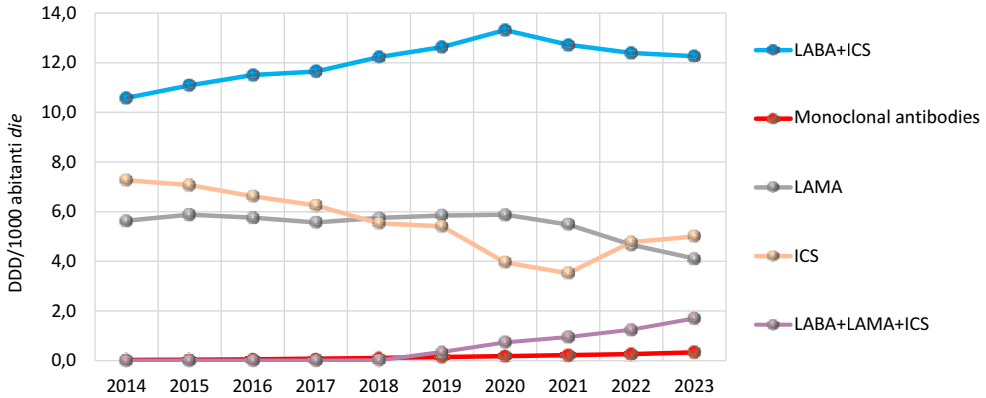


Table 3.7.1b Exposure and duration of therapy of medicines for asthma and COPD per subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
LABAs+ICS	3.0	3.4	3.2	61	201.9	135.7	90.0	28.8
Monoclonal antibodies	0.0	0.0	0.0	57	5705.3	217.2	194.4	3.1
LAMAs	0.9	0.7	0.8	75	274.4	183.9	150.0	17.7
ICSs	6.5	7.4	7.0	43	25.7	24.6	13.3	71.8
LABAs+LAMAs+ICSs	0.3	0.2	0.3	75	568.9	212.3	210.0	11.4
LABAs+LAMAs	0.4	0.2	0.3	75	354.1	183.1	150.0	18.9
Antileukotrienics (LTRA)	0.5	0.6	0.5	48	85.1	136.9	84.0	23.5
LABAs	0.1	0.1	0.1	73	191.2	200.9	150.0	21.6
SABAs	2.4	2.3	2.3	30	7.8	34.6	25.0	69.0
SABAs+SAMAs	1.0	1.2	1.1	57	11.6	17.1	10.0	83.7
SABAs+ICSs	0.2	0.2	0.2	60	41.6	34.5	20.0	70.0
SAMAs	0.3	0.3	0.3	69	12.2	42.5	16.7	58.2
Theophylline-based bronchodilators	0.2	0.2	0.2	74	17.8	47.5	10.0	49.6
PDE-4 inhibitors	<0.05	<0.05	<0.05	74	324.5	208.2	210.0	17.0
Medicines for asthma and COPD	**11.0**	**11.9**	**11.5**	**52**	**132.1**	**95.4**	**30.0**	**43.3**

Regional data on expenditure, consumption and exposure

Table 3.7.1c Medicines for asthma and COPD, temporal trend of per capita expenditure, consumption (DDD/1000 inhab. per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use (%)	Cost/user	Median DDD
Piedmont	16.70	28.5	1.60	1.3	0.2	1.2	0.6	-1.0	1.6	8.6	185.5	31.7
Valle d'Aosta	15.68	30.0	1.43	-2.0	-1.6	-0.4	-2.4	-2.8	0.5	9.4	133.3	30.0
Lombardy	17.14	30.6	1.53	2.0	0.5	1.5	0.9	-0.2	1.1	10.2	142.2	30.0
Province of Bolzano	12.96	23.7	1.50	-1.6	-5.1	3.7	0.1	-1.2	1.3	8.3	116.9	28.2
Province of Trento	15.27	31.1	1.35	-5.0	-3.7	-1.4	0.4	-0.2	0.6	12.4	112.6	26.7
Veneto	14.92	27.9	1.46	-0.1	0.0	-0.1	0.9	-0.5	1.4	9.4	128.0	30.0
Friuli V.G.	15.07	29.5	1.40	2.6	2.0	0.6	0.6	-0.3	0.9	9.7	139.8	30.0
Liguria	17.79	32.2	1.51	-1.0	-0.1	-0.9	1.1	-0.4	1.5	11.0	139.5	31.3
Emilia R.	16.40	32.2	1.40	2.7	1.2	1.5	0.9	-0.4	1.3	12.1	103.8	30.0
Tuscany	17.53	31.9	1.50	0.3	-1.0	1.3	0.8	-0.8	1.6	9.2	159.0	42.7
Umbria	14.90	27.5	1.48	-3.3	-2.9	-0.4	-0.1	-1.5	1.4	9.5	137.9	30.0
Marche	15.80	28.3	1.53	0.6	1.9	-1.3	-0.4	-1.0	0.7	10.0	144.4	30.0
Lazio	18.96	34.5	1.51	-0.6	-0.3	-0.3	-0.2	-1.5	1.4	14.0	126.2	30.0
Abruzzo	16.92	30.3	1.53	1.5	2.9	-1.3	1.3	0.2	1.1	11.9	134.0	30.0
Molise	14.90	26.3	1.55	5.7	5.9	-0.2	0.3	-0.7	1.1	11.6	113.6	30.0
Campania	22.80	42.0	1.49	2.5	0.7	1.8	1.0	-0.5	1.5	16.3	126.0	30.0
Puglia	20.00	33.1	1.66	1.1	1.0	0.2	0.3	-2.1	2.4	11.0	133.1	30.0
Basilicata	22.11	33.7	1.80	3.1	0.2	2.9	1.8	-1.4	3.2	11.9	132.1	30.0
Calabria	18.81	29.6	1.74	1.4	-1.1	2.5	0.9	-1.6	2.6	11.8	131.5	30.0
Sicily	18.95	32.0	1.62	4.8	2.1	2.6	1.3	-0.9	2.3	12.2	114.0	30.0
Sardinia	19.13	35.1	1.50	3.6	0.0	3.6	-0.3	-1.5	1.2	13.8	117.1	30.0
Italy	**17.89**	**32.0**	**1.53**	**1.5**	**0.4**	**1.0**	**0.7**	**-0.9**	**1.5**	**11.5**	**132.1**	**30.0**
North	16.39	30.0	1.50	1.3	0.3	0.9	0.8	-0.5	1.3	10.2	136.7	30.0
Centre	17.79	32.3	1.51	-0.3	-0.5	0.1	0.1	-1.2	1.4	11.7	136.9	30.0
South and Islands	20.09	34.8	1.58	2.7	1.0	1.7	0.8	-1.1	1.9	13.2	124.6	30.0

Adherence and persistence to treatment

Figure 3.7.1b Indicators of low adherence to treatment with medicines for COPD in the population aged ≥45 years stratified by gender, trend 2019-2023

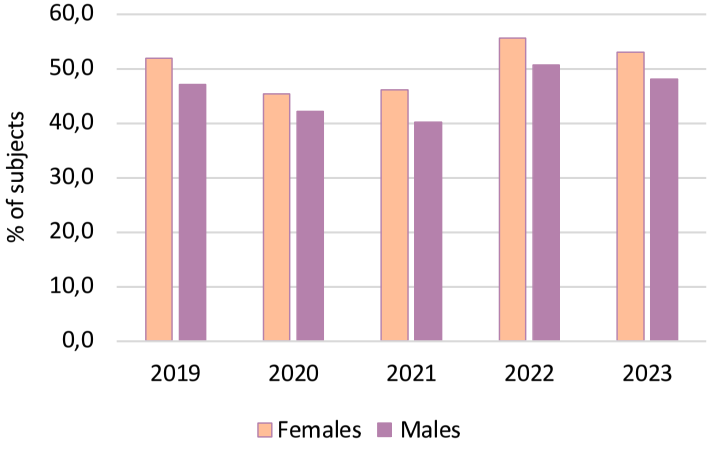
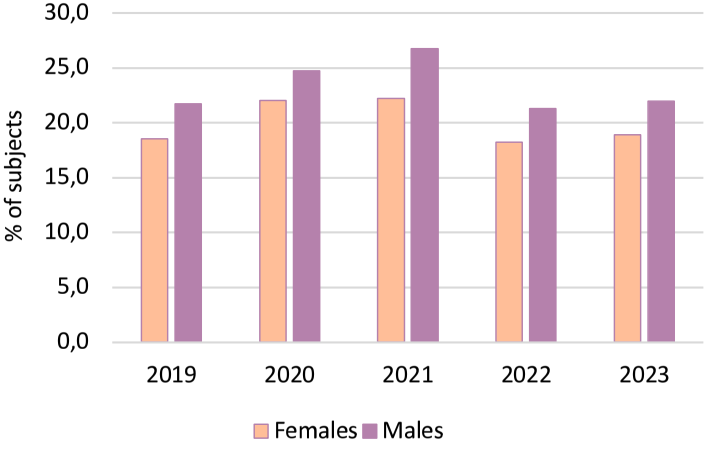


Figure 3.7.1c Indicators of high adherence to treatment with medicines for COPD in the population aged ≥45 years stratified by gender, trend 2019-2023



Adherence to treatment was evaluated only for new users with at least 2 prescriptions. Low adherence to treatment was defined as therapeutic coverage (assessed on the basis of DDD) <40% of the observation period, while high adherence was defined as therapeutic coverage ≥80% of the observation period (for further details please refer to statistical methods)
Adherence to treatment was assessed in the 365 days following the date of the first prescription (index date) only for new users with at least 2 prescriptions. Low adherence to treatment was defined as therapeutic coverage (assessed based on DDD) <40% of the observation period, whereas high adherence was defined as therapeutic coverage ≥80% of the observation period (for further details please refer to the statistical methods).
Percentages of subjects with low/high adherence related to the specified category.
Median follow-up time (IQR): 199 (84-323)

Figure 3.7.1d Time (in days) to discontinuation of treatment with medicines for COPD in the population aged ≥45 years stratified by geographical area; curves are adjusted by gender and age (the Cox model was used to estimate persistence curves)

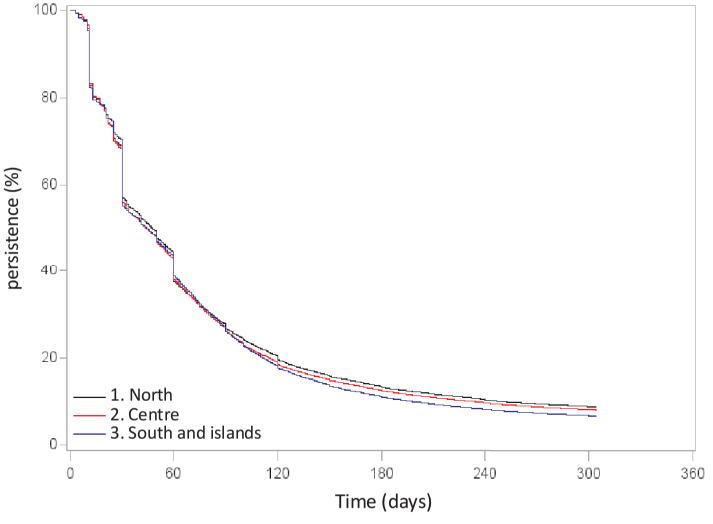
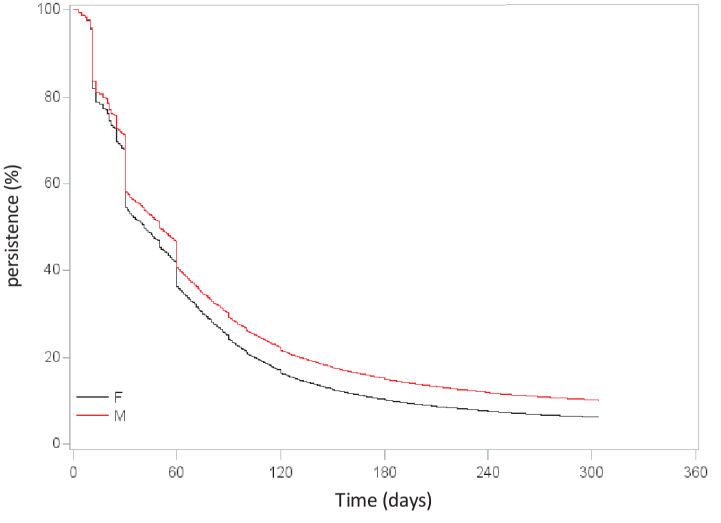


Figure 3.7.1e Time (in days) to discontinuation of treatment with medicines for COPD in the population aged ≥45 years stratified by gender. Curves are adjusted by age (the Cox model was used to estimate persistence curves)



Persistence to treatment was evaluated only for new users with at least 2 prescriptions. Treatment discontinuation occurs if the patient does not receive a prescription within 60 days (for more details please refer to the statistical methods).

3.7.2 Medicines for cystic fibrosis

Medicines for cystic fibrosis recorded an expenditure of 527.2 million euros in 2023, a sharp increase compared to last year (+22.8%). The same trend applies to consumption, with 0.1 DDD/1000 inhabitants per day, up 15.4% compared to 2022 (Box Main indices of expenditure and consumption). Per capita expenditure on drugs for cystic fibrosis has increased significantly over the past decade, reaching 8.96 euros in 2023, +22.8% compared to 2022 and with a +52.5% CAGR over the period 2014-2023. The cost per DDD also recorded a 6.4% increase compared to the previous year, reaching a value of 252.5 euros and a 28.0% average annual variation in the period 2014-2023 (Table 3.7.2a).

The expenditure trend in the category is exclusively due to CFTR modulators, which represent almost 98% of the total, with a 23.5% increase in expenditure compared to 2022 (Table 3.7.2a). The category "Specific action mucolytics", which includes only the active ingredient deoxyribonuclease indicated to improve lung function in patients with cystic fibrosis, had a limited impact on total expenditure in the category and in 2023 it recorded a reduction in both expenditure and consumption (-2.9% for both indicators). Looking at the temporal trend of per capita expenditure on these two subgroups, in the period 2014-2023, a high increase was observed for CFTR modulators with a 52% average annual variation in the period 2015-2023, while mucolytics with specific action remained stable (Figure 3.7.2a).

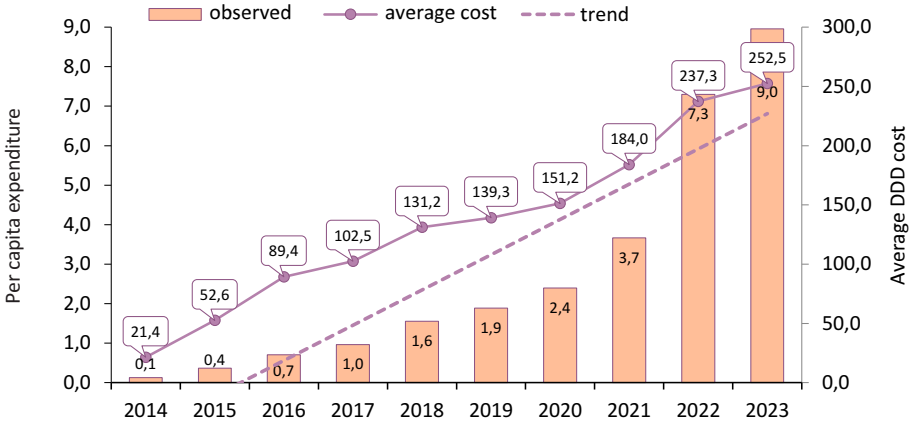
The triple combination elexacaftor/tezacaftor/ivacaftor, recently placed on the market (2021), is the highest-expenditure substance with 4.83 euros per capita (+38.1% compared to 2022). This is followed by ivacaftor, with an expenditure of 3.73 euros per capita, which also increased compared to 2022 (+22.7%). These trends are exclusively due to a consumption increase, of 38.1% and 21.9% respectively, as the average DDD costs of both drugs remained stable compared to last year (+0.0% and +0.7% respectively). The combinations lumacaftor/ivacaftor and ivacaftor/tezacaftor recorded a reduction of approximately 64% in per capita expenditure and of 74.0% and 64.4% in consumption. Only the lumacaftor/ivacaftor combination records a 38.8% increase in the average cost per day of therapy compared to last year (Table 3.7.2a).

There continues to be a marked geographical variability, with the South and the Islands showing a higher per capita expenditure than the rest of Italy (9.20 euros; +2.7% than the national average). However, the Centre recorded the highest increases in expenditure and consumption (respectively +25.1% for expenditure and +17.2% for consumption) compared to 2022 (Table 3.7.2b). The wide variability is also confirmed at a regional level, since the per capita expenditure ranges from a minimum of 5.55 euros in Valle d'Aosta to a maximum of 15.26 euros in Basilicata. The same trend applies to the average DDD cost (167.8 vs 300.6): Valle d'Aosta is the region with the greatest variations in per capita expenditure and average DDD cost (respectively +71.9% and +28.4%) compared to 2022, while Friuli VG records the greatest variation in consumption (+40.0%). At a national level, all expenditure and consumption indicators show an increase compared to last year, except for the Province of Trento, with a 4.5% reduction in consumption (Table 3.7.2b).

MAIN INDICES OF EXPENDITURE AND CONSUMPTION
Medicines for cystic fibrosis

Public expenditure in million euros (% over total)	**527.2**	**(2.0)**
Δ % 2023-2022		22.8
Regional range of gross per capita expenditure:	5.6	15.3
DDD/1000 inhab. per day (% over total)	**0.1**	**(0.0)**
Δ % 2023-2022		15.4
Regional range DDD/1000 inhabitants per day	0.1	0.2

Medicines for cystic fibrosis, temporal trend 2014-2023 of per capita expenditure and average cost per day of therapy



National data on consumption and expenditure by subgroup and substance

Table 3.7.2a Medicines for cystic fibrosis, per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDDcost	Δ % 23-22
CFTR modulators	8.75	23.5	—	0.1	24.2	—	339.52	-0.5
Specific action mucolytics	0.21	-2.9	4.6	<0.05	-2.9	4.7	21.31	0.0
Medicines for cystic fibrosis	**8.96**	**22.8**	**52.5**	**0.1**	**15.4**	**19.1**	**252.49**	**6.4**
elexacaftor/tezacaftor/ivacaftor	4.83	38.1	—	<0.05	38.1	—	289.31	0.0
ivacaftor	3.73	22.7	—	<0.05	21.9	—	431.86	0.7
deoxyribonuclease	0.21	-2.9	4.6	<0.05	-2.9	4.7	21.31	0.0
lumacaftor/ivacaftor	0.17	-64.0	—	<0.05	-74.0	—	607.08	38.8
ivacaftor/tezacaftor	0.03	-64.4	—	<0.05	-64.4	—	169.29	0.0

Figure 3.7.2a Medicines for cystic fibrosis, temporal trend 2014-2023 of per capita expenditure of highest-expenditure subgroups

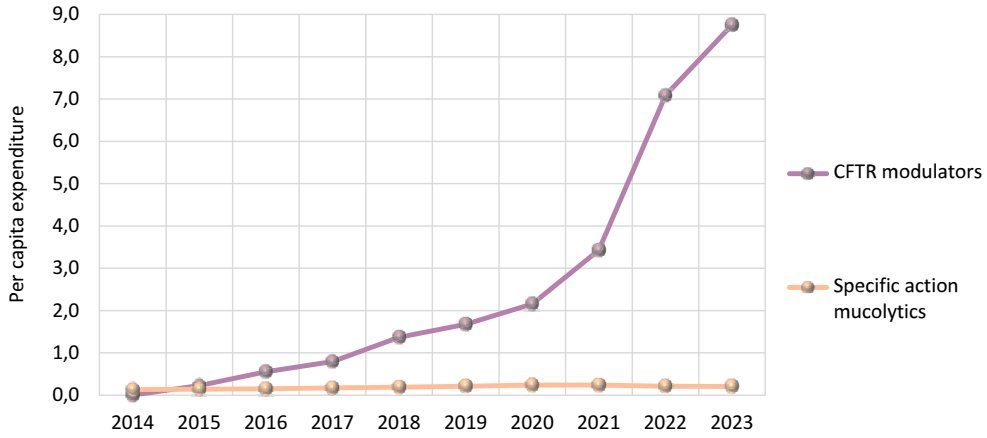


Table 3.7.2b Medicines for cystic fibrosis, regional trend of per capita expenditure, consumption (DDD/1000 inhab. per day) and average cost per day of therapy: comparison 2014-2023

Region	2022			2023			Δ % 23-22			CAGR % 14-23		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost
Piedmont	6.04	0.1	190.84	7.84	0.1	214.43	29.7	15.4	12.4	46.8	16.6	26.0
Valle d'Aosta	3.23	0.1	130.68	5.55	0.1	167.78	71.9	33.9	28.4	45.4	18.5	22.7
Lombardy	7.73	0.1	240.67	9.34	0.1	253.42	20.9	14.8	5.3	55.4	21.5	28.0
Province of Bolzano	10.62	0.2	186.32	15.21	0.2	238.57	43.2	11.9	28.0	42.5	12.1	27.1
Province of Trento	7.60	0.1	206.80	8.39	0.1	239.25	10.5	-4.5	15.7	45.9	14.8	27.1
Veneto	7.01	0.1	212.05	8.52	0.1	228.05	21.6	13.1	7.5	48.8	17.6	26.5
Friuli V.G.	6.28	0.1	274.90	8.94	0.1	279.91	42.5	40.0	1.8	64.8	27.5	29.2
Liguria	8.09	0.1	232.54	10.14	0.1	251.64	25.2	15.7	8.2	49.7	17.2	27.8
Emilia R.	6.71	0.1	291.69	7.62	0.1	287.40	13.5	15.2	-1.5	63.9	26.4	29.7
Tuscany	6.78	0.1	232.69	8.77	0.1	251.74	29.3	19.6	8.2	51.5	18.6	27.8
Umbria	6.43	0.1	218.37	7.76	0.1	241.56	20.6	9.0	10.6	44.3	13.2	27.4
Marche	8.25	0.1	229.87	9.69	0.1	249.63	17.4	8.1	8.6	50.0	17.5	27.7
Lazio	7.28	0.1	244.15	9.13	0.1	255.32	25.5	20.0	4.6	47.4	15.0	28.2
Abruzzo	7.94	0.1	230.08	9.47	0.1	251.54	19.2	9.0	9.3	55.4	21.7	27.8
Molise	5.75	0.1	224.51	8.27	0.1	243.28	43.9	32.8	8.4	46.5	15.1	27.3
Campania	6.67	0.1	241.83	7.71	0.1	252.14	15.7	11.0	4.3	52.1	19.0	27.8
Puglia	7.94	0.1	256.48	9.08	0.1	271.35	14.4	8.1	5.8	59.0	23.4	28.9
Basilicata	12.16	0.1	269.74	15.26	0.1	300.60	25.5	12.6	11.4	42.4	9.5	30.1
Calabria	8.56	0.1	232.05	9.97	0.1	235.56	16.5	14.7	1.5	53.4	20.6	27.2
Sicily	8.44	0.1	266.35	11.20	0.1	280.82	32.7	25.9	5.4	64.0	25.4	30.8
Sardinia	4.62	0.1	198.96	5.67	0.1	219.37	22.6	11.2	10.3	53.4	21.8	26.0
Italy	**7.30**	**0.1**	**237.33**	**8.96**	**0.1**	**252.49**	**22.8**	**15.4**	**6.4**	**52.5**	**19.1**	**28.0**
North	7.15	0.1	230.91	8.78	0.1	246.29	22.7	15.1	6.7	52.4	19.4	27.6
Centre	7.18	0.1	236.55	8.98	0.1	252.47	25.1	17.2	6.7	48.7	16.2	27.9
South and Islands	7.58	0.1	247.07	9.20	0.1	261.50	21.4	14.7	5.8	55.5	20.9	28.6

3.8 Musculo-skeletal system

Medicines for the musculoskeletal system were the eighth category for public expenditure in 2023, with 663.3 million euros, i.e. 2.6% of public expenditure (Box Main indices of expenditure, consumption and exposure). The total per capita expenditure on these drugs was 11.26 euros, divided between approved care regime (5.36 euros per capita) and purchases by public health facilities (5.90 euros). Purchases by public facilities significantly increased compared to the previous year (+30.0%) (Table 3.1).

Consumption for this category of drugs was 45.8 DDD/1000 inhabitants per day, a 0.9% increase compared to 2022. In this case, there is a sharp difference between approved care regime (38.75 DDD/1000 inhabitants per day) and public health facilities (7.05 DDD/1000 inhabitants per day) (Table 3.2).

The analysis of the drug utilization profile, which includes approved care regime and distribution on behalf, confirms the constant increase, in terms of both expenditure and prevalence of use, with increasing age and for both genders. Females report a higher use than males starting from the age of 25, reaching the highest values in the over-seventy-five age group (prevalence: 46.3% in females and 41.8% in males; expenditure: 27.8 euros in females and 13.1 in males). Even the highest consumption values are reached in the age group of over 75 (females 157.9 and males 112.4 DDD/inhabitants per day). This difference is attributable to the higher frequency of use in females of drugs against osteoporosis or other osteorticular diseases.

As for approved care, per capita expenditure was 5.36 euros, with a slight reduction (-0.8%) compared to 2022 (Table 3.9), exclusively due to a decrease in consumption (-1.2%) while prices, the average cost per DDD and the mix effect remained stable. Within this delivery channel, bisphosphonates have the highest impact on expenditure (1.43 euros per capita), up 4.5% compared to 2022 due to an increase in consumption (+5.1%). Next come preparations inhibiting the formation of uric acid, with a per capita expenditure of 0.96 euros, a 4.7% increase due to the combined effect of a 2.3% increase in consumption and a shift towards more expensive molecules (mix effect: +2.4%). “Propionic acid derivatives” and “other nonsteroidal anti-inflammatory and antirheumatic drugs” are the categories with the greatest variation in expenditure and consumption, which respectively range between -9.6% and -12.9% for expenditure and -10.1% and -12.6% for consumption. Among bisphosphonates, alendronic acid is the active ingredient with the greatest impact on expenditure (0.87 euros per capita, equal to 16.2% of the category) with a 7.0% increase compared to 2022, while allopurinol has the highest consumption (8.7 DDD/inhabitants per day and +1.3%) (Table 3.10). Diclofenac is the second active ingredient with the highest expenditure per capita (0.64 euros), representing 12% of the expenditure in the category, followed by etoricoxib (0.62 euros), up 11.5% compared to 2022 (Table 3.10). In 2023 ibuprofen decreased in both expenditure and consumption (of 8.7% and 9.3% respectively). Alendronic acid and febuxostat are among the molecules with the highest increase in expenditure (Table 3.14), while allopurinol is one of the active ingredients with the highest consumption in the approved care regime (Table 3.16).

As for public health care facilities, in 2023 there was an increase in expenditure (+29.6%) determined by both an increase in consumption (+11.5%) and a shift towards more expensive drugs (mix effect: +18.1%), only slightly counterbalanced by a reduction in prices of 1.6%

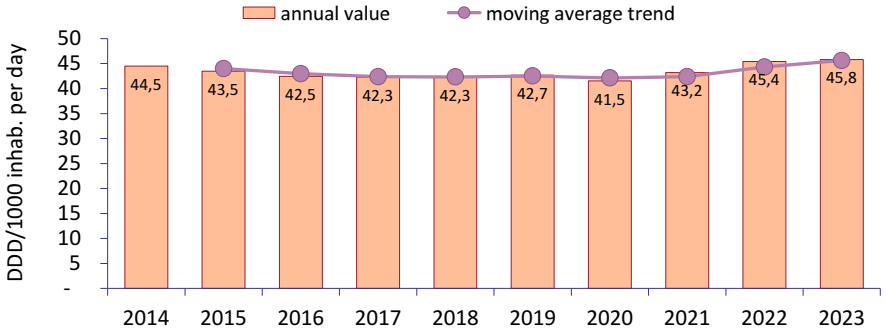
(Table 3.17). The subgroups “other drugs for musculoskeletal disorders” and “other drugs acting on bone structure and mineralization” account for approximately 90% of total expenditure on this category; both recorded increases in expenditure (+23.5% and +43.8%), consumption (+10.4% and +14.5%) and mix effect (+11.8% and +30.7%).

Considering the active ingredients with the highest expenditure, risdiplam, authorised for the treatment of spinal muscular atrophy, is in seventh place among the substances with the highest increase (+72.0%; 1.24 euros per capita) (Table 3.20), while nusinersen (1.09 euros) is among the molecules with the highest reduction in expenditure (-2.2%) (Table 3.21). Both are among the top 30 active ingredients with the highest average cost per DDD (397.3 and 396.1 euros respectively) (Table 3.22). Denosumab ranks third among the substances with the lowest average cost per DDD (0.86 euros per day of therapy) (Table 3.23) and seventh among the top 30 active ingredients by consumption with 5.1 DDD/1000 inhabitants per day (Table 3.24).

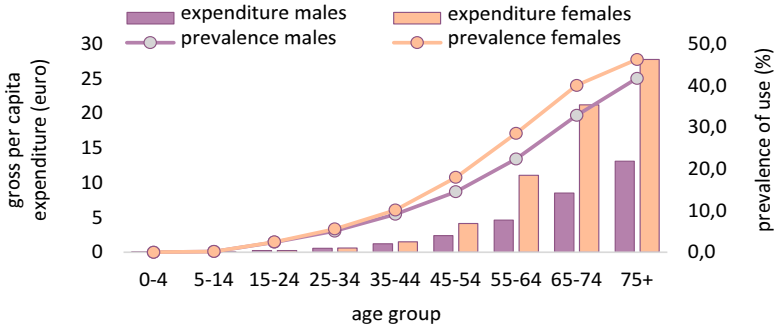
MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Musculo-skeletal system

Public expenditure* in million euros (% over total)	**663.3**	**(2.6)**
Δ % 2023-2022		13.4
Regional range of gross per capita expenditure:	7.4	13.5
DDD/1000 inhabitants per day* (% over total)	**45.8**	**(3.5)**
Δ % 2023-2022		0.9
Regional range DDD/1000 inhabitants per day	34.3	64.8

** includes prescriptions under approved care regime and purchases by public health facilities*



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf by age and gender in 2023 (Figure and Table)



Age group	Gross per capita expenditure			DDD/1000 inhabitants per day		
	Males	Females	Total	Males	Females	Total
0-4	0.0	0.0	0.0	0.0	0.0	0.0
5-14	0.0	0.0	0.0	0.2	0.2	0.2
15-24	0.2	0.2	0.2	1.9	1.7	1.8
25-34	0.6	0.6	0.6	4.2	4.3	4.3
35-44	1.2	1.5	1.4	9.1	9.8	9.5
45-54	2.4	4.1	3.3	18.7	25.1	21.9
55-64	4.6	11.1	7.9	37.5	62.1	50.1
65-74	8.5	21.2	15.2	72.4	116.1	95.4
75+	13.1	27.8	21.8	112.4	157.9	139.3

3.8.1 Medicines for osteoporosis

In 2023, there was a change in the increasing trend in consumption of osteoporosis drugs (including vitamin D and metabolites) observed in recent years, because the doses dispensed decreased by 11.9%, with a value of 140.7 DDD/1000 inhabitants per day. Also expenditure decreased by 2.9%, reaching about 540 million euros, equal to a per capita expenditure of 9.11 euros (Box Main indices of expenditure, consumption and exposure and Table 3.8.1a). This reduction was mainly due to the trend of vitamin D and analogues, whose cost and doses were equal to 4.02 euros and 122.3 DDD, decreasing by approximately 15%. However, they represent approximately 45% and 87% of the entire category. These data confirm the use of cholecalciferol and metabolites for extra-skeletal indications, for which RCTs have not provided evidence of efficacy. Supporting this, in the period 2014-2023 there was a 5.3% average annual increase in consumption (Table 3.8.1a and Figure 3.8.1a).

In 2023, the average DDD cost of osteoporosis drugs increased by 10.2%, returning to the same levels as 2015 (Table 3.8.1a).

As expected based on the prevalence of osteoporotic disease in the population, the prevalence of use and consumption are significantly higher in females than in males. This difference persists in all age groups and reaches a maximum value in people over-75. In this age group, approximately half of women received an osteoporosis drug compared with 20% of men (Box Main indices of expenditure, consumption and exposure).

Monoclonal antibodies, mainly represented by the antiresorptives denosumab, burosumab and romosozumab, rank second in terms of expenditure with 2.08 euros (1.62 euros for denosumab, 0.36 for burosumab and 0.10 for romosozumab). They all record an increase compared to the previous year, despite accounting for a small share of consumption (5.1 DDD/1000 inhabitants per day). In particular, romosozumab, a drug administered once a month subcutaneously with two injections in two different sites, shows increases of more than 100% and has one of the highest average cost per DDD among the category (14.01 euros). Similarly, bisphosphonates alone and teriparatide showed an increase in consumption of 5.5% and 15.7%, respectively (Table 3.8.1a).

The category with the highest exposure among osteoporosis drugs is vitamin D and analogues (total 10.6%; females: 16.3% and males 4.7%). The annual cost per user is 37.2 euros and approximately one in six receives only one prescription during the year (Table 3.8.1b). All other categories have significantly lower levels of exposure in the population. In fact, the second most prevalent category of use is bisphosphonates alone or in combination, which cover 1.5% (1.2% and 0.3% respectively) of the population (Table 3.8.1b). Romosozumab has the highest cost per user of all osteoporosis drugs (2,346 euros), followed by teriparatide (2,242 euros).

The median age of users of osteoporosis drugs is 69 years, ranging from 67 years for users of the “selective estrogen receptor modulators” category to 74 years for users of bisphosphonates, teriparatide, and denosumab. The prevalence of use in females is approximately 3.5 times higher than in males (18% vs 5%) (Table 3.8.1b).

The macro-areas of the North (152.4 DDD/1000 inhabitants per day) show a consumption similar to the South and Islands (141.9 DDD) and 37% higher than the Centre (111.4 DDD/1000 inhabitants per day). All areas show a reduction compared to 2022: -8.2% in the North, -16.0% in the Centre and -15.1% in the South. Expenditure has also decreased,

although to a lower extent, with values ranging from 0.7% in the North to 4.9% in the South and the Islands (Table 3.8.1c).

In the overall population, one in ten people (11.6%) received at least one prescription for drugs belonging to this category in 2023. The prevalence of use is higher in the South (13.3%), while the cost per user in the Centre is 6.3 euros higher than the national average (74.3 vs 68.0 euros) (Table 3.8.1c). The median duration of treatment is approximately three months longer in the North compared to the Centre and the South (336 vs 250 days).

The percentage of subjects with high and low adherence to treatment with osteoporosis drugs was 67.9% and 6.9% respectively, the first stable compared to 2022 while the second decreased by 9%. (Figures 3.8.1b and 3.8.1c). High adherence is higher in women (68.0% vs 66.9% in men), while low adherence shows a higher percentage in men (10.2% vs 6.5% in women).

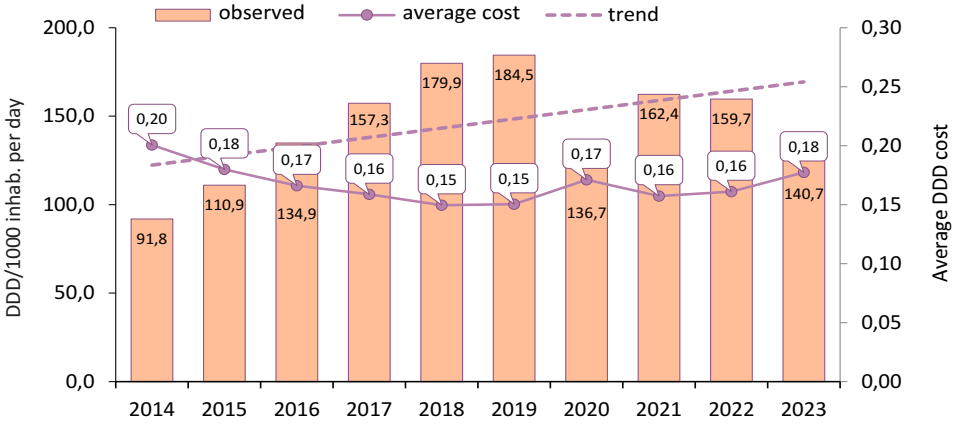
Comparing the persistence data by geographical area (Figure 3.8.1e), no particular differences are noted. However, for these drugs the median time to discontinuation exceeds 365 days, with the exception of the South where it reaches 266 days. This time of discontinuation decreases progressively with age. In the population over 85 years, it is 246 days. Furthermore, there are is a gender difference: in men, persistence to treatment is 255 days while in women it is higher than 365 days (Figure 3.8.1d).

For further information on regional data on exposure and duration of therapy and on indicators of adherence and persistence to treatment stratified by age, gender and geographical area, please refer to the supplementary documents published online.

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Medicines for osteoporosis

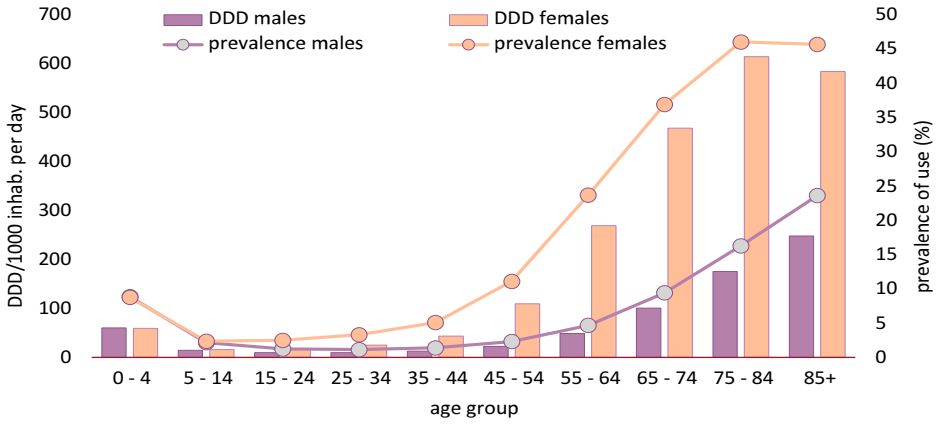
Public expenditure in million euros (% over total)	**536.0**	**(2.1)**
Δ % 2023-2022		-2.9
Regional range of gross per capita expenditure:	6.0	11.3
DDD/1000 inhab. per day (% over total)	**140.7**	**(10.6)**
Δ % 2023-2022		-11.9
Regional range DDD/1000 inhabitants per day	90.9	194.2

Medicines for osteoporosis, temporal trend of consumption and average cost per day of therapy (2014-2023)



** excluding raloxifene*

Distribution of prevalence of use and consumption of medicines for osteoporosis under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.8.1a Medicines for osteoporosis, per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDDcost	Δ % 23-22
Vitamin D and analogues	4.02	-14.7	7.0	122.3	-14.0	5.3	0.09	-0.9
Monoclonal antibodies-enosumab	1.62	16.0	17.2	5.1	14.3	17.4	0.86	1.5
Bisphosphonates alone	1.46	4.3	-1.0	7.5	5.5	0.8	0.53	-1.1
Teriparatide	0.75	-1.1	-1.5	0.2	15.7	3.3	9.99	-14.5
Biphosphonates in combination	0.40	-0.4	-10.1	1.9	-1.6	-6.1	0.59	1.1
Monoclonal antibodies-urosumab	0.36	23.7	—	0.0	64.1	—	142.18	-24.6
Calcium and vitamin D	0.29	-4.7	-5.7	3.1	-5.0	-6.1	0.26	0.4
Monoclonal antibodies-Romosozumab	0.10	>100	—	<0.05	>100	—	14.01	0.1
Calcium	0.09	-6.9	-3.3	0.5	-11.5	-11.2	0.50	5.2
SERM (selective estrogen-receptor modulators)	0.01	2.1	-3.7	<0.05	1.5	-3.7	0.77	0.6
Medicines for osteoporosis	**9.11**	**-2.9**	**3.1**	**140.7**	**-11.9**	**4.4**	**0.18**	**10.2**
denosumab	1.62	16.0	17.2	5.1	14.3	17.4	0.86	1.5
alendronic acid	0.87	7.1	3.5	4.7	8.3	5.0	0.50	-1.2
teriparatide	0.75	-1.1	-1.5	0.2	15.7	3.3	9.99	-14.5
alendronic acid/cholecalciferol	0.40	-0.4	-10.1	1.9	-1.6	-6.1	0.59	1.1
risendronic acid	0.37	1.6	-4.1	2.1	2.3	-2.7	0.47	-0.7
burosumab	0.36	23.7	—	<0.05	64.1	—	142.18	-24.6
calcium/cholecalciferol	0.29	-4.7	-5.7	3.1	-5.0	-6.1	0.26	0.4
calcifediol	0.22	-4.8	10.7	0.2	-4.6	10.6	3.62	-0.2
alfacalcidol	0.21	2.5	9.7	1.3	2.9	10.0	0.45	-0.4
calcitriol	0.21	-1.6	-0.2	1.0	-1.6	-0.5	0.60	0.0

Figure 3.8.1a Medicines for osteoporosis, 2014-2023 temporal trend of consumption (DDD/1000 inhabitants per day) of the highest-expenditure subgroups

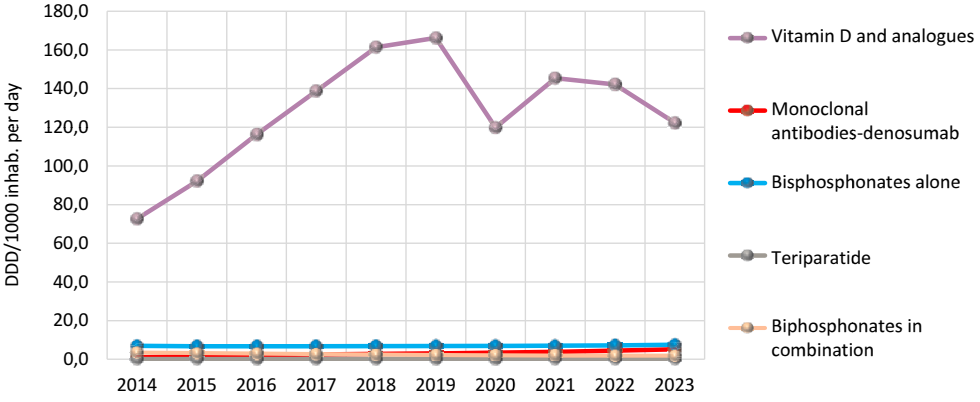


Table 3.8.1b Exposure and duration of therapy with medicines for osteoporosis by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
Vitamin D and analogues	4.7	16.3	10.6	69	37.2	403.5	250.0	16.3
Monoclonal antibodies-denosumab	0.1	0.6	0.3	74	343.1	338.6	363.6	31.4
Bisphosphonates alone	0.2	2.2	1.2	73	113.3	224.6	240.0	9.8
Teriparatide	<0.05	0.1	<0.05	74	2,242.3	205.7	196.0	9.9
Biphosphonates in combination	<0.05	0.6	0.3	74	131.5	224.3	224.0	7.7
Calcium and vitamin D	0.2	1.5	0.9	73	31.8	121.4	90.0	23.5
Monoclonal antibodies-romosozumab	—	<0.05	<0.05	71	2,346.9	166.1	150.4	11.8
Calcium	0.2	0.5	0.3	71	24.1	45.3	30.0	26.8
SERM (selective estrogen-receptor modulators)	<0.05	<0.05	<0.05	67	185.4	242.3	280.0	5.8
Medicines for osteoporosis	**5.0**	**18.0**	**11.6**	**69**	**68.0**	**418.4**	**250.0**	**15.0**

Regional data on expenditure, consumption and exposure

Table 3.8.1c Medicines for osteoporosis, regional trend of per capita expenditure, consumption (DDD/1000 inhab. per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use (%)	Cost/user	Median DDD
Piedmont	7.57	130.7	0.16	-2.1	-10.9	9.9	3.2	5.3	-2.0	10.7	64.6	280.0
Valle d'Aosta	7.21	128.3	0.15	4.0	-1.3	5.4	3.4	8.1	-4.4	10.3	64.4	312.5
Lombardy	10.00	169.8	0.16	-2.4	-7.7	5.7	5.1	7.0	-1.8	12.0	75.3	375.0
Province of Bolzano	9.44	176.3	0.15	6.1	2.7	3.3	5.3	2.9	2.4	9.1	61.2	375.0
Province of Trento	8.16	161.8	0.14	-0.2	-2.9	2.7	5.1	6.2	-1.1	11.6	62.3	315.0
Veneto	7.37	146.0	0.14	4.9	-7.5	13.5	1.4	-3.1	4.6	9.1	66.1	375.0
Friuli V.G.	9.81	172.2	0.16	4.4	-3.8	8.6	6.0	7.1	-1.0	13.1	73.5	344.0
Liguria	8.29	129.1	0.18	-4.5	-14.8	12.0	3.1	4.9	-1.8	11.5	69.2	250.0
Emilia R.	6.85	142.5	0.13	-1.3	-9.2	8.7	1.7	2.7	-1.0	10.6	44.4	250.0
Tuscany	6.25	91.3	0.19	-5.6	-22.4	21.7	0.2	-1.5	1.7	8.1	62.3	250.0
Umbria	6.03	90.9	0.18	-15.2	-24.0	11.4	2.4	3.3	-0.9	9.3	63.3	250.0
Marche	9.52	122.4	0.21	-0.6	-8.2	8.3	3.5	4.9	-1.3	11.0	80.1	250.0
Lazio	10.42	125.3	0.23	-3.2	-13.5	11.8	2.5	5.8	-3.1	11.7	79.6	250.0
Abruzzo	11.32	143.2	0.22	-7.1	-15.7	10.1	2.5	3.7	-1.2	14.7	69.6	250.0
Molise	9.83	151.4	0.18	-2.4	-9.0	7.3	4.5	7.7	-3.0	14.3	64.9	250.0
Campania	10.62	148.3	0.20	-7.6	-19.0	14.1	6.3	10.3	-3.7	12.6	65.8	250.0
Puglia	10.12	145.9	0.19	-7.2	-18.3	13.5	1.2	3.6	-2.3	14.0	64.2	250.0
Basilicata	11.28	172.9	0.18	-3.5	-8.0	4.9	5.2	9.3	-3.8	15.8	68.7	250.0
Calabria	9.57	122.1	0.21	-7.5	-15.2	9.1	3.2	7.9	-4.3	13.7	62.1	250.0
Sicily	9.70	115.9	0.23	-1.9	-14.0	14.0	2.3	6.9	-4.3	12.3	68.3	250.0
Sardinia	11.25	194.2	0.16	6.2	-2.6	9.1	0.7	6.6	-5.5	13.8	75.9	375.0
Italy	**9.11**	**140.7**	**0.18**	**-2.9**	**-11.9**	**10.2**	**3.1**	**4.4**	**-1.2**	**11.6**	**68.0**	**250.0**
North	8.47	152.4	0.15	-0.7	-8.2	8.2	3.6	3.5	0.1	11.0	66.5	336.0
Centre	8.64	111.4	0.21	-4.1	-16.0	14.2	2.1	3.0	-0.9	10.3	74.3	250.0
South and Islands	10.31	141.9	0.20	-4.9	-15.1	12.1	3.0	6.8	-3.5	13.3	66.9	250.0

Figure 3.8.1b Indicators of low adherence to treatment with medicines for osteoporosis in the population aged ≥45 years stratified by gender, trend 2019-2023

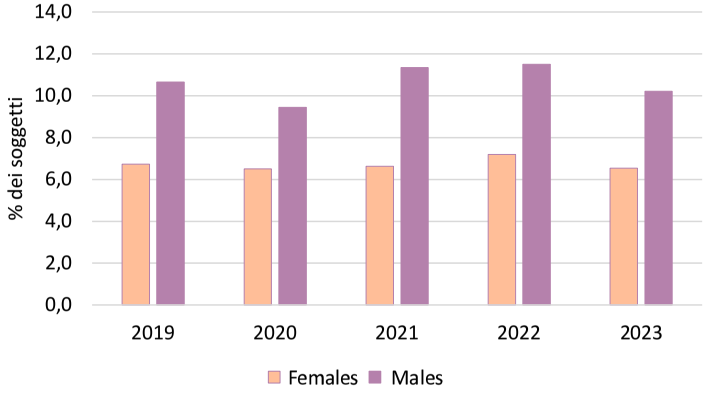
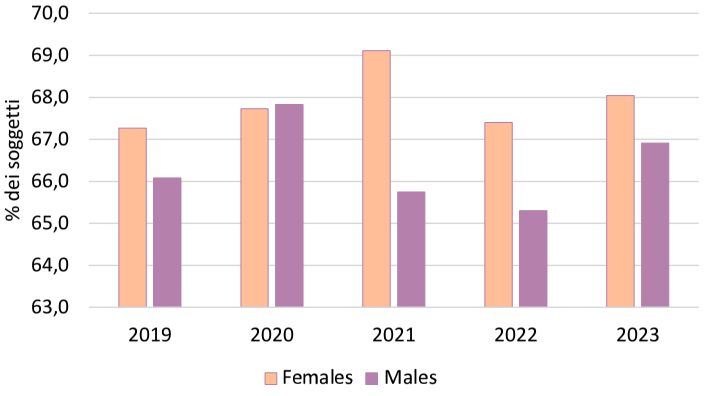


Figure 3.8.1c Indicators of high adherence to treatment with medicines for osteoporosis in the population aged ≥45 years stratified by gender, trend 2019-2023



*Adherence to treatment was evaluated only for new users with at least 2 prescriptions. Low adherence to treatment was defined as therapeutic coverage (assessed on the basis of DDD) <40% of the observation period, whereas high adherence was defined as therapeutic coverage ≥80% of the observation period (for further details please refer to the statistical methods).

Figure 3.8.1d Time (in days) to discontinuation of treatment with medicines for osteoporosis in the population aged ≥45 years stratified by gender. Curves are adjusted by age (the Cox model was used to estimate persistence curves)

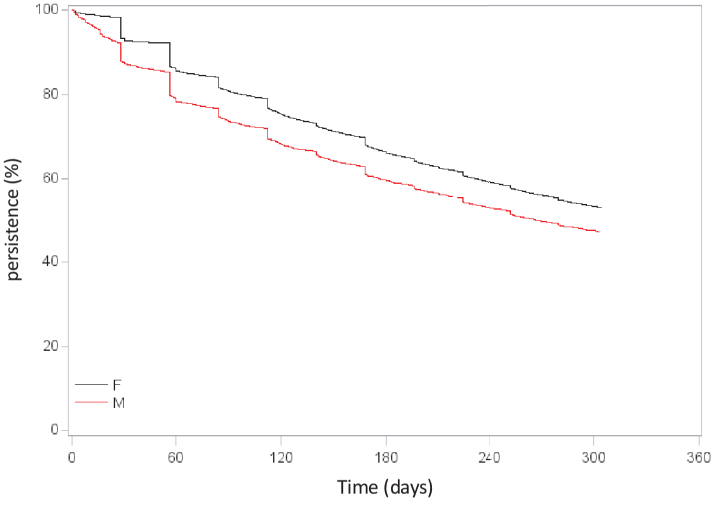
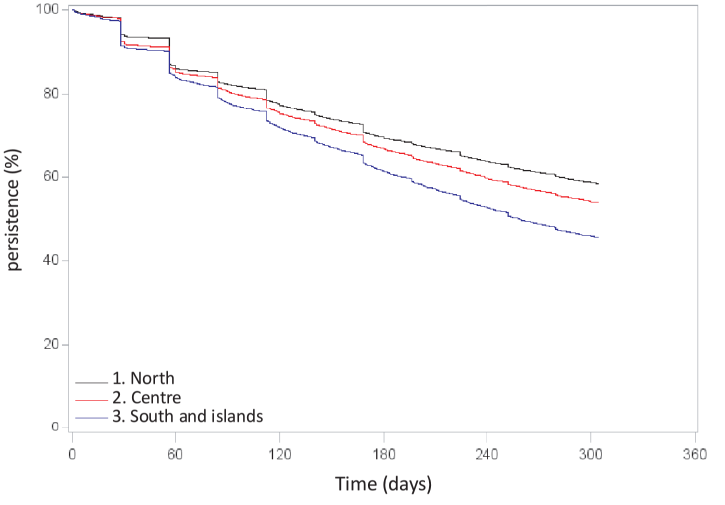


Figure 3.8.1e Time (in days) to discontinuation of treatment with medicines for osteoporosis in the population aged ≥45 years stratified by geographical area. Curves are adjusted by gender and age (the Cox model was used to estimate persistence curves)



3.8.2 Nonsteroidal anti-inflammatory drugs (NSAIDs)

In 2023, total public expenditure on NSAIDs reached 148.9 million euros and 18.1 DDD/1000 inhabitants per day. However, both indicators show a decrease of approximately 5% compared to the previous year. Over the last decade, the use of these drugs has decreased on average each year (CAGR) by 2.3%; at the same time, the average cost per DDD has also recorded a -1.8% annual variation, settling in 2023 at 0.38 euros, a value similar to the previous three years (Box Main indices of expenditure, consumption and exposure).
Using the Health Card data, an analysis was conducted to estimate the exposure and intensity of use of NSAIDs in the population. In 2023, approximately 15 out of 100 citizens received at least one prescription. As expected, based on the epidemiology of clinical conditions such as arthritis and osteoarthritis, where these drugs are indicated, consumption increases with age up to a maximum of 49.4 and 34.4 DDD/1000 inhabitants per day in females and males aged between 75 and 84. In this same age group, the prevalence of use varies between 34.9% in females and 28.8% in males, while up to the age of 44 it does not reach 10%. In all age groups considered, females show higher values than males.

The two main therapeutic categories (traditional NSAIDs and coxibs) account for approximately 97% of expenditure and consumption. For traditional NSAIDs both indicators have decreased (expenditure: -4.8% and DDD: -5.6%), while the prescription of coxibs remains stable (Table 3.8.2a). From 2014 to 2020, consumption of these categories recorded a progressive reduction, and then increased slightly in the last three years for coxibs, whereas for traditional NSAIDs, in 2023, the value returned to a level comparable to 2019 (Figure 3.8.2a).

In 2023, diclofenac was confirmed as the active ingredient with the highest expenditure (0.65 euros), followed by etoricoxib (0.62 euros) and ibuprofen (0.42 euros). The first two molecules show increases of 0.8% and 1.1%. On the contrary, after the increases observed in particular in 2021 and 2022, the consumption of ibuprofen has decreased by 5.7% in terms of expenditure and by 7.0% in terms of doses (Table 3.8.2a). Even greater reductions were found for two other traditional NSAIDs: ketoprofen (DDD: -10.3%) and nimesulide (DDD: -11.9%). In the interpretation, it should be considered that the data in this section do not include private purchases by citizens. For further information on this category, please refer to section 2.6 (NSAIDs and antipyretics).

Ketorolac, approved only for the short-term treatment (maximum five days) of moderate-severe post-operative pain, is among the molecules with the highest average cost per DDD (0.46 euros) and shows a slight increase (+0.8%) in the prescribed doses (Table 3.8.2a).

As expected, this category of drugs is used as needed and for short periods. In fact, half of the users take NSAIDs for one month per year and 50.8% receive only one prescription. The cost per user is 16.2 euros (Table 3.8.2b).

Approximately 13% of the Italian population has received at least one prescription for traditional NSAIDs and 3.3% for Coxibs, which have a cost per user (21.4 euros) 65% higher than traditional NSAIDs and 35% higher than the average (Table 3.8.2b). The median age of Coxib users is 67 years, four years higher than traditional NSAIDs (63 years) and the median use differs by 10 days between the two categories (20 for NSAIDs and 30 for Coxibs).

By analysing the regional variability of NSAID consumption (Table 3.8.2c), in the South consumption is more than double compared to the North (26.2 vs 12.9 DDD/1000 inhabitants

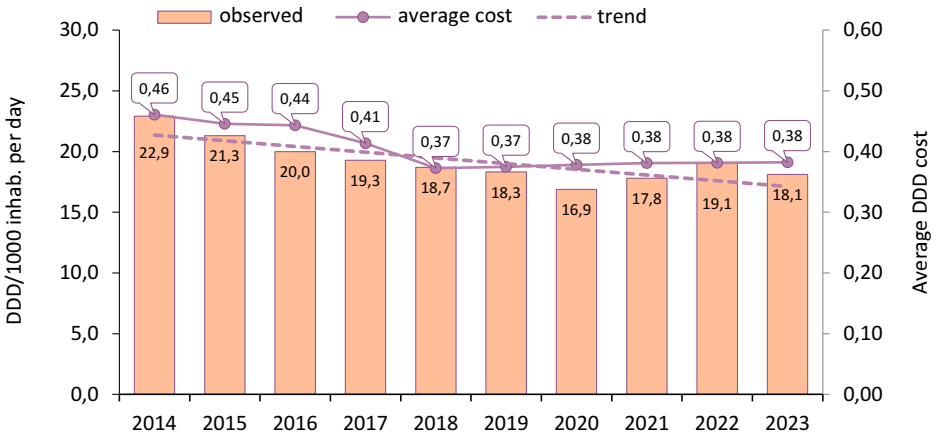
per day) and over 50% higher than the Centre (17.1 DDD/1000 inhabitants per day). However, the average cost per DDD is similar across all geographic areas. The reduction in consumption ranges between 3.3% in the North and 8.7% in the Centre. In the Southern regions, one person in five (prevalence of use: 20.8%) received at least one prescription for NSAIDs in the year, compared to 15.7% in the Centre (1 person in 9) and 10.3% in the North (1 person in 10). When evaluating these territorial differences, it is necessary to take into account the possible greater amount of private purchase of class A drugs or self-medication in the Northern Regions.

For further information on regional data on exposure and duration of therapy, please refer to the supplementary material published online.

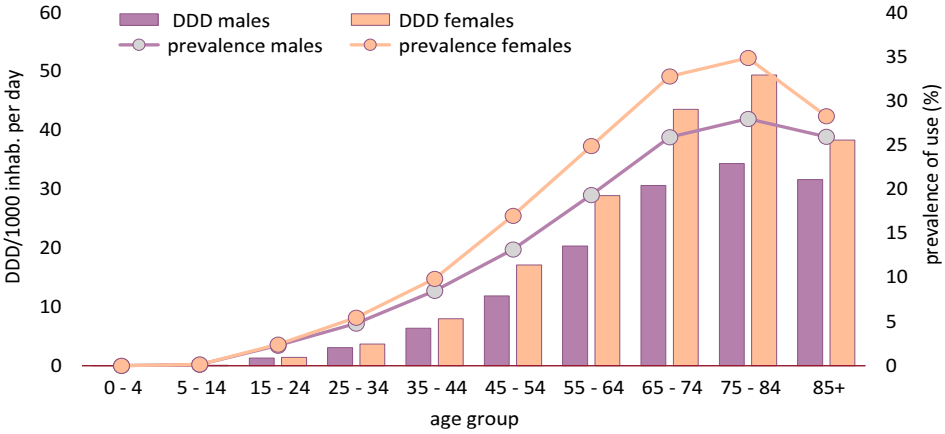
MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Nonsteroidal anti-inflammatory drugs (NSAIDs)

Public expenditure in million euros (% over total)	**148.9**	**(0.6)**
Δ % 2023-2022		-4.6
Regional range of gross per capita expenditure	1.5	4.0
DDD/1000 inhab. per day (% over total)	**18.1**	**(1.4)**
Δ % 2023-2022		-4.9
Regional range DDD/1000 inhabitants per day	10.8	29.1

Nonsteroidal anti-inflammatory drugs (NSAIDs), 2014-2023 temporal trend of consumption and average cost per day of therapy



Distribution of prevalence of use and consumption of nonsteroidal anti-inflammatory drugs (NSAIDs) under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.8.2a Nonsteroidal anti-inflammatory drugs (NSAIDs), per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Traditional NSAIDs	1.74	-4.8	-2.0	13.2	-5.6	-2.3	0.36	0.9
Coxib	0.72	-0.1	-7.2	4.3	0.8	-1.0	0.46	-0.9
Oxicam	0.06	-33.7	-9.9	0.5	-24.1	-8.6	0.31	-12.7
Other nonsteroidal anti-inflammatory/antirheumatics	<0.005	-32.6	-14.5	<0.05	-33.3	-16.8	0.67	1.1
NSAIDs combined with congestant	0.00	-2.1	22.8	0.0	-11.1	19.2	6.42	10.1
Nonsteroidal anti-inflammatory drugs (NSAIDs)	**2.53**	**-4.6**	**-4.1**	**18.1**	**-4.9**	**-2.3**	**0.38**	**0.3**
diclofenac	0.65	0.8	0.7	4.5	0.8	0.6	0.40	0.0
etoricoxib	0.62	1.1	-6.5	3.7	2.0	-0.2	0.46	-0.9
ibuprofen	0.42	-5.7	2.2	2.8	-7.0	2.2	0.41	1.4
ketoprofen	0.25	-10.2	-6.0	2.4	-10.3	-5.6	0.28	0.1
nimesulide	0.13	-11.8	-5.2	1.6	-11.9	-5.5	0.22	0.1
celecoxib	0.10	-6.9	-10.1	0.6	-5.9	-4.7	0.46	-1.1
ketorolac	0.10	-3.6	-3.2	0.6	0.8	-1.2	0.46	-4.4
aceclofenac	0.06	-7.6	-8.8	0.3	-6.6	-7.8	0.49	-1.0
dexibuprofen	0.05	-9.2	-2.3	0.3	-9.2	-2.3	0.49	0.0
naproxen	0.05	-9.0	-4.7	0.5	-8.4	-5.1	0.26	-0.7

Figure 3.8.2a Nonsteroidal anti-inflammatory drugs (NSAIDs), temporal trend of consumption (DDD/1000 inhab. per day) of the most expensive subgroups (2014-2023)

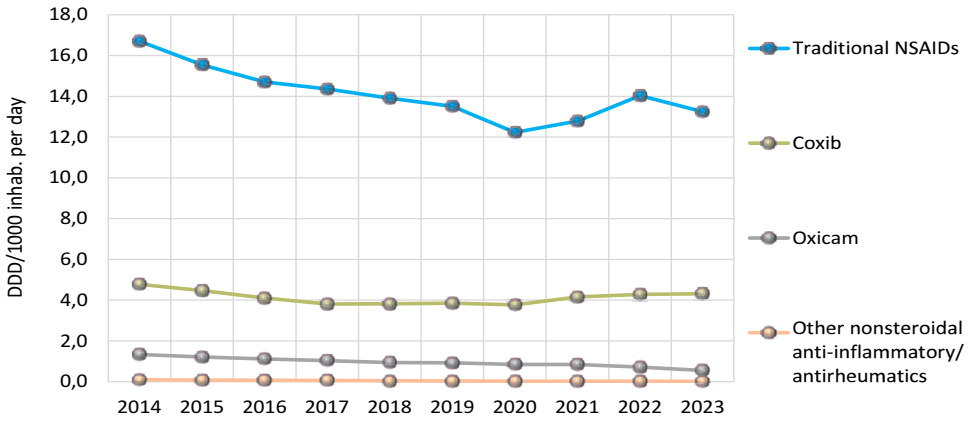


Table 3.8.2b Exposure and duration of therapy with nonsteroidal anti-inflammatory drugs (NSAIDs) by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
Traditional NSAIDs	11.0	14.3	12.7	63	12.9	34.7	20.0	54.0
Coxib	2.4	4.2	3.3	67	21.4	46.8	30.0	61.5
Oxicam	0.5	0.7	0.6	67	10.3	33.1	30.0	70.5
Other non-steroidal anti-inflammatory/anti-rheumatic pharmaceuticals	<0.05	<0.05	<0.05	68	31.2	46.5	30.0	76.8
NSAIDs	**12.7**	**17.0**	**14.9**	**64**	**16.2**	**41.3**	**30.0**	**50.8**

Regional data on expenditure, consumption and exposure

Table 3.8.2c Nonsteroidal anti-inflammatory drugs (NSAIDs), temporal trend of per capita expenditure, consumption (DDD/1000 inhab. per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use (%)	Cost/user	Median DDD
Piedmont	2.09	15.0	0.38	-2.1	-2.0	-0.1	-3.7	-2.0	-1.7	12.8	16.3	27.5
Valle d'Aosta	2.42	17.2	0.38	2.3	2.9	-0.5	-4.2	-2.6	-1.7	12.7	17.9	30.0
Lombardy	1.64	11.7	0.38	-2.0	-3.1	1.0	-3.5	-1.4	-2.2	9.1	16.3	30.0
Province of Bolzano	1.63	12.1	0.37	-0.9	0.6	-1.6	-5.3	-2.7	-2.7	6.3	20.4	30.0
Province of Trento	2.28	16.9	0.37	-4.5	-4.1	-0.3	-2.1	0.2	-2.2	13.1	16.0	30.0
Veneto	1.59	11.4	0.38	-4.5	-4.9	0.4	-5.3	-3.2	-2.1	8.4	17.6	30.0
Friuli V.G.	2.57	18.8	0.38	-0.7	-3.7	3.1	-3.1	-1.1	-2.0	14.5	17.3	30.0
Liguria	1.94	13.2	0.40	-1.6	-2.4	0.8	-4.1	-1.9	-2.2	12.3	15.6	21.0
Emilia R.	1.66	12.9	0.35	-3.7	-3.9	0.2	-2.8	-0.8	-2.0	10.8	13.7	20.0
Tuscany	1.59	11.4	0.38	-14.0	-14.9	1.1	-5.9	-4.6	-1.4	11.2	13.5	20.0
Umbria	1.47	10.8	0.37	-16.6	-16.6	-0.1	-6.0	-4.5	-1.6	11.5	12.8	18.8
Marche	1.88	13.0	0.40	-6.2	-7.0	0.8	-5.3	-3.4	-1.9	13.0	14.3	20.0
Lazio	3.20	23.0	0.38	-6.2	-6.2	0.0	-4.8	-2.5	-2.4	19.8	15.6	27.0
Abruzzo	2.99	21.2	0.39	-3.7	-3.8	0.1	-2.5	-0.8	-1.7	19.4	14.1	20.0
Molise	3.82	26.0	0.40	1.4	1.0	0.4	-3.0	-0.9	-2.2	22.3	16.6	26.7
Campania	4.05	29.1	0.38	-2.9	-2.9	-0.1	-2.7	-1.2	-1.5	21.8	17.0	30.0
Puglia	3.75	26.2	0.39	-6.7	-7.2	0.5	-5.2	-3.9	-1.3	22.3	16.0	30.0
Basilicata	3.75	26.7	0.38	-2.0	-1.7	-0.3	-2.0	-0.5	-1.5	23.2	15.8	30.0
Calabria	4.00	28.6	0.38	-4.7	-4.7	0.0	-4.0	-2.4	-1.6	20.7	18.9	30.0
Sicily	3.27	22.9	0.39	-5.2	-5.1	0.0	-4.7	-2.8	-1.9	17.9	17.4	30.0
Sardinia	3.81	27.2	0.38	-2.9	-3.0	0.1	-4.3	-2.7	-1.7	22.5	17.3	30.0
Italy	**2.53**	**18.1**	**0.38**	**-4.6**	**-4.9**	**0.3**	**-4.1**	**-2.3**	**-1.8**	**14.9**	**16.2**	**30.0**
North	1.78	12.9	0.38	-2.6	-3.3	0.6	-3.8	-1.7	-2.1	10.3	16.1	30.0
Centre	2.39	17.1	0.38	-8.4	-8.7	0.4	-5.1	-3.1	-2.0	15.7	14.8	21.0
South and Islands	3.69	26.2	0.39	-4.3	-4.4	0.1	-3.9	-2.4	-1.6	20.8	16.9	30.0

3.9 Systemic hormonal preparations, excluding sex hormones and insulins

In 2023, the therapeutic category of systemic hormonal preparations, excluding sex hormones and insulins (ATC H), was ninth by public expenditure, amounting to 479.5 euros and 1.8% of total public expenditure (Box Main indices of expenditure, consumption and exposure). The total per capita expenditure on these drugs was 8.14 euros, resulting from both purchases by public health facilities (4.09 euros per capita, a 4.9% decrease compared to 2022) and from approved care regime (4.05 euros per capita, with a 1.9% increase) (Table 3.1). Consumption reached 45.0 DDD/1000 inhabitants per day in 2023, a 2.3% increase compared to 2022, confirming the increasing trend of the last ten years, which places this category in seventh rank in terms of consumption (Table 3.2).

The analysis of the drug-utilization profile, which includes both approved care regime and distribution on behalf, shows an increasing use of this category with age, in both genders, with a greater increase starting from the age of 35. Furthermore, starting from the age of 25, the prevalence of use of these drugs remains higher in the female population than in the male population, up to the age group over 75, where at least one woman in three received prescriptions during the year. At the same time, per capita expenditure also increases with the age of the patients, with higher values in females, until reaching the maximum value of 11.6 euros per capita in patients over 75.

As regards approved care regime, the increase in expenditure (+1.6%) was due to an increase in consumption (+2.4%) and a mix effect of +1.7%, while there was a reduction in prices (-2.4%) compared to 2022 (Table 3.9).

The categories with the highest expenditure under approved care regime are glucocorticoids (1.53 euros per capita, 38% of the total category), followed by thyroid hormones (1.51 euros per capita). The prescription of glucocorticoids is stable compared to the previous year, while thyroid hormones, which have the highest consumption of the entire group of systemic hormonal preparations (23.5 DDD/1000 inhabitants per day), record increases in terms of both expenditure and consumption compared to 2022 (+5.8% and +3.2% respectively), with a shift towards more expensive drugs (mix effect: +2.5%). The active ingredient with the highest expenditure and consumption is levothyroxine (1.48 euros and 23.5 DDD), followed by prednisone (0.70 euros and 7.2 DDD) and teriparatide (0.66 euros and 0.2 DDD) (Table 3.10). Levothyroxine is also the only active ingredient in the category among the top 30 with the highest expenditure (Table 3.11) and consumption (Table 3.16) and among those that, in 2023, recorded the highest increase in expenditure (+6.3%) (Table 3.14), reaching an expenditure value of 87 million euros under the approved care regime, although it is ranked among the top 30 active ingredients with the lowest average cost per DDD (Table 3.13). Teriparatide (11.08 euros) is in second place among the drugs with the highest cost per day of therapy (Table 3.12) and in 29th place among the active ingredients with the greatest reduction in expenditure (-1.9%) in 2023 (Table 3.15).

As regards purchases by public health facilities, there was a -5.2% reduction in expenditure, -0.5% in consumption, -4.6% in prices, with a slight shift towards less expensive medicinal products (mix effect: -0.2%) (Table 3.17).

The category with the greatest impact on expenditure is somatostatin and analogues (1.43 euros per capita), down 12.0% compared to 2022, although consumption increased by 2.9%, followed by somatropin and somatropin agonists (1.10 euros per capita), for which both expenditure (-5.3%) and consumption (-2.7%) decreased (Table 3.17).

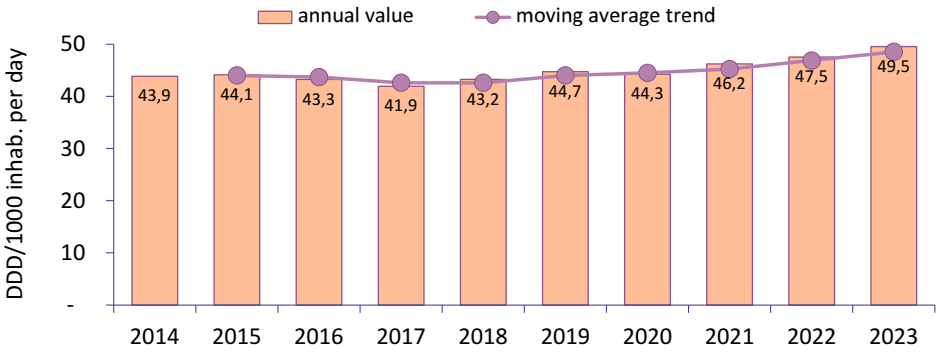
Somatropin is the active ingredient with the highest consumption (0.3 DDD/1000 inhabitants per day) and expenditure per capita (1.09 euros), down 5.6% compared to 2022; etelcalcetide is the active ingredient with the highest increase in expenditure (+12.4%); lanreotide shows the highest reduction in expenditure (-28.4%) and pegvisomant is the active ingredient with the highest average cost per DDD (65.37 euros), although it decreased by 4.3% compared to the previous year (Table 3.18). Furthermore, somatropin is among the top 30 active ingredients with the greatest reduction in expenditure compared to 2022 and with the lowest average cost per day of therapy among drugs purchased by public health facilities (Tables 3.21 and 3.23). Levothyroxine is in eighth place among the top 30 highest-consumption active ingredients related to drugs provided under approved care regime and purchased by public health facilities (Table 3.26).

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

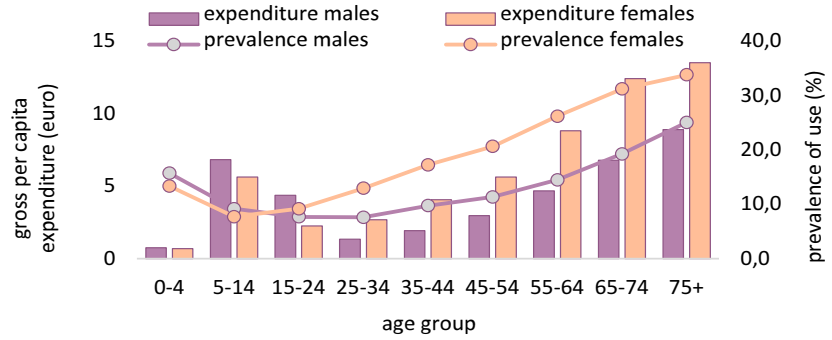
Systemic hormonal preparations, excluding sex hormones

Public expenditure* in million euros (% over total)	**479.5**	**(1.8)**
Δ % 2023-2022		-1.5
Regional range of gross per capita expenditure:	6.1	10.0
DDD/1000 inhabitants per day* (% over total)	**45.0**	**(3.4)**
Δ % 2023-2022		2.3
Regional range DDD/1000 inhabitants per day	30.6	56.9

** includes prescriptions under approved care regime and purchases by public health facilities*



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf by age and gender in 2023 (Figure and Table)



Age group	Gross per capita expenditure			DDD/1000 inhabitants per day		
	Males	Females	Total	Males	Females	Total
0-4	0.7	0.7	0.7	3.8	3.2	3.5
5-14	6.8	5.6	6.2	5.4	4.6	5.0
15-24	4.4	2.2	3.3	7.1	9.5	8.2
25-34	1.3	2.7	2.0	9.0	21.4	15.1
35-44	1.9	4.1	3.0	13.5	36.1	24.8
45-54	3.0	5.6	4.3	19.8	52.5	36.3
55-64	4.7	8.8	6.8	30.9	76.8	54.4
65-74	6.8	12.4	9.7	46.7	100.0	74.8
75+	8.9	13.5	11.6	63.1	106.3	88.7

3.9.1 Thyroid medicines

In 2023, public expenditure on thyroid medicines was 93 million euros, corresponding to a consumption of 25.2 DDD/1000 inhabitants per day, a 3.4% increase compared to 2022 (Box Main indices of expenditure, consumption and exposure). Over the last ten years, the consumption of these drugs has recorded slight annual increases. In the same years, the average cost per day of therapy has also increased, from 0.11 euros in 2014 to 0.17 euros in 2023, probably due to the use of more expensive products.

In line with epidemiological evidence, females use more drugs than males. Consumption increases progressively with age until reaching higher values in the over-85 age group: 76.4 DDD in females and 28.9 DDD in males. The prevalence trend is in line with consumption and, in the 65-74 and 75-84 age groups, females recorded percentages of 15.6% and 17.1% respectively, more than three times higher than males. However, the greatest differences are in the 45-54 age group (females: 8.2% vs. males: 15%).

Thyroid hormones represent almost all of the expenditure and consumption of the category, with 1.52 euros per capita and 23.9 DDD/1000 inhabitants per day. In the period 2014-2023, despite a modest increase in consumption (CAGR: +1.9%), there were more significant variations in expenditure (CAGR: +6.8%), with a 6.1% increase compared to 2022 (Table 3.9.1a and Figure 3.9.1a). This also applies to the analysis of the individual active ingredients. Levothyroxine, a drug authorised for various types of hypothyroidism, accounts for almost all of the prescriptions for this subgroup. In 2023, it recorded an expenditure of 1.48 euros per capita, a 6.3% increase and a progressive increase over the years (CAGR: +7.0%), with consumption levels of 23.8 DDD/1000 inhabitants per day, up 3.6% compared to 2022. In contrast, the consumption of antithyroid preparations (thiamazole) has slightly decreased over the years (CAGR: -0.7%).

The prevalence of use of thyroid medications in 2023 was 5.4%, with significant differences between males (2.0%) and females (8.6%). The median age of users is 65 years, with a difference of 7 years between antithyroid preparations (71 years) and thyroid hormones (64 years). Each user, on average, remained on treatment for approximately 5.5 months, and half of the users for less than 5 months. Approximately one-third of users of antithyroid preparations received only one prescription compared to 4.1% for thyroid hormones (Table 3.9.1b).

The Centre shows the highest levels of consumption, with a value of 30.5 DDD/1000 inhabitants per day in 2023, a 2.7% increase compared to 2022 (Table 3.9.1c), even if the greatest variation is recorded in the North (+3.8%). Basilicata has the highest consumption (34.1 DDD; +5.2% compared to 2022), followed by Molise (33.9 DDD). All regions, with the exception of Abruzzo (+4.8%), Lazio and Valle d'Aosta (+3.7%) and the Province of Bolzano (+2.3%), recorded expenditure increases above 5%. In the North there is a lower prevalence of use (4.9%) than in the South (5.4%) and in the Centre (6.6%).

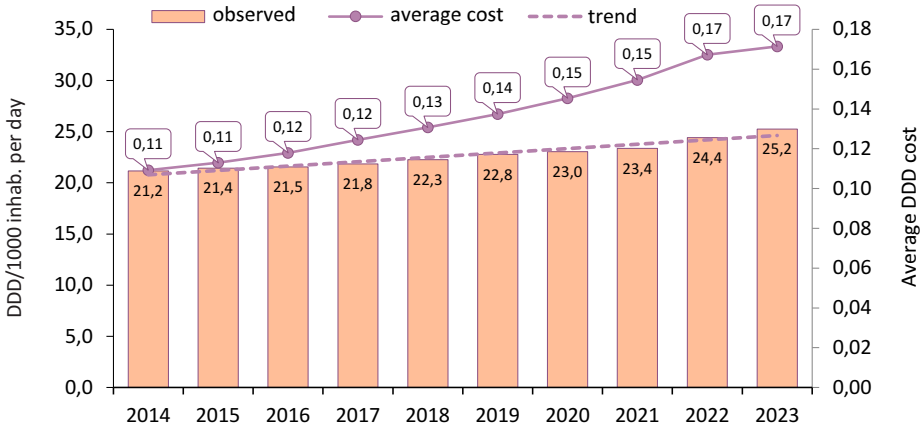
For further information on regional data on exposure and duration of therapy, please refer to the supplementary documents published online.

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Thyroid medicines

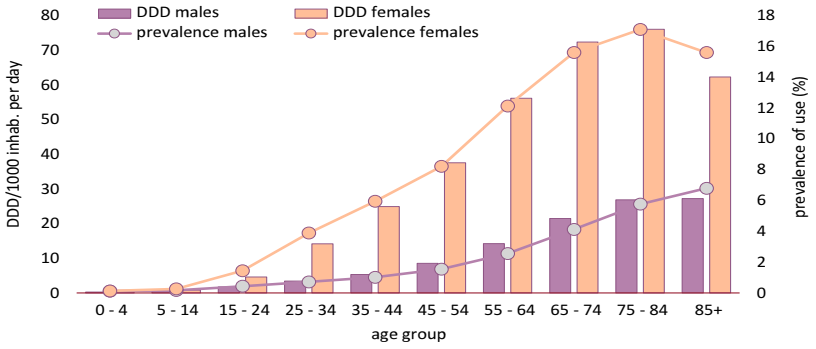
Public expenditure* in million euros (% over total)	**93.0**	**(0.4)**
Δ % 2023-2022		6.0
Regional range of gross per capita expenditure:	0.8	2.3
DDD/1000 inhabitants per day* (% over total)	**25.2**	**(1.9)**
Δ % 2023-2022		3.4
Regional range DDD/1000 inhabitants per day	12.1	34.1

* includes prescriptions under approved care regime and purchases by public health facilities

Thyroid medicines, temporal trend 2014-2023 of per capita expenditure and average cost per day of therapy



Distribution of prevalence of use and consumption of thyroid medicines under approved care regime and distribution on behalf (year 2023)



National data on consumption and expenditure by subgroup and substance

Table 3.9.1a Thyroid medicines, consumption (DDD/1000 inhab. per day) by therapeutic category and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Thyroid hormones	1.52	6.1	6.8	23.9	3.6	1.9	0.17	2.4
Antithyroid preparations	0.06	4.0	0.8	1.4	0.6	-0.7	0.12	3.3
Thyroid medicines	**1.58**	**6.0**	**6.5**	**25.2**	**3.4**	**1.8**	**0.17**	**2.5**
levothyroxine	1.48	6.3	7.0	23.8	3.6	1.9	0.17	2.6
tiamazole	0.06	4.0	0.8	1.4	0.6	-0.7	0.12	3.3
liothyronine	0.03	-0.3	1.3	0.0	-0.3	1.3	2.06	-0.1

Figure 3.9.1a Thyroid medicines, temporal trend of consumption (DDD/1000 inhab. per day) of most expensive subgroups (2014-2023)

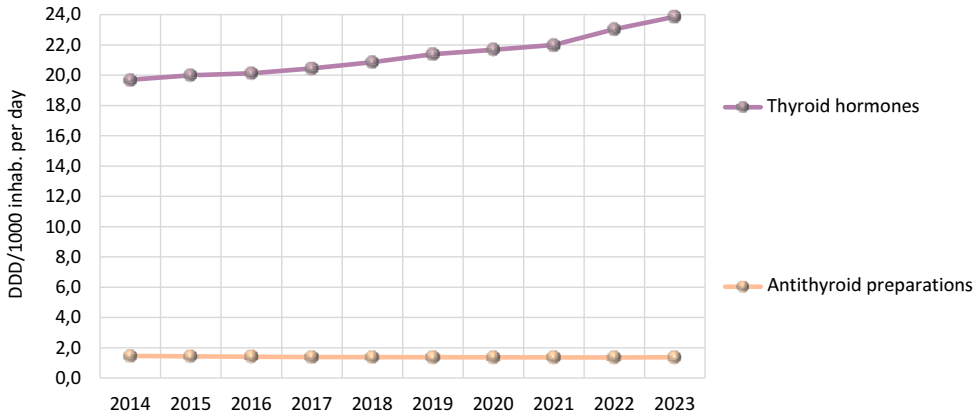


Table 3.9.1b Exposure and duration of therapy with thyroid medicines by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)			Median age	Cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
	males	females	total					
Thyroid hormones	1.8	8.2	5.1	64	29.5	167.1	150.0	4.1
Antithyroid preparations	0.2	0.5	0.3	71	16.6	135.3	100.0	27.2
Thyroid medicines	**2.0**	**8.6**	**5.4**	**65**	**28.7**	**165.4**	**150.0**	**5.5**

Regional data on expenditure, consumption and exposure

Table 3.9.1c Thyroid medicines, regional trend of per capita expenditure, consumption (DDD/1000 inhab. per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use (%)	Cost/user	Median DDD
Piedmont	1.48	24.9	0.16	7.9	4.2	3.5	6.9	2.4	4.4	5.9	25.8	141.7
Valle d'Aosta	1.20	21.3	0.15	3.7	2.5	1.2	1.5	-1.5	3.0	4.9	24.4	133.3
Lombardy	1.20	18.1	0.18	8.9	5.4	3.3	8.2	2.7	5.4	3.8	30.3	150.0
Province of Bolzano	1.13	23.2	0.13	2.3	2.0	0.2	4.1	0.9	3.1	4.6	22.5	150.0
Province of Trento	1.98	31.9	0.17	4.9	2.7	2.1	6.8	2.3	4.4	6.6	29.1	150.0
Veneto	1.72	22.3	0.21	6.3	3.6	2.5	9.0	2.3	6.6	4.5	37.5	155.0
Friuli V.G.	1.66	28.4	0.16	5.2	3.5	1.7	6.5	2.3	4.1	6.5	26.9	150.0
Liguria	0.85	12.1	0.19	5.7	1.2	4.4	6.2	0.2	5.9	3.0	29.2	130.0
Emilia R.	1.66	32.3	0.14	4.8	2.3	2.4	5.0	1.5	3.5	6.6	24.2	150.0
Tuscany	1.42	27.7	0.14	5.1	3.1	1.9	5.5	2.2	3.3	6.3	22.7	150.0
Umbria	1.99	33.3	0.16	5.6	4.0	1.5	6.9	2.8	4.0	7.5	27.5	150.0
Marche	1.50	28.5	0.14	6.4	3.7	2.6	5.3	1.9	3.3	6.4	23.9	150.0
Lazio	2.15	32.4	0.18	3.7	2.0	1.7	5.5	0.5	5.0	6.7	31.3	150.0
Abruzzo	1.67	27.5	0.17	4.8	3.3	1.4	6.9	2.6	4.2	5.6	28.0	150.0
Molise	2.26	33.9	0.18	5.5	2.8	2.6	5.9	1.2	4.7	7.2	30.8	150.0
Campania	1.38	20.4	0.19	5.9	3.4	2.5	6.0	1.5	4.4	4.5	28.7	133.3
Puglia	1.97	31.1	0.17	6.7	4.6	2.0	6.6	2.4	4.1	6.6	29.0	150.0
Basilicata	1.82	34.1	0.15	7.8	5.2	2.4	6.2	2.7	3.4	7.0	26.0	166.7
Calabria	1.58	25.2	0.17	6.3	2.9	3.3	5.4	0.9	4.5	5.4	28.8	150.0
Sicily	1.59	23.6	0.18	5.4	2.6	2.7	6.8	1.7	5.0	4.9	31.5	150.0
Sardinia	1.83	30.2	0.17	6.0	2.9	3.0	5.2	0.3	4.9	6.2	30.9	175.0
Italy	**1.58**	**25.2**	**0.17**	**6.0**	**3.4**	**2.5**	**6.5**	**1.8**	**4.6**	**5.4**	**28.7**	**150.0**
North	1.43	22.7	0.17	6.9	3.8	3.0	7.2	2.1	4.9	4.9	28.9	150.0
Centre	1.82	30.5	0.16	4.5	2.7	1.8	5.6	1.4	4.2	6.6	27.5	150.0
South and Islands	1.65	25.7	0.18	6.0	3.5	2.5	6.2	1.7	4.5	5.4	29.5	150.0

3.10 Sensory organs

In 2023, medicines for sensory organs (ATC S) were the eleventh category for public expenditure, with 400.5 million euros (1.5% of total expenditure), corresponding to a consumption of 23.7 DDD/1000 inhabitants per day, 1.8% of the consumption of drugs covered by the NHS (Box Main indices of expenditure, consumption and exposure).

The overall per capita expenditure was 6.80 euros per capita, of which 3.76 euros were due to approved care regime, a 3.1% increase compared to the previous year. The share of purchases by public health facilities is slightly lower (3.04 euros per capita), with a 7.3% decrease compared to 2022 (Table 3.1). Consumption for this category was 23.7 DDD/1000 inhabitants per day, up 1.9% compared to the previous year (Table 3.2). This is mainly due to the approved care regime, with a consumption value of 21.8 DDD.

The analysis of the drug utilization profile by age group and gender, including approved care regime and distribution on behalf, confirms a limited use of these drugs up to the age of 55 and an increase in subsequent age groups up to almost 10% in people aged over 75. Consumption remains slightly higher in males in females in all age groups, with values that differ most in the +75 age group (98.3 DDD in males vs 85.9 in females). Per capita expenditure also increases with age, reaching a maximum value of 15.7 euros among people over 75, with a higher level for males (17.0 euros) than for females (14.8 euros).

Overall, expenditure under approved care regime shows a 2.8% increase, linked to a consumption increase (+2.1%) rather than to price variations or the mix effect (+0.2 and +0.4% respectively), with a stable average cost per DDD (+0.6%) (Table 3.9). In this delivery channel, beta-blockers have the highest expenditure (2.14 euros) and consumption (12.2 DDD). They are followed by prostaglandin analogues, with 1.21 euros and 5.8 DDD respectively. In 2023, the greatest increases in terms of consumption are reported for the dorzolamide/timolol combination (+13.9%), with per capita expenditure representing 14.7% of the category. In detail, timolol alone or in combination with other active ingredients accounts for over 46% of expenditure on the entire category (Table 3.10). The same combination is among the first 30 molecules with the highest increase in approved care (+15.4%) compared to the previous year (Table 3.14).

Purchases by public health facilities recorded a 7.5% reduction in expenditure, due to a decrease in prices and consumption (-12.9% and -3.7% respectively), but with a shift towards more expensive substances (mix effect: +10.2%) (Table 3.17). The therapeutic category with the greatest impact on expenditure (70%) is antineovascularization substances, which include drugs for the treatment of exudative neovascular age-related macular degeneration (AMD) and those for the treatment of visual impairment caused by diabetic macular edema (DME). This category records a 12.2% decrease in expenditure, mainly related to a reduction in consumption and prices (-12.1% and -18.6% respectively). In this case, there is a greater purchase of more expensive products (mix effect: +22.9%). Within this subgroup, aflibercept is the active ingredient with the highest expenditure (1.42 euros), accounting for 46.6% of the expenditure in the category, followed by ranibizumab (0.52 euros and an incidence of 17.2%). In 2023 this active ingredient decreased in expenditure (-34.0%), consumption (-15.0%) and average cost per DDD (-22.4 euros), probably due to the patent expiry of the molecule in July 2022 (Table 3.18). Aflibercept is among the molecules with the greatest reduction in expenditure (-4.3%) as regards purchases by public health facilities (Table 3.21) and is the only active ingredient of this ATC on the list of substances with the highest average

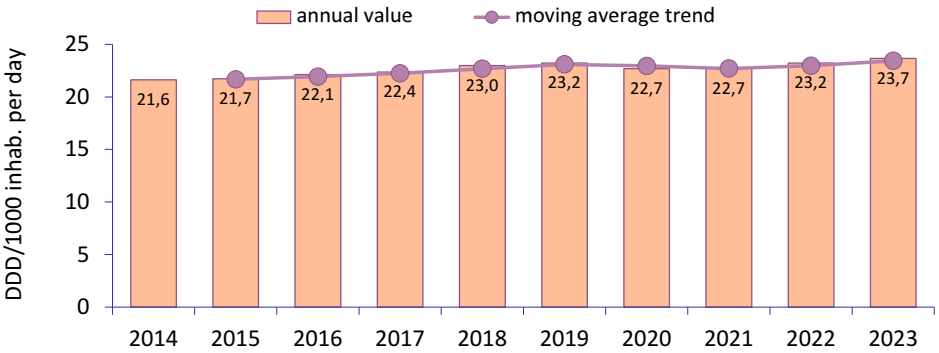
cost per day of therapy (Table 3.22), with a value of 400.8 euros – despite decreasing compared to the previous year (-18.7%).

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

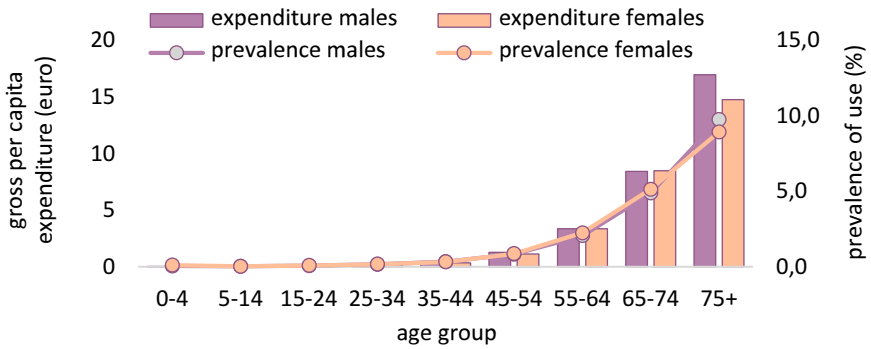
Sensory organs

Public expenditure* in million euros (% over total)	**400.5**	**(1.5)**
Δ % 2023-2022		-1.8
Regional range of gross per capita expenditure:	5.7	10.3
DDD/1000 inhabitants per day* (% over total)	**23.7**	**(1.8)**
Δ % 2023-2022		1.9
Regional range DDD/1000 inhabitants per day	18.8	33.7

** includes prescriptions under approved care regime and purchases by public health facilities*



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf by age and gender in 2023 (Figure and Table)



Age group	Gross per capita expenditure			DDD/1000 inhabitants per day		
	Males	Females	Total	Males	Females	Total
0-4	0.0	0.0	0.0	0.2	0.3	0.2
5-14	0.0	0.0	0.0	0.2	0.2	0.2
15-24	0.1	0.1	0.1	0.5	0.5	0.5
25-34	0.2	0.2	0.2	1.2	1.0	1.1
35-44	0.5	0.4	0.4	2.7	2.1	2.4
45-54	1.3	1.1	1.2	7.4	6.6	7.0
55-64	3.4	3.4	3.4	19.6	19.5	19.6
65-74	8.4	8.5	8.5	48.8	48.8	48.8
75+	17.0	14.8	15.7	98.3	85.9	91.0

3.10.1 Medicines for eye disorders

Public expenditure on drugs for eye disorders reached approximately 390 million euros in 2023, down 1.9% compared to 2022. Doses increased by 2.5%, reaching 22.0 DDD/1000 inhabitants per day, 1.7% of the consumption of drugs covered by the NHS. Consumption has increased slightly over the last ten years, from 20.0 DDD in 2014 to 22.0 DDD in 2023, with a 1.0% average annual increase. In the same period, the average cost per day of therapy also increased by 17.0%, going from 0.74 euros in 2014 to 0.82 euros in 2023 (Box Main indices of expenditure and consumption).

Antiglaucoma preparations (21.5 DDD, approximately 98% of the total) are the category with the highest consumption: in particular, antiglaucoma preparations/beta-blockers alone or in combination (12.7 DDD/1000 inhabitants per day) and antiglaucoma preparations/prostaglandin analogues (5.8 DDD) (Table 3.10.1a). Both categories recorded increases of 2.5% and 2.8% respectively (Table 3.10.1a). This trend is also evident in per capita expenditure, which is 2.20 euros for the former (+3.5% compared to 2022) and 1.21 euros for the latter (+1.8%). However, while antiglaucoma preparations/beta-blockers alone or in combination recorded a 0.8% average annual increase from 2014 to 2023, in the same period antiglaucoma preparations/prostaglandin analogues remained almost stable (Figure 3.10.1a). Recombinant anti-VEGF fusion proteins (aflibercept) showed a 4.3% expenditure decrease and a 17.8% consumption increase. The expenditure variation was due to the reduction in the average cost per day of therapy (-18.7%), which however remains among the highest in the entire category (400.79 euros). Anti-VEGF monoclonal antibodies (brolucizumab), corticosteroids (intravitreal implants) and antiglaucoma-parasympathomimetic preparations are the categories with the greatest expenditure increases (+28.2%, +14.6% and +12.8% respectively) (Table 3.10.1a). Timolol alone or in combination is the molecule with the highest expenditure (1.80 euros per capita) and consumption (10.5 DDD). In terms of expenditure, aflibercept (1.42 euros; -4.3% compared to 2022) and ranibizumab (0.52 euros; -34.0%) follow. Such drugs are indicated in the treatment of neovascular (exudative) age-related macular degeneration (AMD) (Table 3.10.1a). The patent expiry drove the reduction in expenditure on ranibizumab at the end of 2022. It is worth noting that AIFA Note 98 regulates the prescription, intravitreal administration, and use of anti-VEGF drugs for the treatment of maculopathy at the expense of the NHS.

There are no significant geographical differences in expenditure (Table 3.10.1b). The North shows a slightly higher expenditure (6.94 euros per capita), compared to the Centre (6.21 euros) and the South (6.42 euros). Friuli VG has the highest per capita expenditure (9.02 euros), while Sicily records the lowest value (5.59 euros). Valle d'Aosta shows the greatest increase in expenditure compared to 2022 (+52.1%), while the Province of Trento has the greatest reduction (-8.2%). There is a clear regional variability in consumption, from a minimum of 16.9 DDD in the Province of Bolzano to a maximum of 32.3 DDD in Marche (a difference of 89%), with increases in all regions, with the exception of Valle d'Aosta (-0.9%). The most expensive drugs are used in Valle d'Aosta, 1.39 euros per DDD compared to a national average of 0.82 euros, while the least expensive drugs are used in Tuscany (0.62 euros).

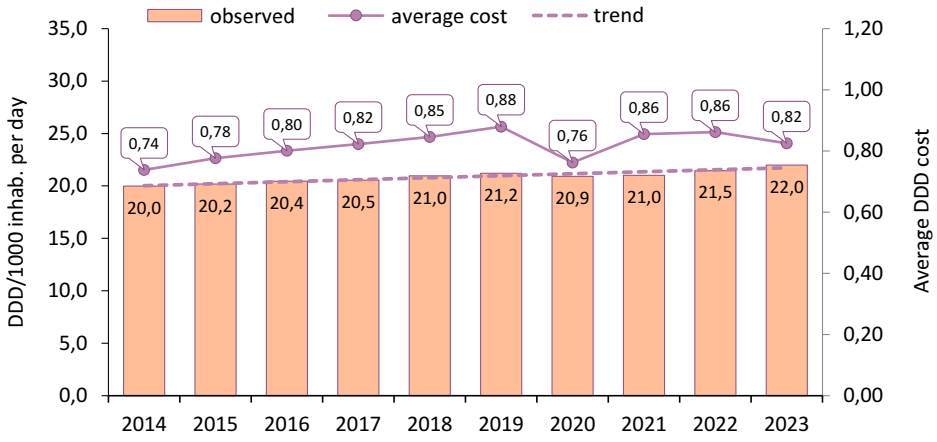
MAIN INDICES OF EXPENDITURE AND CONSUMPTION

Medicines for eye disorders

Public expenditure in million euros (% over total)	**389.7**	**(1.5)**
Δ % 2023-2022		-1.9
Regional range of gross per capita expenditure:	5.6	10.1
DDD/1000 inhab. per day (% over total)	**22.0**	**(1.7)**
Δ % 2023-2022		2.5
Regional range DDD/1000 inhabitants per day	16.9	32.3

*includes prescriptions under approved care regime and purchases by public health facilities

Medicines for eye disorders, temporal trend of consumption and average cost per day of therapy (2014-2023)

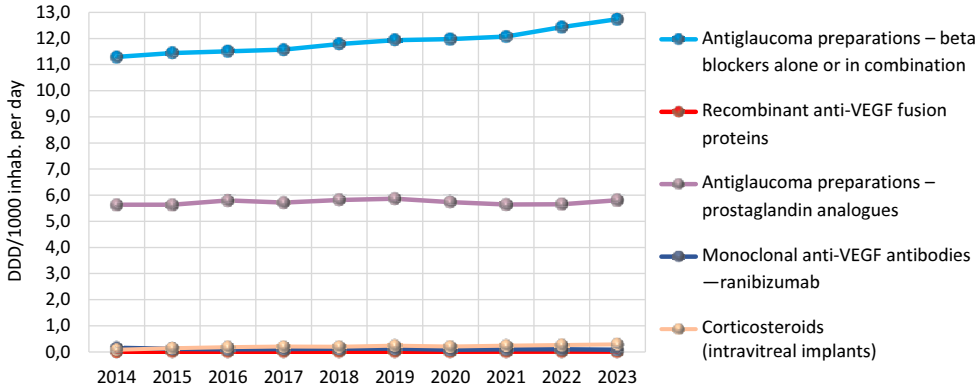


National data on consumption and expenditure by subgroup and substance

Table 3.10.1a Medicines for eye disorders, per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and substance: comparison 2014-2023

Subgroups and substances	Expenditure per capita	Δ % 23-22	CAGR % 14-23	DDD/ 1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Antiglaucoma preparations – beta blockers alone or in combination	2.20	3.5	0.8	12.7	2.5	1.2	0.47	1.0
Recombinant anti-VEGF fusion proteins	1.42	-4.3	23.7	<0.05	17.8	30.4	400.79	-18.7
Antiglaucoma preparations – prostaglandin analogues	1.21	1.8	-0.8	5.8	2.8	0.3	0.57	-0.9
Monoclonal anti-VEGF antibodies—ranibizumab	0.52	-34.0	-8.8	0.1	-15.0	-6.4	17.39	-22.4
Corticosteroids (intravitreal implants)	0.52	14.6	12.5	0.3	9.2	13.0	5.03	4.9
Antiglaucoma preparations – carbonic anhydrase inhibitors alone or in combination	0.23	6.9	-1.9	1.4	1.1	-0.3	0.44	5.8
Monoclonal anti-VEGF antibodies—brolucizumab	0.20	28.2	—	<0.05	28.0	—	401.52	0.1
Other ophthalmological medicines (gene therapy)	0.11	-15.1	—	<0.05	-15.1	—	297000.00	0.0
Antiglaucoma preparations—sympathomimetics	0.10	2.4	2.3	1.6	2.5	2.2	0.18	-0.1
Other ophthalmological drugs	0.07	6.4	29.4	<0.05	51.3	25.0	8.35	-29.7
Antiglaucoma preparations-parasympathomimetics	0.01	12.8	2.9	<0.05	-1.4	-5.6	1.20	14.4
Corticosteroids alone	0.01	-4.1	13.4	<0.05	-8.5	-3.7	2.96	4.9
Antineovascularising agents (photodynamic therapy)	0.01	-42.5	-11.1	<0.05	-43.0	-11.1	797.05	0.8
Other ophthalmological medicines (cell therapy)	0.01	—	—	<0.05	—	—	91.41	—
Antiglaucoma preparations - others	<0.005	-49.8	—	<0.05	-49.8	—	94310.54	0.0
Medicines for eye disorders	**6.62**	**-1.9**	**2.1**	**22.0**	**2.5**	**1.0**	**0.82**	**-4.3**
aflibercept	1.42	-4.3	23.7	<0.05	17.8	30.4	400.79	-18.7
dorzolamide/timolol	0.55	15.4	6.5	3.6	13.9	6.0	0.41	1.3
ranibizumab	0.52	-34.0	-8.8	0.1	-15.0	-6.4	17.39	-22.4
dexamethasone	0.52	17.7	12.3	0.3	9.4	11.7	4.89	7.6
tafluprost	0.52	-0.4	6.7	1.7	0.0	6.8	0.85	-0.4
timolol	0.39	4.1	3.1	3.2	1.7	0.0	0.34	2.4
bimatoprost	0.32	1.0	-3.2	1.8	1.4	-0.2	0.49	-0.4
timolol/bimatoprost	0.32	3.5	-1.2	1.4	1.1	1.7	0.62	2.4
tafluprost/timolol	0.30	9.0	—	0.9	8.9	—	0.96	0.1
timolol/brinzolamide	0.24	-8.1	-2.2	1.4	-7.4	1.9	0.47	-0.8

Figure 3.10.1a Medicines for eye disorders, temporal trend of consumption (DDD/1000 inhab. per day) of the most expensive subgroups (2014-2023)



Regional data on consumption and expenditure

Table 3.10.1b Medicines for eye disorders, regional trend of per capita expenditure, consumption (DDD/1000 inhab. per day) and average cost per day of therapy: comparison 2014-2023

Region	2022			2023			Δ % 23-22			CAGR % 14-23		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost
Piedmont	7.60	23.9	0.87	7.62	24.5	0.85	0.3	2.6	-2.2	3.8	1.1	2.6
Valle d'Aosta	6.67	20.2	0.90	10.14	20.0	1.39	52.1	-0.9	53.5	7.1	-0.3	7.5
Lombardy	6.09	17.8	0.94	6.03	18.2	0.91	-1.0	2.5	-3.4	1.3	1.2	0.1
Province of Bolzano	6.78	16.5	1.13	6.71	16.9	1.09	-1.0	2.6	-3.5	3.3	1.8	1.4
Province of Trento	6.68	17.3	1.06	6.14	17.6	0.96	-8.2	1.8	-9.8	2.8	1.6	1.2
Veneto	6.80	19.7	0.95	6.95	20.2	0.94	2.1	2.7	-0.5	3.7	1.3	2.3
Friuli V.G.	8.68	23.7	1.00	9.02	24.4	1.01	3.9	3.0	0.9	2.5	0.8	1.7
Liguria	8.42	21.8	1.06	7.94	22.2	0.98	-5.7	1.8	-7.4	1.1	0.5	0.6
Emilia R.	7.23	28.6	0.69	7.36	29.2	0.69	1.8	2.0	-0.2	3.0	1.5	1.5
Tuscany	6.67	26.7	0.68	6.14	26.9	0.62	-8.0	0.8	-8.7	-0.9	0.5	-1.4
Umbria	7.48	25.1	0.82	6.97	25.7	0.74	-6.8	2.5	-9.1	2.4	1.1	1.3
Marche	8.02	31.3	0.70	8.19	32.3	0.69	2.2	3.1	-0.9	1.7	1.3	0.4
Lazio	5.98	22.1	0.74	5.60	22.5	0.68	-6.4	1.7	-7.9	0.0	0.0	0.0
Abruzzo	8.31	26.6	0.86	8.02	27.2	0.81	-3.5	2.1	-5.5	2.3	0.7	1.6
Molise	7.98	16.7	1.31	7.89	17.1	1.26	-1.2	2.8	-3.9	3.9	0.7	3.1
Campania	6.73	18.6	0.99	6.49	19.3	0.92	-3.5	3.8	-7.1	4.3	1.3	2.9
Puglia	7.23	19.6	1.01	6.81	20.4	0.91	-5.7	4.2	-9.5	2.5	1.1	1.5
Basilicata	7.31	21.9	0.91	7.33	22.8	0.88	0.3	4.2	-3.7	2.3	1.8	0.6
Calabria	5.96	19.7	0.83	5.95	20.2	0.81	-0.1	2.1	-2.2	2.4	0.5	1.9
Sicily	5.58	17.9	0.85	5.59	18.4	0.83	0.2	2.9	-2.6	2.2	1.3	0.9
Sardinia	6.54	20.2	0.89	6.30	20.9	0.83	-3.7	3.1	-6.6	1.5	0.6	0.9
Italy	**6.75**	**21.5**	**0.86**	**6.62**	**22.0**	**0.82**	**-1.9**	**2.5**	**-4.3**	**2.1**	**1.0**	**1.1**
North	6.92	21.3	0.89	6.94	21.8	0.87	0.3	2.4	-2.1	2.5	1.2	1.3
Centre	6.58	25.0	0.72	6.21	25.4	0.67	-5.6	1.6	-7.1	0.1	0.4	-0.3
South and Islands	6.61	19.5	0.93	6.42	20.1	0.87	-2.8	3.3	-5.9	2.8	1.1	1.7

3.11 Genito-urinary system and sex hormones

In 2023, medicines for the genito-urinary system and sex hormones were the 10th therapeutic category with the highest public expenditure, i.e. 423.1 million euros and 1.6% of overall public expenditure (Box Main indices of expenditure, consumption and exposure). The overall per capita expenditure on these drugs was approximately 7.17 euros, mainly due to the approved care regime (5.70 euros per capita), up 2.1% compared to 2022. The expenditure of public health facilities is lower than the approved care regime (1.48 euros per capita) but records a significant increase (+14.2%) compared to the previous year (Table 3.1).

This category of drugs ranks fifth in terms of NHS-covered consumption, with 49.52 DDD/1000 inhabitants per day, up 4.2% compared to 2022. As expected, consumption has a greater impact in the approved care regime (46.35 vs 3.16 DDD) (Table 3.2).

The analysis of the drug utilization profile by age group and gender, including approved care and distribution on behalf, confirms an almost exclusive use in males aged 55 and over, essentially due to the treatment of prostatic hypertrophy. The prevalence of such drugs in men over 75 years exceeds 40% of the population in this age group. At the same time, per capita NHS expenditure also increases with the age of patients, reaching a maximum of 52.7 euros in males over 75 years. In women, however, significant consumption can be observed in the 25-64 age group, which can be justified by the use of hormonal preparations; the largest expenditure is reached in the 35-44 age group, with 13.2 euros per capita.

As for the approved care regime, per capita expenditure of genitourinary drugs was 5.70 euros, with a slight increase compared to 2022 (+1.8%). This increase was mainly due to a 3.3% increase in consumption, while there was a shift towards less expensive medicinal products (mix effect: -1.4%) and a practically zero change in prices, which led to a 1.5% decrease in the average cost per DDD (Table 3.9). In this delivery channel, alpha-adrenergic receptor antagonists are the predominant therapeutic subcategory, representing over half of the expenditure and consumption of the entire category, with 3.04 euros of expenditure per capita and 29.8 DDD/1000 inhabitants per day. Testosterone-5-alpha reductase inhibitors follow, with a per capita expenditure of 1.59 euros and 11.2 DDD/1000 inhabitants per day (Table 3.9). Testosterone-5-alpha reductase inhibitors show a slight increase in expenditure compared to 2022 (+0.5%), while alpha-adrenergic receptor antagonists show increases in both consumption (+3.7%) and expenditure (+2.9%). The molecules with the greatest impact on per capita expenditure are tamsulosin (1.17 euros) and dutasteride (1.03 euros), which accounts for over 38% of the entire category (Table 3.10). Several highest-cost active ingredients, except finasteride, are among the 30 molecules with the lowest average cost per DDD (Table 3.13). Furthermore, alfuzosin is among the top 30 active ingredients recording the greatest expenditure increases (Table 3.14) and, together with tamsulosin and dutasteride, it is among the top 30 higjhest-consumption molecules under approved care regime (Table 3.16).

As regards purchases by public health facilities, there was an expenditure increase (+13.8%) and a corresponding consumption increase (+13.8%), with a shift towards more expensive medicinal products (mix effect: +13.4%). On the contrary, there was an 11.7% price reduction (Table 3.17). The gonadotropins subcategory records the highest per capita expenditure (1.07 euros), representing over 72% of the category. These drugs, analogues of adenopituitary

hormones, are used to re-establish correct hormone levels in the treatment of infertility, and to treat conditions that require a decrease in hormone levels (for example, prostate cancer, surgical removal of fibroids or early menarche).

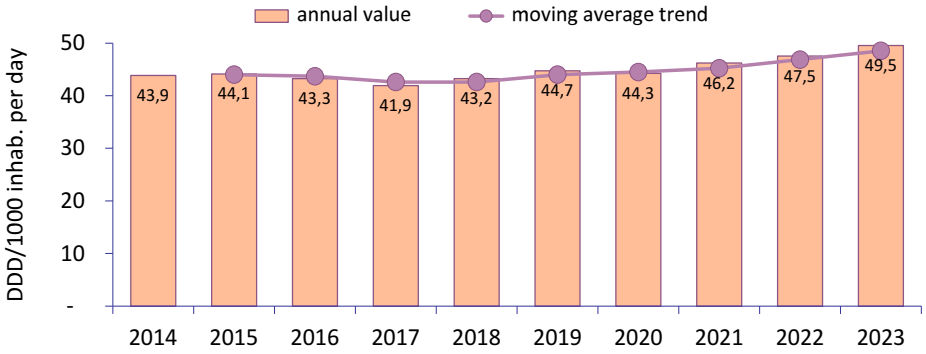
The combination follitropin alfa/lutropin alfa is the active ingredient with the highest incidence on expenditure (26.1%), up +75% compared to 2022, with a high average cost per day of therapy (355.55 euros), while consumption remains lower than 0.05 DDD. Recombinant DNA follitropin alfa, with 0.1 DDD, accounts for 1.7% of the entire category, also increasing both in terms of per capita expenditure (+15.1%) and consumption (+20.6%) compared to the previous year (Table 3.18). On the contrary, menotropin recorded the greatest decreases in expenditure (-46.2%) and consumption (-50.4%). The top 30 active ingredients for consumption under approved care regime and purchased by public health facilities include tamsulosin with 11.9 DDD/1000 inhabitants per day (+3.8% compared to 2022), alfuzosin with 10.4 DDD/1000 inhabitants per day (+5.7%) and dutasteride with 8.6 DDD/1000 inhabitants per day (+1.6%) (Table 3.26).

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

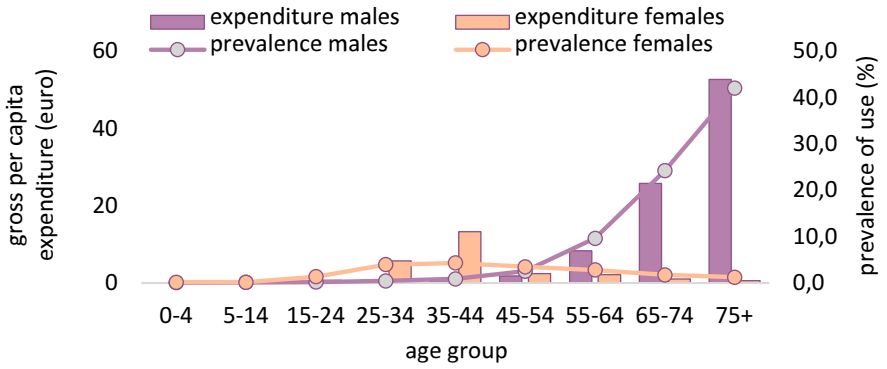
Genito-urinary system and sex hormones

Public expenditure* in million euros (% over total)	**423.1**	**(1.6)**
Δ % 2023-2022		4.4
Regional range of gross per capita expenditure:	5.2	8.3
DDD/1000 inhabitants per day* (% over total)	**49.5**	**(3.7)**
Δ % 2023-2022		4.2
Regional range DDD/1000 inhabitants per day	33.7	59.1

** includes prescriptions under approved care regime and purchases by public health facilities*



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf by age and gender in 2022 (Figure and Table)



Age group	Gross per capita expenditure			DDD/1000 inhabitants per day		
	Males	Females	Total	Males	Females	Total
0-4	0.0	0.0	0.0	0.0	0.1	0.0
5-14	0.1	0.1	0.1	0.1	0.2	0.2
15-24	0.3	0.6	0.4	0.5	3.6	2.0
25-34	0.6	5.7	3.1	1.2	11.0	6.0
35-44	1.1	13.2	7.1	2.7	15.5	9.1
45-54	1.8	2.4	2.1	12.5	14.9	13.7
55-64	8.3	2.1	5.1	70.4	15.9	42.5
65-74	25.8	1.0	12.7	223.4	8.4	110.0
75+	52.7	0.6	21.9	441.9	4.6	183.2

3.11.1 Medicines for genitourinary disorders

In 2023, expenditure on drugs for genitourinary disorders reached approximately 280 million euros, up 2.8% compared to the previous year. Consumption also increased by 3.8%, reaching 42.1 DDD/1000 inhabitants per day (Box Main indices of expenditure, consumption and exposure).

From the in-depth study conducted in the male population, an increase in the use of drugs for genitourinary disorders is observed with age, reaching the highest values in people over 85, with a prevalence of use of 50% and consumption of 527.62 DDD, in line with the epidemiological data on benign prostatic hyperplasia (BPH). Even starting from the age of 65, the prevalence exceeds 20%, going from 23.6% in the 65-74 age group to 38.8% in the 75-84 age group, with a corresponding increase in consumption from 220 to 409 DDD (Box Main indices of expenditure, consumption and exposure).

Since 2014, the consumption of these drugs has steadily increased, with a 2.8% CAGR (Table 3.11.1a). Over the same period, the average cost per day of therapy decreased from 0.48 euros in 2014 to 0.31 euros in 2023 (CAGR: -4.2%).

BPH drugs account for almost all consumption in the category (41.6 out of 42.1 DDD). Among these, alpha-blockers with 30.2 DDD account for the majority of consumption, followed by 5-alpha-reductase inhibitors with 11.4 DDD. Alpha-blockers recorded a 4.1% increase compared to 2022 (and +23.7% in combination), while 5-alpha-reductase inhibitors had a more modest variation, equal to +2.2%. Although the use of drugs for urinary incontinence remains low, in 2023 there was a significant increase in expenditure (+20.3%) and consumption (+26.0%), with an average cost per DDD double than alpha-blockers (0.52 vs 0.28 euros) (Table 3.11.1a). Over the last ten years, the average annual growth rate (CAGR) of consumption of drugs for urinary incontinence has been significantly higher (+13.2%) than alpha-blockers (+2.9%) and 5-alpha reductase inhibitors (+2.1%) (Table 3.11.1a and Figure 3.11.1a).

The most commonly used substances include tamsulosin, dutasteride, alfuzosin and silodosin, with variations ranging between +5.7% for alfuzosin and +4.1% for silodosin, compared to the previous year. These molecules show the lowest average cost per DDD in the category, ranging between 0.26 euros (alfuzosin) and 0.33 euros (dutasteride), approximately half of tolterodine, a drug indicated in the symptomatic treatment of urgency incontinence and/or increased urinary frequency and urgency in patients with overactive bladder syndrome, which has the highest average cost per DDD in the entire category (0.63 euros) (Table 3.11.1a). Solifenacin recorded the highest increases in expenditure and consumption (+57.1% and +58.2% respectively), while terazosin is the only molecule among those with the highest expenditure showing a 6.1% reduction in expenditure and a 5.2% reduction in doses. Solifenacin, together with oxybutynin and tolterodine, is included in AIFA Note 87, which limits its reimbursement only to the packages negotiated in class A/RR for patients suffering from urgent urinary incontinence, in cases where the urinary disorder is related to central nervous system pathologies such as stroke, Parkinson's disease, trauma, tumors, spina bifida and multiple sclerosis.

8.0% of the male population received at least one prescription for alpha-blockers during the year, while the prevalence of use for 5-alpha-reductase inhibitors is 3.2%. Users of alpha-blockers are on average younger (74 vs 77 years for 5-alpha-reductase inhibitors) and have

a 25 euros lower average cost (75.7 vs 99.8 euros). For both categories, the share of users with a single prescription is lower than 10% (Table 3.11.1b).

As for geographical areas, there is a North-South gradient both in terms of expenditure, which ranges from 4.26 euros in the North to 5.33 euros in the South, and in terms of consumption, which varies from 38.8 DDD in the North to 45.7 DDD in the South, with a difference of approximately 20% for both indicators (Table 3.11.1c). In all regions, there were increases in consumption, with variations ranging from 0.8% in the Province of Bolzano to 4.9% in Campania and Sardinia.

The Health Card data were used to estimate the exposure and intensity of use of drugs for genitourinary disorders. 99% of such drugs are used for the treatment of BPH. Patient adherence and persistence to treatment were assessed only for BPH drugs.

At the national level, the prevalence among males is 8.9% overall, with a minimum of 8.1% in the North and a maximum of 9.6% in the South. At the regional level, the highest prevalence is recorded in Marche (10.5%), while the lowest in the Province of Bolzano (5.3%). In line with the main guidelines for the management of BPH, now a chronic condition, each user on average received at least one dose of the drug per day for approximately 11 months of therapy, with no significant regional variation. However, the cost per user varies from 91.8 euros in Valle d'Aosta to 113.7 in Marche. The median age of users is 74 years, with no particular regional difference (Table 3.11.1c).

Adherence and persistence analyses for BPH medications refer to a cohort of new male users aged 45 years and older, followed up for one year. The study population includes 101,749 new users, with a median age of 69 years (IQR 62-76). In 2023, the percentage of subjects with high adherence was 64.8%, stable compared to the years 2019-2022, while the proportion of subjects with low adherence to treatment decreased by 5% compared to 2022, reaching a value of 9.3% (Figure 3.11.1b). Analysing the persistence data, in 2023 over half of the users (52.9%) were still undergoing treatment one year after starting therapy, a value 4% higher than in 2022 (Figure 3.11.1c)

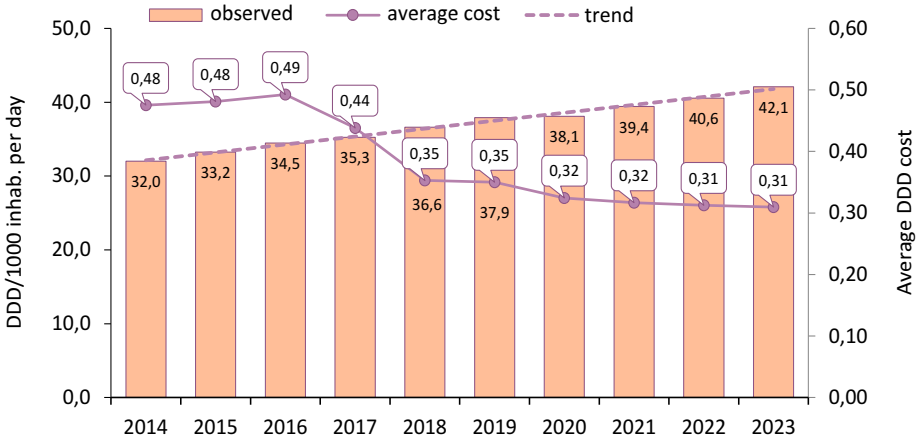
For further information on regional data on exposure and duration of therapy and on indicators of adherence and persistence to treatment stratified by age, gender and geographical area, please refer to the supplementary documents published online.

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

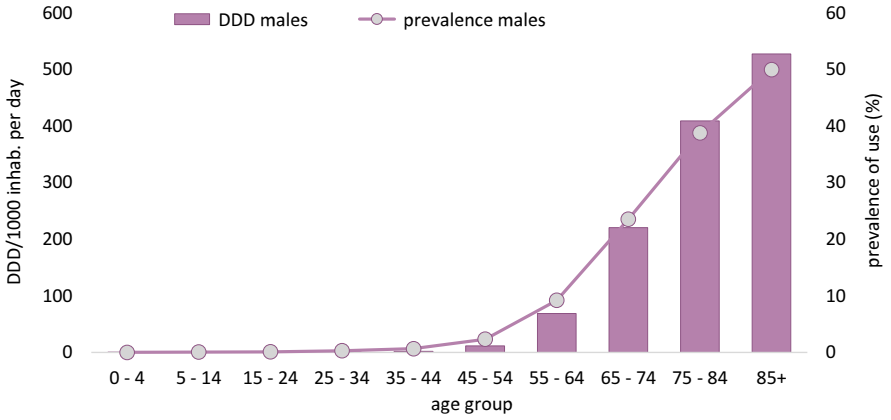
Medicines for genitourinary disorders

Public expenditure in million euros (% over total)	**279.8**	**(1.1)**
Δ % 2023-2022		2.8
Regional range of gross per capita expenditure:	2.7	5.9
DDD/1000 inhab. per day (% over total)	**42.1**	**(3.2)**
Δ % 2023-2022		3.8
Regional range DDD/1000 inhabitants per day	25.3	51.0

Medicines for genitourinary disorders, temporal trend of consumption and average cost per day of therapy (2014-2023)



Distribution of prevalence of use and consumption of medicines for genitourinary disorders under approved care regime and distribution on behalf (year 2023)



Note: the use of drugs for genitourinary disorders in females is negligible, so the graph shows only the data relating to the male population

National data on consumption and expenditure by subgroup and substance

Table 3.11.1a Medicines for genitourinary disorders, per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Medicines for benign prostatic hypertrophy (alpha-blockers)	3.05	3.3	1.6	30.2	4.1	2.9	0.28	-0.8
Medicines for benign prostatic hypertrophy (5-alpha reductase inhibitors)	1.59	0.8	-5.8	11.4	2.2	2.1	0.38	-1.3
Medicines for incontinence and urinary frequency disorders (anticholinergics)	0.11	20.3	10.2	0.6	26.0	13.2	0.52	-4.6
Other medicines for benign prostatic hypertrophy	<0.005	8.0	0.3	<0.05	4.7	-1.0	1.18	3.2
Medicines for incontinence and urinary frequency disorders (beta-3 adrenergic antagonists)	<0.005	8.2	8.3	<0.05	11.4	7.1	1.55	-2.9
Medicines for benign prostatic hypertrophy (alpha-blockers in combination)	<0.005	9.8	62.2	<0.05	23.7	65.0	1.12	-11.2
Medicines per genitourinary disorders	**4.76**	**2.8**	**-1.5**	**42.1**	**3.8**	**2.8**	**0.31**	**-1.0**
tamsulosin	1.17	2.5	1.7	11.9	3.8	2.2	0.27	-1.2
dutasteride	1.04	0.3	-7.7	8.6	1.6	2.8	0.33	-1.3
alfuzosin	0.97	5.7	2.9	10.4	5.7	3.0	0.26	0.1
silodosin	0.76	3.5	1.8	6.7	4.1	7.1	0.31	-0.6
finasteride	0.56	1.8	-0.5	2.8	4.0	0.3	0.55	-2.1
terazosine	0.13	-6.1	-5.1	1.1	-5.2	-4.7	0.33	-1.0
oxybutynin	0.05	2.5	3.5	0.2	2.9	3.7	0.61	-0.4
solifenacin	0.04	57.1	34.3	0.3	58.2	48.9	0.42	-0.7
doxazosin	0.02	-9.7	-7.4	0.1	-9.7	-7.5	0.42	0.0
tolterodine	0.01	9.2	22.6	0.1	10.9	36.9	0.63	-1.5

Figure 3.11.1a Medicines for genitourinary disorders, temporal trend of consumption (DDD/1000 inhabitants per day) of highest-expenditure subgroups (2014-2023)

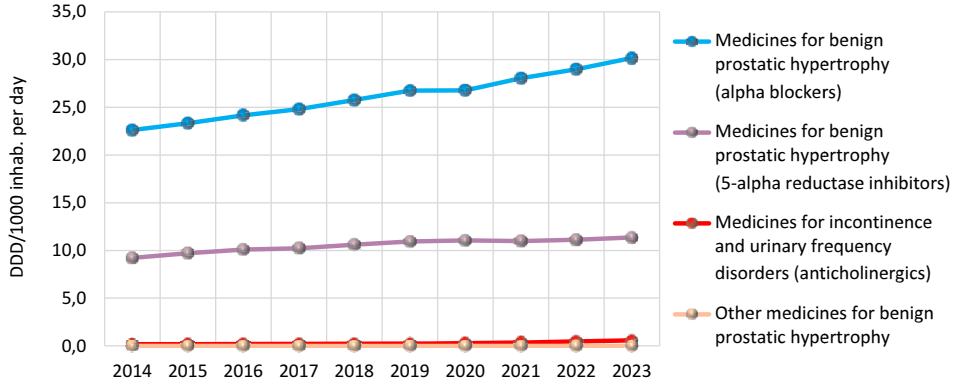


Table 3.11.1b Exposure and duration of therapy with medicines for genitourinary disorders by subgroup under approved care regime and distribution on behalf (year 2023)

Subgroup	Prevalence of use (%)	Median age	Cost per user	DDD per user	Median DDD	Users with 1 prescription (%)
Other medicines for benign prostatic hypertrophy	<0.05	71	197.2	135.8	96	23.7
Medicines for incontinence and urinary frequency disorders (beta-3 adrenergic antagonists)	<0.05	79	408.1	157.2	120	30.4
Medicines for incontinence and urinary frequency disorders (anticholinergics)	0.2	72	69.4	133.1	80	19.3
Medicines for benign prostatic hypertrophy (alpha blockers)	8.0	74	75.7	270.2	300	7.4
Medicines for benign prostatic hypertrophy (alpha-blockers in combination)	<0.05	82	196.8	163.8	120	20.5
Medicines for benign prostatic hypertrophy (5-alpha reductase inhibitors)	3.2	77	99.8	256.7	300	5.0
Medicines for genitourinary disorders	**8.9**	**74**	**104.8**	**334.9**	**320**	**6.9**

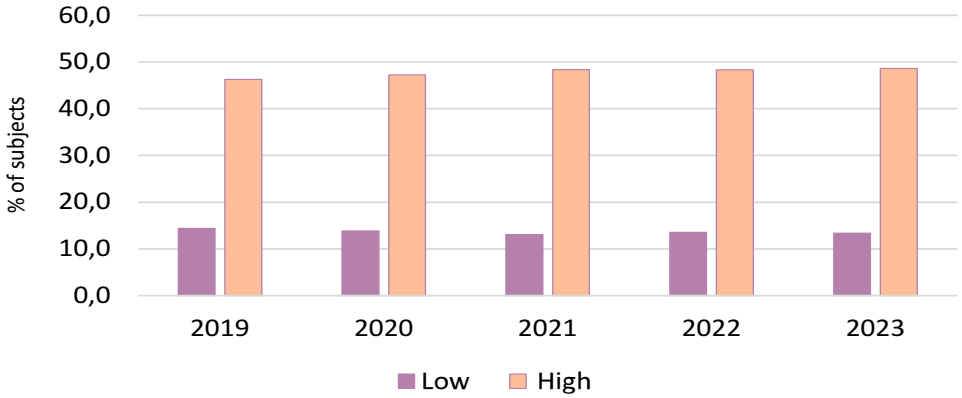
Regional data on expenditure, consumption and exposure

Table 3.11.1c Medicines for genitourinary disorders, regional trend of per capita expenditure, consumption (DDD/1000 inhab. per day) and average cost per day of therapy: comparison 2014-2023

Region	2023			Δ % 23-22			CAGR % 14-23			2023		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Prevalence of use (%)	Cost/user	Median DDD
Piedmont	4.25	39.1	0.30	1.3	3.6	-2.2	-2.4	2.1	-4.4	9.0	98.0	320.0
Valle d'Aosta	3.71	34.1	0.30	2.8	4.4	-1.5	-3.0	1.8	-4.7	7.9	91.8	300.0
Lombardy	4.14	38.2	0.30	2.9	4.1	-1.2	-1.9	2.9	-4.7	7.7	103.0	330.0
Province of Bolzano	2.68	25.3	0.29	0.1	0.8	-0.7	-2.6	1.6	-4.1	5.3	87.5	300.0
Province of Trento	4.36	39.0	0.31	3.0	3.6	-0.5	-1.7	3.1	-4.7	7.5	108.3	330.0
Veneto	4.12	36.7	0.31	2.1	3.1	-1.0	-1.7	2.7	-4.3	7.5	107.1	336.0
Friuli V.G.	4.02	36.6	0.30	2.2	3.7	-1.4	-2.2	2.6	-4.6	7.9	106.6	336.0
Liguria	4.74	42.8	0.30	2.6	3.7	-1.0	-2.2	2.4	-4.5	9.9	102.1	320.0
Emilia R.	4.73	43.1	0.30	1.8	3.6	-1.7	-0.6	2.6	-3.1	8.7	105.3	330.0
Tuscany	4.47	41.2	0.30	1.5	3.3	-1.8	-1.7	2.7	-4.3	9.4	96.7	320.0
Umbria	5.40	48.1	0.31	0.7	3.0	-2.2	-2.2	2.7	-4.8	10.4	109.3	340.0
Marche	5.85	51.0	0.31	2.6	3.4	-0.8	-2.2	2.5	-4.6	10.5	113.7	360.0
Lazio	5.02	43.0	0.32	2.3	3.0	-0.7	-2.2	2.0	-4.1	9.2	106.0	320.0
Abruzzo	4.95	43.9	0.31	2.7	3.4	-0.7	-1.4	3.1	-4.4	8.9	104.0	320.0
Molise	4.94	41.9	0.32	3.6	4.4	-0.7	-1.0	3.3	-4.1	9.0	106.5	320.0
Campania	5.52	46.2	0.33	4.7	4.9	-0.2	0.0	3.8	-3.7	9.8	104.4	320.0
Puglia	5.54	47.3	0.32	4.0	4.3	-0.3	-1.0	3.5	-4.4	9.5	112.2	340.0
Basilicata	5.94	49.7	0.33	2.9	3.1	-0.2	-0.6	3.7	-4.1	10.4	111.9	330.0
Calabria	5.14	43.4	0.32	3.5	4.3	-0.7	-2.0	2.3	-4.2	9.5	106.0	320.0
Sicily	5.22	45.3	0.32	3.4	4.1	-0.6	-1.5	2.7	-4.1	9.5	107.0	330.0
Sardinia	4.91	44.4	0.30	3.6	4.9	-1.3	-0.8	3.5	-4.1	9.6	103.5	336.0
Italy	**4.76**	**42.1**	**0.31**	**2.8**	**3.8**	**-1.0**	**-1.5**	**2.8**	**-4.2**	**8.9**	**104.8**	**320.0**
North	4.26	38.8	0.30	2.2	3.7	-1.4	-1.8	2.6	-4.3	8.1	103.1	320.0
Centre	4.98	43.9	0.31	2.0	3.1	-1.1	-2.0	2.3	-4.3	9.5	104.5	320.0
South and Islands	5.33	45.7	0.32	3.9	4.4	-0.5	-0.9	3.3	-4.1	9.6	106.8	325.0

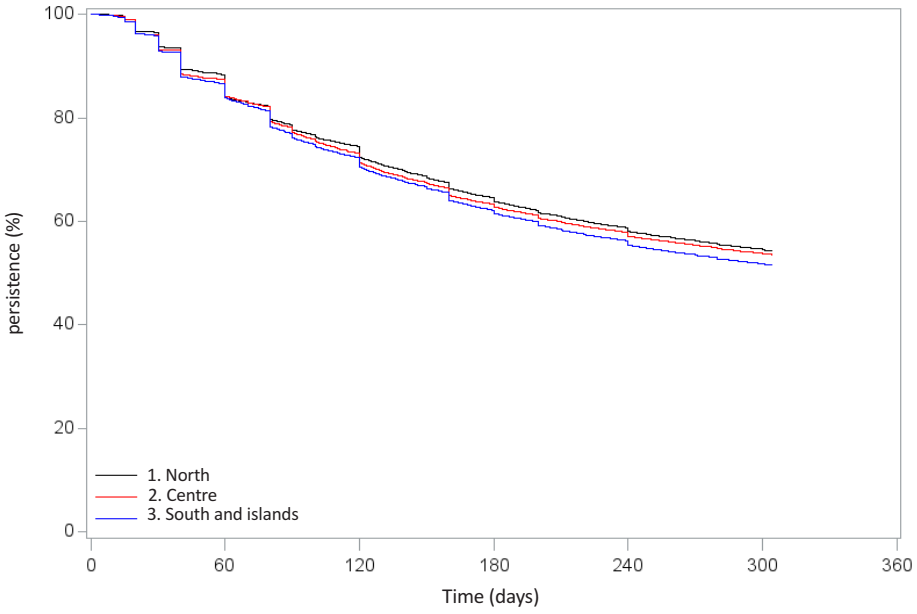
Adherence and persistence to treatment

Figure 3.11.1b Indicators of low and high adherence to treatment with medicines for genitourinary disorders in the population aged ≥45 years, trend 2019-2023



*Adherence to treatment was evaluated only for new users with at least 2 prescriptions. Low adherence to treatment was defined as therapeutic coverage (assessed on the basis of DDD) <40% of the observation period, while high adherence was defined as therapeutic coverage ≥80% of the observation period (for further details please refer to statistical methods)

Figure 3.11.1c Time (in days) to discontinuation of treatment with drugs for genitourinary disorders in the population aged ≥ 45 years stratified by geographical area; the curves are adjusted by gender and age (the Cox model was used for the estimation of persistence curves)



3.12 Various

Also in 2023, the therapeutic category of "Various" drugs ranks twelfth in terms of public expenditure, with 375.2 million euros, i.e. 1.4% of the total (Box Main indices of expenditure, consumption and exposure). The overall per capita expenditure on these drugs, net of the value of medical air (V03AN), reached 6.37 euros, a 2.1% decrease compared to the previous year. Approximately 97% of the expenditure is due to purchases by public health facilities (6.19 euros per capita) (Table 3.1). Consumption for this category of drugs was 3.59 DDD/1000 inhabitants per day, up 10.3% compared to 2022, with a stable trend over the last 7 years (Table 3.2).

The analysis of the drug utilization profile by age group and gender, including approved care regime and distribution on behalf, highlights a reduced use for both genders up to the age group between 45 and 54 years, followed by progressive growth in the subsequent age groups. The prevalence of use is higher in people over 75e, recording values of 3.5% for males and 3.2% for females. A similar trend is present for the per capita expenditure covered by the NHS, which reaches the maximum level of 8.6 euros per capita for males and 7.1 for females over 75 years.

As regards approved care regime, per capita expenditure was 0.19 euros, with a significant increase compared to 2022 (+35.0%), due to a shift in prescription towards more expensive medicinal products (mix effect: +34.0%), while consumption (+0.9%) and prices (-0.2%) were stable (Table 3.9). The subgroup with the greatest impact on the approved care expenditure of this category is drugs for the treatment of hyperkalemia and hyperphosphatemia (0.12 euros per capita) (Table 3.9). Even in 2023, the active substance with the highest expenditure (0.06 euros) is sevelamer, authorised for the control of hyperphosphatemia in patients undergoing haemodialysis or peritoneal dialysis and in patients with chronic kidney disease (CKD) not undergoing dialysis, but with a serum phosphorus concentration ≥1.78 mmol/L, which has an incidence of 32.3% on total expenditure. This is followed by deferasirox, approved for the treatment of chronic iron overload due to frequent blood transfusions in patients with beta-thalassemia major aged over 6 years or in some subgroups of pediatric patients (<6 years) when deferoxamine is contraindicated or inadequate. With a per capita cost of 0.05 euros, it records an incidence of 27.5%. Next comes polystyrene sulfonate, indicated in the treatment of hyperkalemia in patients with acute and chronic renal failure, with a per capita value of 0.04 euros. These three active ingredients account for more than 80% of the approved care expenditure on this ATC (Table 3.10).

As for drugs purchased by public health facilities, there was a reduction in expenditure (-3.2%), prices (-2.6%) and average cost per day of therapy (-12.2%), with a shift towards lower-cost medicinal products (mix effect: -9.8%). Prices remained unchanged, and consumption increased by over 10% (Table 3.17).

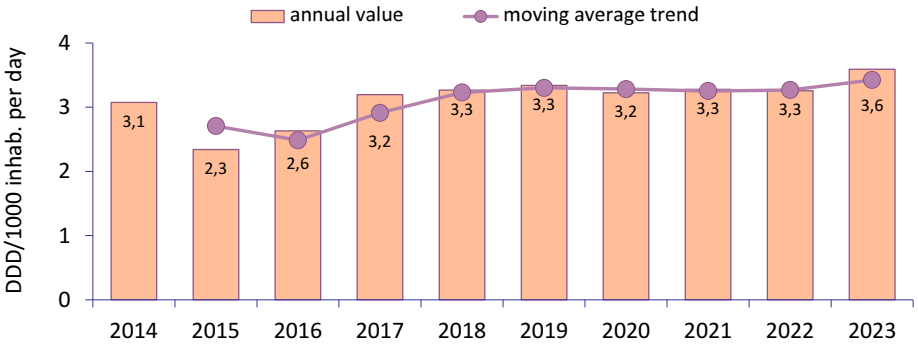
The category of water-soluble, nephrotropic, low-osmolarity radiological contrast media has the greatest impact on expenditure (1.36 euros per capita), followed by antidotes (1.18 euros), with a significant shift towards more expensive products (mix effect: +11.2%). Iron chelating substances show the highest decrease in expenditure (-49.3%) and a shift towards less expensive drugs (mix effect: -44.4%) corresponding to a reduction in the average DDD cost (-47.0%) and consumption (-4.2%) (Table 3.17). Among iron chelators, deferasirox, with a category incidence of 7.1%, recorded a 53.7% reduction in per capita expenditure compared to 2022, due to the decrease in the cost per day of therapy (-50.2%) (Table 3.18). Top of the

list, with a 14.4% incidence on the category expenditure, is sugammadex, an antagonist of the neuromuscular blockade from rocuronium and vecuronium, with a per capita expenditure of 0.89 euros. This drug recorded a 7.5% expenditure decrease and is on the list of the drugs purchased by public health facilities recording the greatest expenditure reduction (Table 3.21). Instead, consumption increased by 8% compared to the previous year (Table 3.18). Second on the list, with a value of 0.53 euros per capita, is the diagnostic product iomeprol, an active ingredient used as a contrast medium, showing a reduction in both expenditure (-2.5%) and consumption (-4.2%), and a slight increase in the average DDD cost (+1.8%).

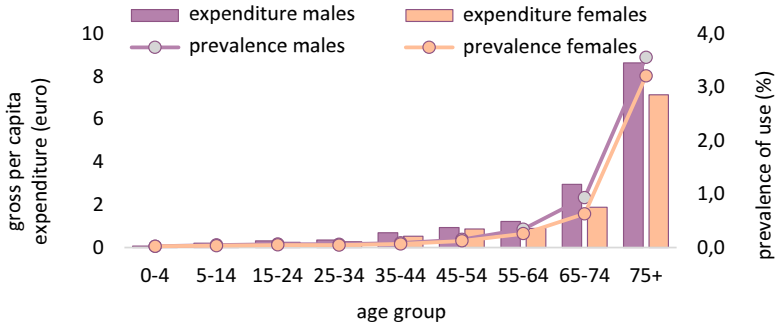
MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE
Various

Public expenditure* in million euros (% over total)	**375.2**	**(1.4)**
Δ % 2023-2022		-2.1
Regional range of gross per capita expenditure:	4.6	10.4
DDD/1000 inhabitants per day* (% over total)	**3.6**	**(0.3)**
Δ % 2023-2022		10.3
Regional range DDD/1000 inhabitants per day	1.8	7.9

** includes prescriptions under approved care regime and purchases by public health facilities*



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf by age and gender in 2023 (Figure and Table)



Age group	Gross per capita expenditure			DDD/1000 inhabitants per day		
	Males	Females	Total	Males	Females	Total
0-4	0.1	0.1	0.1	0.0	0.0	0.0
5-14	0.2	0.1	0.2	0.1	0.1	0.1
15-24	0.3	0.2	0.3	0.2	0.1	0.2
25-34	0.4	0.3	0.3	0.1	0.1	0.1
35-44	0.7	0.5	0.6	0.2	0.1	0.1
45-54	0.9	0.9	0.9	0.2	0.2	0.2
55-64	1.2	0.9	1.1	0.4	0.2	0.3
65-74	3.0	1.9	2.4	0.7	0.3	0.5
75+	8.6	7.1	7.7	1.0	0.4	0.7

3.12.1 Contrast media

In 2023, public expenditure on contrast media was 110.6 million euros, corresponding to a per capita expenditure of 1.88 euros, stable (+0.3%) compared to 2022, but with a 2.1% average annual variation since 2014 (Box Main indices of expenditure and consumption and Table 3.12.1a). The use of contrast media decreased by 1.4%, remaining at 0.1 DDD, while the average cost per DDD reached 53.01 euros in 2023, up 1.7% compared to the previous year (Table 3.12.1a and Figure 3.12.1a).

The therapeutic category with the highest per capita expenditure (1.37 euros) is radiological contrast media, which increased by 2.4% and accounts for 73% of the expenditure on the entire category. Over the period 2014-2023, they had a 1.9% average annual increase in expenditure (Table 3.12.1a). Contrast media for Magnetic Resonance Imaging (MRI) follow, with 0.46 euros, up 2.5% compared to 2022. Contrast media for ultrasound, despite a limited expenditure (0.05 euros), recorded a marked reduction in per capita value (-42.3%) but had the highest average cost per DDD in the category (67.5 euros), in sharp reduction compared to the previous year (-39.7%) (Table 3.12.1a). Analysing the trend of the different subgroups, radiological contrast media showed a significantly higher per capita expenditure, compared to the other categories, which recorded a significant reduction in 2020 and a significantly lower one for ultrasound contrast media (Figure 3.12.1a)

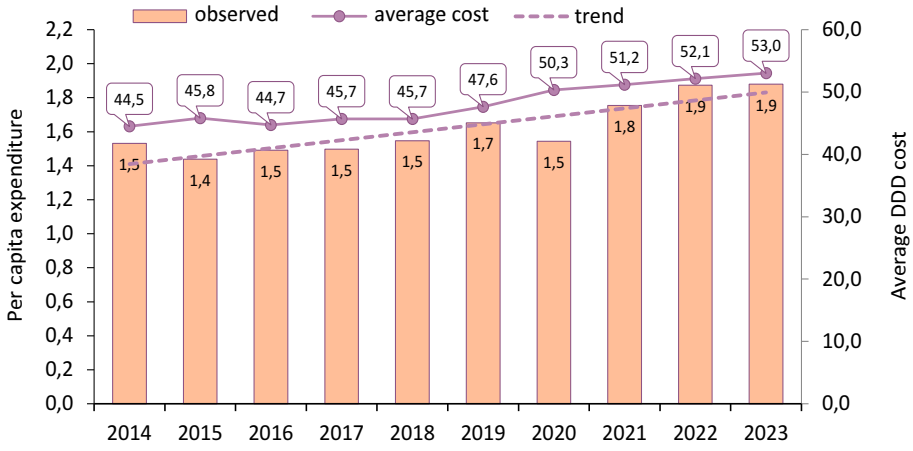
The most expensive active ingredient is iomeprol (0.53 euros; -2.5% compared to 2022), a radiological contrast agent (iodinated, non-ionic, monomeric), with high solubility in water, combined with low chemotoxicity, osmolarity and viscosity. In second place is iodixanol (0.25 euros; +6.9%), another iodinated radiological drug (dimeric, non-ionic, low osmolarity), with a diagnostic efficacy similar to other drugs in the same category. The active ingredients gadobutrol, a drug used for contrast enhancement in MRI and containing gadolinium and the related macrocyclic ligand butrol, and iopromide, an iodinated diagnostic agent used for angiography, contrast enhancement in computed tomography, urography, and visualization of body cavities, have a per capita expenditure of 0.23 and 0.18 euros, respectively. The active ingredient with the highest expenditure increase in 2023 was iohexol (+20.3%), a low-osmolarity monomeric non-ionic contrast medium used for myelograms, angiograms, urography and arthrography. Finally, gadoxetic acid, used to detect focal liver lesions, showed the highest average cost per DDD in the category (176.01).

As for geographical areas, the highest expenditure is recorded in the Centre (2.12 euros) compared to the North and the South and Islands (both 1.82 euros). The Centre is the only macro-area that has increased compared to 2022 (+1.6%). The greatest regional variations in expenditure are in Liguria- with the highest increase (+12.4%) and in Puglia - with the highest decrease (-16.0%). The Southern Regions use drugs with a higher cost per DDD (73.35 euros) compared to the national average of 53.0 euros (Centre 56.08 and North 43.39 euros): Puglia records the highest value (81.05 euros) while the Province of Bolzano shows the lowest figure (30.38 euros) (Table 3.12.1b).

MAIN INDICES OF EXPENDITURE AND CONSUMPTION
Contrast media

Public expenditure in million euros (% over total)	**110.6**	**(0.4)**
Δ % 2023-2022		0.3
Regional range of gross per capita expenditure:	1.3	2.7
DDD/1000 inhab. per day (% over total)	**0.1**	**(0.0)**
Δ % 2023-2022		-1.4
Regional range DDD/1000 inhabitants per day	0.1	0.2

Contrast media, temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)

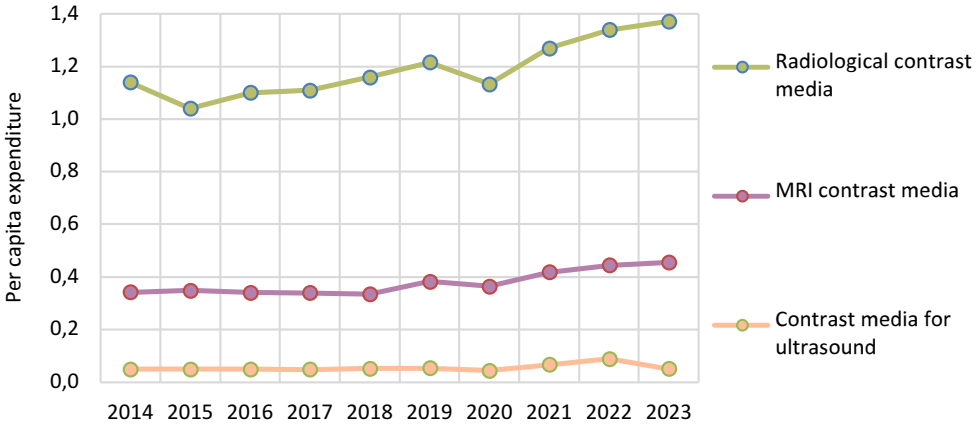


National data on consumption and expenditure by subgroup and substance

Table 3.12.1a Contrast media, per capita expenditure and consumption (DDD/1000 inhabitants per day) by therapeutic category and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Radiological contrast media	1.37	2.4	1.9	0.1	-2.7	-0.4	54.37	5.3
MRI contrast media	0.46	2.5	2.9	<0.05	2.7	2.6	48.22	-0.1
Contrast media for ultrasound	0.05	-42.3	0.3	<0.05	-4.3	0.3	67.50	-39.7
Contrast media	**1.88**	**0.3**	**2.1**	**0.1**	**-1.4**	**0.3**	**53.01**	**1.7**
iomeprol	0.53	-2.5	2.7	<0.05	-4.2	-0.5	76.83	1.8
iodinaxol	0.25	6.9	1.4	<0.05	4.3	0.9	79.57	2.5
gadobutrol	0.23	5.2	5.9	<0.05	5.2	6.4	77.79	0.0
iopromide	0.18	-2.0	-1.6	<0.05	-10.0	-2.2	59.77	8.8
iobitridol	0.13	7.0	0.7	<0.05	-3.0	0.5	51.96	10.3
iopamidol	0.13	4.0	5.5	<0.05	-0.2	0.4	28.39	4.2
ioexol	0.11	20.3	8.4	<0.05	5.8	7.1	37.28	13.7
gadoxetic acid	0.09	-0.7	7.4	<0.05	-0.8	6.5	176.01	0.1
gadoteridol	0.07	2.2	21.6	<0.05	-1.5	19.1	26.37	3.8
hexafluoride sulfur	0.05	-4.2	0.3	<0.05	-4.2	0.3	67.50	0.0

Figure 3.12.1a Contrast media, temporal trend of per capita expenditure of highest-expenditure subgroups (2014-2023)



Regional data on consumption and expenditure

Table 3.12.1b Contrast media, regional trend of per capita expenditure, consumption (DDD/1000 inhab. per day) and average cost per day of therapy: comparison 2014-2023

Region	2022			2023			Δ % 23-22			CAGR % 14-23		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost
Piedmont	1.74	0.1	47.11	1.72	0.1	47.59	-1.1	-2.2	1.0	0.9	0.7	0.1
Valle d'Aosta	2.70	0.1	65.33	2.73	0.1	68.58	0.7	-4.0	5.0	0.0	-3.4	3.6
Lombardy	1.50	0.1	44.40	1.54	0.1	47.00	2.5	-3.2	5.8	0.6	-0.4	1.0
Province of Bolzano	1.70	0.2	28.19	1.83	0.2	30.38	7.7	0.0	7.7	2.8	-0.6	3.4
Province of Trento	1.40	0.1	33.79	1.43	0.1	34.27	1.9	0.5	1.4	2.6	0.1	2.4
Veneto	2.01	0.1	42.28	2.05	0.1	45.00	2.1	-4.1	6.4	2.0	1.2	0.8
Friuli V.G.	2.31	0.1	60.99	2.26	0.1	62.52	-2.4	-4.8	2.5	0.4	-0.1	0.5
Liguria	1.54	0.2	27.94	1.73	0.1	33.24	12.4	-5.6	19.0	4.6	1.3	3.3
Emilia R.	2.26	0.2	37.50	2.19	0.2	36.88	-3.2	-1.6	-1.7	2.6	0.6	2.0
Tuscany	2.41	0.1	50.17	2.43	0.1	50.83	1.0	-0.3	1.3	2.6	0.1	2.5
Umbria	2.33	0.1	51.90	2.44	0.1	52.65	4.7	3.2	1.5	1.0	-0.6	1.7
Marche	2.26	0.1	46.20	2.29	0.1	46.11	1.2	1.4	-0.2	2.2	1.5	0.7
Lazio	1.72	0.1	67.64	1.81	0.1	68.47	5.4	4.1	1.2	1.9	-0.3	2.1
Abruzzo	2.25	0.1	60.17	2.20	0.1	62.49	-2.1	-5.7	3.9	2.3	0.0	2.3
Molise	1.41	0.1	55.85	1.34	0.1	59.91	-4.7	-11.1	7.3	-0.4	-3.3	3.1
Campania	1.29	0.1	62.24	1.29	0.1	65.34	0.3	-4.5	5.0	4.7	2.6	2.0
Puglia	2.53	0.1	103.11	2.13	0.1	81.05	-16.0	6.9	-21.4	3.0	-0.2	3.2
Basilicata	2.19	0.1	69.47	2.11	0.1	72.26	-3.7	-7.4	4.0	0.5	-2.1	2.7
Calabria	1.78	0.1	70.15	1.75	0.1	77.21	-1.4	-10.4	10.1	3.2	-0.6	3.8
Sicily	1.76	0.1	75.91	1.93	0.1	76.25	9.5	9.0	0.5	3.1	0.8	2.3
Sardinia	2.20	0.1	71.23	2.22	0.1	76.35	1.2	-5.6	7.2	1.1	-1.7	2.8
Italy	**1.87**	**0.1**	**52.13**	**1.88**	**0.1**	**53.01**	**0.3**	**-1.4**	**1.7**	**2.1**	**0.3**	**1.8**
North	1.80	0.1	41.70	1.82	0.1	43.39	1.0	-3.0	4.0	1.5	0.4	1.1
Centre	2.06	0.1	55.32	2.12	0.1	56.08	3.0	1.6	1.4	2.0	0.1	2.0
South and Islands	1.87	0.1	75.04	1.82	0.1	73.35	-2.5	-0.2	-2.2	2.9	0.3	2.7

3.12.2 Radiopharmaceuticals

Per capita expenditure on radiopharmaceuticals in 2023 was 1.32 euros, i.e. approximately 78 million euros, recording a 10% growth trend compared to the previous year, and 8.0% in the last ten years (Box Main indices of expenditure and consumption and Table 3.12a). The average cost per day of therapy increased on average each year (CAGR) by 4.9% in the same period, going from 300.7 euros in 2014 to 486.9 euros in 2023.

The highest-expenditure category is radiodiagnostics for tumour detection (0.53 euros per capita), followed by other radiopharmaceuticals for therapeutic use (0.26 euros) and CNS radiodiagnostics (0.24 euros). These three categories account for over 80% of total expenditure; the first increased by 12.5% and the third by 15.1% compared to 2022, while other radiopharmaceuticals decreased by 15.4%. Thyroid radiodiagnostics, on the other hand, show a per capita expenditure of 0.17 euros, with a significant 40% increase. The category of other radiodiagnostics showed a 13.0% increase in expenditure and a 34.4% increase in the average cost (35,165 euros), the highest in the category after therapeutic radiopharmaceuticals (55,000 euros), which however have a negligible per capita expenditure. Diagnostic drugs for cancer detection recorded a 10.2% average annual increase, as did other radiopharmaceuticals for therapeutic use, which recorded a 41.5% CAGR increase (Table 3.12.2a). By analyzing the overall trend of the different subgroups, since 2019 there has been a constant increase of radiodiagnostics for cancer detection; in 2020 there was a decrease in CNS radiodiagnostics and a fluctuating trend of other radiopharmaceuticals for therapeutic use (Figure 3.12.2a).

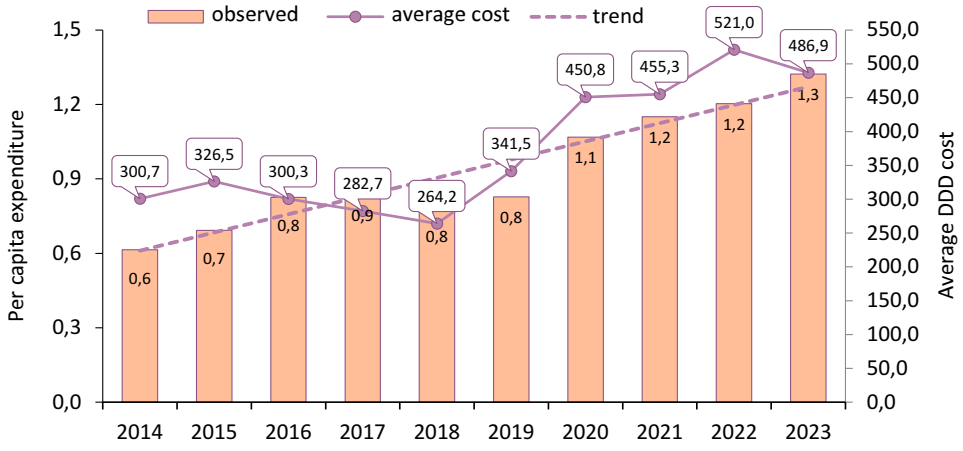
The first active ingredient in terms of expenditure is fluorodeoxyglucose (18F), a radiodiagnostic for cancer detection, which records a per capita expenditure of 0.41 euros, up 16% compared to 2022. This is followed by lutetium (177Lu) oxodotreodite (0.20 euros, down 17.8% compared to 2022), indicated in adult patients for the treatment of well-differentiated, progressive, non-removable or metastatic gastroenterohepatic neuroendocrine tumors (NET-GEP) that are positive for somatostatin receptors. Iodine ioflupane (123I) and technetium (99mTC) pertechnetate, two diagnostic radiotherapy products used respectively for the CNS and the thyroid, recorded a per capita expenditure of 0.20 and 0.14 euros respectively (both up 15.7% and 31.2%).

The Centre shows the highest expenditure (1.40 euros per capita) compared to the North (1.33 euros) and the South and Islands (1.26 euros), which have values comparable to the national average (1.32 euros). There are marked regional differences with higher values in Basilicata (3.32 euros) and Valle d'Aosta (2.99 euros) while Campania (0.72 euros) and Umbria (0.74 euros) record the lowest expenditure (Table 3.12.2b). The expenditure variation compared to 2022 ranges from an 82.4% increase in Valle d'Aosta to a 12.9% reduction in Lazio. Drugs more expensive than the national average are used in the North (590.2 vs 486.9 euros), and in particular, Valle d'Aosta has a cost that is almost four times higher than Sicily (897.03 vs 245.13 euros).

MAIN INDICES OF EXPENDITURE AND CONSUMPTION
Radiopharmaceuticals

Public expenditure in million euros (% over total)	**77.8**	**(0.3)**
Δ % 2023-2022		10.0
Regional range of gross per capita expenditure:	0.7	3.3
DDD/1000 inhab. per day (% over total)	**<0,05**	**(0.0)**
Δ % 2023-2022		17.7
Regional range DDD/1000 inhabitants per day	<0.05	<0.05

Radiopharmaceuticals, temporal trend of per capita expenditure and average cost per day of therapy (2014-2023)

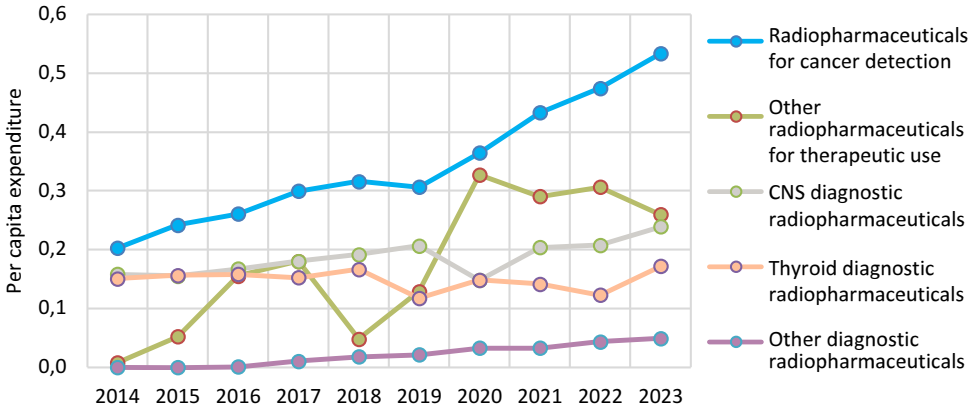


National data on consumption and expenditure by subgroup and substance

Table 3.12.2a Radiopharmaceuticals, per capita expenditure and consumption (DDD/1000 inhabitants per day) by subgroup and substance: comparison 2014-2023

Subgroups and substances	Expenditure *per capita*	Δ % 23-22	CAGR % 14-23	DDD/1000 inhab. per day	Δ % 23-22	CAGR % 14-23	Average DDD cost	Δ % 23-22
Radiopharmaceuticals for cancer detection	0.53	12.5	10.2	<0.05	8.0	0.9	558.38	4.1
Other radiopharmaceuticals for therapeutic use	0.26	-15.4	41.5	<0.05	0.7	50.2	2072.91	-16.0
CNS diagnostic radiopharmaceuticals	0.24	15.1	4.2	<0.05	7.7	2.2	752.77	6.9
Thyroid diagnostic radiopharmaceuticals	0.17	39.7	1.3	<0.05	32.1	13.3	251.59	5.7
Other diagnostic radiopharmaceuticals	0.05	13.0	—	<0.05	-15.9	—	35165.32	34.4
Diagnostic radiopharmaceuticals of the cardiovascular system	0.04	32.1	-2.8	<0.05	10.5	1.4	110.53	19.6
Diagnostic radiopharmaceuticals of the skeletal system	0.01	68.3	—	<0.05	75.5	—	75.89	-4.1
Diagnostic radiopharmaceuticals of the renal system	0.01	66.2	7.0	<0.05	85.3	-0.8	114.42	-10.3
Therapeutic radiopharmaceuticals	0.00	—	—	<0.05	—	—	55000.00	—
Diagnostic radiopharmaceuticals of the respiratory system	0.00	-13.4	-5.4	<0.05	-13.4	-13.5	150.00	0.0
Radiopharmaceuticals for detection of inflammation and infections	0.00	35.2	-19.7	<0.05	37.4	-24.0	566.14	-1.6
Diagnostic radiopharmaceuticals of the hepatic and reticuloendothelial system	0.00	-3.1	-29.2	<0.05	-4.8	-39.5	458.61	1.7
Radiopharmaceuticals with analgesic/anti-inflammatory action	0.00	-66.2	-38.4	<0.05	-71.3	-29.1	925.50	17.9
Radiopharmaceuticals	**1.32**	**10.0**	**8.0**	**<0,05**	**17.7**	**2.9**	**486.90**	**-6.5**
fluoride deoxyglucose (18F) (18 F)	0.41	16.4	10.4	<0.05	7.8	1.1	460.32	8.0
lutetium oxodotreotide (177Lu)	0.20	-17.8	—	<0.05	6.3	—	12858.52	-22.7
iodine ioflupane (123I)	0.20	15.7	3.8	<0.05	17.0	4.3	808.09	-1.1
pertecnetate technetium (99 mTc)	0.14	31.2	-0.6	<0.05	36.6	6.9	372.16	-4.0
fluorocholine (18F)	0.07	4.6	—	<0.05	7.4	—	2359.39	-2.6
sodium iodide (131I)	0.05	51.5	104.0	<0.05	19.7	117.7	126.62	26.6
germanium chloride/gallium chloride (68Ge/68Ga)	0.05	17.9	—	<0.05	3.9	—	98413.67	13.5
flutemetamol (18F)	0.03	7.0	—	<0.05	7.4	—	1216.26	-0.3
radium dichloride (223Ra)	0.03	-24.0	25.7	<0.05	-24.1	30.6	3240.68	0.1
technetium tetrophosmin (99 mTc)	0.02	11.4	-4.6	<0.05	20.0	-0.6	134.00	-7.2

Figure 3.12.2a Radiopharmaceuticals, temporal trend 2014-2023 in per capita expenditure of most expensive subgroups



Regional data on consumption and expenditure

Table 3.12.2b Radiopharmaceuticals, regional trend of per capita expenditure, consumption (DDD/1000 inhab. per day) and average cost per day of therapy: comparison 2014-2023

Region	2022			2023			Δ % 23-22			CAGR % 14-23		
	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost	Expenditure per capita	DDD/1000 inhab. per day	Average DDD cost
Piedmont	1.01	<0.05	511.01	1.25	<0.05	471.76	24.2	34.5	-7.7	6.8	3.3	3.4
Valle d'Aosta	1.64	<0.05	565.30	2.99	<0.05	897.03	82.4	14.9	58.7	4.1	-4.1	8.6
Lombardy	1.13	<0.05	605.02	1.20	<0.05	577.03	6.2	11.3	-4.6	8.1	-0.1	8.2
Province of Bolzano	0.88	<0.05	537.06	1.51	<0.05	611.65	70.2	49.5	13.9	9.8	2.3	7.4
Province of Trento	0.83	<0.05	591.90	1.02	<0.05	497.37	23.2	46.6	-16.0	6.8	6.3	0.5
Veneto	1.29	<0.05	770.15	1.54	<0.05	699.26	19.8	31.9	-9.2	8.6	3.8	4.6
Friuli V.G.	1.06	<0.05	515.89	1.38	<0.05	458.68	31.0	47.3	-11.1	8.2	5.9	2.1
Liguria	0.76	<0.05	531.63	0.75	<0.05	441.08	-1.4	18.9	-17.0	-1.2	-5.4	4.5
Emilia R.	1.69	<0.05	738.50	1.66	<0.05	722.01	-2.1	0.1	-2.2	7.3	-2.2	9.7
Tuscany	1.45	<0.05	490.53	1.79	<0.05	482.29	24.0	26.1	-1.7	4.8	0.6	4.2
Umbria	0.67	<0.05	368.44	0.74	<0.05	346.71	10.4	17.3	-5.9	1.0	3.2	-2.2
Marche	1.79	<0.05	300.86	2.10	<0.05	261.99	17.1	34.4	-12.9	3.9	2.7	1.1
Lazio	1.20	<0.05	700.69	1.05	<0.05	541.19	-12.9	12.7	-22.8	13.2	6.2	6.5
Abruzzo	1.41	<0.05	488.56	1.60	<0.05	487.76	13.6	13.8	-0.2	9.8	9.5	0.3
Molise	0.69	<0.05	724.57	1.00	<0.05	647.56	45.0	62.2	-10.6	2.8	-13.0	18.2
Campania	0.62	<0.05	397.83	0.72	<0.05	429.45	16.9	8.3	7.9	7.2	7.1	0.1
Puglia	1.79	<0.05	621.21	1.60	<0.05	619.61	-10.3	-10.0	-0.3	11.0	-0.7	11.9
Basilicata	3.05	<0.05	423.08	3.32	<0.05	342.96	8.6	34.0	-18.9	9.6	1.6	7.9
Calabria	1.97	<0.05	673.57	1.98	<0.05	628.03	0.4	7.7	-6.8	20.1	14.2	5.2
Sicily	0.79	<0.05	226.63	1.16	<0.05	245.13	47.1	36.0	8.2	16.9	20.9	-3.3
Sardinia	0.63	<0.05	322.35	0.76	<0.05	706.57	20.0	-45.2	119.2	-1.9	-4.9	3.2
Italy	**1.20**	**<0,05**	**521.01**	**1.32**	**<0,05**	**486.90**	**10.0**	**17.7**	**-6.5**	**8.0**	**2.9**	**4.9**
North	1.20	<0.05	631.83	1.33	<0.05	590.24	11.6	19.4	-6.6	7.3	0.6	6.6
Centre	1.32	<0.05	493.67	1.40	<0.05	423.30	6.2	23.8	-14.3	6.5	2.6	3.8
South and Islands	1.14	<0.05	425.96	1.26	<0.05	418.64	10.3	12.2	-1.7	10.4	6.5	3.7

3.13 Dermatological drugs

In 2023, dermatological drugs were the 13th therapeutic category with the highest public expenditure, amounting to 332.7 million euros, i.e. 1.3% of total public expenditure (Box Main indices of expenditure, consumption and exposure). The overall per capita expenditure on these drugs is 5.64 euros, a sharp increase compared to the previous year (+27.6%). This increase was mainly due to purchases by public health facilities, which reached 4.29 euros per capita, up 37.3% compared to 2022. The approved care expenditure was 1.35 euros per capita, a 4.2% increase (Table 3.1).

Total consumption in this category was equal to 13.8 DDD/1000 inhabitants per day, a 0.9% increase compared to 2022, stable for public facilities and up 3.0% in the context of the approved care regime (Table 3.2).

The analysis of the drug utilization profile by age group and gender, including approved care regime and distribution on behalf, highlights an increase in the prevalence of use and consumption starting from the age of 15 for both genders, with a higher prevalence in males in the population over 65. In particular, males over 75 years reach a prevalence of 3.73% and a consumption of 12.7 DDD/1000 inhabitants per day, while in females the trend is less evident with increasing age. However, even among females the prevalence of use reaches its maximum in the over-75 age group, standing at 2.32%. The per capita expenditure covered by the NHS increases with age, reaching a maximum of 2.5 euros per capita in the over-75 age group (3.6 euros in males and 1.7 euros in females).

The increase in approved care expenditure was mainly due to an increase in prescribed doses (+2.7%), a shift towards higher-cost products (mix effect: +1.2%) and to an increase in the average DDD cost (+1.1%). Other antipsoriatic drugs for topical use (0.91 euros per capita) are the category with the greatest impact on approved care expenditure (Table 3.9). The drug with the highest expenditure and consumption is the combination calcipotriol/betamethasone, which represents approximately 65% of the gross expenditure of the category and half of the consumption (Table 3.10), with the latter growing by 5.7% compared to 2022. In 2023, the decline continued in prescriptions for isotretinoin, a drug indicated for the treatment of severe acne in patients resistant to both systemic antibiotics and topical therapy. The decrease was recorded in terms of both expenditure (-1.9%) and consumption (-1.8%).

As for drugs purchased by public health facilities, there was a high expenditure increase (+36.9%), almost exclusively due to the shift towards more expensive drugs (mix effect: +36.7%), with stable consumption and prices (Table 3.17). Drugs used to treat dermatitis (excluding corticosteroids) are the category with the highest per capita expenditure (3.80 euros) and cover approximately 90% of the total.

The most expensive active ingredient is dupilumab (3.65 euros per capita), a monoclonal antibody indicated for the treatment of moderate to severe atopic dermatitis in adult patients, children and adolescents (aged 6 to 17 years) eligible for systemic therapy. This drug accounts for 85.0% of the entire category and increased by 36.6% compared to 2022, in terms of both expenditure and consumption. The average cost per day of therapy of 28.03 euros has not changed compared to the previous year (Table 3.18). Tralokinumab, a monoclonal antibody inhibiting IL-33, indicated for atopic dermatitis and marketed in 2022, is the second substance in terms of expenditure (0.14 euros) and shows the highest cost per DDD in the category (300.94 euros) (Table 3.18). Dupilumab ranks seventh among the highest-

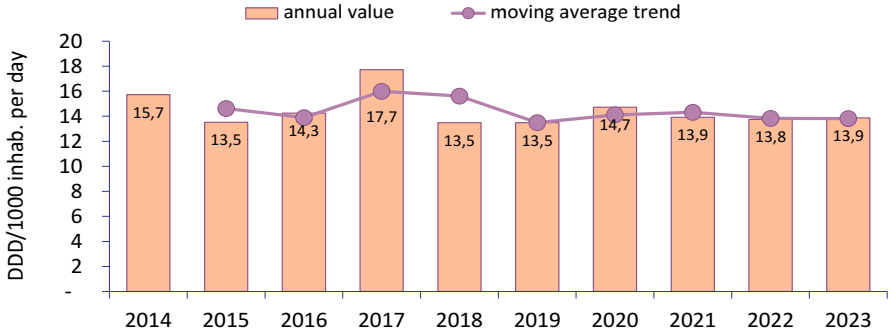
expenditure active ingredients purchased by public health facilities (Table 3.19) and is among the top 30 with the greatest variation in expenditure compared to last year (Table 3.20). Sodium hypochlorite is among the top thirty active ingredients by consumption, with 2.7 DDD per 1000 inhabitants per day, a 4.8% increase compared to 2022 (Table 3.24).

MAIN INDICES OF EXPENDITURE, CONSUMPTION AND EXPOSURE

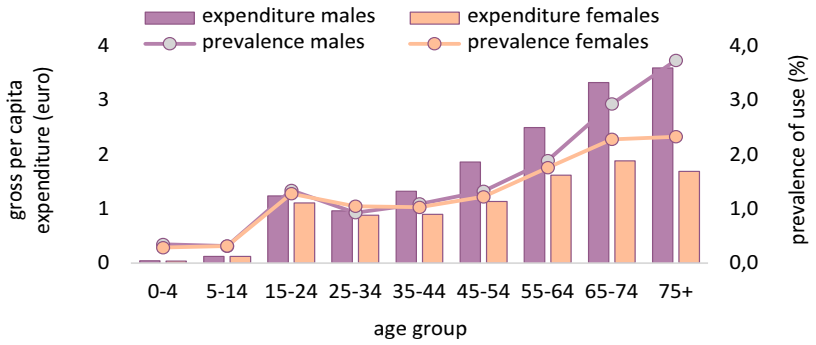
Dermatological drugs

Public expenditure* in million euros (% over total)	**332.7**	**(1.3)**
Δ % 2023-2022		27.6
Regional range of gross expenditure (per capita):	4.3	7.9
DDD/1000 inhabitants per day* (% over total)	**13.8**	**(1.0)**
Δ % 2023-2022		0.9
Regional range DDD/1000 inhabitants per day	8.7	22.1

** includes prescriptions under approved care regime and purchases by public health facilities*



Distribution of prevalence of use and consumption under approved care regime and distribution on behalf by age and gender in 2023 (Figure and Table)



Age group	Gross per capita expenditure			DDD/1000 inhabitants per day		
	Males	Females	Total	Males	Females	Total
0-4	0.0	0.0	0.0	0.5	0.4	0.5
5-14	0.1	0.1	0.1	0.6	0.6	0.6
15-24	1.2	1.1	1.2	3.3	3.1	3.2
25-34	1.0	0.9	0.9	3.1	2.9	3.0
35-44	1.3	0.9	1.1	4.2	3.1	3.7
45-54	1.9	1.1	1.5	5.6	3.8	4.7
55-64	2.5	1.6	2.0	7.7	5.4	6.6
65-74	3.3	1.9	2.6	10.9	7.2	8.9
75+	3.6	1.7	2.5	12.7	7.1	9.4

Section 4

Monitoring registries and conditional reimbursement agreements

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4.1 Medicines Monitoring Registries

AIFA Monitoring Registries constitute an information system that, through a web-based platform, manages both the prescription and dispensing of medicines reimbursed by the NHS, in line with the indications authorised by the European Medicines Agency (EMA) and within the limits identified and set by AIFA Scientific and Economic Committee for Medicines. Thus, AIFA Registries ensure that the appropriateness of use of medicines is monitored in accordance with both regulatory constraints, which derive from the authorisation, and constraints related to the conditions of eligibility for reimbursement set by the advisory bodies of the Agency.

Another fundamental characteristic of the AIFA Registries is that of allowing access to relevant and often high-cost therapies in a homogeneous way on the national territory, regardless of the patients' location or their change of residence.
Monitoring Registries impact also the monitoring of national pharmaceutical expenditure, because they allow the application of specific conditions of eligibility for reimbursement of a medicine, intended for a specific therapeutic indication, which are agreed by AIFA with the pharmaceutical company in the so-called *Managed Entry Agreements* (MEA). In other words, the AIFA Monitoring Registries are the means by which economic agreements, some of which are based on the efficacy of the medicine itself in clinical practice, are made effective.
Furthermore, in application of the legislation introduced in 2015, the AIFA Registries are also used for the distribution among the Regions of the economic resources allocated by the State to finance innovative medicines.

Last but not least, the AIFA Registries are useful in assessing the clinical-therapeutic impact of medicines in the specific Italian healthcare context. Accordingly, Registries are a tool to support the production of technical-scientific information useful for the decision-making processes of doctors and health professionals.

Types of monitoring

AIFA Monitoring Registries are organised according to different types of monitoring: firstly, the Registries in the strict sense, which are aimed at detail monitoring the use of a medicine in clinical practice, from the eligibility criteria to the treatment outcome, including the possible application of a MEA. Secondly, there are the Registries that, with substantially similar methods used by the Registries in the strict sense, monitor medicines reimbursed by the NHS according to law 648/96. On the other hand, web-based therapeutic plans (web-based TPs) focus on aspects related to the prescription of medicines and their eligibility criteria, as well as on the possible evaluation and re-evaluation of the therapy results, less frequently. Lastly, at the end of 2019, Simplified Monitoring Registries (single or multi- drug) were introduced; these are tools to prescribe and monitor the use of a medicine or multiple medicinal products within the same therapeutic indication. This particular type of Register is simplified compared to web-based TPs or Registries in the strict sense, in order to allow non-detailed monitoring and rapid compilation by doctors and pharmacists of the data required by the AIFA platform.

AIFA Registries: legal basis

Starting from 2012, the AIFA Monitoring Registries became an integral part of the National Health Service Information System (Article 15, paragraph 10 of Legislative Decree 95/2012, converted with modification into Law n. 135 of 7 August 2012). Subsequently, further legislation (Law 125/2015; Law 232/2016; Law 205/2017; Law 302/2018) assigned to the Regis-

tries additional tasks related to the evaluation of medicines efficacy for the purpose of renegotiating the medicines subject to monitoring, the control of expenditure for innovative medicines (Article 1, paragraph 578 of Law n. 145 of 30 December 2018), the allocation of resources to the Regions for the purchase of innovative medicines (Article 1, paragraph 401-404 of Law n. 232 of 11 December 2016; Ministerial Decree dated 9 October 2015 published in the Italian Official Journal n. 264 of 12 November 2015 "Costs reimbursed to Regions for the purchase of innovative medicines" and Ministerial Decree dated 16 February 2018 published in the Italian Official Journal n. 81 of 7 April 2018 "Operating procedures for the disbursement of resources allocated as a contribution to the reimbursement for the purchase of innovative and oncological medicines") and support in quantifying the so-called avoidable costs in healthcare.

AIFA Registries and the Regions

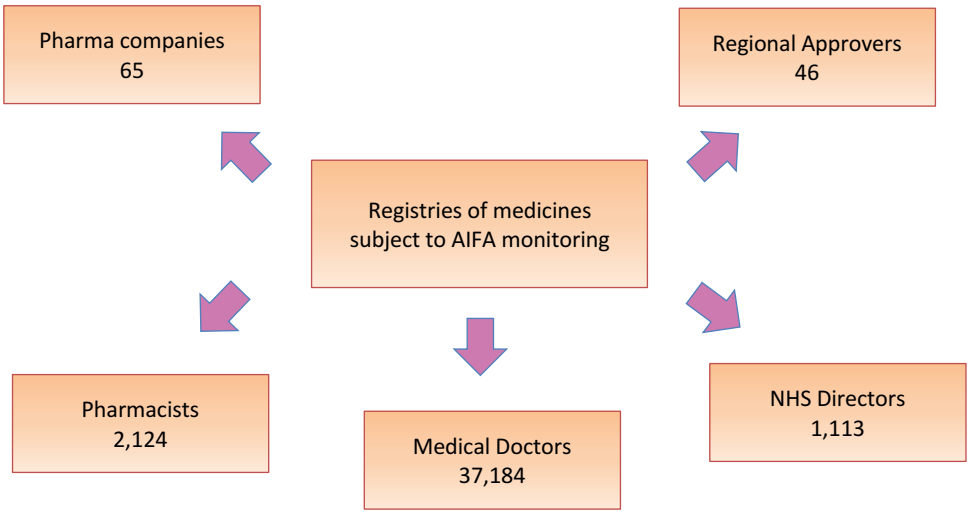
The AIFA Monitoring Registries are a support infrastructure for the Regions. Through the functions of the AIFA Registries, Regions exercise their responsibility in coordinating health facilities and consequently enabling doctors to prescribe medicines subject to monitoring register and enabling pharmacists responsible for their dispensing. In managing the infrastructure, the Regions approve the authorisation of prescribing centres; subsequently, health directors of the health facilities including such prescribing centres, in turn, authorise doctors and pharmacists to use the platform. Licensed doctors and pharmacists are responsible for the correct and timely entry of the collected data in the AIFA Monitoring Registries. The legislation in force (Article 15, paragraph 10, of Decree-Law No. 95/2012) also provides that the LEA (Essential Levels of Care) Committee and the Working group on the Verification of the fulfilments established at the Ministry of Economy and Finance, (as per Articles 9 and 12 of the State-Regions Agreement of 23 March 2005), shall annually check that each Region has ensured both activation and operation of the AIFA registries of medicines subject to monitoring, as well as the activation of the procedures to obtain any reimbursement by the pharmaceutical companies concerned (fulfilment L.2). The positive outcome of that legal obligation, together with that of all the other legal provisions in force, is preliminary to the disbursment of the bonus share of ordinary funding (Article 2, paragraph 68, letter b of Law 191/2009).

The collaborative network of AIFA Registries

AIFA monitoring registries constitute a collaborative network that allows the exchange of information between AIFA, Regions, health facilities, doctors, pharmacists and pharmaceutical companies. This network includes about 2,129 active health facilities (with at least one treatment started in 2023), in all 21 Italian Regions and Autonomous Provinces, 46 regional approvers, 1,113 NHS directors, 37,184 medical doctors registered on the platform and 2,124 pharmacists (Figure 4.1.1). 65 pharmaceutical companies owning at least one monitoring register managed by the AIFA platform also contribute to this network. Moreover, through specific profiling pharmaceutical companies interact with the pharmacies of the authorised health facilities, in the case of registries of medicines owned by them that are admitted for reimbursement with a MEA based on the register.

In this network, the Monitoring Registries Office is responsible for elaborating the monitoring form and the process leading to its approval, for testing the production of the register within the AIFA web platform and for interacting with all stakeholders in order to manage the activities concerning the registries and the related reporting.

Figure 4.1.1 Personnel participating in the Registries Network in 2023



Access and structure of AIFA Registries

Access to the AIFA Monitoring Registries is possible through the following web page: https://servizionline.aifa.gov.it/; users may select the option: "Registries of medicines subject to monitoring" so as to access the registries by entering their credentials, or proceed with their registration if they are logging in for the first time. In general terms, the navigation in the platform allows the doctors to select the pre-filled therapeutic indication for which they intend to prescribe the monitored medicine for which they have previously been enabled. Thereafter, prescribers may select the medicine they intend to prescribe or choose it from a list, in the event that they have been enabled and more than one monitored medicine is available in the same therapeutic indication.

At this point, the structure of the Registries has a modular architecture, designed in order to allow the collection of both clinical-therapeutic and administrative data. This path involves the compilation of the following forms by medical doctors and pharmacists:

1. Patient data (unique for all Registries and/or AP Therapeutic Plans)
2. Eligibility and clinical data (EDC)
3. Prescriptions (Medicine Request RF)
4. Medicine dispensing (Medicine Dispensing DF)
5. Follow-up (Re-evaluations RIV)
6. End of therapy (End of Treatment FT)
7. Pregnancy (GV) (for medicines with Risk Management Plan).

As previously indicated, in addition to the Registries in the strict sense, the web-based TPs are in place. For this type of registries, the participation of specialist doctors is required, with

the compilation of the following forms:

1. Patient data (unique for all Registries and/or AP Therapeutic Plans)
2. Eligibility and clinical data (EDC)
3. Prescriptions (Medicine Request RF)
4. Follow-up (Re-evaluations RIV)
5. End of therapy (End of Treatment FT)

The simplified multi-medicine cards share a very similar structure to those reported above, but provide for a very limited collection of data. It should be noted that, in the case of simplified multi-medicine monitoring, it is possible to select the used medicine and the associated therapeutic indication in the eligibility form.

In 2023, 301 registries were active (at least one day of monitoring). It is important to specify that during 2023 the Monitoring Registries Office published on its page of the Agency's portal (https://www.aifa.gov.it/registri-e-piani-terapeutici1) a new definition of 'Monitoring Register' that goes beyond the 'IT' approach used in past editions of this Report and takes on a more regulatory profile. Indeed, a 'Registrer' (or Therapeutic Plan or simplified single-medicine monitoring) is considered to be the monitoring action applied to a specific medicinal product in a specific reimbursed therapeutic indication. The pair 'medicine/reimbursed indication' thus becomes crucial in the definition of AIFA monitoring and synonym for Registry (or Therapeutic Plan or simplified single-medicine monitoring) accessible through the AIFA Platform.

The numbers shown here take into account this new definition and, in particular, consider each 'medicinal/indication' pair with at least 1 day of active monitoring during the year 2023. The Registries activated in 2023 were 53, while the registries closed during the same period were 35, representing an increase of 18 monitoring registries compared to 2022 (Table 4.1.1).

Table 4.1.1 Summary data of the Monitoring Registries on the web platform: cumulative trend 2021-2023

	No.			Δ %
	2021	2022	2023	23-22
Registries	241	283	301	6.4
PT *web-based*	16	20	17	-15.0
Simplified monitoring	3	6	6	0.0
Therapies	3,792,875	4,441,193	5,004,033	12.7
Patients	3,094,980	3,536,714	3,901,134	10.3

In general, in 2023 the increase in new patients compared to 2022 appears smaller when compared to the previous two-years: this circumstance is attributable to a variety of factors such as, for instance, the fading effect of the COVID-19 emergency impact, as well as the smaller number of new registries activated compared to last year. It should be noted that for ATC category A 'Gastrointestinal tract and metabolism' there is a much larger increase than for the other categories, since patients started in 2023 are almost three times as many as in 2022 (124,473 vs 43,518) (Table 4.1.2).

The following categories showed smaller increases than those observed in the last two years: group J 'Antimicrobials for systemic use', for which the approximately 81,000 new patients in 2023 remain a far cry from the more than 222,000 in 21-22, and group R 'Respiratory system', which saw its increase almost halve in the last observation period, after two consecutive two-year periods of increases close to 60%.

With regard to category B 'Blood and haemopoietic organs', the trend of the years 21-22 is confirmed at under 5%.

Table 4.1.2 Number of patients* in ATC categories (1st level) for the period 2021-2023

ATC 1st level	No. of patients			Incidence %			Δ %	
	2021	2022	2023	2021	2022	2023	23-22	22-21
A	320	43,518	124,473	0.0	1.1	2.9	186.0	13,499.4
B	1,681,501	1,764,408	1,828,441	50.8	45.5	42.0	3.6	4.9
C	107,214	153,785	212,431	3.2	4.0	4.9	38.1	43.4
D	12,756	17,373	22,120	0.4	0.4	0.5	27.3	36.2
H	263	284	289	0.0	0.0	0.0	1.8	8.0
J	335,927	558,089	639,459	10.2	14.4	14.7	14.6	66.1
L	520,604	580,312	646,514	15.7	15.0	14.9	11.4	11.5
M	307,019	359,624	420,931	9.3	9.3	9.7	17.1	17.1
N	27,352	37,069	48,152	0.8	1.0	1.1	29.9	35.5
R	7,933	12,663	16,763	0.2	0.3	0.4	32.4	59.6
S	305,389	345,701	386,692	9.2	8.9	8.9	11.9	13.2
V	1492	1,931	2,340	0.0	0.0	0.1	21.2	29.4
Total	**3,307,770**	**3,874,757**	**4,348,605**	**100**	**100**	**100**	**12.2**	**17.1**

* The table reports the number of "naïve" patients for ATC cathegory. For each patient, only the first treatment with a medicine belonging to an ATC category (1st Level) is counted. Given the approximation to one decimal place, some totals may not add up to 100%.

Table 4.1.3 Number of registries and active PT in ATC categories (1st level) for the period 2021-2023

ATC 1st level	No. of Registries			No. of PT			Total		
	2021	2022	2023	2021	2022	2023	2021	2022	2023
A	5	9	11	0	2	2	5	11	13
B	2	3	3	10	11	7	12	14	10
C	8	7	4	1	1	2	9	8	6
D	3	4	3	0	0	0	3	4	3
H	1	1	1	0	0	0	1	1	1
J	10	13	12	0	0	0	10	13	12
L	183	209	235	0	0	0	183	209	235
M	4	5	6	3	4	4	7	9	10
N	8	8	10	1	1	1	9	9	11
R	12	20	12	1	1	1	13	21	13
S	3	2	2	0	0	0	3	2	2
V	2	2	2	0	0	0	2	2	2
Total	**241**	**283**	**301**	**16**	**20**	**17**	**257**	**303**	**318**

Table 4.1.4 Number of patients* enrolled for ICD-11 category (years 2021-2023)
ICD: International Classification of Diseases

ICD-11	No. of patients			Incidence %			Δ %	
	2021	2022	2023	2021	2022	2023	23-22	22-21
Mental and behavioural disorders	4,962	6,899	10,158	0.2	0.2	0.2	47.2	39.0
Developmental disease	0.0	22	190	0.0	0	0.0	763.6	-
Diseases of the blood and hematopoietic organs	6,870	7,615	8,440	0.2	0.2	0.2	10.8	10.8
Diseases of the circulatory system	1,726,694	1,844,541	1,967,807	53.4	49.0	47.0	6.7	6.8
Diseases of the immune system	2,608	3,244	3,941	0.1	0.1	0.1	21.5	24.4
Diseases of the musculoskeletal system and the connective tissue	271,973	320,251	377,043	8.4	8.5	9.0	17.7	17.8
Diseases of the nervous system	24,706	31,618	38,662	0.8	0.8	0.9	22.3	28.0
Diseases of the digestive system	3,125	3,125	3,125	0.1	0.1	0.1	0.0	0.0
Diseases of the genitourinary system	793	996	6838	0.0	0.0	0.2	586.6	25.6
Diseases of the respiratory system	17,650	21,442	24,579	0.5	0.6	0.6	14.6	21.5
Skin Diseases	15,830	24,335	32,809	0.5	0.6	0.8	34.8	53.7
Eye Diseases	323,926	363,637	404,263	10.0	9.7	9.7	11.2	12.3
Diseases of the endocrine glands of the nutrition and metabolism and immune disorders	33,595	52,401	80,156	1.0	1.4	1.9	53.0	56.0
Infectious and parasitic diseases	331,333	553,532	634,335	10.2	14.7	15.2	14.6	67.1
Tumours	469,879	527,944	592,018	14.5	14.0	14.1	12.1	12.4
Total	**3,233,944**	**3,761,602**	**4,184,364**	**100**	**100**	**100**	**11.2**	**16.3**

*The Table reports the number of naïve patients by ICD-11 code. For each patient, only the first treatment carried out with a medicine whose indication belongs to a specific ICD-11 code is counted. Given the approximation to one decimal place, some totals may not add up to 100%.

Demographic characteristics of patients being treated in Registries and *web-based* TPs

Regulatory decisions are based on information obtained considering the characteristics of the population that was enrolled and studied in pivotal clinical trials, with the awareness that the consequences of use in real clinical practice may vary – in terms of health benefits – compared to those registered in a clinical trial context.

In this regard, in 2015 the European Medicines Agency (EMA) began to draw up a document that aims to define how to assess the degree of fragility of the elderly population with the aim of being able to include them in the clinical trials of medicines in a more adequate fashion (adopted by the CHMP in January 2018). Indeed, although elderly people are among the major users of medicines, due to the concomitant (often chronic) pathologies they suffer from, they are not always enrolled in studies; moreover, the effects of medicines in the over 65-year-olds can vary considerably with respect to those observed in younger adult population, in terms of efficacy and safety. Therefore, the collection and analysis of data relating to clinical practice (Real World Data) becomes essential, also for the purposes of any re-evaluation. To this aim, post-marketing monitoring through the AIFA Registries constitutes an important information basis.

The percentage distribution of treatments by gender and age is shown below. As can be seen from the data, the high presence of patients above the age threshold (>65 years) is evident. In particular, Tables 4.1.5 and 4.1.6 show the distribution of treatments by age and gender in Registries and Therapeutic Plans, respectively. As regards the Registries, the highest number of treatments was detected in the age group between 70 and 79 years, both for women and for men, while for the TPs the highest number of treatments was observed in the same age group for men, while for women there is a higher incidence in the over 80 years group. Compared with the previous two-year period, the distribution by age group and ATC code again confirms that in younger patients the most populated ATCs are related to categories B, J, L and N (Table 4.1.7). From the age of 50 onwards, the ATC category B is the one that counts the highest number of patients entered in a Registry. At the same time, the number of patients entered in Registries referred to ATC categories C and S begins to be relevant. In particular, ATC category S registers up to 100,000 patients entered both in the age group 70-79 and over 80 years.

Table 4.1.5 Number of patients by age group and gender in the Registries (year 2023)*

Age group	Donne		Men		Total	
	No. of patients	Inc %	No. of patients	Inc %	No. of patients	Inc %
<40	42,410	5.48	43,360	5.05	85,770	5.25
40-49	65,227	8.43	74,566	8.69	139,793	8.56
50-59	127,415	16.47	157,006	18.29	284,421	17.42
60-69	171,321	22.14	208,160	24.25	379,481	23.25
70-79	216,529	27.98	244,534	28.49	461,063	28.25
≥80	150,938	19.51	130,802	15.24	281,740	17.26
Total	**773,840**	**100**	**858,428**	**100**	**1,632,268**	**100**

Tabele 4.1.6 Number of patients by age group and gender in Therapeutic Plans (year 2023)*

Age group	Women		Men		Total	
	No. of patients	Inc %	No. of patients	Inc %	No. of patients	Inc %
<40	17,688	1.43	24,628	2.37	42,316	1.86
40-49	33,005	2.67	34,919	3.37	67,924	2.99
50-59	86,121	6.98	94,746	9.14	180,867	7.96
60-69	201,735	16.35	206,432	19.9	408,167	17.97
70-79	400,302	32.44	351,916	33.93	752,218	33.12
≥80	495,182	40.13	324,529	31.29	819,711	36.09
Total	**1,234,033**	**100**	**1,037,170**	**100**	**2,271,203**	**100**

* Patients registered both in a *web-based* PT and in a Registry in strict sense are counted in both Tables 4.1.5 and 4.1.6.

Table 4.1.7 Number of patients* by age group in ATC categories (1st level) up to 2023

1st level ATC	<40			40-49			50-59		
	Males	Females	Total	Males	Females	Total	Males	Females	Total
A	564	1,627	2,191	984	3,901	4,885	2,867	11,625	14,492
B	11,211	13,720	24,931	18,084	28,414	46,498	37,615	77,107	114,722
C	946	2,892	3,838	2,397	10,040	12,437	8,684	29,161	37,845
D	5,457	5,733	11,190	1,288	1,334	2,622	1,613	1,470	3,083
H	60	24	84	71	11	82	42	15	57
J	14,921	22,601	37,522	23,010	44,798	67,808	44,416	79,992	124,408
L	12,180	7,905	20,085	29,518	16,433	45,951	59,165	47,100	106,265
M	3,840	1,250	5,090	15,670	1,755	17,425	51,054	5,752	56,806
N	7,549	9,776	17,325	8,089	2,694	10,783	8,566	2,837	11,403
R	3,653	2,672	6,325	1,571	840	2,411	1,641	904	2,545
S	2,311	2,264	4,575	4,557	5,857	10,414	15,330	18,661	33,991
V	21	21	42	61	77	138	138	244	382
Total	**62,713**	**70,485**	**133,198**	**105,300**	**116,154**	**221,454**	**231,131**	**274,868**	**505,999**
1st level ATC	**60-69**			**70-79**			**≥80**		
	Males	Females	Total	Males	Females	Total	Males	Females	Total
A	5,871	20,478	26,349	11,330	28,612	39,942	14,085	22,529	36,614
B	112,660	177,613	290,273	292,494	319,425	611,919	433,878	306,220	740,098
C	16,128	44,533	60,661	19,278	46,360	65,638	10,675	21,337	32,012
D	1,101	1,245	2,346	804	1,026	1,830	463	586	1,049
H	29	12	41	18	2	20	5	0	5
J	52,712	67,103	119,815	74,753	78,719	153,472	71,815	64,619	136,434
L	83,400	95,600	179,000	90,689	120,703	211,392	39,495	44,326	83,821
M	93,903	13,020	106,923	122,838	18,949	141,787	80,290	12,610	92,900
N	3,619	1,674	5,293	852	1,409	2,261	184	903	1,087
R	1,394	1,271	2,665	881	1,291	2,172	244	401	645
S	35,417	40,370	75,787	72,578	64,355	136,933	74,538	50,454	124,992
V	195	490	685	179	628	807	41	245	286
Total	**406,429**	**463,409**	**869,838**	**686,694**	**681,479**	**1,368,173**	**725,713**	**524,230**	**1,249,943**

*The Table reports the number of 'naïve' patients by ATC category. For each patient, only the first treatment carried out with a medicine belonging to an ATC category (1st level) is counted.

4.2 Financial impact of conditional reimbursement agreements

Italy is one of the first European countries to have adopted the so-called *Managed Entry Agreements* (MEAs), i.e. tools that allow access to new therapies which, although promising, are characterised by high costs and/or uncertainties related to clinical benefits and economic impact. AIFA negotiates with pharmaceutical companies various MEAs that can provide for the management of conditional reimbursement at single patient level through the Monitoring Registries platform (*Patient level*) and at the level of the entire population (*Population level*) through the information flows for monitoring expenditure and consumption by the NHS (i.e. OsMed Flow and Medicine Traceability Flow).

Conditional reimbursement agreements managed through the Registries (*patient level*)

On the basis of an international taxonomy, the MEAs managed through the AIFA Registries can be classified in two main categories: a) outcome-based risk-sharing arrangements (*Outcome-based schemes*) and b) purely financial arrangements (*Financial-based schemes*) (Figure 4.2.1). The first category includes two macro types of agreements, namely *Payment-by-result* (PbR) and *Risk-sharing* (RS). In the case of PbR, the entire cost of treatment failure is borne by the pharmaceutical company holder of the MA. The PbR has two variants: *Success-Fee* (SF), where the entire cost of treatment is borne by the NHS only when representing therapeutic success, and *Payment-at-result* (PaR), in which the entire cost of treatment borne by the NHS is broken down over time following the verification of the maintenance of therapeutic success. Finally, the second type relates to *Risk-sharing* (RS), in which the cost of failure is shared between the NHS and the pharmaceutical company with a variable breakdown, depending on the medicine and the pathology (N.B. in case of early failure of treatment, the PaR actually coincides with a *Risk-sharing* model, in economic terms).

With regard to *Financial-based schemes,* only *Cost-Sharing* (CS) and *Capping* are among those manageable through the Monitoring Registries. In the case of CS, part of the treatment cost is returned by the pharmaceutical company to the NHS health facilities, regardless of the treatment outcome (i.e. it is applied to each patient initiating treatment), with various methods of financial compensation (credit note, *pay-back,* ecc).

In contrast, in the case of *Capping*, when a patient's treatment reaches a predetermined threshold of dispensed packages, or amount of medicine, the relative cost of each additional package in continuation of treatment is returned by the pharmaceutical company to the NHS healthcare facilities.

Figure 4.2.1 Taxonomy of MEAs related to AIFA Monitoring Registries

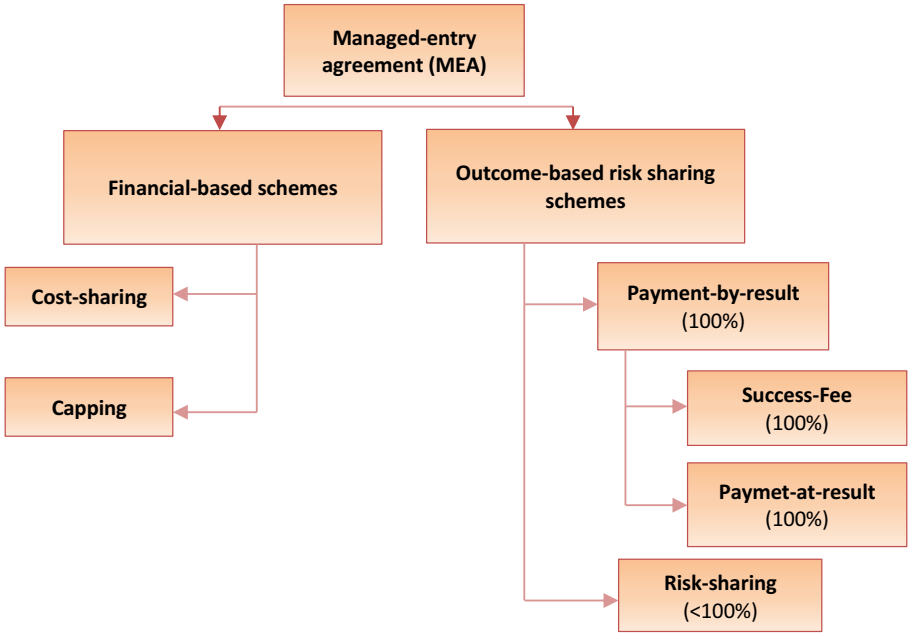


Figure 4.2.2. Percentage distribution of the types of risk sharing agreements (as of 31/12/2023)

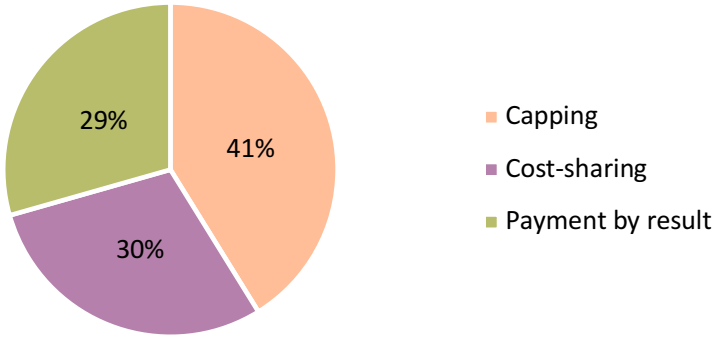


Figure 4.2.2 shows the percentage of each agreement, as of 31/12/2023.

As of that date, 5 agreements based on the clinical outcome of the treatment (29% of total agreements) were active on the AIFA Monitoring Registries platform, expressed in PbRs, while financial agreements accounted for the remaining 71%, related to a total of 12 agreements: 5 *Cost-sharing* type (30% of total agreements) and 7 *Capping* type (41% of total agreements). Table 4.2.1 shows the reimbursements relating to MEAs detected by the Registries platform

for the three-year period 2021-2023, divided by Region. 81% of the reimbursement obtained in 2023 (approximately 60 mln Euro) relates to financial agreements (Figure 4.2.3), of which 67% for *Cost Sharing* agreements and 14% for *Capping* agreements.

The reimbursement rate of the "*outcome-based*" MEAs is 19% and it is entirely attributable to *Payment-by-result* agreements. As in the last two-year period, the remaining (and now entirely marginal) share attributable to *Risk-sharing* agreements still derives from administrative reimbursement procedures related to MEAs that have been closed for years.

It is important to note that *PaR*-type agreements provide for deferred invoicing over time and do not contemplate reimbursements. Therefore, this type of agreement does not contribute to the values shown in Table 4.2.1 and Figures 4.2.3 and 4.2.4.

At ATC level (Figure 4.2.4), almost all of the reimbursement (90%) is attributable to antineoplastic and immunomodulatory medicines (L); musculoskeletal medicines (M) account for more than 6% of the reimbursements generated in 2023, followed by antimicrobials for systemic use (J), which account for just under 3% of the total. The report is closed by a few residual categories in terms of reimbursment, such as medicines for the nervous system and sense organs.

In the overall assessment of the MEAs' effectiveness, it is necessary to take into account the value derived from their management within the AIFA Registries Platform, which represents a unique experience in the European context. In this regard, it is important to consider the economic impact deriving from the appropriate use of medicines guaranteed by the Registries, which allow to supply medicines to selected patients for whom the treatment efficacy was highly demonstrated during the authorisation phase. Nevertheless, in a counterfactual scenario, the unquantifiable costs of dispensing the medicine in patients in whom that medicine is not indicated and/or not reimbursed (inappropriateness), or in whom the expected efficacy would be lower (because they are excluded on the basis of the criteria of the register eligibility form), should also be considered. For similar reasons, it should be emphasised that when assessing the effectiveness of *outcome*-based MEAs, it is not sufficient to consider the value of the reimbursements obtained, as such reimbursements are exclusively linked to treatment failures and do not take into account the benefit for the NHS in terms of appropriateness. Indeed, in an apparently paradoxical way, a relatively high reimbursement value from an *outcome-based* MEA implies a relatively higher clinical-therapeutic inappropriateness compared to the same register that, since it was developed with more selective criteria in terms of eligibility for reimbursement by the NHS, would lead to lower reimbursements and higher clinical-therapeutic appropriateness because it has been.

Table 4.2.1 Reimbursement obtained (€) for online MEAs years 2021-2023*

Region	Reimbursement 2021	Reimbursement 2022	Reimbursement 2023
Abruzzo	1,775,971	1,404,213	2,051,926
Basilicata	1,106,373	697,721	583,567
Calabria	1,872,137	1,425,621	1,349,580
Campania	15,569,723	12,448,257	8,239,891
Emilia Romagna	9,652,272	4,401,804	4,738,350
Friuli Venezia Giulia	2,508,802	926,697	1,792,588
Lazio	10,750,137	6,690,372	3,026,175
Liguria	2,266,187	2,996,866	1,279,920
Lombardy	19,686,427	15,344,503	9,290,508
Marche	2,519,704	1,208,274	993,892
Molise	501,225	150,014	314,989
Piedmont	7,044,898	3,379,371	2,074,020
Province of Bolzano	1,015,011	628,667	276,270
Province of Trento	456,463	477,298	590,143
Puglia	12,288,125	7,094,415	6,182,141
Sardinia	2,319,411	1,385,282	1,929,790
Sicily	7,740,633	7,152,221	5,263,461
Tuscany	12,343,935	8,017,432	3,777,770
Umbria	966,506	1,067,861	796,735
Valle d'Aosta	423,464	295,449	24,905
Veneto	8,647,254	3,708,336	5,361,108
Total	**121,454,657**	**80,900,674**	**59,937,729**

*Reimbursements reported for 2021, 2022 and 2023 are obtained using data updated to May 2022, 2023 and 2024 respectively. Values rounded to the nearest whole number.

Table 4.2.2 Reimbursements obtained by type of MEA (year 2023)

Region	Capping	Cost-sharing	Payment by result	Risk-sharing	Total
Abruzzo	131,137	1,321,027	599,762	-	2,051,926
Basilicata	41,233	452,229	90,105	-	583,567
Calabria	177,340	1,063,603	108,637	-	1,349,580
Campania	1,669,147	5,069,901	1,500,843	-	8,239,891
Emilia Romagna	687,857	2,631,523	1,418,970	-	4,738,350
Friuli Venezia Giulia	42,953	1,682,641	66,993	-	1,792,587
Lazio	232,516	2,457,323	336,336	-	3,026,175
Liguria	95,384	992,541	191,994	-	1,279,919
Lombardy	653,448	6,416,049	2,221,011	-	9,290,508
Marche	36,742	813,909	143,241	-	993,892
Molise	186,439	128,551	0	-	314,990
Piedmont	48,182	1,721,855	303,982	-	2,074,019
Province of Bolzano	119,955	152,765	3,549	-	276,269
Province of Trento	-	572,452	17,691	-	590,143
Puglia	1,117,757	3,825,028	1,239,357	-	6,182,142
Sardinia	393,926	983,822	549,697	2,346	1,929,791
Sicily	892,086	3,737,352	634,023	-	5,263,461
Tuscany	759,982	2,440,406	577,383	-	3,777,771
Umbria	108,341	640,319	48,075	-	796,735
Valle d'Aosta	3,348	21,557	-	-	24,905
Veneto	1,255,694	2,904,985	1,200,429	-	5,361,108
Total	**8,653,467**	**40,029,838**	**11,252,078**	**2,346**	**59,937,729**

*Values rounded to the nearest whole number

Figure 4.2.3 2023 Reimbursements, percentages by type of agreement

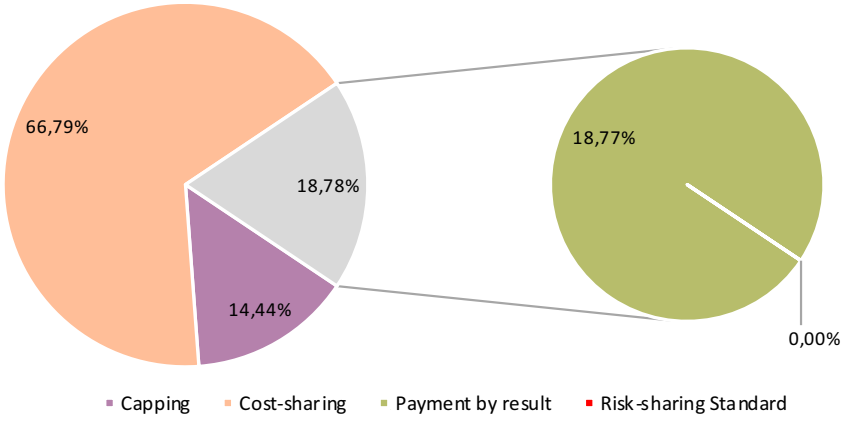
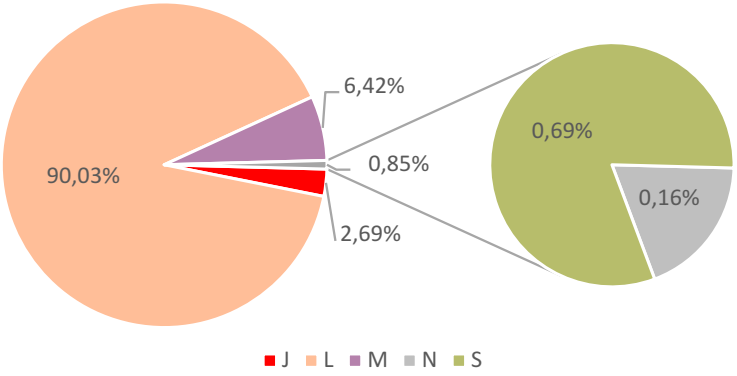


Figure 4.2.4 2023 Reimbursements, percentages for ATC 1st level



Conditional reimbursement agreements managed through information flows for monitoring expenditure and consumption (*Population level*)

Agreements managed in a manner other than the Registries are of a financial nature and can be mainly classified into "expenditure ceilings by product" and "price/volume agreements".

The expenditure ceilings are used in order to promote the appropriate use of medicines. In the case of setting an expenditure ceiling, the Agency, upon proposal of the Scientific and Economic Committee for Medicines, finalises the agreement with the pharmaceutical company, both in relation to the medicine price and the maximum expenditure sustainable by the NHS in the first 12/24 months of marketing. The latter is calculated on the basis of the estimated number of patients expected in Italy according to epidemiological data available for the reimbursed therapeutic indication. According to this logic, if the monitoring of pharmaceutical expenditure, at the end of the period defined by the contract, shows that the expenditure for that product exceeds the agreed ceiling, AIFA notifies the pharmaceutical company of the *payback* to be paid to the Regions.

On the other hand, the price/volume agreements provide for progressive discounts on the price of a medicine on the basis of the volumes reached during the contract period. Those discounts can be obtained through a reduction in the price of the medicine or, if mentioned in the agreement, through a *payback* in favour of the Regions.

Furthermore, in some cases AIFA can negotiate confidential discounts with pharmaceutical companies, which however do not result into a *payback* in favour of the Regions but into a reduction in the price in favour of the NHS healthcare facilities, directly on the invoice. It should be noted that the aforementioned confidentiality is limited to the extent of the discounts and not to the presence or absence of this negotiation agreement.

Table 4.2.3 shows the legal measures that gave rise to reimbursements by companies for the application of expenditure ceilings and price/volume agreements in 2023. The medicines involved were 36 (23 payback) (Tables 4.2.3). In total, pharmaceutical companies paid 157.7 million euros. In particular, 134.1 million euros were paid for the application of the expenditure ceilings and the remaining 23.6 million for the application of price/volume agreements. Considering the reimbursement class, € 103.4 million was paid for class A products and € 54.3 million for class H products (Table 4.2.4).

Table 4.2.3 List of medicines subject to the payback mechanism for the application of expenditure ceilings and price/volume agreements

Medicine	Class	Total €	Italian Official Journal	Type of agreement
Libtayo	H	5.9	GU Serie Generale n.31 of the 07 -02 -2023	Expenditure ceiling
Samsca	H	0.9	GU Serie Generale n.32 of the 08 -02 -2023	Expenditure ceiling
Xtandi	H	8.9	GU Serie Generale n.32 of the 08 -02 -2023	Expenditure ceiling
Orkambi	A	1.3	GU Serie Generale n.60 of the 11-03-2023	Expenditure ceiling
Zytiga	H	4.3	GU Serie Generale n.60 of the 11-03-2023	Expenditure ceiling
Aimovig	A	2.1	GU Serie Generale n.74 of the 28-03-2023	Expenditure ceiling
Emgality	A	0.3	GU Serie Generale n.74 of the 28-03-2023	Expenditure ceiling
Reblozyl	A	6.1	GU Serie Generale n.107 of the 09-05-2023	Price/volume
Brineura	H	3.4	GU Serie Generale n.228 of the 29-09-2023	Expenditure ceiling
Xadago	A	6.3	GU Serie Generale n.228 of the 29-09-2023	Price/volume
Fetcroja	H	11.5	GU Serie Generale n.255 of the 31-10-2023	Expenditure ceiling
Ocaliva	H	6.4	GU Serie Generale n.271 of the 20-11-2023	Expenditure ceiling
Accuretic and Zoton	A	0.1	GU Serie Generale n.271 of the 20-11-2023	Price/volume
Cystadrops	A	0.0	GU Serie Generale n.271 of the 20-11-2023	Expenditure ceiling
Micardis and Micardis Plus	A	1.5	GU Serie Generale n.271 of the 20-11-2023	Price/volume
Cipralex, Entact, Elopram and Seropram	A	3.3	GU Serie Generale n.275 of the 24-11-2023	Price/volume
Zavicefta	H	2.3	GU Serie Generale n.275 of the 24-11-2023	Expenditure ceiling
Oralair	A	0.0	GU Serie Generale n.275 of the 24-11-2023	Expenditure ceiling
Cluviat	A	0.3	GU Serie Generale n.275 of the 24-11-2023	Expenditure ceiling
Kaftrio, Kalydeco, Orkambi and Symkevi	A	75.8	GU Serie Generale n.280 of the 30-11-2023	Expenditure ceiling
Sinvacor, Hizaar, Forzaar, Sinertec, Enapren, Fosamax Lortaan, Vasoretic	A	6.1	GU Serie Generale n.291 of the 14-12-2023	Price/volume
Xtandi	H	10.9	GU Serie Generale n.291 of the 14-12-2023	Expenditure ceiling

Table 4.2.4 Amounts paid by companies to the Regions in 2023 for class A and H products

Region	Class A (EUR million)	Class H (EUR million)	Total (EUR million)
Piedmont	6.82	3.77	10.59
Valle d'Aosta	0.12	0.06	0.19
Lombardy	18.20	6.28	24.48
Province of Bolzano	1.06	0.35	1.41
Province of Trento	0.92	0.43	1.35
Veneto	7.46	1.31	8.77
Friuli Venezia Giulia	2.20	1.70	3.90
Liguria	3.22	4.57	7.79
Emilia Romagna	7.10	4.18	11.28
Tuscany	6.33	1.12	7.44
Umbria	1.45	1.73	3.17
Marche	2.89	6.42	9.32
Lazio	10.11	1.37	11.48
Abruzzo	2.71	0.20	2.91
Molise	0.46	5.42	5.89
Campania	8.01	3.96	11.97
Puglia	7.54	0.49	8.03
Basilicata	1.51	1.91	3.42
Calabria	3.47	4.11	7.58
Sicily	9.47	1.31	10.78
Sardinia	2.31	3.65	5.96
Italy	**103.36**	**54.33**	**157.70**

Section 5

New therapeutic entities and orphan medicines

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5.1 New therapeutic entities

Comparison between new therapeutic entities authorised by EMA and those negotiated by AIFA

This section presents a comparison between the number of new medicines authorised under the centralised procedure of the European Medicines Agency (EMA) and those for which the pricing and reimbursement procedure at national level has been concluded. The new medicines authorised by EMA have been identified through the list published on the European Agency's [1] website and the Union Register of medicinal products [2] and excluding generics, biosimilars and vaccines (ATC J07). Medicines authorised by EMA from 2018 up to 2023 were included.

For the identification of medicines that have concluded the pricing and reimbursement procedure in Italy, the first date of approval by the AIFA Board of Directors is considered, and if not available, the date of transmission to the Official Journal. Only medicines of reimbursability class A and H are taken into consideration.

The "Pricing and Reimbursement Negotiation system", known as NPR, was used to obtain this information.

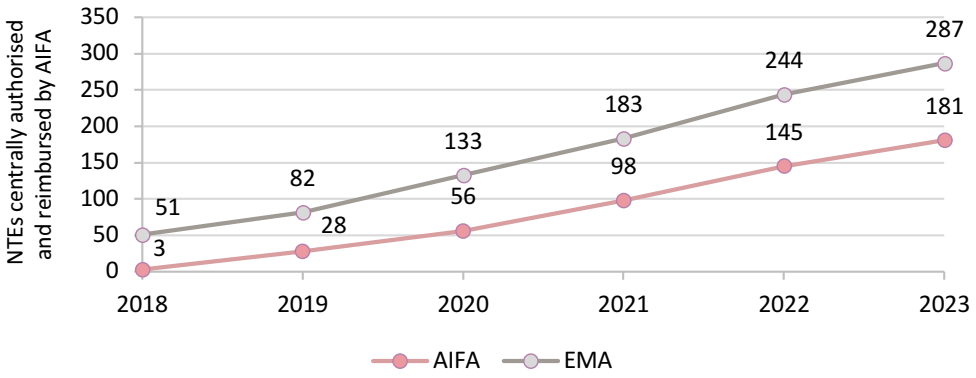
Figure 5.1.1 shows that the availability rate over the period 2018-2023 is 63.1%, well above the European average of 43% (EFPIA 2024)[3]. The highest availability rate was recorded for EMA-authorised medicines in 2020 (94.1%), while for the years 2022-2023 the availability rate is affected by the difference between EMA authorisation and the closing of the pricing and reimbursement process. Indeed, without considering the years 2022-2023, the average availability rate rises to 85.4%.

[1] https://www.ema.europa.eu/en/medicines/download-medicine-data

[2] https://ec.europa.eu/health/documents/community-register/html/reg_hum_act.htm?sort=a

[3] EFPIA Patients W.A.I.T. Indicator 2023 Survey https://efpia.eu/media/vtapbere/efpia-patient-wait-indicator-2024.pdf

Figure 5.1.1 Trend over time of new therapeutic entities authorised and approved by EMA and AIFA from 2018 to 2023 (Figure and Table)



Year of EMA Authorisation	EMA (a)	AIFA* (b)	Availability rate % (b/a)	AIFA cumulative
2018	51	47	92.2	3
2019	31	24	77.4	28
2020	51	48	94.1	56
2021	50	39	78.0	98
2022	61	23	37.7	145
2023	43	0	0.0	181
Total	**287**	**181**	**63.1**	

* medicines reimbursed by AIFA in the period 2018-2023 by year of authorisation
**cumulative number of medicines reimbursed by AIFA

Analysis of new therapeutic entities in the period 2014-2023

An analysis of new therapeutic entities for the period 2014-2023 is presented in this section in order to monitor their impact on the NHS pharmaceutical expenditure, the turnover trend and the average cost per therapy day over time. The new therapeutic entities were selected from class A and H medicines marketed in the period 2014-2023, whose movements were tracked in the OsMed flow and the Italian Medicines Traceability system. The definition of the list of new therapeutic entities provided for the following steps (Table 5.1.1):

1) **Selection of molecules with at least one movement:** only molecules moving at least one package in institutional flows (OsMed Flow or Medicines Traceability database) were considered in each year from 2014 to 2023.
2) **Selection of molecules with a single speciality:** For each year, molecules with only one specialty (6-digit marketing authorisation) were considered. Such molecules are not considered also in the following years, even if only one specialty should remain on the market.

3) **Selection of molecules with patent coverage:** patent-expired molecules were excluded from the year in which the patent expires and the following years in which they are moved. As a *proxy* for patent expiry, the inclusion into the transparency list was used. For this purpose, the transparency lists published monthly by AIFA over the period 2008 to 2023 were used.
4) **Selection of molecules with time from the first authorisation ≤ 15 years:** in order to exclude molecules with time from the first authorisation above 15 years, information on the authorisation date contained in the list of authorised medicines available on the European Medicines Agency (EMA) website was used. For medicines not included in the EMA list, information on the year of first commercialisation was collected both through data flows (OsMed and Traceability) and from the Farmadati database.
5) **Exclusion of associations of known active ingredients:** associations of known active ingredients have been eliminated.
6) **Selection of class A and H molecules:** only molecules with a prevalence class in each year A and H were selected.
7) **Exclusion of Vaccines (ATC J07)**

In conclusion, according to the criteria described above, the molecules analysed relating to new therapeutic entities followed from 2014 to 2023 in Italy are 469. (Table 5.1.1).

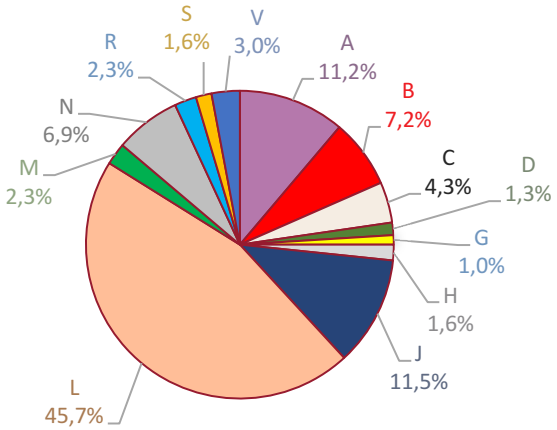
Table 5.1.1 shows the number of new therapeutic entities for each year, both incident in the year and prevalent, as the respective movement over time is followed. The percentage of new therapeutic entities that have been granted the innovative status or have been designated and authorised as orphan medicines is also reported. It is observed that on average there are 29 new therapeutic entities each year, with a higher peak in 2017, 2018, 2021, 2022 and 2023 with 33, 33, 41 and 37 new medicines, respectively. The percentage of orphan medicines is increased over time from 13% in 2014 to 31% in 2023. Innovative medicines represent 16% of the new therapeutic entities marketed in 2023. The new therapeutic entities are mainly classified in class H, 68% in 2023.

Table 5.1.1 New therapeutic entities marketed in 2014-2023

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
No. new therapeutic entities (Incident and prevalent)	**203**	**212**	**223**	**232**	**243**	**244**	**246**	**269**	**293**	**304**
No. new therapeutic entities (incident)	27	25	23	33	33	19	21	33	41	37
No. new therapeutic entities (exited: loss of requirements in the new year)	15	16	12	24	22	18	19	10	17	26
Of which orphans (%)	26 (13)	30 (14)	38 (17)	49 (21)	55 (23)	61 (25)	64 (26)	74 (28)	88 (30)	95 (31)
Of which innovative (%)	9 (4)	17 (8)	19 (9)	20 (9)	37 (15)	35 (14)	40 (16)	45 (17)	50 (17)	50 (16)
Of which Class A (%)	81 (40)	87 (41)	89 (40)	93 (40)	93 (38)	88 (36)	91 (37)	94 (35)	96 (33)	97 (32)
Of which class H (%)	122 (60)	125 (59)	134 (60)	139 (60)	150 (62)	156 (64)	155 (63)	175 (65)	197 (67)	207 (68)

Figure 5.1.2 represents the subdivision of medicines into incident and prevalent analysis for ATC 1st level. The largest share of medicines in 2023 is confirmed to be attributable to the category 'L: antineoplastics and immunomodulators', which accounts for 45.7% of these medicines, in second place is the category 'J: anti-infectives for systemic use' with 11.5%, and in third place is the category 'A: gastrointestinal system and with 11.2%. In a lower share there are the categories 'B: blood and haemopoietic system', 'C: cardiovascular system' and 'N: central nervous system', which will be seen in the following tables as categories of increasing economic importance.

Figure 5.1.2 New incident and prevalent therapeutic entities (No. = 304) for ATC 1st level (year 2023)



Expenditure of new incident and prevalent therapeutic entities amounted to €5,160 million in 2014 rising to €9,625 million in 2023 (Table 5.1.2). On average, expenditure on medicines dispensed under approved care regime from 2014 to 2023 accounts for a minority share (5% on average) of the total expenditure for new therapeutic entities, while medicines purchased by public health facilities constitute the predominant share (95%) Over the period observed, 36% of the expenditure for incident and prevalent new therapeutic entities is accounted for by class A medicines while 64% by class H medicines. From 2014 to 2023, the expenditure of new therapeutic entities increases corresponding to the increase in new entries that are not balanced by medicines that lose their new therapeutic entity status, as defined above. Thus, the market of new therapeutic entities is growing steadily, with an average annual increase of 6.4% (the CAGR value of expenditure from 2014 to 2023) (Table 5.1.4). The impact of expenditure for new therapeutic entities in total NHS expenditure (A and H) has increased over the years, from 26% in 2014 to 39% in 2023, but as can be seen in Figure 5.1.3, it accounts for more than half in the direct purchasing channel. The impact increased especially in the year 2015, in the years 2018-2019 ad in the years 2021-2022. Although the number of orphan medicines is higher than the number of innovative medicines, the impact of the latter on the total expenditure for new therapeutic entities is higher than that of orphan medicines. On average, each year the expenditure incurred by the NHS for new therapeutic entities marketing for the first time in the year (incidents) is EUR 190.6 million, with the highest values being recorded in 2015 (EUR 514.2 million) and 2017 (EUR 435.5 million) (Table 5.1.2).

Table 5.1.2 NHS Expenditure (in millions) for new therapeutic entities in the period 2014-2023

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
New therapeutic entities (Incident and prevalent) (€)	**5,160.2**	**6,634.5**	**6,488.5**	**6,061.9**	**6,674.0**	**7,916.8**	**7,707.9**	**8,182.8**	**8,798.2**	**9,625.4**
Of which incident (€)	62.2	514.2	178.0	435.5	156.0	51.7	49.2	124.0	151.2	184.3
Of which approved care regime class A	472.5	329.3	328.3	395.5	397.9	306.4	306.1	284.4	254.9	239.4
Of which direct purchases class A	1290.5	2615.3	2496.7	1744.9	1971.5	2643.1	2233.6	2267.7	2710.8	3036.2
Total class A medicines (€)	1763.0	2944.6	2825.0	2140.4	2369.3	2949.5	2539.8	2552.1	2965.7	3275.7
Of which approved care regime class H (€)	0.01	0.024	0.11	0.195	0.15	0.25	0.95	0.01	0.01	0.01
Of which direct purchases class H (€)	3,397.1	3,689.8	3,663.4	3,921.4	4,304.5	4,967.0	5,167.2	5,630.7	5,832.4	6,349.7
Total Class H (€)	3,397.2	3,689.8	3,663.5	3,921.6	4,304.7	4,967.3	5,168.2	5,630.7	5,832.4	6,349.7
of which orphans (%)	9.0	8.8	12.0	16.0	156.0	19.9	23.8	26.1	28.1	28.6
of which innovative (%)	3.26	23.00	24.01	16.992	397.9	34.51	30.09	30.65	33.50	33.94
% on NHS total Expenditure	**25.9**	**30.1**	**29.6**	**28.1**	1971.5	**35.1**	**34.6**	**36.3**	**37.1**	**38.6**

Among the incident NTEs in 2023, the highest-spending molecules are 50% represented by the antiviral active ingredient remdesivir, approved for the treatment of COVID-19 disease caused by the SARS-CoV-2 virus, reclassified from class C-NN to class H in July 2023. It is followed by the active ingredient trastuzumab deruxtecan for the treatment of adult patients with HER2-low unresectable or metastatic breast cancer, which accounts for 20% of incident therapy expenditure with EUR 36 million, and the active ingredient bulevirtide for the treatment of chronic hepatitis delta virus (HDV) infection in plasma (or serum) HDV-RNA positive adult patients with compensated liver disease, which with EUR 14.5 million accounts for 8%. Among the first 10 incident molecules in 2023, it can be noted that they are related to ATCs J and L.

ATC L category is not only the one with the highest number of new therapeutic entities, but also the one with the highest expenditure, which is increasing over the period 2014-2023 (from €2,621 million to €5,212 million, increasing by 99%, CAGR 2014-2023 +7,1%) (Table 5.1.3 and Figure 5.1.3). The second and third categories, A and J, have different behaviours over time: the A category increased from 2014 to 2023 (CAGR 2014-2023 of +4.5%), reaching EUR 704 million in 2023; while the J category initially increased and then decreased with a CAGR 2014-2023 of -3.1%, attributable to the trend in expenditure on medicines for the treatment of hepatitis C. The category B (CAGR 2014-2023: +12.3%), category C (CAGR 2014-2023: +11.7%), category R (CAGR 2014-2023: +39.8%) and especially category D (CAGR 2014-2023: +53.6%) are on the increase (Table 5.1.4).

Table 5.1.3 NHS Expenditure (in million) for new therapeutic entities in 2014-2023

ATC	Molecules	No. Packages (consumption in thousands)		NHS Expenditure (EUR mln)	
		No.	%	Values *(decreasing order)*	%
J05AB16	remdesivir*	256	43	91.3	50
L01FD04	trastuzumab deruxtecan	54	9	36.0	20
J05AX28	bulevirtide	3	1	14.5	8
C10BA10	ezetimibe/bempedoic acid	118	20	6.9	4
C10AX15	bempedoic acid	102	17	5.8	3
L01XX75	tebentafusp	1	0	4,5	2
L01FX13	enfortumab vedotin	26	4	4.2	2
L01XX67	tagraxofusp	0.2	0	2.8	2
N07XX18	vutrisiran	0.03	0	1.7	1
H02CA02	osilodrostat	2	0	1.6	1
Total top 10 molecules per expenditure		563	96	169.4	92
Others		26	4	14.9	8
Total		**589**	**100**	**184.3**	**100**

* this medicine was re-classified from class C-NN to class H with AIFA Resolution of 17 July 2023 (Official Gazette, General Series, No 174 of 27-07-2023).

Figure 5.1.3 Annual trend in NHS Expenditure for incident and prevalent new therapeutic entities and NHS expenditure on direct purchases (A and H)

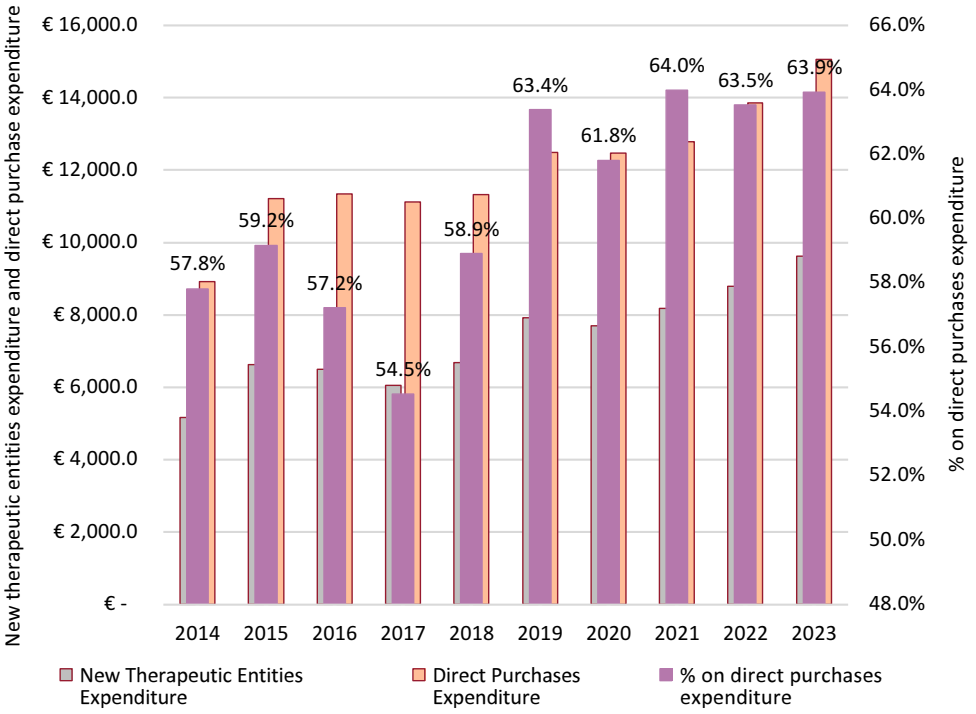
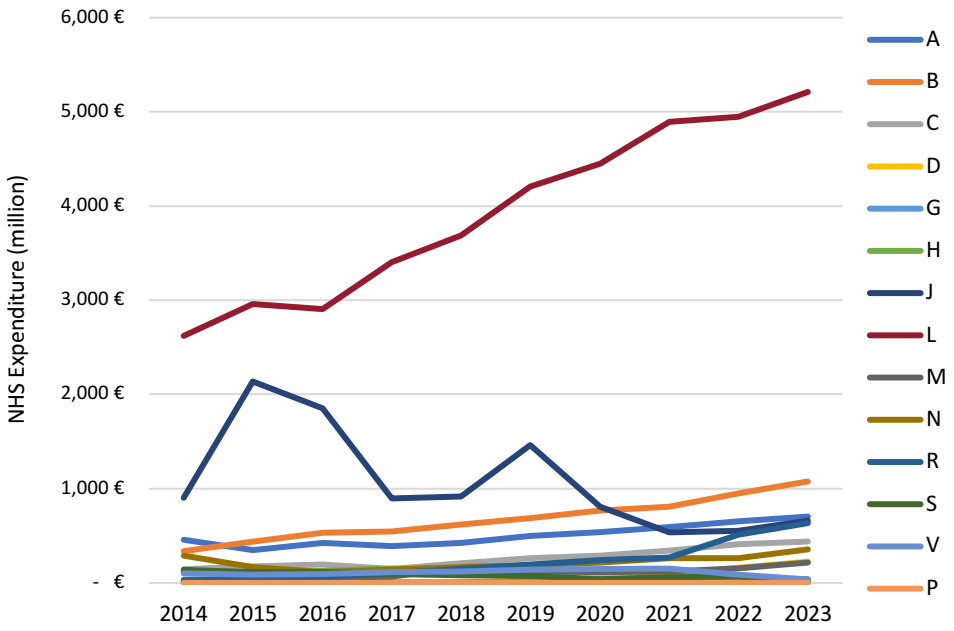


Table 5.1.4 Annual trend in NHS Expenditure for incident and prevalent new therapeutic entities per ATC 1st level (Table and Figure)

ATC 1st level	Expenditure CAGR % from 2014 to 2023	Δ % 2023-2022
A	4.5	52.4
B	12.3	127.6
C	11.7	31.3
D	53.6	67.7
G	-7.0	-14.7
H	-9.0	6.1
J	-3.0	105.4
L	7.1	262.4
M	20.6	62.7
N	2.0	96.6
R	39.8	122.5
S	-18.1	-45.3
V	-9.2	-47.6
P	0.0	0.0
Total	**6.4**	**86.5**



L	Antineoplastic and immunomodulatory medicines	N	Central nervous system	G	Genitourinary system and sexual hormones
A	Gastrointestinal system and metabolism	H	Systemic hormonal preparations, excluding sexual hormones	J	General antimicrobials for systemic use
C	Cardiovascular system	R	Respiratory system	D	Dermatological medicines
B	Blood and haemopoietic organs	V	Various	S	Sense organs
		M	Musculoskeletal system		

Figure 5.1.4 shows the trend of the average cost for new therapeutic entities by DDD: the trend is increasing from 9.09 EUR in 2014 to 9.27 EUR in 2023. It picked in 2015 when it reached 13.70 EUR, during the following two years a decrease was observed while in 2018 and 2019 there was another increase, in the last 4 years a decreasing trend was recorded.

Figure 5.1.4 Annual trend of average cost per DDD of new therapeutic entities over the period 2014-2023

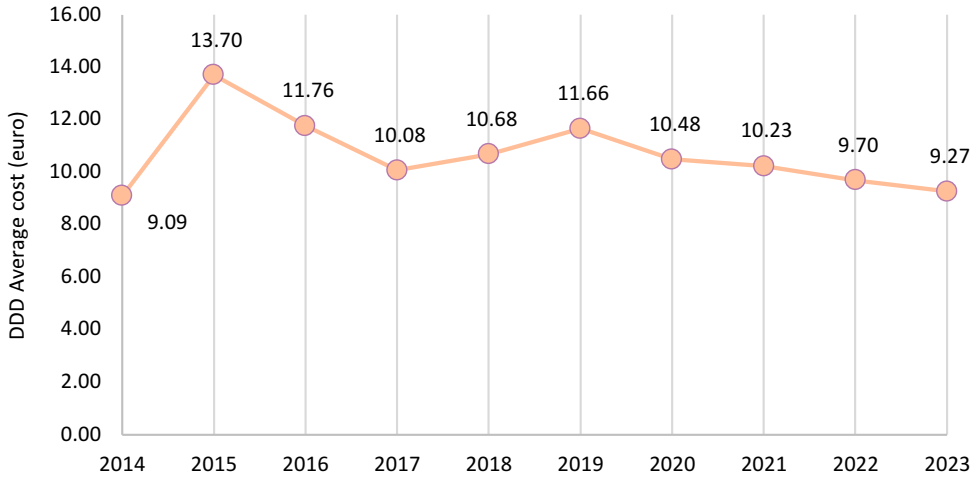


Table 5.1.5 shows the regional distribution of 2023 *per capita* expenditure on medicines concerning new therapeutic entities. At national level, the *per capita* expenditure on new therapeutic entities was EUR 163.1 with a wide regional variability: the Regions with the highest values were Liguria (EUR 193.0), Friuli Venezia Giulia (EUR 188.6) and Marche (EUR 183.6), while the lowest values were recorded in the Province of Trento with EUR 125.3 and in Valle d'Aosta with EUR 134.8. The regional expenditure trend from 2014 to 2023 is marked by an average annual increase in all Regions, which at national level was 6.43%. Major variations were reported in Valle d'Aosta (+8,4%), in Friuli Venezia Giulia (+7,8%) and in Emilia Romagna (+7,6%). At national level, the average DDD cost was EUR 9.3 in the year 2023, but it fluctuates between the minimum value of EUR 7.6 in the Province of Trento and a maximum of EUR 11.4 in the Province of Bolzano. The latter has one of the lowest *per capita* expenditures (EUR 155.2); this may be due to a lower consumption of DDD in this Region, but related to medicines with a higher average cost.

Table 5.1.5 Regional variability in expenditure and average DDD cost of new therapeutic entities in the year 2023 and comparison 2014-2023

Region	Expenditure 2023 *per capita*	Δ% compared to the Italian Average	CAGR % 2014-2023	Average cost DDD 2023	Δ% compared to the Italian Average	CAGR % 2014-2023
Piedmont	170.2	4.4	6.9	9.2	-1.1	0.9
Valle d'Aosta	134.8	-17.4	8.4	8.4	-9.7	0.4
Lombardy	151.6	-7.1	6.7	9.3	0.6	0.0
Province of Bolzano	155.2	-4.9	7.6	11.4	22.6	-1.8
Province of Trento	125.3	-23.2	7.5	7.6	-17.6	-1.7
Veneto	150.3	-7.9	6.9	8.6	-7.0	-1.3
Friuli VG	188.6	15.6	7.8	9.4	1.9	0.3
Liguria	193.0	18.3	7.2	9.7	5.0	1.4
Emilia R.	173.4	6.3	7.7	9.9	7.0	-0.3
Tuscany	175.9	7.8	5.8	9.5	2.8	-0.3
Umbria	181.9	11.5	6.6	9.3	0.2	1.3
Marche	183.6	12.6	6.5	10.0	8.3	-0.1
Lazio	153.4	-6.0	5.5	9.0	-2.9	0.3
Abruzzo	182.7	12.0	6.1	9.4	1.6	0.5
Molise	161.6	-0.9	6.3	9.2	-0.5	0.2
Campania	173.5	6.4	6.9	9.7	4.3	0.7
Apulia	168.7	3.4	5.3	8.9	-4.4	-0.6
Basilicata	165.5	1.5	6.1	9.1	-1.6	0.7
Calabria	153.3	-6.0	5.5	8.9	-3.4	1.0
Sicily	147.7	-9.4	6.4	9.2	-0.7	1.3
Sardinia	165.1	1.2	4.1	8.5	-8.0	-0.6
Italy	**163.1**		**6.4**	**9.3**		**0.2**
North	161.2	-1.2	7.1	9.3	0.3	0.0
Centre	166.3	2.0	5.8	9.3	0.6	0.2
South	164.0	0.5	6.0	9.2	-0.8	0.5

A detailed analysis on the expenditure trend and average cost of new therapeutic entities was carried out on the basis of time passed since the first marketing. For this purpose, only molecules with first commercialisation in 2014 were selected: 2013 was used as a *wash-out* window to allow the definition of the first entries in 2014 and to study their evolution from that year onwards (No. molecules: 125). Of these molecules, only specialities with the criterion of 'new therapeutic entity for a period of at least six years' were selected and followed, in order to have the same number of molecules in each year of marketing. Figure 5.1.5 shows the average turnover from the first year of marketing up to the 6th year. It may be observed that all 125 molecules start an upward trend from the moment they enter the market, rising from an average of 1.5 million in the first year of marketing to 3.7 million in the last year analysed. However, the *box plots* show a wide variability of turnover across marketing years which can be seen from the length of the whiskers; in particular, the upper whisker is longer and therefore the most dispersed values are the highest (Figure 5.1.7). It should also be noted that the median starts to fall after the sixth year, showing that the greatest expansion is during the first five years, going from a median of EUR 18 million in the 4th year to EUR 19 million in the 5th year, and falling back to EUR 17 million in the 6th year.

Figure 5.1.6 shows the percentage ratio of turnover in each year compared to turnover in the first year. It can be seen that in the third year of marketing the turnover is doubled compared to that of the first year until it reaches a plateau in the sixth year.

Figure 5.1.5 Average turnover by time since first placing on the market (molecules with at least 5 observation points; N=125)

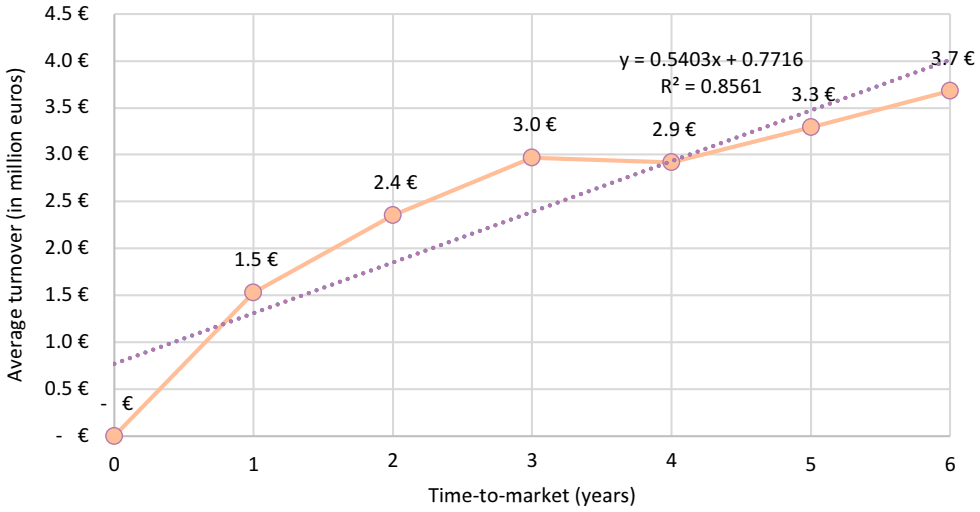


Figure 5.1.6 Percentage ratio between total expenditure at time T_i compared to expenditure at time of first marketing (T_1) (molecules with at least 6 observation points; N=125)

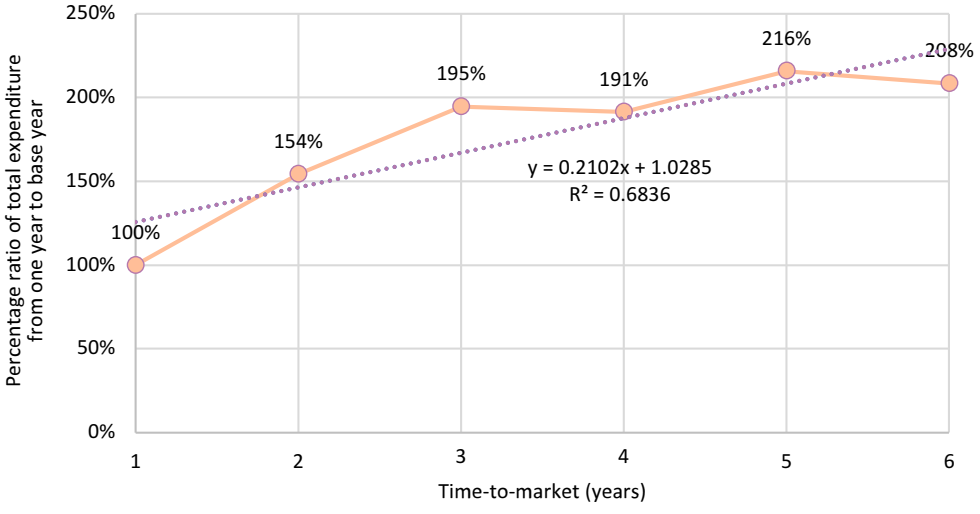


Figure 5.1.7 Variability of NTE sales by year from the first year of marketing (molecules with at least 6 observation points; N=125)

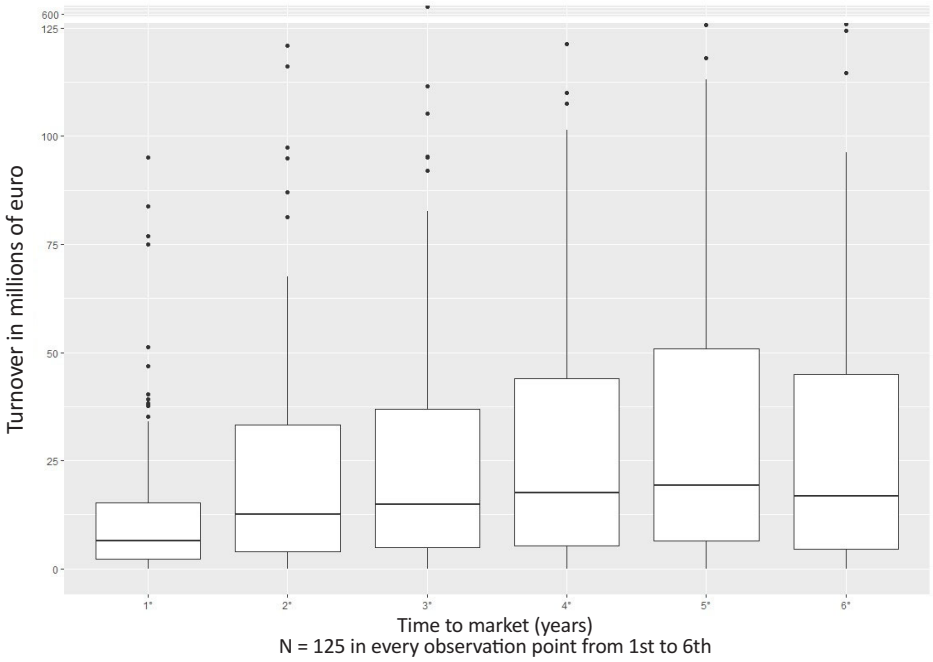
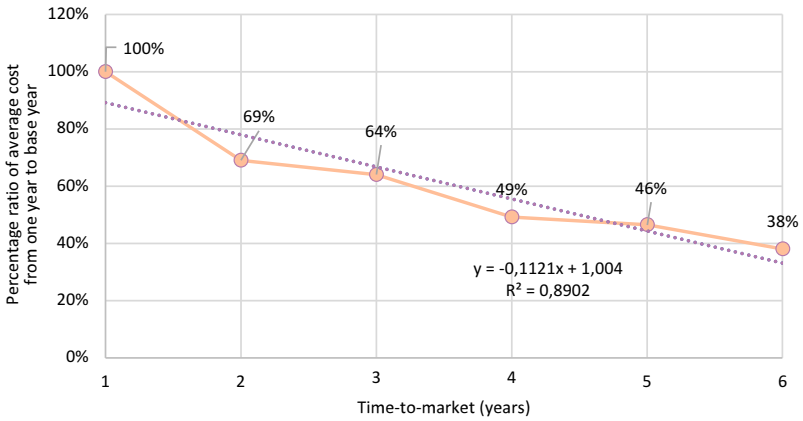


Figure 5.1.8 shows the percentage ratio between the average cost per DDD in each year and the average cost in the first year of marketing. A downward trend can be observed, with a shift from 69% in the second year to 38% in the last year. This trend could be due to the effect of renegotiations, also following the extension of indications and purchasing procedures at regional level.

Figure 5.1.8 Percentage ratio of the average cost per DDD at time T_i compared to the average cost at the time of first placing on the market (T_1) (molecules with at least 6 observation points; N=125)



5.2 Orphan medicines and rare diseases

Orphan medicines: authorisation through EMA centralised procedure and access in Italy

Orphan medicines are medicinal products used for the diagnosis, prevention and treatment of rare diseases. In Europe a disease is considered to be rare when it affects no more than 5 people per 10,000 inhabitants. Generally, even if orphan medicines meet the needs of treatment of a disease, such medicines may require investments in research and development that may not be profitable for the manufacturer because they are intended for the treatment of a few patients. For this reason, orphan medicines have been excluded from the payback mechanism initiated in application of the governing discipline for hospital pharmaceutical expenditure (Article 15, paragraph 8, letters i and i-bis, of Law 135/2012, as amended by Article 1, paragraph 228, of Law 147/2013 - 2014 Stability Law - and most recently amended by Article 1, paragraph 578, of Law 145/2018 - Budget Law 2019).

Starting from 2019, Art. 1, paragraphs 575-584, of Law 145/2018 (Stability Law 2019) modified the provisions of the Stability Law of 2014 by establishing that the only medicines that will benefit from exclusion from the payback mechanism are the following: orphan medicines authorised by means of the EMA centralised procedure, excluding the so-called "*Orphan Like*" medicines, medicines included in the Orphanet register and all medicines that were authorised as orphan by the EMA but that have exhausted their period of market exclusivity.

It should be noted that the EMA provides for the marketing authorisation of orphan medicines, but it is up to the individual country to define the reimbursement class. It therefore appears clear that there is a time gap between the marketing authorisation by the EMA and the definition of price and reimbursement class by AIFA in Italy. However, this is not a limitation for citizens to access their treatment because, in Italy, a patient suffering from a rare disease can have access to the medicine through various legislative instruments.

The centralised authorisation procedure represents the main access rule. Alternatively, due to the lack of marketing authorisation for an orphan medicine indicated for a rare disease, a patient can access the medicine through one of the following procedures:

- Law 648 of 1996 allows the use of a medicine on a national basis;
- Law 326 of 2003, art. 48 (AIFA fund);
- Ministerial Decree 7 September 2017 (so-called "Compassionate use");
- Law 94 of 1998 (former Di Bella Law) which, differently from Law 648/96, regulates the prescription of the medicine for the single patient, on a nominal basis;
- non-repetitive use of advanced therapies.

In 2023, the EMA granted authorisation for a total of 12 new orphan medicines. The main therapeutic areas of medicines authorised under the centralised procedure by the EMA are:

- Oncology: glofitamab (Columvi), dabarfenib (Finlee), talquetamab (Talvey), epcoritamab (Tepkinly), ivosidenib (Tibsovo)
- Dermatology: sirolimus (Hyftor)
- Endocrinology: palopegteriparatide (Yorvipath)

- Haematology: etranacogene dezaparvovec (Hemgenix)
- Infectious diseases: rezafungin (Rezzayo)
- Metabolism: pegzilarginase (Loargys)
- Neurologia: Vamorolone (Agamree), ganaxolone (Ztalmy)

Out of the 12 drugs authorised by the EMA, 6 began the process of price negotiation and reimbursement, 1 has been on the market since March 2024 and for 2 medicines the procedure is suspended. However, 4 of these medicines are available because they are in class C-NN. The remaining 3 medicines did not apply for price and reimbursement.

There were 15 orphan drugs that applied for pricing and reimbursement in 2023, 2 of which are already on the market, 12 are in the negotiation process and the procedure was suspended for 1 medicine.

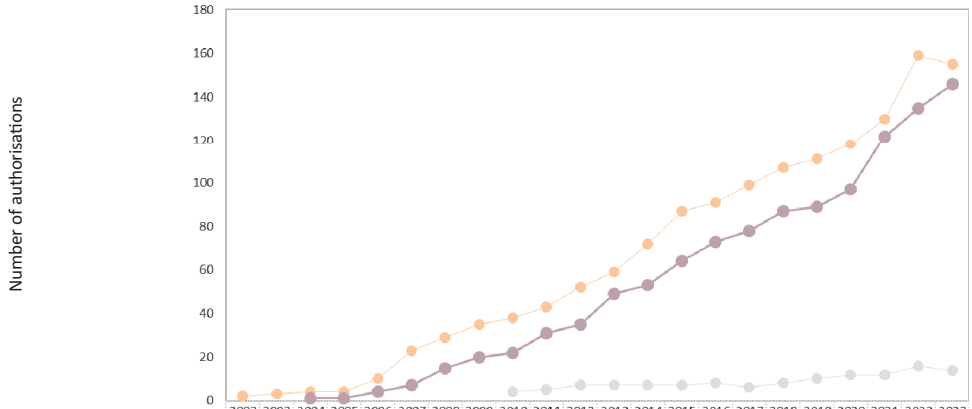
As of 31 December 2023, out of a total of 155 orphan medicines authorised by the EMA (Figure 5.2.1 and Figure 5.2.2), 146 were available in Italy of which:

- 25 (17.1%) in class A;
- 85 (58.2%) in class H;
- 2 (1.4%) in class A-H;
- 14 (9.6%) in class C;
- 1 (0.7%) in class C-H;
- 19 (13.0%) in class C-nn;

The only medicine authorised by the EMA and negotiated and marketed as of 2024 is glofitamab (Columvi), indicated as monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy. Among the medicines that started the P&R process in 2023, and that are currently on the market in addition to glofitamab (Columvi), there is irinotecan (Onivyde Pegylated Liposomal), indicated for the treatment of metastatic adenocarcinoma of the pancreas, in combination with 5-fluorouracil (5-FU) and leucovorin (LV), in adult patients progressing after gemcitabine-based therapy, on the market since December 2023.

45.9% of the 146 medicines included in AIFA's orphan list is subject to a Monitoring Register. Only 4.8% of the orphan medicines currently have a *Managed Entry Agreement* (MEA), which can be either a financial agreement or an *outcome*-based agreement. Moreover, more than 10% of medicines also obtained the innovativeness requirement (5 innovative oncological medicines and 15 innovative non-oncological medicines).

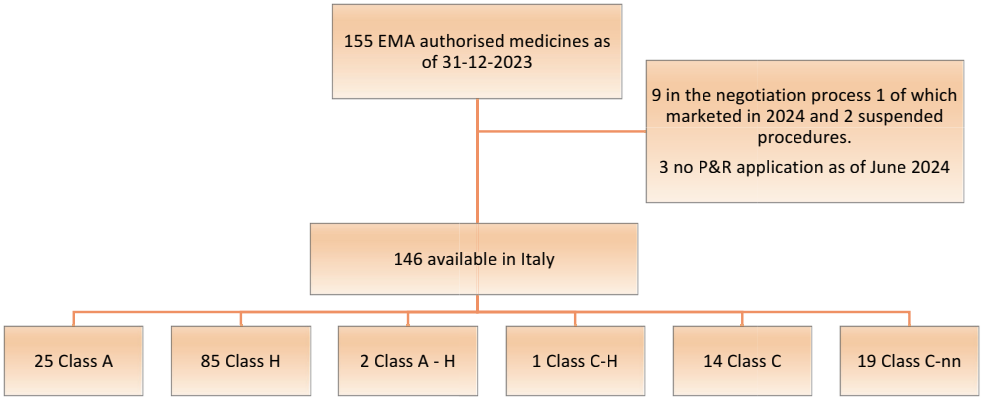
Figure 5.2.1 Comparison between medicines authorised with EMA centralised procedure and available in Italy (cumulative data 2002-2023)



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
EMA	2	3	4	4	10	23	29	35	38	43	52	59	72	87	91	99	107	111	118	130	159	155
AIFA			1	1	4	7	15	20	22	31	35	49	53	64	73	78	87	89	97	122	135	146
Availability rate (AIFA/EMA*100)	0	0	25	25	40	30	52	57	58	72	67	83	74	74	80	79	81	80	82	94	84	94
AIFA classe C									4	5	7	7	7	7	8	6	8	10	12	12	16	14

As can be seen in Figure 5.2.1, in 2023 there is a reduction of orphan medicines in the EMA list compared to 2022. It should be remembered that the list of medicines with orphan status, both EMA and AIFA, is dynamic and its composition varies over time, especially considering that these medicines have a 10-year market exclusivity. Moreover, such medicines may be taken off the list because they have been withdrawn from the market at the request of the company or for safety reasons.

Figure 5.2.2 Comparison between number of orphan medicines authorised with EMA centralised procedure and AIFA as of 31 December 2023



Expenditure and consumption of orphan medicines

The expenditure for orphan medicines, including the purchase by public health structures and the provision under the approved care regime, was approximately 2.23 billion euros in 2023 (+12.5% compared to 2022 and +45.4 compared to 2021), corresponding to 8.5% of the pharmaceutical expenditure borne by the NHS. As for consumption, 14.9 million doses of orphan medicines were dispensed (+30.7 million compared to the previous year), corresponding to 0.052% of the total consumption of medicines. In 2023, the incidence of class C orphan medicines on total orphan medicines consumption was 0.3%, showing a considerable reduction compared to 2022 and 2021, when the incidence was 1.9% and 2.2% respectively (Table 5.2.1).

Table 5.2.1 Expenditure and consumption trend (agreed and direct purchases) for orphan medicines, years 2013-2023 in reimbursement class A-SSN, H-SSN, C, C-NN

	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Expenditure for orphan medicines* (million)	608.9	716.2	822.2	947.6	1,022.7	1,306.9	1,554.9	1,402.7	1,535.1	1,983.17	2,231.54
Incidence % of orphan medicines on total pharmaceutical expenditure*	6.4	7.1	6.7	4.2	4.5	5.8	6.8	6.1	6.4	7.9	8.5
Incidence % orphan medicines direct purchase expenditure vs orphan medicines total expenditure	100.0	100.0	100.0	99.7	99.6	99.7	99.9	100.0	100.0	99.9	100.0
Orphan medicines* consumption (millions of DDD)	5.6	6.1	6.7	7.0	7.2	8.8	10.1	8.1	8.4	11.4	14.9
Incidence % of orphan medicines on total consumption*	0.002	0.002	0.003	0.026	0.026	0.031	0.035	0.029	0.030	0.040	0.052
Incidence % of C class orphan medicines on total consumption of orphan medicines	1.2	0.1	0.1	0.8	0.6	0.9	1.3	1.39	2.2	1.9	0.3

*including expenditure and consumption of all medicines dispensed under approved care regime and purchased from public health facilities

Analysing consumption at the regional level, a greater use of orphan medicines is always observed in the Northern Regions, and therefore also a greater absolute expenditure. The Regions with the highest per capita expenditure are Umbria and Emilia Romagna with an expenditure of EUR 46.55 and EUR 45.26 respectively, which are higher than the national average of EUR 37.92. The Regions with the lowest expenditure are again Valle d'Aosta and Molise with EUR 18.35 and EUR 29.71 respectively. On the other hand, the Regions with the largest variations in per capita expenditure are Valle d'Aosta (+30.2%), Liguria (+22.0%), Umbria (+20.4%), Piedmont (+19.0%) and Veneto (+16.6%). The Region with the greatest variation in consumption is Valle d'Aosta (+65.5%), while the Region with the least variation is Marche (+18.5%) compared to the national average of +30.3% (Table 5.2.2).

Table 5.2.2 Consumption and expenditure (agreed and direct purchases) for orphan medicines by Region in 2023 (A-SSN, H-SSN, C, C-NN)

Region	Expenditure *(million)*	DDD *(thousand)*	Inc.% expenditure*	% direct purchases	Expenditure *per capita*	Δ % 23-22	DDD 1000 inhab. per day	Δ % 23-22
Piedmont	161.9	1,010.6	7.3	100.0	36.62	19.0	0.63	34.6
Valle d'Aosta	2.3	17.6	0.1	100.0	18.35	30.2	0.38	65.5
Lombardy	381.6	2,427.8	17.1	99.9	38.77	13.6	0.68	26.8
Province of Bolzano	19.9	151.9	0.9	100.0	40.37	3.7	0.84	23.2
Province of Trento	16.5	136.9	0.7	100.0	30.98	13.0	0.71	38.1
Veneto	195.2	1,406.2	8.8	100.0	40.09	16.6	0.79	37.8
Friuli VG	54.6	396.4	2.5	100.0	43.47	14.4	0.86	26.8
Liguria	71.6	471.7	3.2	100.0	43.74	22.0	0.79	37.4
Emilia R.	202.4	1,444.0	9.1	100.0	45.26	9.8	0.88	30.8
Tuscany	152.3	1,078.8	6.8	100.0	40.10	14.7	0.78	33.5
Umbria	41.5	285.0	1.9	100.0	46.55	20.4	0.88	43.4
Marche	63.2	451.0	2.8	100.0	41.41	7.6	0.81	18.5
Lazio	190.3	1,283.3	8.5	99.9	33.69	11.5	0.62	34.6
Abruzzo	52.8	366.2	2.4	100.0	40.77	16.5	0.77	28.8
Molise	9.0	58.3	0.4	100.0	29.71	14.6	0.53	19.8
Campania	189.2	1,152.9	8.5	100.0	36.34	12.0	0.61	28.5
Apulia	144.5	957.2	6.5	100.0	37.37	5.8	0.68	23.4
Basilicata	16.7	105.4	0.8	100.0	30.69	3.8	0.53	32.4
Calabria	56.8	348.3	2.5	100.0	31.40	5.6	0.53	24.8
Sicily	155.3	936.8	7.0	100.0	33.32	11.9	0.55	25.4
Sardinia	53.9	381.7	2.4	100.0	32.61	10.6	0.63	36.5
Italy	**2,231.5**	**14,867.9**	**100.0**	**100.0**	**37.92**	**12.8**	**0.69**	**30.3**
North	1,106.1	7,463.1	49.6	100.0	40.00	14.5	0.74	31.4
Centre	447.4	3,098.1	20.1	100.0	37.70	12.7	0.72	32.3
South and Islands	678.1	4,306.7	30.4	100.0	35.07	10.1	0.61	27.0

* calculated on total orphan medicines expenditure nationwide

In 2023, the expenditure for Class C medicines amounted to €14.72 million, decreasing by 4.8% over the previous year (in 2022 it amounted to 15.5 million euro). Lower expenditure is associated with lower consumption, indeed there is a 77.2% reduction in DDD consumed in 2023. Higher consumption, and consequently a higher expenditure, of class C orphan medicines is observed in the Northern Regions. As regards per capita expenditure, Northern Regions have higher values but in line with the Italian average, while Central and Southern Regions have values below the national average (0,3 euro *per capita* in the North, compared to 0.2 euro in the Centre and in the South) (Table 5.2.3).

Table 5.2.3 Consumption and expenditure (approved care regime and direct purchases) for class C orphan medicines by Region in 2023

Region	DDD *(thousand)*	Δ % 23-22	Expenditure *(thousand)*	Δ % 23-22	Expenditure *per capita*	% Incence on consumption^	% Incence on expenditure**
Piedmont	4.1	-80.1	796.0	-18.2	0.2	0.4	0.5
Valle d'Aosta	0.4	-60.4	4.7	-60.0	<0.05	2.2	0.2
Lombardy	7.3	-79.6	2,518.6	-30.8	0.3	0.3	0.7
Province of Bolzano	0.8	-68.5	284.5	-33.7	0.6	0.5	1.4
Province of Trento	0.3	-78.7	3.8	-95.4	<0.05	0.2	0.0
Veneto	4.8	-76.7	2,070.5	7.0	0.4	0.3	1.1
Friuli VG	0.7	-82.3	821.3	13.8	0.7	0.2	1.5
Liguria	1.1	-78.6	240.5	68.5	0.2	0.2	0.3
Emilia R.	6.9	-69.2	839.3	-29.3	0.2	0.5	0.4
Tuscany	3.7	-74.8	554.5	-49.4	0.2	0.3	0.4
Umbria	1.0	-82.7	229.3	-2.6	0.3	0.3	0.6
Marche	1.5	-79.9	550.5	-29.5	0.4	0.3	0.9
Lazio	4.4	-82.1	1,306.5	50.7	0.2	0.3	0.7
Abruzzo	1.8	-78.8	836.3	4.7	0.7	0.5	1.6
Molise	-	-100.0	-	-100.0	-	-	-
Campania	2.8	-75.0	617.9	-5.2	0.1	0.2	0.3
Apulia	1.9	-77.7	390.6	9.7	0.1	0.2	0.3
Basilicata	0.3	-81.7	3.3	-98.7	<0.05	0.3	0.0
Calabria	0.1	-97.9	452.8	23.0	0.3	0.0	0.8
Sicily	3.7	-68.3	1,117.0	422.5	0.2	0.4	0.7
Sardinia	1.5	-57.5	1,086.4	53.2	0.7	0.4	2.0
Italy	**49.0**	**-77.2**	**14,724.2**	**-4.8**	**0.3**	**0.3**	**0.7**
North	26.5	-76.8	7,579.2	-16.9	0.3	0.4	0.7
Centre	10.5	-79.8	2,640.7	-11.3	0.2	0.3	0.6
South and Islands	12.0	-75.7	4,504.3	34.0	0.2	0.3	0.7

* C-NN medicines excluded; ^calculated on total orphan medicines consumption; ** calculated on total orphan medicines expenditure

In 2023, only 8 out of the 14 available Class-C active ingredients have been used, and their expenditure is approximately EUR 14.72 million, the largest part of which is attributable to the active ingredient defibrotide, indicated for the treatment of severe hepatic veno-occlusive disease (VOD) also known as sinusoid obstruction syndrome (SOS) in haematopoietic stem cell transplantation (HSCT), whose expenditure was EUR 5.7 million. The second and third medicines with highest expenditure are Treosulfan (about EUR 3.6 million) and Asphotase alpha (EUR 3.4 million euro). As for consumption, expressed in total DDD, the first active principle is pitolisant which is indicated for narcolepsy (85.1% on total Class C medicines consumption) (Table 5.2.4).

Table 5.2.4 Class C orphan medicines in descending order of expenditure 2023

Class	Active ingredient	Expenditure (€)	%*	Consumption (DDD)*	%**
C	defibrotide	5,726,295	38.9	1,396.7	2.8
C	treosulfan	3,574,473	24.3	1,201.2	2.5
C	asphotase alpha	3,434,112	23.3	1,459.2	3.0
C	amikacin	609,466	4.1	1,624.0	3.3
C	cenegermin	596,224	4.0	462.0	0.9
C	pitolisant	540,842	3.7	41,722.5	85.1
C	X factor	216,678	1.5	20.0	0.0
C	telotristat	26,120	0.2	1,140.0	2.3
	Class C total	**14,724,210**	**100.0**	**1,396.7**	**100.0**

^ excluding C-NN medicines; * calculated on the total expenditure of Class C orphan medicines; ** calculated on the total consumption of Class C orphan medicine

Considering the three-year period 2021-2023 (Table 5.2.5), in which the top ten most expensive molecules were selected for the first two years, the highest spending active ingredient is defibrotide. The expenditure on asfotase alpha and treosulfan increased in 2023 compared to 2022, by 48.9% and 36.7% respectively, while the expenditure on pitolisant decreased over time with a variation of -74.5% compared to 2021. The reduction in expenditure and consumption for class C orphan medicines is also attributable to the reduction in the number of C-labelled orphan medicines.

Table 5.2.5 Expenditure for Class C orphan medicines* 2021- 2023

Classe	Active ingredient	Expenditure (*thousand*)		
		2021	2022	2023
C	amikacin	-		609.5
C	asphotase alpha	-	2,306.3	3,434.1
C	avapratinib	-	275.1	-
C	belantamab mafodotin	554.5	-	-
C	cenegermin	512.1	770.4	596.2
C	chlormetin	140.1	234.1	-
C	defibrotide	8,303.8	6,103.1	5,726.3
C	X factor	-	-	216.7
C	mannitol	438.7	145.9	-
C	onasemnogene abeparvovec	260.0	-	-
C	pitolisant	2,118.1	2,365.1	540.8
C	polatuzumab vedotin	1,806.6	-	-
C	ridisplan	-	42,400.0	-
C	telotristat	35.9	36.8	26.1
C	tobramycin	1,090.8	792.6	-
C	treosulfan	-	2,614.7	3,574.5

* excluding Class C-NN medicines

In 2023, the active ingredients with the highest consumption (Table 5.2.6) are daratumumab, tafamidis and the combination elexacaftor/tezacaftor/ivacaftor, similarly to 2022. Wheres those with the highest expenditure are daratumumab, the combination elexacaftor/tezacaftor/ivacaftor, tafamidis and eculizumab, whose expenditure increased by 16.8%, 37.7% and 84.4% respectively. Whilst the expenditure for eculizumab decreased by 0.9% with a corresponding increase in consumption of 0.9%. There is a significant increase (>100%) for vosoritide, indicated for the treatment of achondroplasia in patients aged 2 years and older whose epiphyses are not closed, for axicabtagene ciloleucel (>100%) and for tafamidis (+94.9%).

Table 5.2.6 Expenditure and consumption for the first 30 orphan medicines (A, H, C, C-NN) in descending order of expenditure: comparison years 2022-2023

Rank	First 30 orphan medicines *(molecules)*	Prevalent Class in 2023	DDD *(thousand)*	Δ % 23-22	Expenditure (million)	Δ % 23-22	% Incidence on consumption	% Incidence on expenditure	% direct purchases
1	daratumumab	H	5,464.8	32.0	456.2	16.8	20.4	36.8	100.0
2	elexacaftor/ tezacaftor/ ivacaftor	A	981.5	37.7	284.0	37.7	12.7	6.6	100.0
3	tafamidis	H	2,012.4	94.9	123.2	84.4	5.5	13.5	100.0
4	eculizumab	H	164.1	0.9	117.5	-0.9	5.3	1.1	100.0
5	nusinersen	H	162.0	-1.0	64.2	-2.5	2.9	1.1	100.0
6	macitentan	A	657.1	-2.6	57.6	-2.6	2.6	4.4	100.0
7	axicabtagene ciloleucel	H	0.2	25.0	56.6	>100	2.5	0.0	100.0
8	albutrepenon-acog alpha	A	55.8	11.5	54.7	3.1	2.5	0.4	99.9
9	patisiran	H	101.7	33.5	52.5	33.5	2.4	0.7	100.0
10	brentuximab vedotin	H	173.6	14.9	50.9	14.9	2.3	1.2	100.0
11	risdiplam	H	112.7	1.8	44.8	5.6	2.0	0.8	100.0
12	carfilzomib	H	357.4	26.1	42.0	12.4	1.9	2.4	100.0
13	niraparib	H	266.5	19.4	41.0	19.4	1.8	1.8	100.0
14	pomalidomide	H	175.2	-30.4	39.2	-35.8	1.8	1.2	100.0
15	luspatercept	A	359.7	55.2	38.8	55.5	1.7	2.4	100.0
16	caplacizumab	H	8.6	-9.6	29.3	-9.5	1.3	0.1	100.0
17	lanadelumab	A	50.8	36.6	28.2	36.5	1.3	0.3	100.0
18	migalastat	A	61.5	21.9	27.5	17.3	1.2	0.4	100.0
19	tisagenlecleucel	H	0.1	-15.4	26.3	-14.0	1.2	0.0	100.0
20	eliglustat	A	39.0	7.7	24.2	7.5	1.1	0.3	100.0
21	brexucabtagene autoleucel	H	0.1	60.0	23.8	70.5	1.1	0.0	100.0
22	obeticolic acid	H	279.4	24.8	22.6	24.5	1.0	1.9	100.0
23	obinutuzumab	H	346.4	26.7	22.6	26.7	1.0	2.3	100.0
24	ataluren	H	14.9	18.9	22.3	13.8	1.0	0.1	100.0
25	isavuconazolo	A	217.5	19.0	21.8	13.1	1.0	1.5	99.9
26	letermovir	A	61.5	11.8	21.8	15.7	1.0	0.4	100.0
27	vosoritide	H	47.6	>100	21.7	>100	1.0	0.3	100.0
28	burosumab	H	149.6	63.6	21.3	23.3	1.0	1.0	100.0
29	eftrenonacog alpha	A	28.3	8.5	18.9	8.2	0.9	0.2	99.5
30	gilteritinib	H	46.3	15.2	18.8	15.3	0.8	0.3	100.0
	Total top 30		**12,396.4**	**33.2**	**1,874.1**	**20.2**	**84.0**	**83.4**	**100.0**
	Other orphan medicines		2,471.5	15.7	357.5	-15.8	16.0	16.6	99.9
	Total orphan medicines		**14,867.9**	**30.0**	**2,231.5**	**12.5**	**100.0**	**100.0**	**100.0**

Among the top 20 active ingredients of class A and H having the greatest variation in expenditure in 2023, the followings showed the greatest increase: stabentafusp, osilodrostat, vosoritide, satralizumab, tafasitamab, pegcetacoplan, glasdegib and fenfluramine. However, the active ingredients with the highest expenditure values were tafamidis (123, 2 million) with a variation in expenditure of +84.4%, axicabtagene ciloleucel (56.6 million) with a variation in expenditure greater than 100%, brexucabtagene autoleucel with an expenditure of 23.8 million and a variation of +70.5%, and vasoritide with a 21.7 million expenditure and a variation in expenditure greater than 100% (Table 5. 2.7).

Table 5.2.7 Top 20 active ingredients (class A and H) having the highest variation in 2023 compared 2022

Prevalent Class	Active ingredient	Expenditure *(million)*	Δ % 23-22	DDD *(thousand)*	Δ % 23-22
H	tebentafusp	4.5	>100	15.1	>100
A	osilodrostat	1.6	>100	50.9	>100
H	vosoritide	21.7	>100	47.6	>100
H	satralizumab	2.2	>100	9.8	>100
H	tafasitamab	5.0	>100	55.3	>100
H	pegcetacoplan	3.0	>100	2.2	>100
H	glasdegib	1.2	>100	5.7	>100
A	fenfluramine	4.0	>100	128.9	>100
H	odevixibat	6.2	>100	6.2	>100
H	pretomanid	1.2	>100	10.3	>100
H	fedratinib	7.2	>100	87.9	>100
H	pemigatinib	1.5	>100	7.4	>100
H	velmanasi alpha	1.4	>100	2.1	>100
H	axicabtagene ciloleucel	56.6	>100	0.2	27.4
H	pegvaliase	3.5	86.9	15.8	86.9
H	tafamidis	123.2	84.4	2,012.4	94.8
H	brexucabtagene autoleucel	23.8	70.5	0.1	50.9
H	metreleptin	3.2	68.6	3.3	59.5
A	cannabidiol	12.4	66.0	257.8	63.5
H	lumasiran	9.9	65.7	9.6	65.7

* selected among the active ingredients with an expenditure higher than 1 million euros

Orphan medicines having the additional requirement of innovativeness generated an expenditure amounting to 1.096 billion euros in 2023, increasing by 15.3% compared to 2022 and by 128.8% compared to 2021, against an increase in consumption (38.8%) (Table 5.2.8). The number of orphan medicines having the requirement of innovativeness was 17 in 2023, 19 in 2022 and 17 in 2021. Of these innovative orphan medicines, daratumumab, elexacaftor/tezacaftor/ivacaftor, tafamidis and eculizumab are also among the top 30 most expensive orphan medicines, ranking first, second, third and fourth respectively.

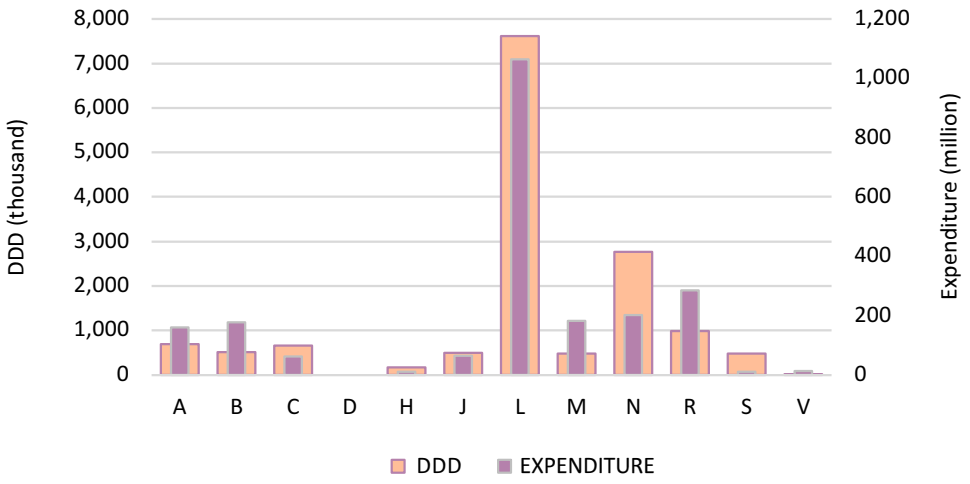
Table 5.2.8 Orphan medicines accessing the fund for oncology and non-oncology innovative medicines: expenditure and consumption, years 2019-2023 (direct purchases)

Active ingredient	Expenditure (million)					DDD				
	2019	2020	2021	2022	2023	2019	2020	2021	2022	2023
axicabtagene ciloleucel		3.4	17.4	20.2	4.7		56	95	124	39
blinatumomab				3.2	12.0				1,946	7,381
brexucabtagene autoleucel (CD3 cells + autologous transduced anti-CD-19 cells)				13.9	23.8				53	80
cenegermin	4.0	2.8				15,232	10,976			
cerliponase alpha			4.1	8.1	3.2			3,101	6,073	2,401
cytarabine/daunorubicin	2.4	8.6	9.2	4.5		608	2,249	2,396	1,170	
daratumumab	156.3	211.0	240.8	390.6	456.2	838,428	1,131,465	1,611,193	4,139,895	5,464,760
dinutuximab beta	3.2	5.1	3.4		0.0	926	1,414	886		
eculizumab				36.2	117.5				52,084	164,122
elexacaftor/tezacaftor/ivacaftor			36.4	206.2	284.0			167,692	712,796	981,512
givosiran			4.6	8.9	12.1			5,344	10,460	14,142
ivacaftor			40.0	105.6				119,215	242,293	
letermovir	10.8	18.7	15.1			26,653	50,020	42,417		
lumasiran				6.0	9.9				5,769	9,561
lutetium oxodotreotide (177lu)	3.5	15.1	13.2	3.8		244	948	935	258	
midostaurin	12.6	15.8	10.7			23,543	29,443	20,182		
nusinersen	102.2	70.2				242,400	166,320			
odevixibat				1.0	6.2				988	6,195
onasemnogene abeparvovec			12.5	7.5	8.1			49	42	30
patisiran		9.5	26.7	39.3	4.7		18,400	51,720	76,200	9,150
ripretinib					1.1					2,550
setmelanotide					1.0					2,853
tafamidis			1.6	66.8	123.2			13,476	1,032,839	2,012,442
tisagenlecleucel	1.2	13.2	31.0	20.5		12	84	151	83	
voretigene neparvovec			12.2	7.7	6.5			41	26	22
vosoritide				0.5	21.7				1,000	47,620
Total	**296.3**	**373.5**	**479.0**	**950.5**	**1,095.8**	**1,148,046**	**1,411,375**	**2,038,892**	**6,284,098**	**8,724,861**

With reference to therapeutic categories, most of the expenditure concerned antineoplastic and immunomodulatory medicines (47.6%), followed by medicines for the respiratory system (12.8%), the central nervous system (9.1%), the musculoskeletal system (8.2%), the blood and haemopoietic organs (7.9%), the gastrointestinal and metabolic system (7.1%) and others (15.2%) (Figure 5.2.3).

As regards consumption, the most affected categories are antineoplastics and immune-modulators (51.2%), nervous system medicines (18.6%), respiratory system medicines (6.7%), gastrointestinal tract and metabolism medicines (4.6%) and cardiovascular system medicines (4.4%), while the remaining 14.5% of consumption is accounted for by other categories (Figure 5.2.3).

Figure 5.2.3 Expenditure and consumption of orphan medicines in Italy for ATC level I, year 2023 (A, H, C, C-NN Class)



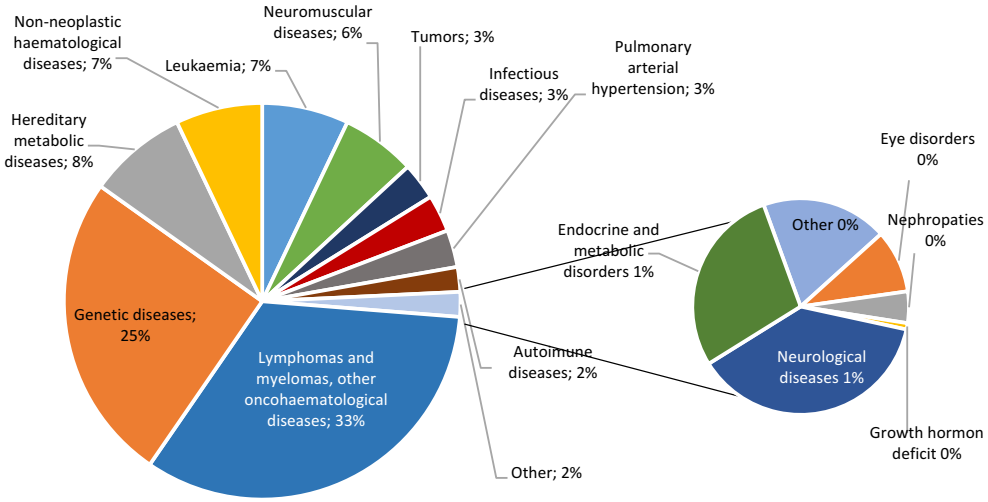
L	Antineoplastic and immunomodulatory medicines	N	Central nervous system	G	Genito-urinary system and sexual hormones
A	Gastrointestinal system and metabolism	H	Systemic hormonal preparations, excluding sexual hormones	J	General antimicrobials for systemic use
C	Cardiovascular system	R	Respiratory system	D	Dermatological medicines
B	Blood and haemopoietic organs	V	Various	S	Sense organs
		M	Musculoskeletal system		

Analysing the distribution of orphan medicines' expenditure by therapeutic area in details, the highest incidence is found to be for medicines intended for the treatment of lymphomas, myelomas and genetic diseases (32.8% and 25.4% respectively), in line with the trend of the previous year. As for consumption, medicines used in lymphomas, myelomas and other onco-haematological diseases top the list, followed by those for genetic diseases and pulmonary arterial hypertension, which have values almost halved (Table and Figure 5.2.9).

Table 5.2.9 Expenditure and consumption of orphan medicines in Italy by therapeutic area: year 2023 (Table and Figure) (A, H, C, C-NN Class)

Therapeutic Area	Expenditure (million)	Δ % 23-22	Expenditure per capita	DDD (*thousand*)	Δ % 23-22	DDD 1000 inhab. per day	Inc.% * expenditure*
Lymphomas and myelomas, other oncohaematological diseases	732	15.2	12.44	6,543.7	30.2	0.30	32.8
Genetic diseases	568	41.1	9.65	3,293.4	64.7	0.15	25.4
Hereditary metabolic diseases	188	25.3	3.19	442.8	38.2	0.02	8.4
Non-neoplastic haematological diseases	166	10.0	2.82	537.7	30.9	0.03	7.4
Leukaemia	150	8.9	2.55	546.9	9.7	0.03	6.7
Neuromuscular diseases	139	2.9	2.37	289.7	0.9	0.01	6.2
Tumors	67	5.3	1.14	314.6	6.1	0.01	3.0
Infectious diseases	63	57.7	1.07	414.6	59.9	0.02	2.8
Pulmonary arterial hypertension	58	-2.5	0.98	657.7	-2.5	0.03	2.6
Autoimmune diseases	56	10.0	0.95	299.3	28.2	0.01	2.5
Neurological diseases	19	82.9	0.32	614.6	78.7	0.03	0.8
Endocrine and metabolic diseases	12	20.3	0.21	246.0	-13.4	0.01	0.6
Other	8	27.2	0.14	194.8	315.9	0.01	0.4
Eye disorders	4	1.2	0.07	472.2	41.6	0.02	0.2
Nephropathies	2	96.3	0.03	0.1	100.0	<0.005	0.1
Total	**2,232**	**12.5**	**37.92**	**14,867.9**	**30.0**	**0.69**	**100.0**

*Calculated on the total expenditure of orphan medicines nationwide

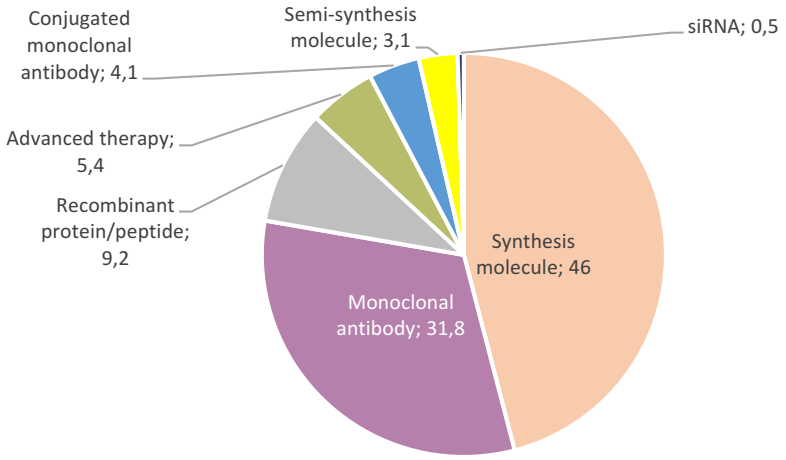


The analysis by product type shows that most orphan medicines are synthesis molecules (incidence on expenditure of about 46%), followed by monoclonal antibodies (incidence on expenditure of about 31.8%) (Table and Figure 5.2.10). In comparison with 2022, the largest increase in expenditure and consumption is observed for *short-interfering* RNA (siRNA) molecules.

Table 5.2.10 Expenditure and consumption of orphan medicines in Italy by therapeutic area: year 2023 (Table and Figure) (A, H, C, C-NN Class)

Type of medicines	No. of molecules	Expenditure *(million)*	Δ % 23-22	DDD *(thousand)*	Δ % 23-22	Expenditure *per capita*	DDD 1000 inhab. per day	Inc. % on expenditure*
Synthesis molecule	56	1,026.9	18.9	6,671.1	34.5	17.45	0.31	46.0
Monoclonal antibody	14	708.8	13.3	6,319.8	32.0	12.04	0.29	31.8
Recombinant protein/peptide	21	204.5	36.3	702.1	50.5	3.47	0.03	9.2
Advanced therapy	7	121.4	41.1	0.5	9.8	2.06	<0.005	5.4
Conjugated monoclonal antibody	5	90.4	11.1	278.8	20.4	1.54	0.01	4.1
Semi-synthesis molecule	12	68.0	55.1	883.1	58.1	1.16	0.04	3.1
siRNA	2	11.6	93.7	12.6	118.7	0.2	<0.005	0.5
Total	**117**	**2,231.5**	**12.5**	**14,867.9**	**30.0**	**37.92**	**0.69**	**100.0**

siRNA: *short-interfering* RNA



Access to medicines for rare diseases pursuant to Law 648, AIFA 5% fund and Ministerial Decree 7 September 2017

Despite notable medical advances in diagnosing and treating many diseases, there are still the so-called "niche" therapeutic areas which refer to unmet clinical needs and which represent a challenge and a healthcare goal for medicine. And it is precisely in this niche position that Law n. 648/96, the National Fund and compassionate use are inserted at a regulatory level.

Law no. 648 of 1996

In the absence of a valid therapeutic alternative, this rule allows the National Health Service to provide:

- innovative medicines whose marketing is authorised in other countries, but not in Italy;
- medicines not yet authorised, but undergoing clinical trials;
- medicines to be used for a therapeutic indication other than that authorised in Italy.

In all the above-mentioned cases, the inclusion in list 648 must be supported by the results of concluded clinical studies, which are at least in phase II and which have demonstrated adequate efficacy with an acceptable risk profile.

Since Law no. 79 of 2014 entered into force, medicines may be included in the list even in the presence of alternatives, after the evaluation of AIFA. These medicines can be used for a therapeutic indication other than that authorised, provided that this indication is known and compliant with research conducted within the national and international medical-scientific community, according to parameters of cost-effectiveness and appropriateness.

The inclusion in the list is carried out by AIFA upon documented request by Patient Associations, Scientific Societies, Health Authorities, Universities or upon recommendation of the AIFA Scientific Technical Committee.

The list of orphan medicines and medicines for the treatment of rare diseases that are reimbursed pursuant to Law no. 648/96 can be downloaded from the Agency's website at the following link: https://www. aifa.gov.it/legge-648-96/.

Law no. 326/2003 (AIFA 5% Fund)

Law no. 326 of 2003 provided for the establishment at AIFA of a national fund for the use of orphan medicines for the treatment of rare diseases and medicines that represent a hope of therapy, pending marketing, for particular and serious diseases.

The Fund consists of 50% of the contribution that pharmaceutical companies pay to AIFA on an annual basis. This contribution corresponds to 5% of the annual expenses that pharmaceutical companies incur on promotional activities aimed at healthcare professionals.

Ministerial Decree 7 September 2017

In Italy, the Ministerial Decree of 7 September 2017- "Therapeutic use of medicinal products undergoing clinical trials" is the regulatory instrument establishing procedures and methods to access experimental pharmacological therapies for the treatment of serious diseases, rare diseases, rare cancers or diseases that put the patient in danger of life when there are no further valid therapeutic alternatives, in the doctor's opinion, or in the event that the patient cannot be included in a clinical trial or for patients who were already treated with clinical benefit in a completed clinical trial, for therapeutic continuity purposes.

Access to experimental medicines requires the Ethics Committee within whose sphere of competence this request originated, to grant an authorisation for use, given the prior de-

clared willingness of the manufacturing pharmaceutical company to supply the medicine free of charge.
The regulatory references for this Decree of the Ministry of Health are art. 83 of Regulation (EC) no. 726/2004, as required pursuant to art. 158, paragraph 10, of the D.L. 219/2006 for aspects relating to compassionate use programs and art. 5 (1) of Directive 2001/83 for accesses on a nominal basis.

If the company is willing to provide the medicine free of charge and the conditions described in the aforementioned Decree are met, the treating physician can use this tool to provide clinical trial medicines to patients who are not part of the trials themselves, or to supply market-authorised medicines for indications other than those approved, or for medicines authorised but not yet available on the national territory.

Access to medicines for rare diseases pursuant to Law 648, AIFA 5% fund and Ministerial Decree 7 September 2017

The data provided refer only to List 648, which is subject to clinical and expenditure monitoring; therefore, these data do not include the lists of medicines for consolidated use.
Table 5.2.11 lists the medicines included in List 648 in 2023, intended for the treatment of rare diseases, both with and without the status of orphan medicine.

Table 5.2.11 Medicines included in List 648 in 2023, intended for the treatment of rare diseases, both with and without the status of orphan medicine

Active ingredient	Therapeutic indication
dabrafenib + trametinib	Treatment of anaplastic thyroid carcinoma
emicizumab	Treatment of acquired A haemophilia
etuvetidigene autotemcel/Telethon 003	Treatment of patients, aged 6 months or older, with the severe form of Wiskott-Aldrich syndrome, who have a mutation in the WAS gene and for whom a suitable HLA-identical familial haematopoietic stem cell donor is not available.
human normal immunoglobulin (IVIg)	Treatment of Rasmussen's encephalitis
rituximab (originator or biosimilar)	Maintenance therapy in patients with mantle cell lymphoma after first-line therapy
rituximab (originator and biosimilar) + vemurafenib	Treatment of hairy cell leukaemia
lomitapide	Treatment of familial chylomicronemia syndrome (type I hyperlipoproteinemia)
somatropin	Treatment of stature deficit due to Noonan syndrome

Source: AIFA Pre-Authorisation Division

During 2023, 26 compassionate use programs were activated for rare diseases, 12 of which contained medicines that received orphan designation by the COMP, with a total of 2,198 patients treated.
It should be noted that the figures reported are updated to 30 November 2023; the reported figure is cumulative for programmes opened before 2023.

Table 5.2.12 shows the list of programmes and the number of patients included in each of them.

Table 5.2.12 Medicines intended for the treatment of rare diseases for which a program was activated in 2023 pursuant to Ministerial Decree 7th September 2017

Medicine	Therapeutic indication	Number of patients included in the programme
efgartigimod*	Treatment of patients with generalised Myasthenia Gravis (gMG) who do not benefit from currently available therapies	116
avacopan (Tavneos)*	In combination with a rituximab or cyclophosphamide-based regimen, for the treatment of adult patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) in active and severe phase	47
capmatinib (Tabrecta)	Treatment of patients with metastatic non-small cell lung cancer (NSCLC) with c-MET mutation	57
glofitamab*	Treatment of patients diagnosed with relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL), relapsed/refractory high-grade lymphoma (R/R HGL), relapsed/refractory transformed follicular lymphoma (R/R trFL), relapsed/refractory primary mediastinal lymphoma (R/R PMBCL).	115
odevixibat (Bylvay)*	Treatment of Alagille syndrome	11
durvalumab (Imfinzi)	In combination with gemcitabine and cisplatin for the first-line treatment of adult patients with metastatic or locally advanced biliary tract cancer	1368
mosuNTEuzumab (Lunsumio)*	Treatment of adult patients with relapsed/refractory follicular lymphoma	32
polihexanide collirio*	Treatment of acanthamoeba keratitis	58
pembrolizumab (Keytruda)	In combination with chemotherapy, with or without bevacizumab, in the treatment of persistent, recurrent or metastatic cervical cancer in adults whose tumour expresses PD-L1 with a PCD ≥ 1.	174
spesolimab (Spevigo)	Treatment of generalised pustular psoriasis (GPP) undergoing recrudescence	13
rezafungin*	Treatment of candidaemia and/or invasive candidiasis	7
Sutimlimab (Enjaymo)	Treatment of adult patients (> 18 years old) with primary cold agglutinin anaemia (Cold Agglutin Disease - CAD), limited to the treatment of haemolytic anaemia of moderate to severe grade, unfit, non-responders or relapsed after previous treatment with rituximab.	9
pegunigalsidase alpha (Elfabrio)*	Treatment of Fabry disease	3
ivacaftor/tezacaftor/ elexacaftor (Kaftrio)*	Treatment of patients aged 2 to 5 years with cystic fibrosis who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene	18
ravulizumab (Ultomiris)	Adjunctive therapy to standard therapy for the treatment of adult patients with generalised Myasthenia Gravis (gMG) who are positive for antibodies against the acetylcholine receptor (AChR+) and for whom there are no approved therapeutic alternatives	66

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Table 5.2.12 – *continued*

Medicine	Therapeutic indication	Number of patients included in the programme
talquetamab*	Treatment of relapsed or refractory multiple myeloma in patients for whom there are no approved therapeutic alternatives	91
TAK-755 (rADAMTS13)	Treatment and prophylaxis of severe thrombotic thrombocytopenic purpura, hereditary or congenital	1
berotralstat (Orladeyo)*	Prevention of recurrent attacks of hereditary angioedema (HAE) in adult and adolescent patients - 12 years of age and older.	9
sparsentan*	Treatment of adult patients with A immunoglobulin nephropathy	1
dupilumab (Dupixent)	Treatment of eosinophilic oesophagitis in adults and adolescents - 12 years of age or older, weighing at least 40 kg, not adequately controlled by/ intolerant to/ or who are not candidates for conventional drug therapy (TCS for ingestion or PPI).	35
zilucoplan*	Adjunctive therapy to standard therapy for the treatment of adult patients with generalised myasthenia gravis (MGg) who are positive for antibodies against the acetylcholine receptor (AChR+) and who are unresponsive, intolerant or ineligible for authorised therapeutic alternatives.	2
iptacopan	Treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH) for whom there are no authorised therapeutic alternatives	2
iptacopan	Treatment of adult patients with C3 glomerulopathy (C3G), transplanted and non-transplanted, for whom there are no authorised therapeutic alternatives	0
mavacamten (Camzyos)	Treatment of symptomatic hypertrophic obstructive cardiomyopathy (HCM) (class II-III according to the New York Heart Association, NYHA classification) in adult patients who have exhausted authorised therapeutic alternatives	0
repotrectinib	Treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) with ROS1 rearrangements:- in patients pre-treated with TKIs who have seen no benefit or have shown evidence of disease progression or- in patients ineligible for authorised treatments	29

* medicines with orphan designation by the COMP.
Source: AIFA Pre-Authorisation Division

The resources allocated in the 5% fund for 2023 amounted to € 15,088,347. The total number of applications to access the fund received during 2023 was 538; 289 of these applications concerned patients with a rare disease, 147 were related to patients with a rare tumour. The fund was authorised for 149 applications related to rare diseases, of which 75 related to rare tumours (Table 5.2.13).

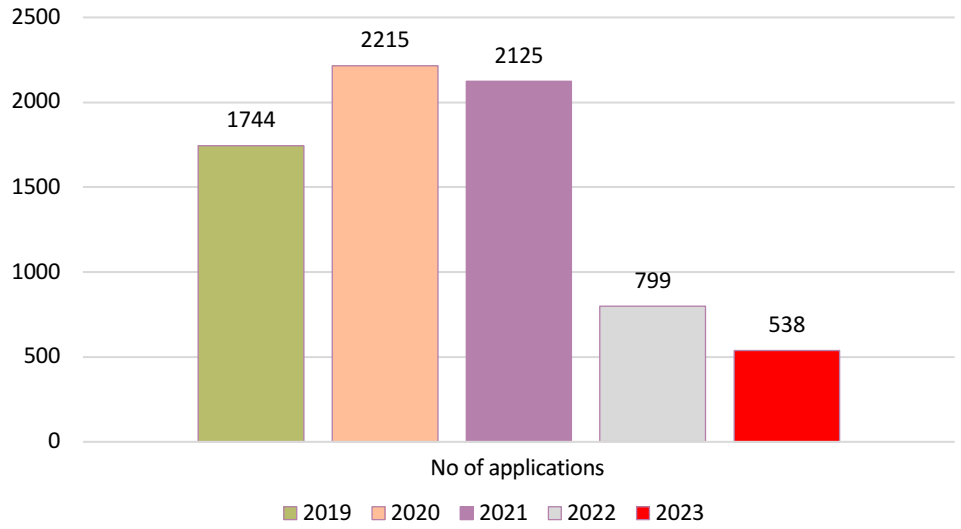
Table 5.2.13 Number of applications to access the fund and number of actual accesses obtained in 2023

Year	Number of patients who applied for access to the AIFA fund		Number of patients who received a positive response to the application for accessing the AIFA fund	
	with rare disease	with rare tumour	with rare disease	with rare tumour
2023	289	147	149	75

Source: AIFA Pre-Authorisation Division

Over the last five years (2019-2023), there has been a downward trend in applications for access to the 5% fund, from 1744 applications in 2019 to 538 in 2023 (Figure 5.2.4).

Figure 5.2.4 Applications to access to the 5% fund in the period 2019-2023



The decrease in applications is related to the adoption of new criteria for accessing the fund which were introduced at the end of 2021 and subsequently amended in June 2023. Those new criteria are aimed to protect the sustainability of the fund itself and to guarantee access to medicines that are not yet marketed in Italy and that represent a hope of cure for patients with rare and serious diseases, i.e., the treatment of individual cases characterised by a major or maximum therapeutic need.

Finally, it should be noted that as of 1 July 2022, AIFA activated the new online service that allows the submission and monitoring of the processing status of applications for access and reimbursement of the 5% fund.

Applications for the top 10 active substances account for about 46% of the total applications (174 out of a total of 376 applications that received an opinion from the Support and Coordination Secretariat of the Pre-Authorisation Division).

As can be seen from Tables 5.2.14 and 5.2.15, most of the requests concern the active ingredients pembrolizumab, ruxolitinib and nivolumab.

Table 5.2.14 Top 10 active principles by number of applications for accessing the 5% fund in 2023(*)

Active ingredient	No. of requests
pembrolizumab	45
ruxolitinib	29
nivolumab	23
lutetium (177Lu) vipivotide tetraxetan	20
sebelipase alpha	12
trametinib; dabrafenib	10
trastuzumab deruxtecan	10
eltrombopag	9
alpelisib	8
ivosidenib	8

Source: AIFA Pre-Authorisation Division;(*) Table produced without considering applications withdrawn by the applicants.

Table 5.2.15 shows the top 10 active ingredients with the greatest expenditure impact in descending order. These medicines accounted for about 70% of the total authorised expenditure. The medicines with the greatest expenditure impact are sebelipase alpha, beremagene geperpavec and belinostat.

Table 5.2.15 Top 10 active principles with the greatest expenditure impact on the AIFA 5% fund for 2023(*)

Active ingredient	Authorised expenditure (€)
sebelipase alpha	2,208,142.37
beremagene geperpavec	1,411,410.00
belinostat	979,100.00
lutetium (177Lu) vipivotide tetraxetan	572,000.00
eculizumab	537,192.16
triheptanoin	490,500.00
blinatumomab	423,591.36
leniolisib	367,999.92
pembrolizumab	305,837.80
burosumab	299,712.84

Source: AIFA Pre-Authorisation Division;(*) Table produced without considering applications withdrawn by applicants.

Section 6

Environmental impact of medicines

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Introduction

As in the previous year, a section on the environmental impact of medicines is introduced in the Osmed Report 2023. The sustainable use of medicines represents one of the multiple challenges for human activity with respect to the environment. Surface waters, although not the only environment affected, are contaminated by the use of medicines since after they are taken, medications are released into the water via urinary or faecal excretion, either in unaltered form or as metabolites. Moreover, topical formulations and unused medicines, if disposed of incorrectly, e.g. through toilets, may reach the waters in virtually unaltered form[1]. Once in the water, these medicines can alter the aquatic ecosystem[2–4]. Therefore, it is important to remember that the health status of ecosystems can directly or indirectly influence that of human beings [5].

Calculation of environmental risk

With the aim of estimate the environmental risk of medicines for human use in Italy, 114 active ingredients were selected on the basis of three criteria: highest use, highest environmental toxicity and inclusion/application in at least one version of the European Watch List[6–9]. The active ingredients, which were selected according to the criteria of highest environmental toxicity and inclusion in the European Watch List, remained unchanged from the previous year. On the other hand, the number of most frequently used molecules has increased, taking into consideration the most consumed OsMed subgroups both NHS-covered and privately purchased by citizens. Within each subgroup, the top 3 active ingredients with the highest consumption were included (Table 6.1). On the basis of the NHS consumption, the following subgroups were included: ACE inhibitors, acetylsalicylic acid alone and in combination, other antipyretics - salicylic acid and derivatives, SSRI antidepressants, beta-blockers, dihydropyridine calcium channel blockers, traditional NSAIDs, proton pump inhibitors, statins alone and vitamin D and analogues. Considering private consumption, the followings were analysed: other antipyretics-salicylic acid and derivatives, benzodiazepines, oral contraceptives, erectile dysfunction medicines, thyroid hormones, paracetamol alone and in combination. Table 6.1 shows the active substances by inclusion criteria and ATC 1st and 2nd level. The environmental risk is estimated at national level, by geographical area and region.

Table 6.1 List of active substances included in the analysis by inclusion criteria

ATC I	ATC II	Inclusion criteria	Active substances
A	A02	Most consumed	esomeprazole, lansoprazole, omeprazole
	A07	High environmental toxicity	rifaximin
	A10	Watch List	metformin
	A11	Most consumed	alfacalcidol, calcitriol, cholecalciferol
B	B01	Watch List	dipyridamole
	B02	High environmental toxicity	lusutrombopag
	B03	Most consumed	cyanocobalamin
C	C02	High environmental toxicity	bosentan
	C07	Most consumed	atenololo, bisoprolol, nebivolol
		Watch List	propranolol
	C08	Most consumed	amlodipine, barnidipine, lercanidipine
		High environmental toxicity	clevidipine, felodipine, isradipine, lacidipine, nisoldipine
	C09	Most consumed	candesartan, enalapril, olmesartan, ramipril, valsartan, zofenopril
		Watch List	irbesartan
	C10	Most consumed	ezetimibe, atorvastatin, rosuvastatin, simvastatin
		High environmental toxicity	lomitapide
		Watch List	gemfibrozil
D	D01	Watch List	clotrimazole
G	G03	Most consumed	desogestrel, dienogest, drospirenone, **estradiol, ethinylestradiol**, gestodene, norgestimate
		High environmental toxicity	**estradiol, ethinylestradiol levonorgestrel**
		Watch List	**estradiol, ethinylestradiol, levonorgestrel,** noretisterone
	G04	Most consumed	sildenafil, tadalafil, vardenafil
H	H03	Most consumed	levothyroxine, liothyronine
J	J01	Watch List	amoxicillin, azithromycin, cephalexin, ciprofloxacin, clarithromycin, clindamycin, erythromycin, ofloxacin, sulfamethoxazole, trimethoprim
	J02	Watch List	fluconazole, miconazole
	J04	High environmental toxicity	bedaquiline
	J05	High environmental toxicity	elbasvir, grazoprevir, rilpivirine
L	L01	High environmental toxicity	ceritinib, dabrafenib, fedratinib, imatinib, lapatinib, midostaurin, nilotinib, vinflunine
		Watch List	cyclophosphamide, daunorubicin, doxorubicin, fluorouracil
	L02	High environmental toxicity	toremifene
	L04	Watch List	mycophenolate
M	M01	Most consumed	**diclofenac,** ibuprofen, ketoprofen
		High environmental toxicity	proglumetacin
		Watch List	**diclofenac**
	M04	Watch List	allopurinol

continued

Table 6.1 - *continued*

ATC I	ATC II	Inclusion criteria	Active substances
N	N02	Most consumed	acetylsalicylic acid, lysine acetylsalicylate, paracetamol
		Watch List	fentanyl, gabapentin
	N05	Most consumed	alprazolam, brotizolam, delorazepam, eszopiclone, lorazepam, lormetazepam, **midazolam**, remimazolam, triazolam, zolpidem, zopiclone
		Watch List	**midazolam**
	N06	Most consumed	escitalopram, paroxetine, sertraline
		Watch List	venlafaxine
P	P01	High environmental toxicity	atovaquone
		Watch List	piperaquine
	P02	Watch List	mebendazole
	P03	High environmental toxicity	permethrin
R	R03	High environmental toxicity	montelukast
	R06	High environmental toxicity	ebastine
S	S01	High environmental toxicity	verteporphine

Note: active substances selected according to more than one criterion are shown in bold.

The medicines' environmental risk for surface waters was assessed by calculating the ratio between the medicine estimated concentration (PEC - *Predicted Environmental Concentration)* and the substance toxicity to aquatic animal and plant species (PNEC- *Predicted No Effect Concentration).* The resulted environmental risk was classified as high when the PEC/PNEC ratio was greater than or equal to 10, moderate when between 1 and 10, low when between 0.1 and 1 and insignificant when less than or equal to 0.1[10].

To calculate the PEC of each active substance the following formula was used:

$$PEC(\mu g/L) = \frac{A \times 10^9 \times (100 - R)}{365 \times P \times V \times D \times 100}$$

Where:

- $A\ (kg)$ is the total amount of active substance consumed in Italy, in geographic areas and in the Regions in 2023. Consumption for all reimbursement classes (approved care regime, hospital and private) was considered for each selected active ingredient. For all active ingredients, both individual consumption and consumption in combination were considered.

- $R\ (\%)$ represents the removal rate of the substance due to loss by volatilization, hydrolysis or biodegradation. As no specific information is available, a value of 0 % was considered[11].
- P is the numerosity of the Italian population, in macro-areas and regions in 2023, calculated as the average of the resident population on 1 January 2023 and 1 January 2024[12].
- $V\ (L/die)$ is the volume of waste water *per capita* per day and it is set at 200 l according to the European Chemical Agency (ECHA)[11] proposal.
- D represents the dilution factor of the waste water by river flow and was set at 10 according to the ECHA proposal[11].

The PNEC values used to estimate the environmental risk have been extracted from the NORMAN ecotoxicology database[13]. These data derived from the study of animals or plants in natural environments or artificially exposed to concentrations of individual active ingredients. In cases where more than one PNEC value was available for a specific active substance, the lowest value was selected[14].

Environmental risk in Italy

The environmental risk was calculated for 109 of the 114 selected active ingredients, due to the absence of PNEC data for 5 of them. The active substances estimated at high risk are 10, while those at moderate risk are 25. Most of the examined therapeutic classes contain at least one active substance of high or moderate risk (figure 6.1) with results that are in line with those of the previous year. The active substances of high or moderate risk by therapeutic class are outlined below:

- NSAIDs and antipyretics: diclofenac and ibuprofen have been estimated to be as high risk.
- Antibiotics: macrolide azithromycin and penicillin amoxicillin were rated as high risk, while macrolide clarithromycin, ciprofloxacin and ofloxacin fluoroquinolones and lincosamide clindamycin as moderate risk.
- Antifungals and antivirals: clotrimazole and miconazole, together with the anti-HIV antiviral rilpivirine, were identified as moderate risk.
- Medicines used in oncology: nilotinib, imatinib and dabrafenib were confirmed to be as moderate risk, while lapatinib, which was estimated to be at moderate risk last year, was found to be as low risk.
- Contraceptive medicines: oestradiol, ethinylestradiol, levonorgestrel and norethisterone were classified as moderate risk. Last year estradiol was indicated as high risk but its risk quotient decreased from 12.5 to 4.8 in 2023.
- Antihistamines and anti-asthmatics: ebastine and montelukast, the only active ingredients in their respective classes that were included in the analysis, were found to be of moderate risk.
- Pesticides: permethrin and atovaquone were estimated as high risk.
- Medicines that act on the nervous system: antidepressants venlafaxine and sertraline were estimated to be as high risk, while the anxiolytic delorazepam was found to be as moderate risk.

- Among proton pump inhibitors, esomeprazole was found to be as moderate risk. In contrast, lansoprazole, which was classified as as moderate risk in 2022 report, was classified as low risk in 2023 (from 1.4 to 0.8).
- Medicines that act on the cardiovascular system: the hypolipidemic drug rosuvastatin, which was low risk last year, rose to moderate risk. Among the calcium channel blockers, lercanidipine was estimated as high risk, while lacidipine (high risk in last year's report) and barnidipine as moderate risk, and felodipine (moderate risk in last year's report) as low risk. ACE inhibitors zofenopril and ramipril were identified as moderate risk. Among the others antihypertensives, olmesartan was classified as high risk and bosentan as moderate risk.
- Antidiabetics: the only active ingredient included for this class, metformin, was estimated to be of moderate risk.

Most of the differences in risk classes of individual active substances between one year and the next relate to the shift between adjacent classes, mainly towards the lower one. For the most part, these transitions are due to small differences in risk quotients and thus small variations in consumption. Of particular interest is the increased environmental risk for rosuvastatin, linked to an increase in consumption, which may have been brought about by the implementation of the new European Society of Cardiology (ESC) guidelines regarding cholesterolaemia control, with lower target values and consequently the need for more prescriptions of high-intensity statins, as well as a possible enlargement of the number of patients [15].

Figure 6.1 shows the relation between the estimated risk level and the level of consumption. It is important to note that amoxicillin, the most widely used antibiotic with a consumption of about 340 tonnes per year, along with the NSAIDs diclofenac and ibuprofen, with a cumulative consumption of more than 200 tonnes, are among the medicines having high environmental risk, despite their low toxicity. Similarly, metformin has a moderate risk due to its widespread use, just under 1400 tonnes. On the other hand, paracetamol (around 1200 tonnes) and acetylsalicylic acid (around 290 tonnes) are low risk, although widely used.

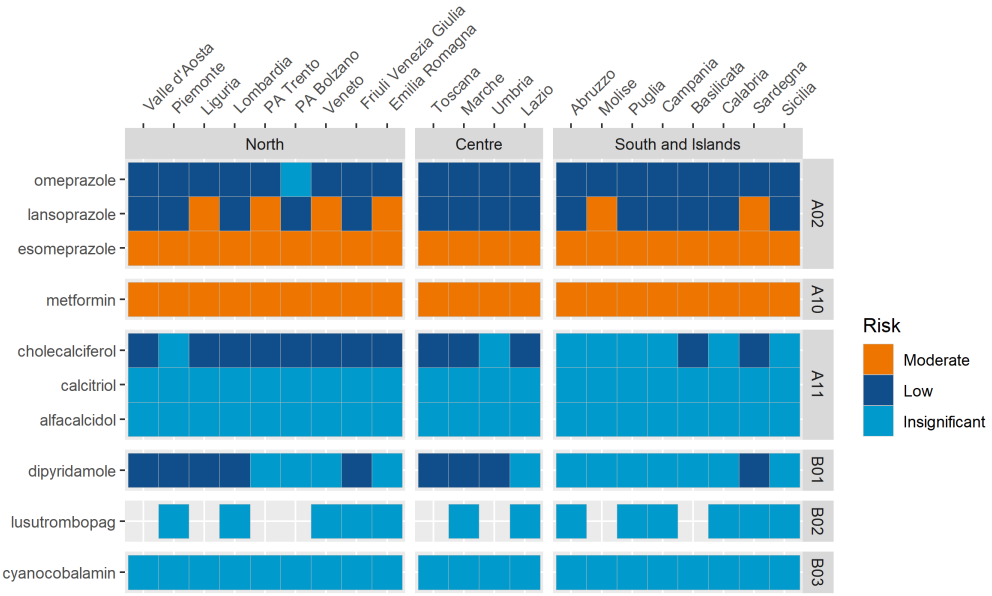
In contrast, the high risk of other medicines is mainly due to their high environmental toxicity (low PNEC). In particular, the medicines with the lowest PNEC are levonorgestreland the ethinylestradiol, 0,000016 µg/L e 0,000035 µg/L respectively. Both medicines are classified as moderate risk despite their consumption of about 5kg and 12 kg.

Figure 6.1 Environmental risk and level of consumption of selected medicines (n=109) in 2023

Note: the figure shows the risk level according to the colour scale in caption. On the other hand, the dimension of the bubble is proportional to the consumption amount in Italy.

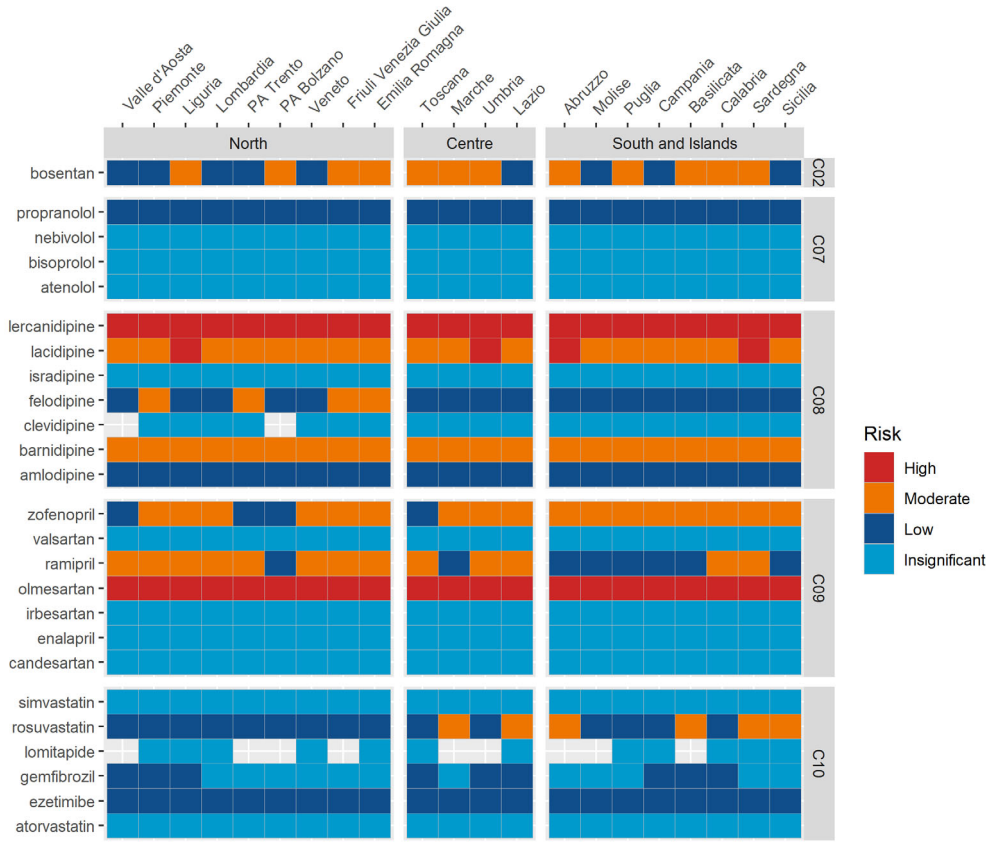
As regards regional data, it was highlighted that some active substances differ by risk class in different Regions (Figures 6.2- 6.8). In particular, risk for ethinylestradiol was estimated high in Sardegna while it was moderate in all the other Regions. This variation was observed also for drospirenone, usually used in combination with ethinylestradiol, which was found as low risk in Sardinia and as insignificant risk in all the other Regions. This trend could be attributable to a greater use of oral contraceptives in the Region of Sardinia, higher than the national average[16] An opposite trend was observed for norethisterone, estimated as moderate risk in all Regions except Sardinia. However, this active ingredient is used in a variety of indications and it is thus difficult to identify the determining factors of this trend in potential variations of specific clinical recommendations. The antileukotrienic montelukast was found to be as moderate risk in all Regions except the Province of Bolzano, where it was esteemed as low risk. This could be due to different recommendations followed by physicians working in the field: in addition to the Italian guidelines (where montelukast is proposed as alternative to ICS for asthma prophylaxis in cases of mild-moderate, moderate and moderate-severe severity for those who suffer from concomitant allergic rhinitis or have preserved pulmonary function), German-language guidelines are also followed in the Bozen area. The latter guidelines propose montelukast as an alternative to ICS only after a case-by-case analysis and in case of incompatibility with prophylactic therapy with ICS, as they are considered less effective[17,18]. Moreover, the antifungal myconazole showed high risk in Calabria while in all other Regions it has moderate risk. The anti-cancer medicine dabrafenib presented low risk in Molise, while it was at moderate risk in all other regions.

Figure 6.2 Environmental risk for selected medicines belonging to ATC A and B classes in the Regions, by geographical area



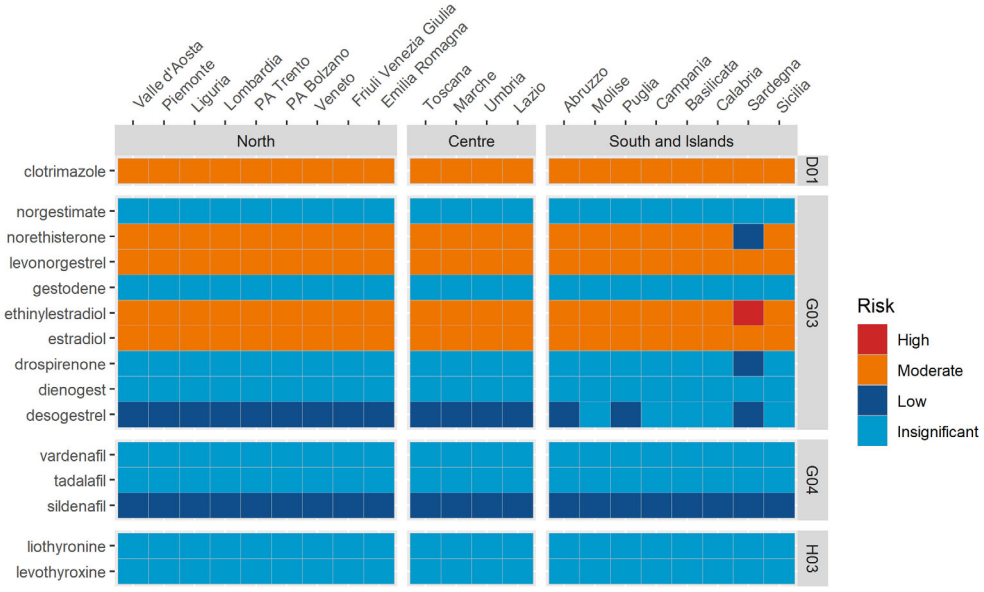
Note: the figure shows the risk level according to the colour scale in caption

Figure 6.3 Environmental risk for selected medicines belonging to ATC C class in the Regions, by geographical area



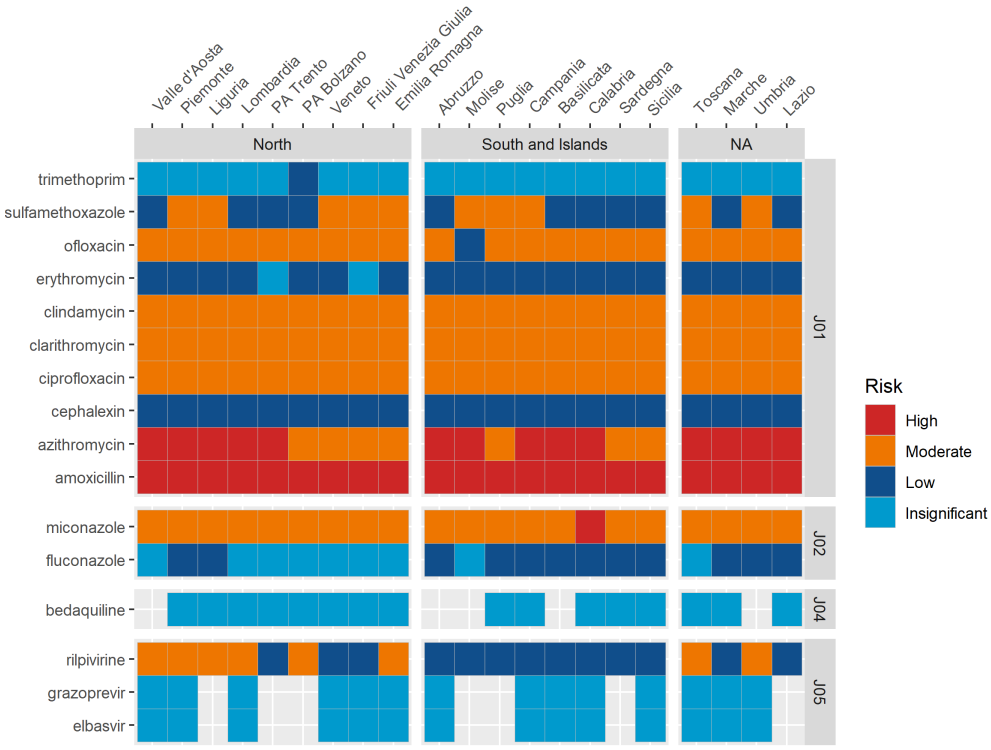
Note: the figure shows the risk level according to the colour scale in caption

Figure 6.4 Environmental risk for selected medicines belonging to ATC D, G and H classes in the Regions, by geographical area



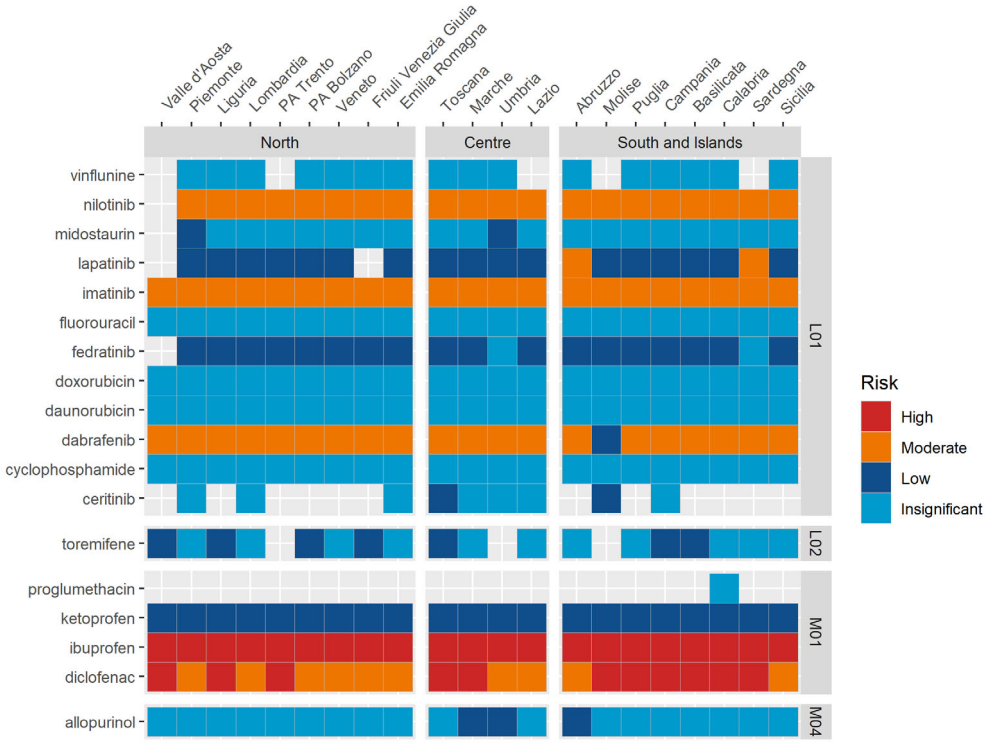
Note: the figure shows the risk level according to the colour scale in caption

Figure 6.5 Environmental risk for selected medicines belonging to ATC J class in the Regions, by geographical area



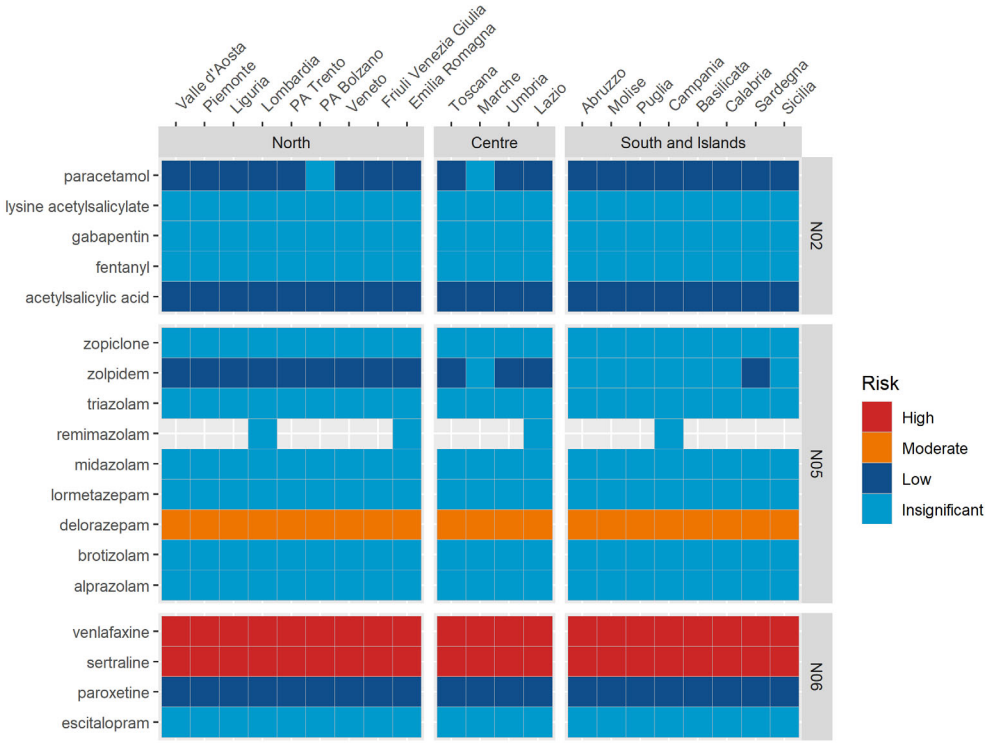
Note: the figure shows the risk level according to the colour scale in caption

Figure 6.6 Environmental risk for selected medicines belonging to ATC L and M classes in the Regions, by geographical area



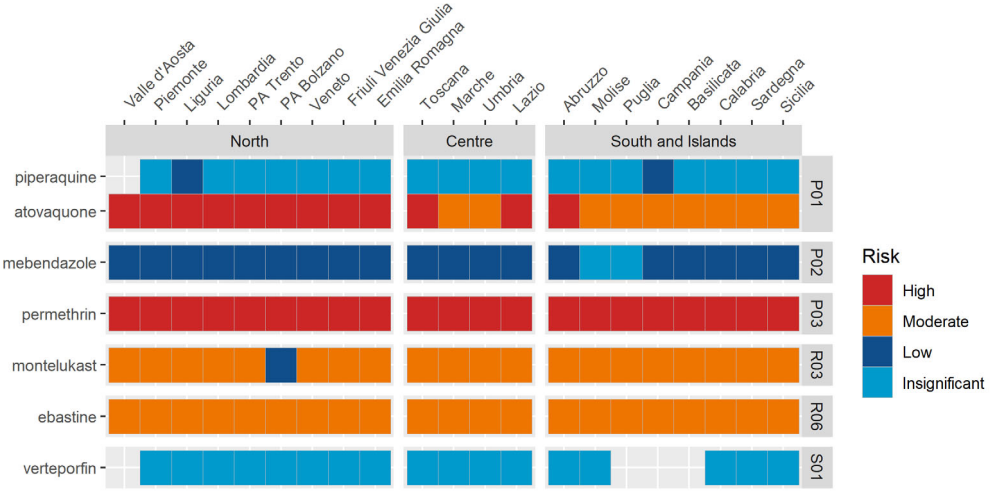
Note: the figure shows the risk level according to the colour scale in caption

Figure 6.7 Environmental risk for selected medicines belonging to ATC N class in the Regions, by geographical area



Note: the figure shows the risk level according to the colour scale in caption

Figure 6.8 Environmental risk for selected medicines belonging to P, R and S ATC classes in the Regions, by geographical area



Note: the figure shows the risk level according to the colour scale in caption

Conclusions

The reference taken for this section on environmental impact of medicines is 114 active ingredients selected on the basis of the following criteria: environmental toxicity, inclusion in the Watch List programme for monitoring European waters and highest consumption in Italy. The analysis provides a starting point for assessing the environmental impact of medicines used in the human domain. However, that analysis has several limitations that call for caution in its direct application to clinical and regulatory practice. In particular, according to the method developed by the EMA, the estimation of aquatic concentrations represents the 'worst case scenario' based on the assumption that all dispensed drugs end up in water unmodified. In reality, several factors influence this concentration from the moment of dispensation to its presence in water, such as metabolic detoxification and wastewater treatment. In addition, environmental toxicity data (PNEC values) were not available for all selected active ingredients, so it was not possible to estimate the risk quotient. The current challenges in research in this field include the collection of more comprehensive data on an increasing number of active ingredients and the development of more accurate estimation methods. With regard to the analysis by geographical area, differences in utilisation were observed between North, Centre and South, leading to different environmental risks between geographical areas. Assessing the environmental impact of medicines and designing interventions to mitigate such impact will involve cooperation between healthcare professionals, to ensure appropriate use of medicines also in a *one-health* perspective, and environmental protection professionals, for the development of organisational and technological solutions to limit residues reaching the environment, without excluding the role of citizens and patients.

References

1. Daughton CG. Chapter 2 - Pharmaceuticals in the Environment: Sources and Their Management. In: Petrovic M, Barcelo D, Pérez S, eds. *Comprehensive Analytical Chemistry*. Vol 62. Analysis, Removal, Effects and Risk of Pharmaceuticals in the Water Cycle. Elsevier; 2013:37-69.
2. Porseryd T, Larsson J, Kellner M, Bollner T, Dinnétz P, Porsch Hällström I. Altered non-reproductive behavior and feminization caused by developmental exposure to 17α-ethinylestradiol persist to adulthood in three-spined stickleback (Gasterosteus aculeatus). *Aquat Toxicol*. 2019;207:142-152.
3. aus der Beek T, Weber FA, Bergmann A, et al. Pharmaceuticals in the environment—Global occurrences and perspectives. *Environ Toxicol Chem*. 2016;35(4):823-835.
4. Grenni P, Ancona V, Barra Caracciolo A. Ecological effects of antibiotics on natural ecosystems: A review. *Microchem J*. 2018;136:25-39.
5. European Environment Agency E. Climate Change as a Threat to Health and Well-Being in Europe: Focus on Heat and Infectious Diseases. Publications Office; 2022.
6. Negrão DCR, Ceriani L, Ippolito A, Lettieri T. Development of the First Watch List under the Environmental Quality Standards Directive. JRC Publications Repository.

7. Loos, R., Marinov, D., Sanseverino, I., Napierska, D. and Lettieri, T., Review of the 1st Watch List under the Water Framework Directive and recommendations for the 2nd Watch List, EUR 29173 EN, Publications Office of the European Union, Luxembourg, 2018.

8. Selection of substances for the 3rd Watch List under the Water Framework Directive - Publications Office of the EU. Accessed August 20, 2023. https://op.europa.eu/en/publication-detail/-/publication/a2ab9f86-d140-11ea-adf7-01aa75ed71a1/language-en.

9. Gomez CL, Marinov D, Sanseverino I, et al. Selection of substances for the 4th Watch List under the Water Framework Directive. JRC Publ Repos. Published online August 3, 2022.

10. Lif. Environmental classification of pharmaceuticals at www.fass.se. Published online 2012. Accessed December 5, 2023. https://www.lif.se/contentassets/b7cf255755504f78a906f3eba8a6ae38/environmental-classification-of-pharmaceuticals-att-wwwfassse.pdf

11. ECHA. Guidance on information requirements and chemical safety assessment Chapter R.10: Characterisation of dose [concentration]-response for environment. Published online May 2008. https://echa.europa.eu/documents/10162/13632/information_requirements_r10_en.pdf/bb902be7-a503-4ab7-9036-d866b8ddce69

12. Popolazione residente al 1° gennaio: per fascia di età. Accessed July 17, 2024. http://dati.istat.it/Index.aspx?QueryId=42869

13. Dulio V, Koschorreck J, van Bavel B, et al. The NORMAN Association and the European Partnership for Chemicals Risk Assessment (PARC): let's cooperate! Environ Sci Eur. 2020;32(1):100. doi:10.1186/s12302-020-00375-w

14. EMA. Environmental risk assessment of medicinal products for human use - Scientific guideline. European Medicines Agency. Published September 17, 2018. Accessed August 20, 2023. https://www.ema.europa.eu/en/environmental-risk-assessment-medicinal-products-human-use-scientific-guideline

15. Arca M, Di Fusco SA. Dislipidemia: i nuovi target e importanza delle terapie di associazione. *G Ital Cardiol*. 2021;22(4):5-8. doi:10.1714/3582.35670

16. Istituto Nazionale di Statistica. La salute riproduttiva della donna. Published online 2017. Accessed July 26, 2024. https://www.istat.it/produzione-editoriale/la-salute-riproduttiva-della-donna/

17. Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin e.V. S2k-Leitlinie Fachärztliche Diagnostik und Therapie von Asthma. Published online March 1, 2023. Accessed July 17, 2024. https://register.awmf.org/assets/guidelines/020-009l_S2k_Fachaerztliche-Diagnostik-Therapie-von-Asthma_2023-03.pdf

18. Paggiaro P, Gruppo GINA Italia, Bacci E. LINEE GUIDA GINA ITALIANE. Published online 2016. Accessed July 17, 2024. https://ginasma.it/wp-content/uploads/materiali/2017/GINA_adattamento_ita_2017_doc.pdf

Appendix 1

Regulations concerning pharmaceutical assistance in Italy

BACK TO CONTENTS

1. Main measures taken in 2023

Budget Law 2024

The Budget Law 2024 (Law December 30, 2023, No. 213) introduced several changes in the area of pharmaceutical assistance:

- restated the cap on pharmaceutical spending for direct purchases to the extent of 8.5% starting from the year 2024. Consequently, the cap on conventional pharmaceutical spending is restated to the value of 6.8% from the same year 2024;
- established that the Italian Medicines Agency (AIFA) shall update the formulary of the continuity of care hospital-local units (PHT) by identifying the binding list of medicines that, due to their pharmacological characteristics, can transit from the A-PHT classification regime, as well as the binding list of PHT medicines not covered by patent that can be assigned to distribution under agreement through pharmacies open to the public;
- introduced, starting March 1, 2024, a new pharmacy remuneration system for the reimbursement of drugs dispensed under the NHS that provides:
  - a percentage share of 6% related to the public price net of VAT per drug package;
  - a fixed fee of 0.55 euros for each drug package with a retail price not exceeding 4.00 euros;
  - a fixed fee of 1.66 euros for each drug package with a retail price between euro 4.01 and euro 11.00;
  - a fixed fee of 2.50 euros for each drug package with a retail price exceeding 11.00 euros;
  - an additional fixed fee of 0.10 euros per drug package belonging to the transparency lists. The public sale price of Class A medicines is intended to be unchanged. The latter share will be restated to EUR 0.115 as of January 1, 2025.

In order to confirm and strengthen the ubiquity of the pharmacy network throughout the country, the following are also recognized:

a) an additional fixed fee of 1.20 euros for each drug dispensed by pharmacies with NHS revenue not exceeding 150,000 euros after VAT;
b) an additional fixed fee of 0.58 euros for each drug dispensed by pharmacies, excluding those referred to in (c), with NHS revenue not exceeding 300,000 euros after VAT;
c) an additional fixed fee of 0.62 euros for each drug dispensed by subsidized rural pharmacies, as defined by Law No. 221 of March 8, 1968, with NHS revenue not exceeding 450,000 euros after VAT.

Without affecting the shares for pharmaceutical companies in the public sale price of Class A drugs and equivalent drugs, and except for drugs that were originally covered by a patent or have benefited from licenses derived from such a patent, a series of discounts cease to apply as of March 1, 2024:

a) discount for the benefit of the NHS proportional to the price of the drug for the different types of pharmacies, defined in accordance withArticle 1, paragraph 40, of Law No. 662 December 23, 1996;

b) discount arranged by determination of AIFA February 9, 2007, published in the Official Gazette No. 43 of February 21, 2007;
c) discount referred to in Article 1, paragraph 3, of Decree-Law No. 156of June 24, 2004, converted, with amendments, by Law No. 202of August 2, 2004;
d) discount referred to in Article 11, paragraph 6, of Decree-Law No. 78of May 31, 2010, converted, with amendments, by Law No. 122of July 30, 2010.

2. Main context indicators of the Italian Health System

Table 2.1 shows the main context indicators for healthcare in Italy. With regard to hospital care, a reduction in the number of hospital discharges in the period 2016-2020 can be observed, going from 9 million in 2016 to 7.3 million in 2021, with a 1.7 million reduction in the period 2016/2021. In 2020, in particular, there was a sharp year-on-year reduction in hospital discharges of about 20% due to the COVID-19 pandemic. At the same time, hospital days also increased from 61.2 million in 2016 to 51.7 million in 2021, with a 9.5 million day reduction in the period 2016/2021. There is evidence, for the first time in the period considered, of an increase in the number of ordinary inpatient beds in acute care, from 151,607 in 2020 to 176,709 beds in 2021, while long-term care beds confirm the downward trend from 8,767 beds in 2016 to 7,989 in 2021. Over the same period, a reduction of more than 2,000 inpatient day hospital beds is observed in accordance with DM70 as amended.

The trend of average stays under long-term care and rehabilitation, after the 2017 reduction compared to 2016, tends to stabilise with a slight increase both in 2018 and 2019. However, the average stay under long-term care shows a limited increase in 2020 (from 24.5 days in 2019 to 24.6 days in 2020), whereas the average stay for rehabilitation under ordinary scheme shows a more substantial increase (from 26.2 days in 2019 to 27.5 days in 2020). In 2021 there is a slight decrease for the average rehabilitation stay and a larger increase for the average long-term care stay from 24.6 days in 2020 to 26.1 days in 2021. The average ordinary acute stay remained broadly stable in the period from 2016 to 2019, equal to around 7 days, and showed an increase to 7.5 and 7.4 days in the year 2020 and 2021, respectively. A steady increase in the average weight of Diagnosis Related Groups (DRGs) was recorded, from 1.19 in 2016 to 1.33 in 2021. The average weight of DRGs is calculated as the ratio between the sum of the DRG points produced and the total number of discharges. This is a measure of the complexity of the cases treated.

With regard to the distribution of medicines, the number of Marketing Authorisation Holders (MAHs) increased from 817 in 2018 to 871 in 2023. The number of pharmacies continues to be registered as increasing from 21,419 in 2021 to 22,798 in 2023; there is also an increase in the number of retail stores from 6,383 in 2020 to 7,411 in 2023. A slight increase was recorded in medicines distributors, from 2,250 units in 2020 to 2,281 units in 2022. In 2023 there is a slight reduction with 2,278.

Regarding community assistance, a reduction in the number of General Practitioners (GPs) has continued, from 44,279 units in 2016 (7.30 GPs per 10,000 inhabitants) to 41,707 units (6.99 GPs per 10,000 inhabitants) in 2020, to 39,366 units in 2022 (6.67 GPs per 10,000 inhabitants). A reduction by more than 2,341 units was observed in the three-year period 2020-2022, compared with a decrease by more than 4,500 units in the period 2016-2022, corresponding to an overall percentage reduction of about 9%.

The number of Free Choice Paediatricians also show a steady decrease, from 7,662 units in 2016 to 6,962 units in 2022 (with a more than 320 unit reduction in the three-year period 2020-2022, and a more than 700 unit reduction in the period 2016-2021, corresponding to an overall percentage reduction of more than 8%).

Considering the incidence of Free Choice Paediatricians (referring to children aged <15 years – values for every 10,000 children) in the period 2016/2021, a gradual increase from 9.30 in 2016 to 9.43 in 2020 and a reduction to the value of 9.20 and 9.29 in 2021 and 2022, respectively, are observed.

Finally, as regards the number of local health authorities on the national territory, their number has remained substantially unchanged, amounting to 99 in 2020/2021 and increasing to 110 in 2023. This increase in 2023 was determined by the territorial reorganisation carried out by the Region of Marche.

Table 2.1 Context indicators of healthcare in Italy

	2016	2017	2018	2019	2020	2021	2022	2023
Total hospital discharges (1)	9,061,064	8,872,090	8,691,638	8,520,801	6,803,328	7,317,074		
Total days paid (1) (2)	61,236,601	59,955,328	59,533,633	58,799,017	49,618,858	51,731,119		
Beds in ordinary acute stay (3)	158,113	155,929	155,446	153,945	151,607	176,709		
Beds in ordinary long-term stay (3)	8,767	8,332	8,373	8,198	8,056	7,989		
Beds in ordinary rehabilitation stay (3)	24,674	24,487	24,632	24,867	24,851	24,870		
Beds in day hospital stay (3)	22,067	21,278	20,886	20,562	20,374	19,896		
Beds in ordinary stay for 1,000 inhabitants (3)	3.16	3.12	3.12	3.13	3.10	3.54		
Beds in day hospital stay for 1,000 inhabitants (3)	0.36	0.35	0.35	0.34	0.34	0.34		
Average ordinary rehabilitation stay (1)	25.80	25.50	26.10	26.20	27.50	27.0		
Average long-term stay (1)	27.60	24.10	24.20	24.50	24.60	26.10		
Relationship between Dh and OR days (acute) (1)	0.12	0.11	0.11	0.10	0.09	0.09		
Average ordinary acute stay (1)	6.90	6.90	7.00	7.00	7.5	7.4		
Average weight (1) (4) (5)	1.19	1.19	1.22	1.24	1.31	1.33		
Average no. of diagnosis for ordinary stay (1) (4)	2.50	2.80	2.50	2.50	2.60	2.60		
Average no. of procedures for ordinary stay (1) (4)	2.90	2.90	3.00	3.10	3.20	3.40		
No. of MAHs (6)			817	849	844	861	875	871
No. of Medicine Distributors (7)			2,273	2,327	2,250	2,276	2,281	2,278
No. of Pharmacies (7)			19,782	20,375	18,871	20,233	21,419	22,798
Pharmacies per 10,000 inhabitants			3	3	3	3	4	4
Inhabitants per pharmacy			3,058	2,962	3,160	2,928	2,755	2,581
No. of Shops (7)			6,438	6,644	6,383	6,901	7,323	7,411
Inhabitants per shop			9,395	9,085	9,344	8,584	8,061	7941
Shops per 10,000 inhabitants			1	1	1	1	1	1
No. of GPs (8)	44,279	43,731	42,987	42,428	41,707	40,250	39,366	
No. of GPs per 10,000 inhabitants (8)	7.30	7.22	7.12	7.03	6.99	6.79	6.67	
No. of Free Choice Paediatricians (8)	7,662	7,590	7,499	7,408	7,285	7,022	6,962	
No. of Free Choice Paediatricians per 10,000 inhabitants <15 years (8)	9.30	9.33	9.35	9.41	9.43	9.20	9.29	
No. of Local Health Authorities (9)	121	101	101	101	99	99	106	110

(1) Ministry of Health - Annual Report on hospital admission activity - Ordinary stay data 2021 (page 92); (2) Total of hospital admissions, including nursery; (3) "Istituti di cura" (Healthcare Facilities) dataset on ISTAT website; (4) Ordinary acute admissions; (5) DRG relative weight pursuant to Ministerial Decree 1997 (up to 2005), Medicare 2002 (2006-2008), pursuant to MD 18/12/2008; (6) Medicines Database, Italian Medicines Agency; (7) Medicines manufacturing and distribution chain dataset, "Open data" section, Ministry of Health; (8) "Assistenza sanitaria di base" (Primary Healthcare) dataset on ISTAT website; (9) "Aziende Sanitarie Locali" (Local Health Authorities) dataset, Open data section, Ministry of Health

3. Analysis of health expenditure in Italy and international comparison

Table 3.1 presents Eurostat data on the development of total health expenditure and GDP in Italy in the years 2012 to 2022. Compared to 2012, 2013 shows a reduction in both GDP and expenditure. During the subsequent years, the total health expenditure shows an upward trend, but maintains a decreasing incidence compared to GDP over time, which is always above 8.6%. In 2020, the incidence of health expenditure over GDP reached 9.6%, equal to an increase of around one percentage point, mainly due to a 7.5% reduction in GDP and, to a greater extent, to the increase in expenditure (+2.6%). In 2021 and 2022, there is again a decline in the share of healthcare spending on GDP (9.4% and 9.0% respectively), while both spending and GDP increase (Table 3.1 and Figure 3.1).

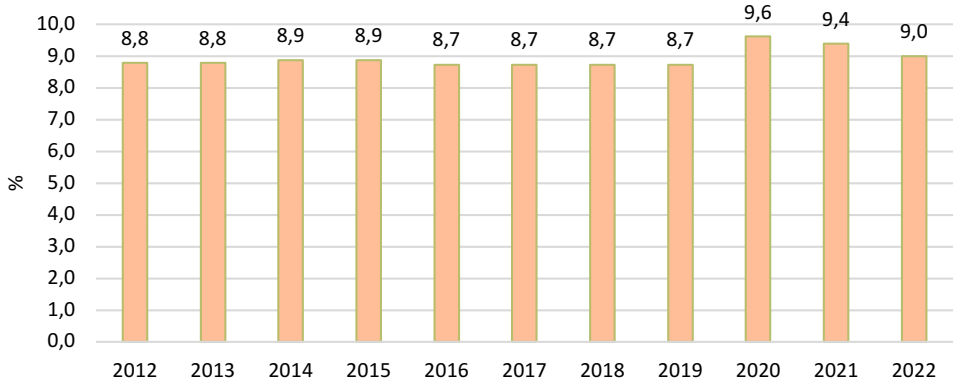
Table 3.1 Impact of total health expenditure over GDP: 2012-2023 comparison

Years	Total health expenditure *(EUR million)*	GDP *(EUR million)*	Incidence %
2012	142,676	1,624,359	8.8
2013	141,526	1,612,751	8.8
2014	144,317	1,627,406	8.9
2015	146,613	1,655,355	8.9
2016	147,963	1,695,787	8.7
2017	150,697	1,736,593	8.7
2018	153,790	1,771,391	8.7
2019	155,523	1,796,649	8.7
2020	159,628	1,661,020	9.6
2021	167,855	1,787,675	9.4
2022	171,867	1,909,154	9.0
2023	-	2,085,376	-

Source: Processing of Eurostat, OECD and ISTAT data

Figure 3.1 Percentage incidence of total health expenditure over GDP in Italy: 2012-2022 comparison

Source: Processing of Eurostat, OECD and ISTAT data



Using OECD data, a comparison was made of the incidence of total health expenditure over GDP in the main countries of the European Union and the United Kingdom (Table 3.2 and Figure 3.2). By analysing the data, the countries in question can be grouped into three main groups: the first consists of Germany and France, with an incidence of total health expenditure over GDP always above 11% as of 2015 and over 12% in the two-year period 2020-2022; the second consists of Austria, the United Kingdom, Belgium, Sweden, Portugal, Spain and Italy, which report a ratio between 9% and 11% of total health expenditure to GDP. Among the countries considered, only Poland shows steady values over time, between 6% and 7%.

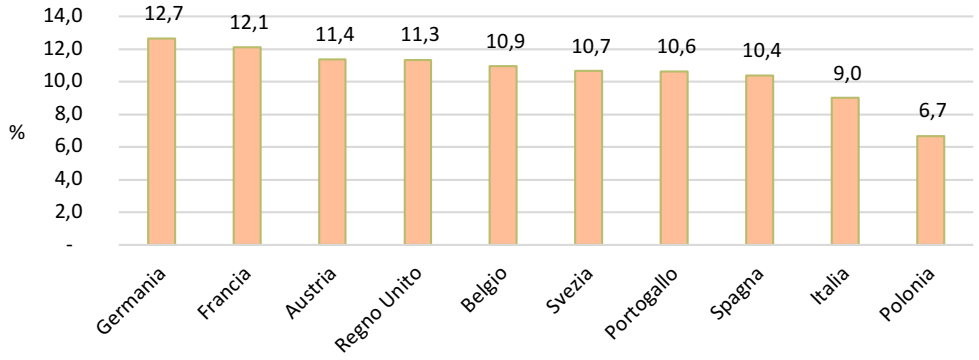
It is noteworthy that all countries, with the exception of Poland, have presented a reduction in the ratio of healthcare spending to GDP in 2022 compared to 2021, especially the United Kingdom, which presented a decrease of one percentage point compared to 2021 (from 12.4% to 11.3%).

Table 3.2 International comparison in the incidence of total health expenditure over GDP: 2013-2022

	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
	%	%	%	%	%	%	%	%	%	%
Germany	11.0	11.0	11.2	11.2	11.3	11.5	11.7	12.7	12.9	12.7
France	11.4	11.5	11.4	11.5	11.4	11.2	11.1	12.1	12.3	12.1
Austria	10.3	10.4	10.4	10.4	10.4	10.3	10.5	11.4	12.1	11.4
United Kingdom	9.8	9.8	9.8	9.7	9.6	9.7	10.0	12.2	12.4	11.3
Belgium	10.6	10.6	10.8	10.8	10.8	10.9	10.8	11.2	11.0	10.9
Sweden	10.9	10.9	10.8	10.9	10.8	10.9	10.8	11.3	11.2	10.7
Portugal	9.4	9.3	9.3	9.4	9.3	9.4	9.5	10.5	11.1	10.6
Spain	9.1	9.1	9.1	8.9	8.9	9.0	9.1	10.7	10.7	10.4
Italy	8.8	8.9	8.9	8.7	8.7	8.7	8.7	9.6	9.4	9.0
Poland	6.4	0.1	6.4	6.6	6.6	6.3	6.5	6.5	6.4	6.7

Source: Processing of OECD data

Figure 3.2 International comparison of the incidence of total health expenditure over GDP in 2022



Source: Processing of OECD data

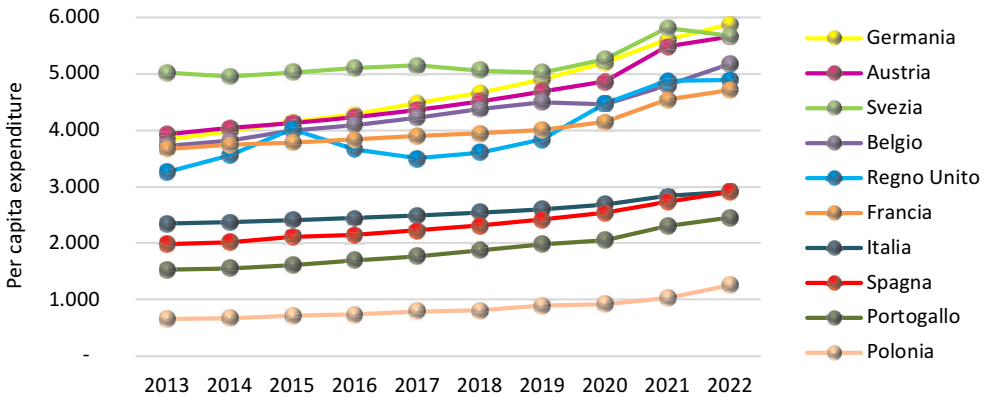
With regard to per capita health expenditure (Table 3.3 and Figure 3.3), countries can be grouped into three main groups. The first consists of Germany, Austria, Sweden and Belgium, which show a per capita health expenditure of more than EUR 5,000 in 2022. The second group consists of United Kingdom and France, with an amount between EUR 4,000 and EUR 5,000. The third group consists of Italy, Spain and Portugal, with a per capita expenditure between EUR 2,000 and EUR 3,000. Poland records an expenditure of just over 1,000 euros per capita.

Comparison of the percentage change in per capita health expenditure between 2013 and 2022 shows the largest increase in Poland (+89.9%), followed by Portugal (+60.1%), Germany (+53.3%) and the United Kingdom (+50.0%). Italy shows a 23.9% increase, while the remaining countries register an increase in per capita expenditure between 46.5% (Spain) and 13.0% (Sweden).

Looking at the 2021-2022 trend, the largest increases can be observed in Poland (+21.6%) and Belgium (+8.0%), while the only country registering a decrease was Sweden (-2.4%). Italy records a 2.6% increase, the lowest after the United Kingdom (+0.3%).

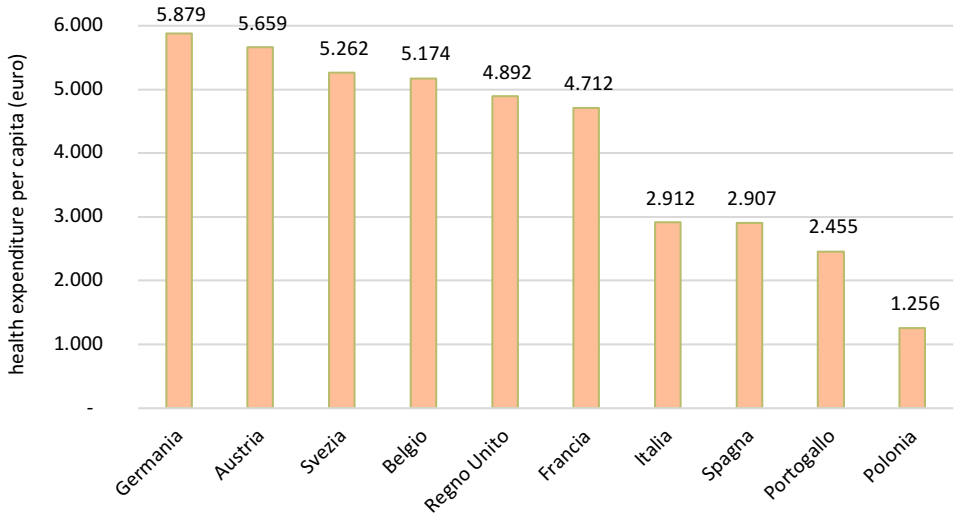
Table 3.3 International comparison – Trend in total per capita health expenditure (amounts in EUR) over the period 2013-2022 (Table and Figure)

	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	Δ% 22-13	Δ% 22-21
Germany	3,834	3,986	4,146	4,279	4,481	4,660	4,897	5,198	5,599	5,879	53.3	5.0
Austria	3,929	4,042	4,130	4,237	4,360	4,510	4,690	4,865	5,486	5,659	44.0	3.2
Sweden	5,019	4,955	5,022	5,099	5,147	5,061	5,025	5,260	5,813	5,670	13.0	-2.4
Belgium	3,724	3,814	3,991	4,097	4,225	4,373	4,498	4,462	4,790	5,174	39.0	8.0
United Kingdom	3,261	3,560	4,021	3,663	3,504	3,608	3,839	4,474	4,876	4,892	50.0	0.3
France	3,668	3,741	3,782	3,841	3,898	3,944	4,011	4,148	4,542	4,712	28.4	3.7
Italy	2,350	2,374	2,414	2,441	2,489	2,545	2,604	2,690	2,837	2,912	23.9	2.6
Spain	1,984	2,018	2,117	2,145	2,232	2,314	2,417	2,536	2,734	2,907	46.5	6.3
Portugal	1,533	1,554	1,616	1,697	1,770	1,878	1,983	2,054	2,308	2,455	60.1	6.4
Poland	661	676	718	738	791	813	896	922	1,032	1,256	89.9	21.6



Source: AIFA processing of OECD data For the year 2022 in all countries data are estimated or forecast. For Sweden and the United Kingdom, data in euros were extracted from Eurostat

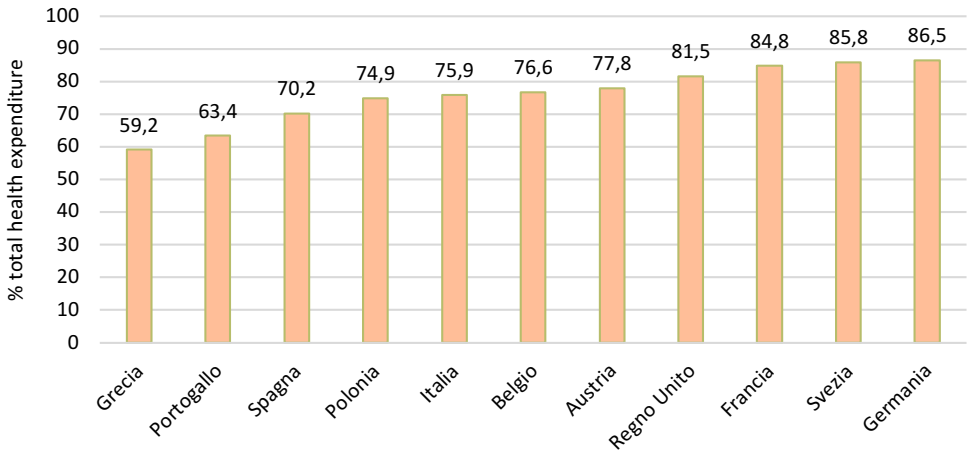
Figure 3.3 Total per capita health expenditure - 2022 (amounts in EUR)



Source: Processing of Eurostat data

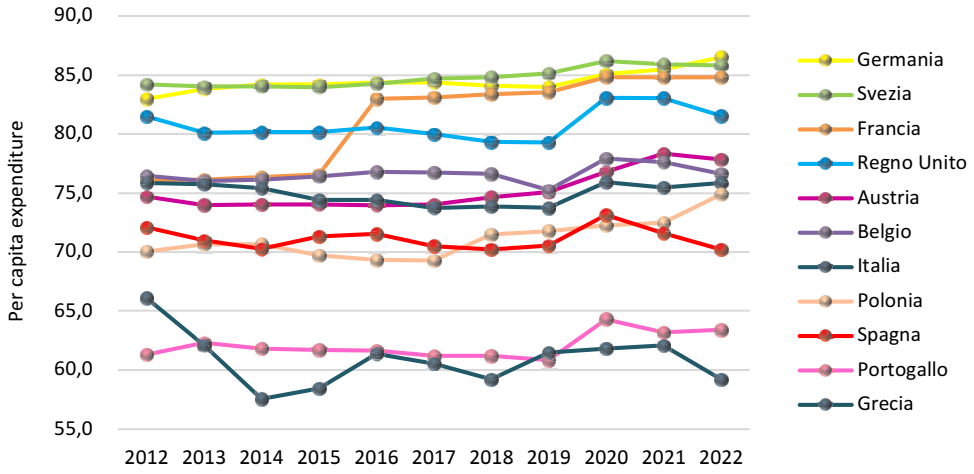
By analysing the incidence of public health expenditure, the countries with the largest share of public expenditure in 2022 were Germany (86.5%) and Sweden (85.8%). Conversely, countries showing the lowest incidence are Greece (59.2%) and Portugal (63.4%) (Figure 3.4). Looking at the trend over the 2021-2022 period, it can be seen that Poland shows an increase in the incidence of public spending (+2.4%), while Greece shows the sharpest decrease (-2.9%) (Figure 3.5).

Figure 3.4 Impact of public health expenditure in 2022: international comparison



Source: Processing of OECD data

Figure 3.5 Time trend in the incidence of public health expenditure over the overall health expenditure in the period 2010-2022: international comparison



Source: Processing of OECD data

4. Medicines reimbursement and supply scheme

The reimbursement and supply scheme, as well as the price of the medicine, is the result of relatively complex and very differentiated decision-making processes between the different European and non-European countries. In the Italian context, these processes depend on AIFA and its advisory bodies. In Italy, the medicinal products in the National Medicines List reimbursed by the NHS are classified in Class A or Class H when they are dispensed by hospitals or similar facilities (Article 8(10)(a) of Law No 537 of 24 December 1993 as amended). Alternatively, medicinal products may be classified in Class C when they are not reimbursed by the NHS, with the exception of people entitled to a direct life war pension (Article 1 of Law No 203 of 19 July 2000) in cases where the general practitioner attests to their proven therapeutic usefulness for the patient.

Medicinal products reimbursed by the NHS include essential medicines intended for the treatment of chronic diseases, reimbursed for any authorised therapeutic indication, unless there is an AIFA Note that restricts reimbursement to only some of them. This is in order to ensure the appropriate use of the medicine in question, guiding, in some cases, the therapeutic choices in favour of more effective and tested molecules. Consequently, Class A medicines, the therapeutic indications of which are not included in the Notes, are fully borne by the patient. Class C medicines are not considered essential medicines (compared with those reimbursed by the NHS) and can be dispensed to the citizen after the presentation of a medical prescription (C with prescription), or can bepurchased directly from the citizen without a prescription.

The latter category includes both Class C-bis medicines (Article 8(10)(c-bis), Law No 537/1993 as amended), called over-the-counter (OTC) medicines, and Class C-without-prescription

medicines, but that are not over the counter. By judgment No 2217 of 12 May 2017, the Italian Council of State (*Consiglio di Stato*) rejected the appeal brought by the Ministry of Health against the decision of the Lazio Regional Administrative Court No 7539/2016, confirming the full admissibility of advertising to the public of medicinal products without prescription not belonging to the category of self-medication medicinal products (OTC). By Ministerial Decree of 18 April 2012, implementing the provisions of Article 32(1) of Decree-Law No 201 of 6 December 2011, converted, with amendments, by Law No 214 of 22 December 2011, AIFA updated the supply scheme for Class C medicines with a prescription obligation, defining which medicines required the presentation of a medical prescription for being dispensed and which could be included in Class C without prescription, thus allowing them to be sold through the shops referred to in Article 32(1) of Decree-Law No 201/2011 (i.e. through large retailers and parapharmacies). Subsequently, Ministerial Decree of 18 April 2012 was updated, as it became necessary to supplement the list of medicines reclassified in Class C without prescription, on the basis of the prior opinion of the CTS (Ministerial Decree of 15 November 2012). This measure was further amended by the Decree dated 21 February 2014, thus amended by Decree dated 8 May 2014 (published in the Official Gazette No 119 of 24 May 2014).

In addition, Article 12(5) of Decree-Law No 158 of 13 September 2012, converted, with amendments, by Law No 189 of 8 November 2012 ('Balduzzi Decree') as amended, provided that medicinal products with a marketing authorisation granted under a centralised, decentralised, national and parallel import procedure are automatically classified in the new grouping 'C - Non Negotiated' (C-NN), pending submission by the MAH of a specific application for classification for the purposes of pricing and reimbursement. The MAH is required to notify AIFA, prior to marketing, the ex-factory price and the price to the public of the medicinal product classified in Class C-NN, as well as the date on which it was placed on the market. Then Law No. 118/2022 (Annual Law on the Market and Competition 2021) eliminated the possibility for the company concerned not to submit the application for the purpose of obtaining a different classification.

In addition, for orphan medicines or other medicines of exceptional therapeutic and social importance, it is established that, in case of non-submission within thirty days of granting the MA, AIFA shall urge the company to submit the request for price and reimbursement within the next thirty days. Once this term has expired, information is given on the AIFA's institutional website and the lowest price is applied within the fourth level of the Anatomic Therapeutic Chemical classification system (ATC) to which the medicine belongs.

When a pharmaceutical company submits the dossier to AIFA requesting pricing and reimbursement, AIFA competent offices and advisory bodies verify the regularity and completeness of the documentation and initiate the procedure aimed at assessing and deciding the place in therapy, as well as the reimbursement of the medicinal product. At the end of the decision-making process and the negotiation process by the Technical Scientific Commission (CTS) and the Price and Reimbursement Committee (CPR), the decision authorising the reimbursement of the medicinal product, its supply scheme and the price borne by the NHS is ratified by the AIFA Board of Directors and sent to the Ministry of Justice for publication in the Official Gazette.

For the purposes of supply, within the meaning of Article 87 of Legislative Decree No 219 of 24 April 2006, as amended, medicines can be classified as follows:

a) medicines subject to medical prescription (RR)
b) medicines subject to medical prescription that can be renewed from time to time (RNR)
c) medicines subject to special medical prescription (RMS) (Consolidated Law on narcotics - Presidential Decree No 309 of 9 October 1990, as amended)
d) medicines subject to restricted medical prescription, including:
   – medicines that can be sold to the general public upon prescription by hospitals or specialists (RRL; RNRL);
   – medicines that can only be used in hospitals or in a similar environment (H);
   – medicines that can only be used by specialists identified in accordance with the provisions of the Regions or Autonomous Provinces (USPL);
e) medicines not subject to medical prescription, including:
   – over-the-counter medicines (OTC)
   – other medicines not subject to medical prescription.

The renewable prescription is the most common form of prescription. It is valid for six months and the patient is automatically authorised to present it at the pharmacy up to ten times within that period. A particular case is the prescription of psychotropic medicines (anxiolytics, sedatives, hypnotics), for which the prescription is valid for thirty days and can be renewed no more than three times.
The non-renewable prescription is necessary for all medicines with potential risks of acute or chronic toxicity, addiction and tolerance and potential for abuse by the patient. This tool is much more rigorous than the previous one, as is based on the inability of the patient to access the medicine without the intervention of the doctor, who issues the necessary prescription from time to time.
The validity of the recipe is fixed at 30 days for the number of packages indicated (otherwise it is valid for three months if it relates to galenic preparations not containing narcotic substances). A particular case is isotretinoin, that can be prescribed and dispensed only within a teratogenic risk prevention program and upon presentation of a non-renewable prescription valid for seven days.
The restricted renewable and non renewable prescriptions are tools that limit the prescription and use of certain types of medicines to certain specialists or in certain settings. These are:

- medicines that can only be used in hospitals (Article 92 of Legislative Decree No 219/2006);
- medicines that can be sold to the public upon prescription by hospitals or specialists (Article 93 of Legislative Decree No 219/2006);
- medicines that can only be used by specialists in an outpatient setting (USPL) (Article 94 of Legislative Decree No 219/2006).

Pharmacies are not allowed to sell medicines included in the USPL category to the public, but may have tem, which can also be supplied directly to the specialist by manufacturers and wholesalers.

AIFA Decision No 1522 of 13 January 2010, published in Ordinary Supplement No 21 of Official Gazette No 25 of 1 February 2010, updated the supply scheme of hospital medicines. In particular, the previous H1 and H2 classifications for supply purposes were abolished and new ones entered into force on 16 February 2010. Medicines previously classified under the

H1 supply scheme were reclassified under the H scheme, without further changes to the already defined conditions and characteristics. Medicines previously classified as H2 had their supply scheme modified to RR, RNR, RRL or RNRL. Subsequently, in view of AIFA implementation of the provisions of Article 11(7)(a) of Decree-Law No 78 of 31 May 2010, converted, with amendments, by Law No 122 of 30 July 2010, as amended, most of Class H medicines with RR, RNR, RRL or RNRL supply scheme were reclassified into Class A-PHT (AIFA Decision of 2 November 2010).

Table 4.1 Number of medicines authorised and marketed in 2023 by reimbursement class

Class	MA number		Medicine		Active substances	
	No.	% over total	No.	% over total	No.	% over total
A	10,854	52.8	4,900	48.6	867	33.5
C	7,591	36.9	4,033	40.0	1,169	45.1
H	2,121	10.3	1,149	11.4	555	21.4
Total	**20,566**	**100.0**	**10,082**	**100.0**	**2,591**	**100.0**

5. Citizen cost-sharing

Law No 405/2001 as amended provided for the possibility for Regions to adopt resolutions to introduce/increase the cost shared by citizens, by introducing or modulating the cost per prescription or packs (the 'ticket'), in order to compensate for any deficits in regional pharmaceutical expenditure compared to the planned ceiling. This provision has been applied primarily in Regions subject to a repayment plan and to date in almost all other regions.

However, the citizen's share in the pharmaceutical expenditure does not derive exclusively from regional tickets, but also from the quota paid on expired patent medicines. Since 1 December 2001, medicinal products without patent coverage reimbursed by the NHS, including generics, have been grouped into AIFA Transparency Lists, currently drawn up on a monthly basis, in order to identify a single reference price for all interchangeable packages. The differential between the price of the prescribed medicine and the cheapest medicine with the same composition shall be borne by the patient. Specifically, if two medicines are available with the same active ingredient, route of administration, pharmaceutical form and dosage units, but with different prices, the NHS reimburses the medicine with the lowest reference price.

Since Article 7 of Law No 405/2001, as amended, defines the level of NHS reimbursement up to the lowest price of the corresponding product available in the normal regional distribution cycle, the possibility has been granted to fix reference prices by means of regional measures. That provision played an important role, in particular, in the early 2000s, when the availability of generic on the whole national territory, generally with the lowest price to the public, could not be guaranteed. As a matter of fact, to date, in most Italian Regions the reference prices correspond to the prices published in the AIFA Transparency Lists. A detailed analysis of the citizen cost-sharing for the reference price of generic is provided in section

2.1. Although citizen cost-sharing, given by the difference between the price to the public of the prescribed medicine and the reference price in the AIFA Transparency Lists, is substantially homogeneous in the national territory, with the exception of some Regions, the procedures for imputing the regional ticket to the citizen are, on the other hand, very diverse (Table 6.1). This condition is expressly permitted by Article 4 Law No 405/2001 as amended, which empowers Regions to apply measures to cover possible management deficits through the introduction of various initiatives, including *the introduction of forms of accountability of the main actors contributing to the determination of expenditure (so-called 'tickets')*. That option has become a legal obligation for regional governments by virtue of Article 5(4) of Decree-Law No 159 of 1 October 2007, converted, with amendments, into Law No 222 of 29 November 2007, which expressly provided for the adoption of measures to contain expenditure, including direct distribution, for an amount equal to at least 30% of the regional pharmaceutical expenditure deficit in relation to the ceiling. These measures constitute a regional fulfilment for accessing supplementary State financing.

There are nine regions that do not have cost-sharing (ticket) in 2023 as a means of containing NHS reimbursed pharmaceutical expenditure (Piedmont, P.A of Trento, Friuli Venezia Giulia, Emilia Romagna, Tuscany, Umbria, Marche, Basilicata and Sardinia).

At national level, the citizen share in the expenditure amounts to EUR 1.5 billion (of which 71% is attributable to the share of the reference price and the remaining 29% to the fixed ticket), representing 15.0% of gross reimbursed pharmaceutical expenditure and with a slight change of 1.36% compared to 2022. Concerning the citizen cost-sharing over the reference price, there is a marked variability at regional level: while the national value is equal to EUR 18.0 per capita (EUR 23.5 in the South and Islands, EUR 19.7 in the Centre and EUR 13.3 in the North), Calabria shows a value of EUR 26.2 per capita, which is more than double compared with the Autonomous Province of Bolzano (average of EUR 11.9 per capita Table 2.1.5).

Table 5.1 shows the main measures related to the ticket in the Italian regions in 2023, with the aim of providing a summary as comprehensive as possible (Source: Federfarma, https://www.federfarma.it/Ticket-Regionali.aspx), without prejudice to the exemptions provided for by current legislation (exemptions for income, chronic diseases, rare diseases, disability and situations of particular social interest).

Table 5.1 Way of application of regional tickets in 2023

Region	Exemption		Ticket (€)			AIFA Transparency List	Notes	Legal basis
	Income (€)	Condition	Package	Max prescription	Share on prescription			
Valle d'Aosta	0-9.999	yes	no	no	no	yes	Patients with chronic and debilitating diseases are exempt from ticket payment	DGR No 1899 of 28/12/2017
	10.000-25.000	no	1	2	no			
	>25.000	no	2	4	no			
Piedmont	N/A	yes	no	no	no	yes	Assisted persons identified by exemption codes E92, G01, G02, V01, V01.2 are excluded from paying the difference between the public price and the reference price for medicines on the transparency list	DGR No 57-5740 of 3/4/2002 DGR No 36-7965 of 28/12/2007 DGR No 16-3096 of 12/11/2011DGR No 39-8425 of 15/2/2019
		no	no	no	no			
Lombardy	>20000.00	no	2	4	no	yes + ticket		DGR No 4230 of 25/10/2012
		yes	1	3	no	yes	Chronic diseases and rare diseases; certain types of invalidity Chronic and rare diseases; some types of disability limited to single-dose antibiotics, IFN for hepatitis, drugs administered by IV (L.405/2001)	
	Up to 20000,00	no	no	no	no	yes		
Province of Bolzano	N/A	yes	no	no	1	yes + ticket	Chronic diseases Rare diseases, people with incapacity for work, civilian disabled, deaf people, victims	DGR No 1862 of 27/05/2002
		no	1	2	no		Fiscally dependent children	
		no	2	4	no			
Province of Trento	N/A	no	no	no	no	yes	No cost sharing	Provincial Law 14 of 23/12/2019
Veneto	>12,000	no	2	4	no	yes + ticket		
	Up to 12,000	yes	no	no	no	yes	Pain Therapy, severe invalidity, chronic diseases, rare diseases	DGR 744 of 11/03/2005

continued

Table 5.1 - *continued*

Region	Exemption		Ticket (€)			AIFA Transparency List	Income (€)	Condition
	Income (€)	Condition	Package	Max prescription	Share on prescription			
Friuli VG	N/A	no	no	no	no	yes	No cost sharing	
Liguria	N/A	no	2	4	no	yes + ticket	Also for single-dose antibiotics and medicines administered by phleboclysis	DGR No 163 of 20/2/2002 DGR No 1116 of 9/9/2011
		yes	no	no	no	yes	The victims of terrorism and people with disability by war are exempt from cost-sharing	
Tuscany	N/A	no	no	no	no	yes	No cost sharing	DGR No 1134 of 3/8/2020
Emilia-Romagna	N/A	no	no	no	no	yes	No cost sharing	DGR No 1044 of 24/8/2020
Umbria	N/A	no	no	no	no	yes	No cost sharing	DGR No 682 of 30/7/2020
Marche	N/A	no	no	no	no	yes	No cost sharing	
Lazio	N/A	yes	2	no	no	yes	Medicines with sale price >EUR 5, not included in the AIFA Transparency List	DCA 45 of 17/11/2008
		no	4	no	no			
		yes	1	no	no		Medicines with sale price ≤EUR 5, not included in the AIFA Transparency List	
		no	2.5	no	no			
Abruzzo	N/A	no	2	6	no		Medicines with sale price >EUR 5	DCA 26 of 4/7/2012
		yes	1	3	no			
		no	0.5	1.5	no		Medicines with sale price ≤EUR 5 and off-patent drugs with public price higher than the reference price	
		yes	0.25	0.75	no	yes + ticket		
		no	no	no	no	yes	Chronic and Disabled Diseases Medicines not covered by a patent with an aligned price	

continued

Table 5.1 - *continued*

Region	Exemption		Ticket (€)			AIFA Transparency List	Notes	Legal basis
	Income (€)	Condition	Package	Max prescription	Share on prescription			
Molise		no	2	6	0.5	yes + ticket	Medicines covered by patent with a sale price >EUR 5	DGR 1188 of 29/7/2002 DD.CC.AA 87 and 97/2011 Circular 4702 of 3/4/2012
			0.5	no			Expired patent medicines with a sale price >EUR 5	
			no	no		yes	Pain therapy	
	Da E01 a E04		no		0.5	yes	Partial exempts	
Campania	N/A	no	1.5	no	2	yes + ticket	Per-package cost sharing does not apply to off-patent drugs with a price aligned with the regional reference price. Apply to oxygen prescriptions and PHT medicines	DCA 67 of 4/11/10, DC 141 of 31/10/2014, DC 147 of 24/12/2014, DC 34 of 13/3/2015
			no	no	2	yes	Off-patent drugs with price aligned to reference price	
		yes	no	no	1	yes	Disability and chronic and debilitating diseases with income lower than €50,000	
		no	no	no	no	yes	Pain therapy	
Puglia	> 23,000	no	2	5.5	1	yes + ticket		DGR 1718 of 19/11/2004 DGR 1198 of 6/8/2005 DGR 2789 of 14/12/2010 DGR 1389 of 21/6/2011, DGR 1391 of 21/6/2011
		yes	0.5	no	1		Single-dose antibiotics, IFN for hepatitis, medicines administered by intravenous injection (L.405/2001)	
		no	no	no	1		Medicines included in the Transparency List	
		no	no	no	1		Disability, pain therapy, victims of terrorism, chronic and disabling diseases, rare diseases	
	< 23,000	no	1	no	1	yes		
		no	no	no	no	yes	Minimum pensions	

continued

Table 5.1 - *continued*

Region	Exemption		Ticket (€)			AIFA Transparency List	Notes	Legal basis
	Income (€)	Condition	Package	Max prescription	Share on prescription			
Basilicata	N/A	no	no	no	no	yes	No cost sharing	DGR 496 of 17/7/2020
Calabria		no	2	5	1	yes		DGR No 247 of 5/5/2009
		yes	no	no	no	yes	Chronic diseases, rare diseases	
			no	no	1	yes	Invalids for work L01-L03, service and civilians C03	
		no	no	no	no	no	War invalids holding lifetime pensions and victims of terrorism and organized crime	
	Da E01 a E04		no	no	no	yes		
Sicily	N/A	no	4	no	no	yes	Medicines with sale price ≤EUR 25	Regional Law 6 of 10/1/2012
		yes	1.5					
		no	2				Generics with sale price ≤EUR 25	
		yes	1					
		no	4.5			yes	Medicines with sale price >EUR 25	
		yes	2					
		no	2.5				Generics with sale price >EUR 25	
		yes	1.5					
			no		no	no	War invalids holding life pensions and victims of terrorism and massacres and their family members (spouse, children or, in the absence of the aforementioned, their parents)	
					no	yes	100% civilian invalids, severely disabled by service or work, prisoners, damaged by vaccinations, transfusions, unemployed according to total household income, persons under 6 or over 65 according to income	
Sardinia	N/A	no	no	no	no	yes	No cost sharing	

* difference between medicine price and reference price

Exemptions

(Source Ministry of Health, 2019; http://www.salute.gov.it/portale/esenzioni/homeEsenzioni.jsp)

Income exemptions

E01: Citizens under six years of age and over sixty-five years of age, belonging to a household with a total annual income not exceeding EUR 36,151.98.

E02: Unemployed and their dependent family members belonging to a household with a total annual income of less than EUR 8,263.31, increased to EUR 11,362.05 if there is a spouse and by additional EUR 516.46 for each dependent child.

E03: Holders of social pensions and their dependent family members.

E04: Holders of pensions aged over sixty and their dependent family members, belonging to a household with a total annual income of less than EUR 8,263.31, increased to EUR 11,362.05 if there is a spouse and by additional EUR 516.46 for each dependent child.

Chronic diseases

The list of chronic diseases exempt from participation in the cost of benefits has been redefined and updated by Annex 8 of the Decree of the President of the Council of Ministers on the new LEAs of 12 January 2017.

Rare diseases

The list of rare diseases exempted from cost sharing has been extended by Annex 7 to Decree of President of the Council of Ministers of 12 January 2017 defining the new Essential Service Levels. The new exemptions for rare diseases entered into force on 15 September 2017, to give the Regions time to identify reference centres experienced in the treatment of new diseases.

Disability

Only people with disability by war, direct pensioners and victims of terrorism have the right to receive free of charge medicines belonging to class “C”, based on GP prescription attesting to their proven therapeutic usefulness.

Other exemptions for situations of particular social interest

Maternity protection, limited to the services defined by the Decree of the President of the Council of Ministers of 12 January 2017 (Annex 10).
Prevention of the spread of HIV infection, limited to the assessment of the state of infection, in favour of subjects belonging to categories at risk, with behaviour at risk or incidentally exposed to risk of infection.
Promotion of donations of blood, organs and tissues, limited to the services related to the donation activity.
Protection of persons damaged by irreversible complications due to mandatory vaccinations, transfusions and administration of blood products referred to in Law No 210 of 25 February 1992, limited to the services indicated therein.
Victims of terrorism and organised crime.

6. Price of medicines

Since 1 January 2004 the price of all medicines reimbursed by the NHS has been set following negotiation between AIFA and the manufacturers, based on methods and criteria that had been previously applied to centralised procedures.
In the context of the negotiations, the parameters set out in Ministerial Decree of 2 August 2019 (OJ General Series n.185 of 24-07-2020) are taken into account, according to which the following supporting documents should be included by the company in its request for negotiation:

- scientific documentation on the potential added therapeutic value of the medicine, in relation to the main treatments with which the product is compared;
- the economic assessment;
- documentation on marketing, consumption and reimbursement in other countries, and in that case, the relevant price and reimbursement conditions, including any further negotiation agreements;
- the annual market shares expected to be acquired over the next 36 months in the specific market segment;
- the certification by the company about its production capacity and management of possible unforeseen events that could put production standards at risk as well as the activities that will be put in place in order to ensure the adequate supply of the medicines to the NHS according to the needs of the population;
- the forecast and changes in expenditure for the NHS resulting from the proposed prices, in their separate components;
- self-certified quantification of any public contributions and incentives aimed at promoting research and development programmes;
- quantifications of the economic and financial impact on the NHS and consumption resulting from the possible inclusion of the medicine in early access programmes.

The pricing and reimbursement process is characterised by four steps:

1. the pharmaceutical company submits the request for the price and reimbursement to AIFA;
2. the CTS assesses the dossier and gives a binding opinion on the therapeutic value of the medicine, defining its place in therapy, its supply regime and its possible innovativeness;
3. the CPR, taking into account the opinion expressed by the CTS, assesses the dossier and, where necessary, convenes the applicant for negotiation;
4. the result of the negotiation, in case of admission to reimbursement, is submitted to the final assessment of the Board of Directors (BoD) of AIFA. The opinions of the CTS and the decisions of the CPR shall be delivered within a total of 180 days from the date of submission of a valid application, and the company's revenue price is published in the Official Gazette.

Decree-Law No. 169 of Nov. 8, 2022, provided for the establishment of a single commission called the Scientific and Economic Commission on Drugs (CSE), which is given the functions of the Scientific and Technical Advisory Commission (STC) and the Committee on Pricing and Reimbursement (CPR). The new Commission took office in March 2024, and in April 2024 the Rules governing its organization and operation were approved.

By way of derogation from those provisions, Decree-Law No 69 of 21 June 2013, converted, with amendments, by Law No 98 of 9 August 2013,amended Decree-Law No 158 of 13 September 2012, converted, with amendments, by Law No 189 of 8 November 2012, by introducing paragraph 5-bis, which provided that orphan medicines, hospital medicines or medicines of exceptional therapeutic and social importance should be assessed as a priority over the proceedings pending on the date of submission of the application, including through the establishment of extraordinary sessions of the CTS and CPR, within the period of 100 days (see also Section 5 Orphan medicines). Moreover, for these medicines, the current legislation provides for a further facilitation, i.e. the right for the company to submit to AIFA – in case of a positive opinion by the EMA – the application for price and reimbursement before the issue of their marketing authorisation by the European Commission.

In order to shorten negotiation time, AIFA has introduced, starting in 2020, simplified procedures for certain categories of drugs/negotiating procedures, such as:

- generic medicines/biosimilars (starting from October 2020)
- parallel imported drugs (starting from March 2021)
- Equivalent or biosimilar drugs, for claims for reimbursement of extension of indications already reimbursed to the originator (from November 2021)
- New packs due to change in primary packaging (from November 2021).

With regard to Class A medicines dispensed through local pharmacies, under agreed disbursement arrangements, the price published in the Official Gazette is the same as the price to the public of the individual pack, including the quota borne by the citizen, any mandatory discounts payable by pharmacies and pharmaceutical companies and the value added tax. Consequently, the price charged to the NHS is the same as the public price net of both discounts and any quota borne by the citizen. The ex-factory price, excluding VAT, is also published in the Official Gazette.

For Class A and H medicines purchased by public health facilities, the price charged to the NHS is the same as the ex-factory price resulting from purchase tenders or determined as a result of direct negotiation by the health authority (or the Region) with the pharmaceutical company, including VAT.

In the case of Class C medicines, the price is determined independently by the pharmaceutical company. It is not published in the Official Gazette, but is communicated to AIFA. For Class C prescription medicines - with the exception of C-bis medicines - the price may be increased only in January of each odd year (Decree-Law No 87 of 27 May 2005, converted, with amendments, by Law No 149 of 26 July 2005), while reductions are always allowed.

Article 9-ter(11) of Decree-Law No 78 of 19 June 2015 (D-L. Local Authorities), converted with amendments by Law 125/2015, with regard to the definition of the price of medicinal products, supplemented Article 48 of Decree-Law No 269 of 30 September 2003, converted, with amendments, by Law No 326 of 24 November 2003 and subsequent amendments thereto. It introduced paragraph 33-bis, which provides that, upon expiry of the patent on the active substance of a biotechnological medicinal product and in the absence of a concomitant price negotiation procedure for a biosimilar or therapeutically equivalent medicinal product, AIFA shall initiate a new price negotiation procedure with the marketing authorisation holder of the same biotechnological medicinal product, in order to reduce the reimbursement price borne by the NHS. Paragraph 33-ter was also included, providing that, for medicines subject to AIFA Monitoring Registries, AIFA will start a new negotiation procedure

with the marketing authorisation holder, in order to reduce the price in case the benefits found, two years after the granting of the MA, have been lower than those identified under the negotiation agreement.

7. Distribution margins and discounts for the NHS

The margins of pharmaceutical companies, wholesalers and pharmacies for medicines payable by the NHS are equal to 66.65%, 3.0% and 30.35% respectively, of the selling price to the public, excluding VAT (Law No 662 of 23 December 1996 as amended). At the same time, the NHS makes a deduction from the pharmacies quota equal to 1.82% of the price for the public exclusive of VAT (this quota does not apply to subsidised rural pharmacies in areas with resident population of less than 3000 inhabitants and with annual turnover not exceeding EUR 387 324,67 as well as to other pharmacies with an annual turnover not exceeding EUR 258 228,45). Pharmaceutical companies pay to the Regions an amount of 1.83% of the price for the public exclusive of VAT. The change in the margins of wholesalers and pharmacists, provided for in Article 11(6) of Decree-Law No 78/2010, converted with amendments by Law No 122/2010 as amended, also involves medicines with expired patent. In the case of generics, excluding medicines originally covered by a patent or which have been licensed under that patent, the share of the pharmaceutical companies remains equal to 58.65%, as provided for by Decree-Law No 39 of 28 April 2009, converted, with amendments, by Law No 77 of 24 June 2009, and the remaining 8% (66.65%) is redistributed among pharmacists and wholesalers in accordance with market rules.

Decree-Law No 95/2012, converted with amendments by Law No 135/2012 as amended, introduced some important provisions concerning the governance of pharmaceutical expenditure, including the increase in the discount for pharmacies from 1.82% to 2.25%, currently in force, and the temporary increase in the burden on pharmaceutical companies from 1.83% to 4.1% until 31 December 2012.

Table 7.1 shows the discounts paid by pharmacies in favour of the NHS, updated by Decree-Law No 148 of 16 October 2017, converted with amendments by Law No 172 of 4 December 2017 (Article 18-bis(2)). These changes have been applied as of 1 January 2018.

Decree-Law No 41 of 22 March 2021 introduced, for 2021 and 2022, an additional remuneration to pharmacies for the reimbursement of medicines dispensed under the NHS scheme, in order to structurally strengthen the resilience, proximity and timeliness of the NHS response to emerging infectious diseases and other health emergencies, as well as the COVID-19 vaccination activity in pharmacies. The remuneration and its regional breakdown was recognised by Ministry of Health Decree dated 11 August 2021, adopted in agreement with the Ministry of Economy and Finance and published in the Official Gazette of 29 October 2021. A total of EUR 200 million was allocated, of which EUR 50 million from 1 September to December 2021 and EUR 150 million for 2022. The 2023 Budget Law confirmed, as from 1 March 2023, the additional remuneration for pharmacies for the reimbursement of medicines dispensed under the NHS scheme, up to EUR 150 million per year from 2023.

As of March 1, 2024, the system of remuneration of pharmacies on drugs dispensed under the NHS replaces the 30.35% provided by the previous legislation with a percentage fee and a series of fixed fees, determined as follows:

a) a percentage share of 6% of the public price net of VAT for each drug pack;
b) a fixed fee of 0.55 euros for each drug pack with a retail price not exceeding 4.00 euros;
c) a fixed fee of 1.66 euros for each drug pack with a retail price ranging from 4.01 to 11.00 euros;
d) a fixed fee of 2.50 euros for each drug pack with a retail price not exceeding 11.00 euros;
e) an additional fixed fee of 0.10 euros per each drug pack belonging to the transparency lists, for the year 2024 only. From January 1, 2025, this fixed fee is set at 0.115 euros.

The new system also provides additional allowances for specific types of pharmacies with low NHS revenue:

a) an additional fixed fee of 1.20 euros for each drug dispensed by pharmacies with NHS revenue not exceeding 150000,00 euros after VAT;
b) an additional fixed fee of 0.58 euros for each drug dispensed by pharmacies, excluding those referred to in (c), with NHS revenue not exceeding 300000,00 euros after VAT;
c) an additional fixed fee of 0.62 euros for each drug dispensed by subsidized rural pharmacies, as defined by Law No. 221 of March 8, 1968, with NHS revenue not exceeding 450000,00 euros after VAT.

Table 7.1 Discounts to pharmacies on medicines dispensed under the NHS scheme

Age price (EUR)	Rates for unsubsidised urban and rural pharmacies (%) not in combination (%)			Rates for subsidised rural pharmacies (%) in combination (%)		
	NHS Turnover					
	higher than 300,000	lower than 300,000 e higher than 150,000	lower than 150.000*	greater than 450,000	lower than 450,000 and higher than 150,000	lower than 150.000*
0 to 25,82	3.75	1.50	Exemption total	3.75	fixed rate 1.5	Exemption total
from 25.83 to 51.65	6.0	2.40		6.0	fixed rate 1.5	
from 51.66 to 103.28	9.0	3.60		9.0	fixed rate 1.5	
from 103.29 to 154.94	12.50	5.0		12.50	fixed rate 1.5	
more than 154.94	19.0	7.60		19.0	fixed rate 1.5	
further deduction	2.25	-		2.25	-	

* introduced by Law No 145 of 30 December 2018

8. Methods of dispensing medicines charged to the NHS

In light of the national legislation regulating the reimbursement of medicinal products and their supply scheme, within the pharmaceutical assistance structure, it is possible to identify different methods for the supply of medicines reimbursed by the NHS, depending on their dispensing and use in both outpatient and inpatient settings. In particular, medicines in the outpatient setting are dispensed based on the prescription by general practitioners and free-choice paediatricians, as well as on the prescription or issuance of therapeutic plans by specialised doctors operating in public health facilities. While in the first case the prescribed medicine is dispensed to the patient by affiliated, public and private, pharmacies that can be found in the national territory (conventional dispensing scheme), in the second case the medicine taken by the patient at home is dispensed either directly by healthcare facilities (direct distribution) or, alternatively, by affiliated pharmacies as a result of specific agreements signed locally (distribution on behalf of the public health facility). Article 8 of Decree-Law No 347 of 18 September 2001, converted, with amendments, by Law No 405 of 16 November 2001, as amended, introduced the direct distribution and the on-behalf distribution as alternative methods for dispensing medicinal products, as opposed to the conventional dispensing scheme. These arrangements provide for the purchase by public facilities of high-consumption medicinal products and their dispensing through:

- direct distribution by public health facilities to the patient for the first course of therapy, following hospital discharge or after specialist outpatient visits, or to patients who need periodic controls. This dispensing scheme does not only contribute to limiting expenditure, but also helps ensuring the clinical safeguard of the patient and the therapeutic continuity from the inpatient to the outpatient setting, as well as the appropriate use of medicines;
- distribution on behalf of local health authorities, by pharmacies open to the public on the basis of specific agreements concluded by the Regions and Autonomous Provinces with the associations of the affiliated pharmacies, to allow patients suffering from chronic diseases and who, therefore, require continuous pharmaceutical assistance, to obtain supplies from local pharmacies.

An overview of DPC agreements in Italian regions and update on Pharmacy of Services

Distribution on behalf (DPC), introduced by Law No. 405 of Nov. 16, 2001, requires the NHS to purchase the drug and territorial pharmacies to distribute it to patients, with compensation agreed for this service. In view of the fact that the health care organization is regional in nature, the management of this distribution also takes on different characteristics depending on the region. In addition to dispensing medication per conto, pharmacies can provide a range of services paid by the NHS, the so-called ''Pharmacy of Services.'' Although some mention can already be found in Law No. 69/2009 (Art. 11), the Pharmacy of Services saw its origins in three ministerial decrees (DMs). 153/2009: Ministerial Decree Dec. 16, 2010 (GU No. 57, March 10, 2011 and GU No. 90, April 19, 2011) and Ministerial Decree July 8, 2011 (GU No. 229, Oct. 1, 2011). Specifically, the two decrees of Dec. 16, 2010 regulate first-line analytical services (e.g., 'self-diagnostic' tests), second-line services that can be delivered with instrumental devices (e.g., spirometry), as well as professional services that can be delivered in pharmacies (e.g., nurse, physical therapist). In contrast, the decree of July 8, 2011 regulates the booking of specialist services at pharmacies. The "Budget Law of 2018" pro-

vided for the possibility for local pharmacies to offer a range of services with charges borne by the NHS. Thus, the Pharmacy of Services represents an evolution of the activity of pharmacies in primary care, the aim of which is to integrate the pharmacy network within local activities of the National Health System, based on new care services provided. The dispensing of drugs, counseling and health education, traditionally carried out by pharmacies, is thus joined by a range of health and prevention-related services. Specifically, the aforementioned 2018 Budget Law provided for the launch in nine regions (for the 2018-2020 three-year period) of a trial for the remuneration of services and care functions under Legislative Decree No. 153/2009, provided by pharmacies at the expense of the NHS, while authorizing the expenditure of 6 million euros for the year 2018, 12 million euros for 2019 and 18 million euros for the year 2020. The Ministerial Decree of May 17, 2018 identified the nine regions involved in this experimentation, including three for the year 2018 (Piedmont, Lazio and Apulia), an additional three for 2019 (Lombardy, Emilia-Romagna and Sicily), and an extra three for 2020 (Veneto, Umbria and Campania).

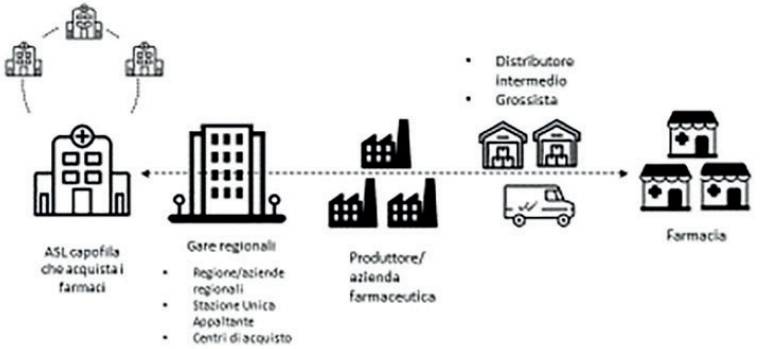
This experimentation was extended by the State-Regions Conference for the two-year period 2021-2022, extending it to the remaining ordinary statute regions, and authorising the expenditure of EUR 25.3 million annually. In addition, the Decree-Law of 30 December 2023 extends the trial of the Service Pharmacy to 2024 and provides for an evaluation of the results of the trial at the end of the same year.

The descriptive analysis, summarised in the figure below (Figure 8.1), aims to take a concise overview of the contents of the regional agreements for the DPC and the state of the art of the 'Pharmacy of Services', in order to provide an insight into the state of the art of distribution 'on behalf' and 'per conto' in Italy, updating the information published in the Osmed 2023 Report. The methodology involved an initial phase of reviewing and updating the agreements for the DPC by the regional pharmaceutical contact persons, which was followed by a request to supplement some of the information provided with a focus on the topic of Service Pharmacy. The variables taken into account, in continuity with previous years, and summarised in the table below are: regional determination of the agreement, duration of the agreement, organisation of DPC distribution, medicines possibly excluded or criteria taken into account, remuneration per pack, DPC ceilings, drug substitutability, management of mixed prescriptions, management of medicines unavailable in the channel and urgent prescriptions, activation of the 'service pharmacy'.

Figure 8.1 DPC organisational models and inter-regional variability (year 2023)

Model 1.
A lead company buys the drugs on the basis of tenders issued by the region or other regional authorities and asks the manufacturer to deliver the DPC drugs directly to the intermediate distributors in charge of storage and distribution to pharmacies under agreement.

Regions: Abruzzo Basilicata, P.A. Bolzano, Campania, Lombardy, Puglia, Sicilia, P.A. Trento, Aosta Valley



Model 1.1
A lead company buys the drugs on the basis of tenders issued by the region or other regional authorities and asks the manufacturer to deliver the DPC drugs directly to the intermediate distributors in charge of storage and distribution to pharmacies under agreement.
Model 1 is also used in Calabria Lazio and Umbria, however with some additions. Calabria provided a lead distributor and intermediate distributors in a radial pattern, and also a software, 'Procuro', to search for the product on all warehouses following a pharmacy order. Umbria, like Calabria, has radial distribution, but no information was received on an integrated DPC software. Lazio has two lead intermediate distributors and an integrated IT system.

Regions: Calabria, Latium, Umbria

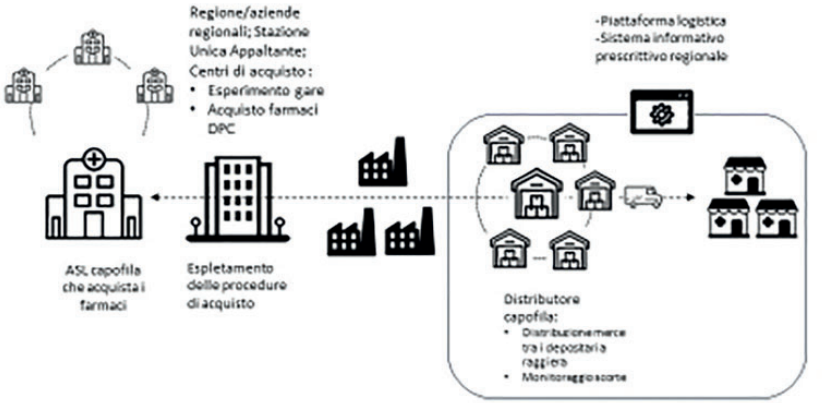


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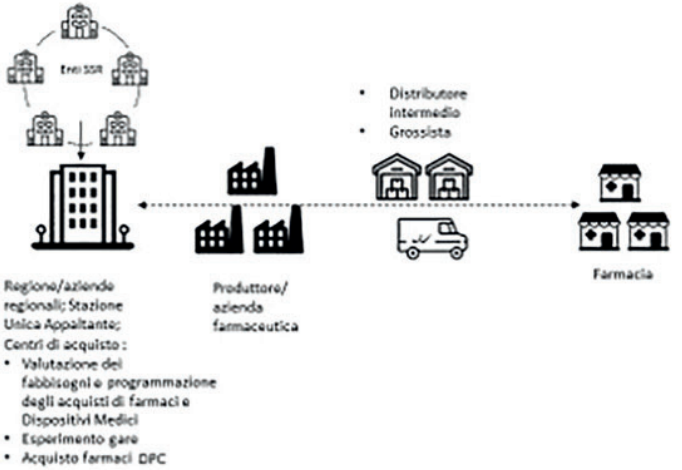
Figure 8.1 - *continued*

Model 2.
A lead company buys the drugs on the basis of tenders issued by the region or other regional authorities and asks the manufacturer to deliver the DPC drugs directly to the intermediate distributors in charge of storage and distribution to pharmacies under agreement.

Regions: Molise, Toscana, Liguria, Veneto, Sardinia



Model 2.2
A lead company buys the drugs on the basis of tenders issued by the region or other regional authorities and asks the manufacturer to deliver the DPC drugs directly to the intermediate distributors in charge of storage and distribution to pharmacies under agreement.
Model 2 is also used in Friuli Venezia Giulia, however with some additions. Friuli Venezia Giulia has provided a lead distributor and intermediate distributors in a radial pattern and also a software, 'goopenDPC System', to search for the product on all warehouses following the pharmacy order.

Regions: Piedmont, Friuli Venezia Giulia

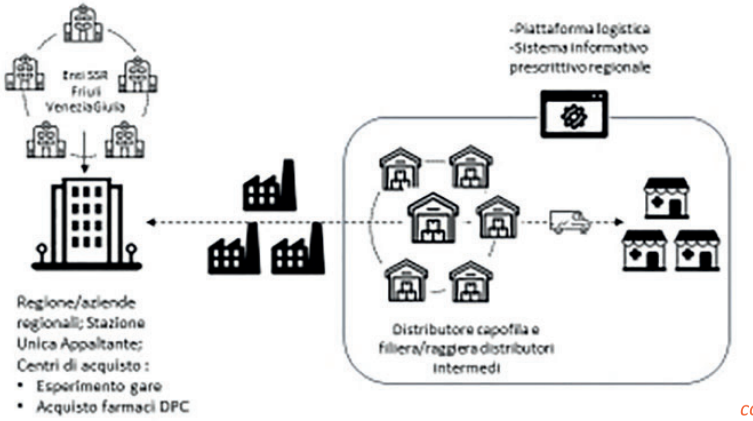


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Figure 8.1 - *continued*

Model 3

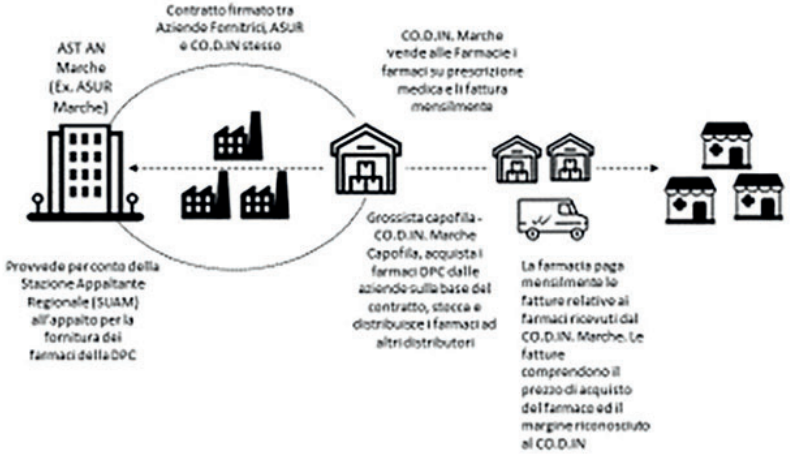
The local health authorities purchase drugs on the basis of tenders issued at regional level. Some local health authorities require the manufacturer to deliver DPC drugs directly to a lead distributor. The latter stores the drugs and distributes them to a series of satellite distributors. These make the delivery to pharmacies under agreement.

In Emilia-Romagna, some local health authorities receive, store and distribute drugs to intermediate distributors.

Regions: Emilia-Romagna

Model 4 – Region Marches

The former ASUR Marche, now replaced by AST AN pursuant to L.r. 19/2022 and DGR 1839/2022, is in charge of the Regional Contracting Authority (SUAM) for the supply of DPC drugs.
A leading wholesaler - CO.D.IN. Marche - buys DPC medicines from the supplier companies on the basis of a contract signed between Suppliers, ASUR and CO.D.IN itself; the lead wholesaler stores and distributes the drugs to other distributors (couriers) who supply the pharmacies under agreement.



In order to collect any updates, the regions were asked to confirm what was reported in last year's edition or to send any changes that occurred in 2023. All regions provided the requested information with the exception of Lazio and Sicily.

The update in 2023 confirmed that the organisation of the DPC service varies widely at regional level, although common models are found among the regions. The most adopted organisational model (Abruzzo Basilicata, PA Bolzano, Campania, Lombardy, Apulia, Sicily, PA Trento, Valle d'Aosta) is the one whereby a lead local health authority buys the drugs on the basis of tenders carried out at regional level and asks the manufacturer to deliver the DPC drugs directly to the intermediate distributors in charge of storage and distribution at the pharmacies under agreement (Model 1) (Figure 8.1). In some regions, this model includes integrative elements such as, for example, a radial distribution organisation with one or more lead distributors and a series of satellite distributors (e.g. Calabria, Lazio and Umbria). In addition, an integrated information system is often provided in these regions (Model 1.1). Another popular organisational model (Molise, Tuscany, Liguria, Veneto, Sardinia) provides for a regional body or other third party body to purchase the drugs on the basis of tenders issued by the region or other regional bodies and to request delivery of the DPC drugs directly to intermediate distributors in charge of storage and distribution at pharmacies under agreement (Model 2). Also for this model, there are integrations with radial distribution organisation and integrated information system (Model 2.2: Piedmont and Friuli Venezia Giulia) There is also a third organisational model, adopted by Emilia Romagna, whereby individual health authorities purchase drugs on the basis of regionally organised tenders, with no lead company. Some local health authorities require the manufacturer to deliver DPC drugs directly to a lead distributor. The latter stores the drugs and distributes them to a series of satellite distributors delivering to pharmacies under agreement (Model 3). In Emilia-Romagna, some local health authorities request that the manufacturer deliver the DPC drugs to a lead distributor, who in turn will distribute them to other satellite distributors to be subsequently delivered to pharmacies under agreement. Other local health authorities, on the other hand, receive, store and distribute the drugs to intermediate distributors, who will then deliver them to pharmacies under agreement. To conclude, the Marche region has a peculiar organisational model that is unique in Italy (Model 4). The former ASUR Marche, now replaced by AST AN pursuant to L.r. 19/2022 and DGR 1839/2022, is in charge of the Regional Contracting Authority (SUAM) for the supply of DPC drugs. A leading wholesaler - CO.D.IN. Marche - buys DPC medicines from the supplying companies on the basis of a contract signed between the supplying companies, ASUR and CO.D.IN itself. The lead wholesaler stores and distributes the drugs to other distributors (couriers) who supply the pharmacies under agreement.

Differences remain in the regional lists of drugs for which distribution through the DPC channel has been envisaged (Table 8.1). The texts of the agreements reveal that each region selects a different set of drugs to be included in the distribution list in DPC, drawing from the list of drugs indicated by AIFA as A-PHT (Determination 29.10.2004 and supplements). For inclusion in the regional DPC list, a number of regions indicate exclusion criteria, others inclusion criteria, and still others combine elements of inclusion and exclusion (e.g. Lombardy, inclusion in the regional list of drugs from the ex-OSP2 list reclassified by AIFA into A-PHT; exclusion of drugs with a public price of less than EUR 50). Specific groups of drugs, although with some interregional diversity, are specifically excluded or included in the DPC list. Among those excluded are frequently narcotics, liquid oxygen, medicines subject to the AIFA monitoring register or, more generally, medicines which, for specific care needs (e.g. therapeutic

monitoring) and organisational requirements, are distributed directly by companies. Variability between regions also persists in the remuneration of the DPC service. The regional fees also vary according to the type of pharmacy (e.g. urban, rural non-subsidised and urban pharmacies with reduced revenue, rural subsidised). The fees vary from a maximum of €15 in Lazio for medicines with retail prices between €600.01 and €1,000.01, and a minimum of €3.20 in Emilia-Romagna. With reference to the type of pharmacy, for example In Emilia-Romagna, there is a remuneration quota of €3.20 for urban pharmacies, €3.88 for non-subsidised rural and urban pharmacies with NHS revenues of less than €300,000, and subsidised rural pharmacies with NHS revenues of less than €450,000. A large part of the regions indicated that the remuneration for the distribution service is paid to the pharmacies and includes the share of intermediate distribution, which is defined in a separate agreement of the pharmacies with the intermediate distributors. Some regions have declared the share for intermediate distribution, which shows limited inter-regional variability. Specifically, in Puglia and Tuscany the charge recognised to the intermediate distributor is €1.10, in Marche €1.28, in Sicily €1.30, in Basilicata €1.40 and in Calabria €1.90. Some agreements also noted that in some regions, ad hoc ceilings had been set for DPC, with tariffs being readjusted as a result of the expenditure being exceeded. A special case is the case of the Marche region, which has provided for incremental ceilings over the years, for which dispensation in DPC is foreseen until 1,600,000 packs are reached in 2022, 1,700,000 in 2023, 1,800,000 in 2024, and 1,900,000 in 2025. If the ceiling is exceeded, the remuneration is reduced from €4.12 to €3.50 + VAT/pack.

Table 8.1 Summary of regional agreements on distribution on account

Abruzzo	
Legal basis	DCA no. 114 of 28.09.2016, supplemented by D.G.R. no. 780 of 28.12.2017 Dispensing instructions arranged with D.G.R. no.606 of 07.08.2018 and DGR 508/2018 supplemented by D.G.R. no.89 of 01.02.2019 Law no. 461 of 09.08.2022
Agreement duration	01.08.2018 – 31.07.2020 renewable
Organisation of DPC distribution	A lead company buys the drugs on the basis of tenders issued by the region or other regional authorities and asks the manufacturer to deliver the DPC drugs directly to the intermediate distributors in charge of storage and distribution to pharmacies under agreement.
Medicines/Criteria Attention for Distribution DPC	Exclusion from the regional list of patent-expired drugs whose price is equal to or lower than the purchase price of the local health authority plus the DPC service. Inclusion in the regional Low Molecular Weight Heparin (EBPM) list for all indications.
Remuneration per pack	Share including costs of intermediate and final distribution: • €8.40 + VAT, urban and rural pharmacies with SSN revenue <€258,000; • €7.10 + VAT rural pharmacies with SSN revenue ≥€258,228 and <€600,000; • €6.10 + VAT, urban pharmacies with SSN revenue ≥€258,228 and rural pharmacies with SSN revenue ≥€600,000
Roofs at the DPC	N.A.
Drug substitutability	Dispensing of the drug awarded in the tender.In the case of a reasoned indication by the doctor of 'non-substitutability': •if thedrug is included in DPC list, dispensed in DPC; •if the drug is not included in DPC list, dispensed under approved care regime In case of a replacement request by the user: • dispensation in agreement with the user sharing the difference from the tender price.

continued

Table 8.1 - *continued*

Abruzzo - *continued*	
Mixed prescriptions	Separate prescriptions for medicines DPC and under approved care regime. It is possible to include different medicinal products in the same DPC prescription.
Medicines not available in the DPC channel/urgent prescriptions	In case of unavailable medicines:if the drug is not patent-expired, dispensation under approved care regime;if the drug is off-patent without a 'non-substitutability' clause, • substitution with a DPC equivalent with the user sharing the difference from the tender price In the case of an urgent prescription, dispensation under approved care regime.
Reference to "service pharmacy"	N.A.
Basilicata	
Legal basis	Law no. 767 of 05.11.2020
Agreement duration	05.11.2020 – 05.11.2023 valid until new agreement is signed
Organisation of DPC distribution	A lead company (Potenza local health authority) buys the drugs on the basis of tenders issued by the region or other regional authorities and asks the manufacturer to deliver the DPC drugs directly to the intermediate distributors in charge of storage and distribution to pharmacies under agreement.
Medicines/Criteria Attention for Distribution DPC	Exclusion from the regional list of: • narcotic drugs • liquid oxygen • medicines subject to AIFA Monitoring Registers • A/PHT drugs with a retail price less than or equal to €30.00 including VAT • coagulation factors (ATC: B02BD) Dispensing in DPC is restricted to resident users only.
Remuneration per pack	Remuneration of the distribution service to the pharmacy including the charge to the wholesaler: • €5.80 + VAT, pharmacies with SSN revenues >€450,000 • €6.80 + VAT, pharmacies with SSN revenues >€150.000 and ≤€450.000 • €7.80 + VAT, pharmacies with SSN revenues ≤€150.000 The charge to the wholesaler is equal to €1.40 for all revenue categories.
Roofs at the DPC	N.A.
Drug substitutability	Dispensing of the drug awarded in the tender. In substitution of biological drugs by the pharmacist. In the case of a reasoned indication by the doctor of 'non-substitutability', or request for replacement by the user, subject to payment of a fixed fee per pack: • if the drug is included in DPC list, dispensed in DPC; • if the drug is not included in the DPC, dispensing in agreement with the user sharing the difference from the tender price.
Mixe d prescriptions	N.A.
Medicines not available in the DPC channel/urgent prescriptions	In case of unavailable medicines, dispensation in agreement with possible payment of the fee according to the transparency lists. Annotation 'MISSING' on the prescription. In the case of urgent prescriptions on Saturday afternoons and/or public holidays, the pharmacy can dispense the drug under approved care regime.
Reference to "service pharmacy"	Inactive service.

continued

Table 8.1 - *continued*

Province of Bolzano	
Legal basis	Provincial Council Resolution No. 1164 of 29.12.2023
Agreement duration	01.01.2021-31.12.2026 (extension of previous agreement: DGR No 1046 of 22/12/2020
Organisation of DPC distribution	The Bolzano local health authority buys drugs on the basis of tenders conducted at provincial level. The local health authority requires the manufacturer to deliver the DPC drugs directly to the intermediate distributors in charge of storage and distribution to pharmacies under agreement.
Medicines/Criteria Attention for Distribution DPC	N.A.
Remuneration per pack	Share including charges for intermediate and final distribution: • €7.50 + VAT for subsidised urban/rural pharmacies with SSN revenues ≤450.000 euro • €6,50 + VAT all other pharmacies If the packs distributed are > 250,000, the amounts indicated are reduced by €0.70 per pack. • Web application provided by pharmacies
DPC ceilings	N.A.
Drug substitutability	Dispensing of the equivalent medicine with the lowest price. In the event of a reasoned indication by the doctor of 'non-substitutability' or a request for substitution by the user, dispensation in agreement with the user sharing the difference between the reimbursement price and the sale price.
Mixed prescriptions	Separate prescriptions for medicines DPC and under approved care regime.
Medicines not available in the DPC channel/urgent prescriptions	In case of unavailable medicines, dispensing under agreement. No information was found on the management of urgent prescriptions.
Reference to "service pharmacy"	Active service 1. booking of specialist services 2. collecting reports 3. payment of participation fees in the expenditure 4. colorectal screening
Calabria	
Legal basis	DGR 28.01.2010, update Resolution no. 398 of 24.05.2010, Law no. 100 of 5.07.2012, Law no. 169 of 9.10.2012, Law no. 184 of 28.11.2012; DCA No. 72 of 03.07.2015; DCA 84/2017;DCA 89/2019; DCA 157/2020;Note n. 118092 of 24.03.2020 Dematerialisation of prescriptions in DPCNote n. 131494 of 19.03.2021 Note n. 544496 of 5.12.22 Modification of DPC list - new modalities
Agreement duration	From 03.07.2015, renewable
Organisation of DPC distribution	A lead local health authority (ASP of Cosenza) takes care of the entire procurement process: from the preparation of tender specifications to the issuing of supply orders for the entire region to the settlement of electronic invoices. Procurement procedures are carried out at regional level by the Procurement Authority. The ordered goods are delivered by the Supplier to the Lead Distributor, who carries out the redistribution of the delivered products among all the radiating dealers. The lead distributor constantly monitors stocks in the distribution chain. The Regional DPC Office oversees the processes with the help of IT platforms that allow the real-time monitoring of all process steps.

continued

Table 8.1 - *continued*

Calabria - *continued*	
Medicines/Criteria Attention for Distribution DPC	Exclusion from the regional list of: • narcotic drugs • methylphenidate, methadone • medicines in Nota 65 • medicines for cystic fibrosis Exclusion from the regional list of: • liquid oxygen • ex-OSP2 reclassified by AIFA into A-PHT • EBPM for prophylaxis of DVT after major orthopaedic or major general surgery, for indications according to law 648/96 and for established uses major.

Remuneration per pack	Share including charges for intermediate and final distribution:
	• €6,50 + VAT, of which:
	  • charge to pharmacy: €4.60
	  • charge at the intermediate distributor: €1.90
	The IT platform used to manage the entire process is purchased and managed by the region. The fee is paid to community pharmacies by Local Pharmaceutical Services upon presentation of the DPC invoice together with the Monthly Summary of Accounting Documents. The pharmacies pay the distributors their due fees.

DPC ceilings	N.A.
Drug substitutability	Dispensing of the drug awarded in the tender for generics Possibility of 'non-substitutability' certification and provision in the DPC channel only for: • second-generation antipsychotic drugs For other generic drugs, in the case of a reasoned indication by the doctor of 'non-substitutability: • if the drug is 'patent expired', dispensation under agreement with the user sharing the difference from the price on the transparency list and any fixed fee per prescription expected. The certificate of 'non-substitutability' is not necessary, as the requirement for: •patent covered drugs • biologics/biosimilars • coagulation factors • tacrolimus drugs
Mixed prescriptions	Separate prescriptions for medicines DPC and under approved care regime. If there is an overlap, the user expresses a preference and will have to make a new prescription for the non-withdrawn drug.
Medicines not available in the DPC channel/urgent prescriptions	In case of unavailable medicines, dispensing under agreement. The IT platform issues a missing product certificate, which must be attached to the prescription sent under approved care regime. Prescriptions with a doctor's certificate of urgency (with a brief justification) are sent through the conventional channel for the minimum quantities to cover the urgency. These prescriptions require the payment of the co-payment and any difference in price from the transparency list.
Reference to "service pharmacy"	Service Pharmacy activities initiated at regional level: 1. Administration of anti-SARS-CoV-2 and influenza vaccination: € 8,16+VAT. 2. Administration of flu vaccines: € 7.66 + VAT. 3. Holter blood pressure: € 40.00 4. Cardiac Holter: € 45.00 5. ECG: € 25,00 6. Simple spirometry

continued

Table 8.1 - *continued*

Campania	
Legal basis	D.C.A. n.97 of 20.09.2016 DD.G.R.C. n.384 of 19.07.2022
Agreement duration	N.A.
Organisation of DPC distribution	The Salerno Local Health Authority, lead DPC for the Campania Region, purchases the drugs on the basis of tenders issued by the regional purchasing centre So.Re.Sa, identifying the delivery point at the designated regional hub in the order. The latter, according to the ordering province, distributes the drugs to the provincial logistics chain indicated in the individual provincial distribution agreements, for subsequent delivery to the affiliated pharmacies. In addition, for drugs and prescriptions for diabetics that have not yet been awarded in So.Re.Sa, the individual AA.SS.LL. provide directly, indicating in the order the delivery point identified in the provincial Agreements. The latter distributes the products directly to community pharmacies or via radial distributors, according to provincial distribution agreements.
Medicines/Criteria Attention for Distribution DPC	The list of DPC medicinal products is regularly updated by a dedicated technical table. Drugs whose price is equal to or less than the sum of the ASL purchase price plus the DPC service are excluded from the regional DPC list.
Remuneration per pack	Maximum tariff including charges for intermediate and final distribution: • €6,00 + VAT; • €7,50 + VAT for subsidised rural pharmacies
DPC ceilings	N.A.
Drug substitutability	Dispensing of the equivalent medicine with the lowest price. In the case of a doctor's indication of 'non-substitutability': dispensation in agreement with the user sharing the difference between the reimbursement price and the sale price. The request for irreplaceability must be accompanied by the preparation of an ADR form in which the doctor reports the problem encountered following the intake of the medicine available in DPC.
Mixed prescriptions	Separate prescriptions for medicines DPC and under approved care regime. If there is an overlap, the user expresses a preference and will have to make a new prescription for the non-withdrawn drug.
Medicines not available in the DPC channel/urgent prescriptions	In the case of unavailable medicines, recourse to the acquisition of other own stocks or borrowing from other health authorities. Lastly, dispensing by agreement with issue of a 'MISSING' notification to be registered in the IT platform and attached to the prescription.In cases of urgency, dispensing in agreement only for the first prescription, in the event that the first course of treatment is not delivered, particularly if that delivery falls on a Saturday afternoon or Sunday, or if the drug cannot be found in the time needed.
Reference to "service pharmacy"	Active service
Emilia Romagna	
Legal basis	Resolution No. 1201 of 17.07.2023 Resolution No. 2303 of 27.12.2022 Law no. 329 of 4.03.2019, Notes from the Director-General for Health and Social Policy PG 322010 of 2013, PG 245837 of 2014, memorandum n18 of 22.11.2013
Agreement duration	17.01.2023 - 31.12.2024
Organisation of DPC distribution	The local health authorities purchase drugs on the basis of tenders issued at regional level. Some local health authorities require the manufacturer to deliver DPC drugs directly to a lead distributor. The latter stores the drugs and distributes them to a series of satellite distributors. These make the delivery to pharmacies under agreement. In Emilia-Romagna, some local health authorities receive, store and distribute drugs to intermediate distributors. These make the delivery to pharmacies under agreement.

continued

Table 8.1 - *continued*

Emilia Romagna - *continued*	
Medicines/Criteria Attention for Distribution DPC	Exclusion from the regional list of patent-expired drugs whose price is equal to or lower than the purchase price of the local health authority plus the DPC service.
Remuneration per pack	Share including charges for intermediate and final distribution: • €3,20 + VAT for urban pharmacies; • €3.88 + VAT for unsubsidised rural and urban pharmacies with NHS revenues <€300,000; subsidised rural pharmacies with NHS revenues <€450,000; pharmacies in their first year of opening
DPC ceilings	N.A.
Drug substitutability	Dispensing of the drug awarded in the tender.In the case of a reasoned indication by the doctor of 'non-substitutability' with approval of the pharmaceutical service: • if the drug is included in DPC list, dispensed in DPC; • if the drug is not included in DPC list, dispensed under approved care regime In case of a replacement request by the user: • the user bears the full cost of the medicine. For antiepileptic drugs (N03A), immunosuppressants (L04A), antiplatelet drugs (B01AC), for which therapeutic continuity is particularly important, in the absence of availability in the DPC, dispensing by agreement is envisaged with an indication on the prescription of 'sic volo for therapeutic continuity'.
Mixed prescriptions	Possibility of simultaneous prescribing of a drug prescribed under approved care regime and a DPC drug on the same prescription.
Medicines not available in the DPC channel/urgent prescriptions	In case of unavailable medicines, dispensing under agreement.
Reference to "service pharmacy"	Service Pharmacy activities initiated at regional level: • administration of anti-SARS-CoV-2 vaccines; remuneration of EUR 10.40 (excluding VAT) per any vaccination administered • administration of anti-SARS-CoV-2 vaccines; remuneration of EUR 6.70 (excluding VAT) per any vaccination administered • administration of COVID-19 antigenic tampons: 15 euro (excluding VAT) per any vaccination administered • activation of the electronic health file both in the component of issuing digital identity and in the component of only recognising citizens who have already preregistered; remuneration of support to citizens in obtaining digital identity (assisted) amounting to 8.296 euro (VAT included); remuneration of recognition of citizens amounting to 4.148 euro (VAT included) • participation in colorectal cancer screening; fees vary among local health authorities. Activities starting by the year 2023: • structured interview with the patient suffering from chronic disease (starting with COPD) to be recorded on a regional computer application, including promotion and measurement of adherence to therapy; medication recognition; collection of suspected ADRs; evaluation of correct use of administration devices through related patient education. The way the project is implemented and the evaluation of its impact • development of involvement of pharmacies in telemonitoring pathways in cardiology. The provision of healthcare services will be shared within a special regional multidisciplinary working group being set up, so that the healthcare intervention of interest is appropriately placed within the patient's diagnostic and therapeutic care pathway.

continued

Table 8.1 - *continued*

Friuli Venezia Giulia	
Legal basis	DGR No. 1007 of 30 June 2023 and DGR 1196 of 27 July 2023
Agreement duration	1/7/2023-30/6/2026
Organisation of DPC distribution	Medicines that can be dispensed under DPC are purchased by the Regional Health Coordination Authority (ARCS), which also provides support for the centralised procurement of goods and services of the Regional Health Service, on the basis of the needs provided by the Regional Health Service. Medicines, ordered by the Regional Health Coordination Authority, are delivered by suppliers directly to intermediate distribution (DI). Namely, a lead partner is identified to distribute DI to the supply chain on the basis of defined algorithms. Following a request from the pharmacy to the distributor, the latter delivers the drug to the pharmacy. A dedicated platform (gopenDPC) is used for this procedure. On a voluntary basis, there is the possibility of activating a ministock at the pharmacy of the medicines with the highest turnover rate, based on defined criteria and algorithms.
Medicines/Criteria Attention for Distribution DPC	Exclusion from the regional list of medicines dispensed in DPC of: • medicines with a retail price/reference price < €30.00, except for clopidogrel 75mg, 28 tablets and quetiapine 25mg, 30 tablets that are on the DPC list • drugs subject to Presidential Decree 309/90 as amended • LMWH • therapeutic oxygen • medicines in Nota 65 • medicines for which exclusive direct distribution is provided for by national provisions or regional indications
Remuneration per pack	From 1/10/2023, the remuneration of the distribution service is: • For pharmacies with annual NHS revenues, net of VAT, <€150,000: – €7.60 + VAT for packs with a retail price/reference price <€51.65 – €10.60 + VAT for packs with a retail price/reference price <€51.65 • for subsidised rural pharmacies with annual NHS revenues, net of VAT, between €150,000 and €450,000 and for rural/urban pharmacies with NHS revenues between €150,000 and €300,000: – €7.60 + VAT/package • for all other pharmacies: €5.80 + VAT/pack for medicines with a public price/reference price ≥ €30 clopidogrel: • €5.80 + VAT for rural/urban pharmacies with annual NHS revenues, excluding VAT, > €300,000; • €6.80 + VAT for rural/urban pharmacies with annual NHS turnover, net of VAT, of less than €300,000 and for subsidised rural pharmacies with annual NHS turnover, net of VAT, of less than €450,000.quetiapine 25mg: • €4.55 + VAT for rural/urban pharmacies with annual NHS revenues, excluding VAT, > €300,000; • €5.35 + VAT for rural/urban pharmacies with annual NHS turnover, net of VAT, <€300,000 and for subsidised rural pharmacies with annual NHS turnover, net of VAT, <€450,000. Remuneration for the distribution service is only paid to pharmacies.The share of intermediate distribution is defined by separate agreement of the pharmacies with the intermediate distributors.
DPC ceilings	N.A.
Drug substitutability	Dispensing of the drug awarded in the tender. In the case of a reasoned indication by the doctor of 'non-substitutability': • if the drug is included in DPC list, dispensed in DPC;if the drug is not included in the DPC list, dispensing by agreement with payment by the user of any differential with the reference price defined by AIFA.
Mixed prescriptions	Separate prescriptions for medicines DPC and under approved care regime. If there is a mixed prescription (DPC drug and prescription drug), the user expresses a preference for the drug to be picked up.

continued

Table 8.1 - *continued*

Friuli Venezia Giulia - *continued*	
Medicines not available in the DPC channel/urgent prescriptions	In the case of unavailable medicines or urgent prescriptions, dispensing under agreement.
Reference to "service pharmacy"	Active service: 1. Single reservation centre (CUP) service: €2/reservation 2. Colorectal screening: € 2.40/sample analysed 3. Performing rapid tests for the detection of SARS-CoV2 in application of the national memorandum of understanding Administration of the anti-SARS-CoV2 vaccination and flu vaccination: €10 (+VAT)/administration as the sum of €6.16/inoculation + €3.84 for administrative tasks.
Liguria	
Legal basis	L.R. 13/2022 DGR 477/2023 Alisa Resolution 130/2023 DGR 375/2024
Agreement duration	01.06.2023 – 31.05.2026
Organisation of DPC distribution	A.Li.Sa. purchases drugs through the A.Li.Sa. Single Centre on the basis of tenders issued by the Regional Single Contracting Station (SUAR). The manufacturer delivers the DPC drugs to intermediate distributors in charge of storage and delivery to contracted pharmacies.
Medicines/Criteria Attention for Distribution DPC	A-PHT drugs according to a list drawn up by the DPC Technical Commission.
Remuneration per pack	Share including charges for intermediate and final distribution: • € 5.69 (incl. VAT and distribution of diabetic devices in DPC)Rural pharmacies with an allowance and NHS turnover, net of VAT, of <€450,000 and other pharmacies with an NHS turnover of <€300,000 are granted a remuneration surcharge of €0.50 per pack plus VAT as per law. • the share of intermediate distribution is defined by a separate Agreement signed by the delegates of Federfarma, Assofarm Liguria and the Intermediate Distributors.
DPC ceilings	Dispensing in DPC up to a number of drugs/year of 2,100,000. If the ceiling is exceeded, the remuneration is reduced from €5.69 to €5.12 (including VAT)/pack.
Drug substitutability	Dispensing of the drug awarded in a tender or framework agreement. In the event of a reasoned indication by the doctor of 'non substitutability' or a request for substitution by the user, if the drug is not included in the framework agreement, dispensing by special agreement with user co-participation according to the AIFA transparency lists and a fixed prescription fee, if applicable. In some cases (branded drugs with justified non-substitutability) centralised purchase and distribution in DPC.
Mixed prescriptions	For both paper and dematerialised prescriptions: separate prescriptions for medicines in DPC and under approved care regime (DGR 375/2024).
Medicines not available in the DPC channel/urgent prescriptions	In the case of unavailable medicines, if certification of unavailability is documented by the warehouses holding the regional medicines, dispensation in agreement with the user sharing the difference from the tender price and any fixed fee per prescription provided. In the case of urgent prescriptions: availability of ministocks in the pharmacy for some drugs, otherwise dispensing under approved arrangements.

continued

Table 8.1 - *continued*

Liguria - *continued*	
Reference to "service pharmacy"	Active substances: 1. COVID-19 PVT organisation and management (remuneration: €1000/pharmacy) concluded 2. Adherence to therapy-hypertension: €43/patient; training (one-off) €60 3. Adherence to therapy-hypertension: €40/patient; training (one-off) €60 4. Adherence to therapy-diabetes2: €33/patient; training (one-off) €80 (one-off for all diabetes-related services) 5. Diabetes screening (questionnaire + capillary blood sample): €20/patient 6. Capillary blood sampling: €14.3/sampling 7. Telemedicine - cardiac holter: €70/patient; training (one-off) €50 8. Telemedicine - cardiac holter: €45patient; training (one-off) €50 9. Telemedicine-ECG: €31/patient; training (one-off) €50 10. Colorectal screening for new subjects 50-74: €5/patient; training (one-off) €30 Services include remuneration for patient activity and training (one-off).
Lazio	
Legal basis	DCA n. U00253 of 31.08.2016
Agreement duration	31.08.2016 – 31-08.2020, under extension
Organisation of DPC distribution	A leading company (ASL Roma1) buys the drugs on the basis of tenders issued by the Regional Purchasing Centre of Lazio. Two lead distributors receive, store and distribute the drugs to intermediate distributors. These make the delivery to pharmacies under agreement. The lead Local Health Authority manages relationships with pharmacies and prescribers via the logistics and prescription information system.
Medicines/Criteria Attention for Distribution DPC	Regional listing of: ulipristal acetate, tadalafil, eslicarbezapine, retigabine, perampanel, metirapone, sevelamer. These are joined by ex-OSP2: linezolid, voriconazole, posaconazole, imatinib mesylate, mycophenolate mofetil, mycophenolic acid, deferiprone, deferasirox, omalizumab. Exclusion from the regional list of medicines with Pp <€25.00, except: clozapine, quetiapine and risperidone. Monthly update of A-PHT drug lists with equal ATC at level IV.
• Remuneration per pack	Share including charges for intermediate and final distribution: as well as the information system managing prescription and logistics: • Pp <€50,00, €7,00 • Pp >€50,01 and €154.93, €10.00 • Pp>154,94 and €600, €11.80 • Pp >€50,01 and €1000.01, €15.00 • For ex-OSP2: €6.00 For subsidised rural pharmacies with NHS turnover <€387,342.64: • Pp <€50,00, €7,00 • Pp >€50.01 and €600, 16% of Pp devolved • Pp >€50.01 and €1000.01, 5% of Pp devolved • Pp>€1000.01, €28.00 • Remuneration remuneration includes charges for the computerised management of the CVD and Webcare (online treatment plans)
DPC ceilings	N.A.
Drug substitutability	Dispensing of the drug awarded in a tenderor framework agreement. In the event of a reasoned indication by the doctor of 'non substitutability' or a request for substitution by the user, if the drug is not included in the framework agreement, dispensing by special agreement with user co-participation according to the AIFA transparency lists and a fixed prescription fee, if applicable.
Mixed prescriptions	Separate prescriptions for medicines DPC and under approved care regime.

continued

Table 8.1 - *continued*

Lazio - *continued*	
Medicines not available in the DPC channel/urgent prescriptions	In case of unavailable medicines: • branded drug unavailable: equivalent generic dispensation in DPC; • generic unavailable: dispensing DPC branded drug if present in framework agreement; • if branded and generic drugs are unavailable: dispensation in agreement with cost-sharing of the user according to the AIFA transparency lists and fixed fee per prescription, if applicable. Emergency prescriptions maximum two packs for haemophilia drugs. There are no exemptions for all other drugs
Reference to "service pharmacy"	Active service 1. colorectal screening: - €4.00 per service (VAT included) 2.Vaccini COVID-19: - €6,00 vaccination - €6,00 personal protective equipment, information system management, AVR reporting 3. Flu vaccines: - €6.16 (VAT included)
Lombardy	
Legal basis	Regulation n. XI/796 dell'12.11.2018
Organisation of DPC distribution	A lead local company (ATS Bergamo) buys the drugs on the basis of tenders issued by ARIA. The lead ATS requests that the manufacturer deliver the DPC drugs to intermediate distributors in charge of storage and delivery to contracted pharmacies.
Medicines/Criteria Attention for Distribution DPC	Regional listing of ex-OSP2 drugs reclassified by AIFA in A-PHTExclusion from the regional list of medicines with Pp <€50.00
Remuneration per pack	Share including charges for intermediate and final distribution: • €7,00 + VAT; • €9.00 + VAT, rural pharmacies with NHS revenue <€450.000 The share of intermediate distribution is defined by separate agreement of the pharmacies with the intermediate distributors. • €6.00 + VAT: ex-OSP2 drugs - all pharmacies (including distributors' fee)
DPC ceilings	N.A.
Drug substitutability	Dispensing of the drug awarded in the tender. In the event of a reasoned indication by the doctor of 'non-substitutability' or a request for substitution by the user, dispensation in agreement with the user sharing the difference between the reimbursement price and the sale price.
Mixed prescriptions	Separate prescriptions for medicines DPC and under approved care regime.
Medicines not available in the DPC channel/urgent prescriptions	In case of unavailable medicines: • For A/PHT drugs dispensed under agreement with user co-payment of the difference between the tender price and any fixed fee per prescription foreseen • For ex-OSP2 medicines - direct distribution In the case of an urgent prescription, dispensation under approved care regime.
Reference to "service pharmacy"	Active service 1. administration of the anti-SARS-CoV vaccination and flu vaccination: €6,16 2. vaccine delivery to GP and pls: €0.30 3. choice of withdrawal of GPs and pls: €1.25 4. colorectal screening: €3,85 5. COVID-19 tampons: €12 Reconciliation of therapies in chronic patients is being activated.

continued

Table 8.1 - *continued*

Marche	
Legal basis	DGR No 1642 of 28 December 20221
Agreement duration	01.01.2022 – 31.12.2025
Organisation of DPC distribution	AST Ancona, as the lead local authority on behalf of the Regional Procurement Authority (SUAM), carries out the tenders for the supply of DPC drugs. CO.D.IN. Marche, the single regional logistics operator identified by a European tender by the former ASUR Marche, is in charge of purchasing the medicines of the DPC from the suppliers on the basis of a contract between the parties. The wholesaler stores and distributes the drugs at its own warehouse and supplies the affiliated pharmacies by means of a request entered on the dedicated portal.
Medicines/Criteria Attention for Distribution DPC	-
Remuneration per pack	Total amount paid by the Region per pack: • €4.12 (€ 4.62 rural pharmacies) or €3.50 (€4.00 rural pharmacies) over the expenditure ceiling (number of di packs supplied in DPC) • €1,28 (wholesaler) • The cost incurred by AST: € 5.40 + VAT 10% or € 4.78 + VAT 10% is the cost per ASTSubsidised rural pharmacies have a surcharge of EUR 0.50 cents.
DPC ceilings	Dispensation in DPC until 1,600,000 for 2022, 1,700,000 for 2023, 1,800,000 for 2024, 1,900,000 for 2025 packages in DPC. If the ceiling is exceeded, remuneration is reduced to €3.50 + VAT/package This margin (€ 24.12 or € 3.50) is further increased by € 0.50 (excluding VAT 10%) for subsidised rural pharmacies receiving the additional contribution under Regional Law No 4/2015. The intermediate distributor according to ASUR Determination No. 263/2021 will be remunerated €1.28 per pack on each drug distributed in DPC and €6 for the IT management of each therapeutic plan.
Drug substitutability	Dispensing of the 'lowest priced' drug (ASUR list). In the event of a reasoned indication by the doctor of 'non-substitutability' or a request for substitution by the user, dispensation in agreement with the user sharing the difference between the reimbursement price and the sale price.
Mixed prescriptions	-
Medicines not available in the DPC channel/urgent prescriptions	-
Reference to "service pharmacy"	The Marche Region with DGR 654 of 30 May 2022 approved the timetable of the experimental activities of the Pharmacy of Services in the Marche Region and, subsequently, it was transmitted to the Joint Committee and Technical Table with note prot. no. 0006442|01/06/2022|R (prot. Siveas 51/2022), pursuant to articles 9 and 12 of the Understanding of 23 March 2005 for approval. By DGR 724 of 30 May 2023 'Approval of projects relating to the experimentation of new services in community pharmacy' the following projects were approved. - 'Reconciliation of drug therapy'; - 'Monitoring adherence to drug therapy in patients with type 2 diabetes'; - 'Monitoring adherence to drug therapy in patients with COPD'; - 'ESF Enrichment and Consultation Service'; - 'Telemedicine services Holter Pulse, Cardiac Holter, ECG, Spirometry'; - 'Supporting screening for colorectal cancer prevention'. 54.7% of the pharmacies affiliated with the Regional Health System participated in at least one of the proposed projects, the distribution sufficiently representing the regional demographic distribution.

continued

Table 8.1 - *continued*

Molise	
Legal basis	DCA N.62 dated 23/12/2023 DCA 30/2023 Regulation DG ASReM N.1580/2022 DCA 90/2020
Agreement duration	-
Organisation of DPC distribution	The Regional Health Authority of Molise (ASReM) buys the drugs on the basis of tenders issued by SCR Piedmont to which the Molise region joins; it requires the manufacturer to deliver the DPC drugs directly to the sole distributor in charge of storage and distribution to affiliated pharmacies.
Medicines/Criteria Attention for Distribution DPC	-
Remuneration per pack	The charge for wholesalers and distributors for the distribution on account (DPC) service of regional PHT drugs, including intermediate distribution costs, is set as follows: • Subsidised pharmacies with an annual turnover of less than/equal to €300,000 are granted a fee of: – €7,50 + VAT per item dispensed for drugs with ex factory cost <€ 40.00 – €9,50 + VAT per item dispensed for drugs with ex factory cost >€ 40.00 • Pharmacies with an annual turnover between EUR300,000.01 and EUR450,000.00 are granted a per-pack fee of EUR 5.82 + VAT per dispensed item • In lieu of the above amounts, the pharmacies referred to above shall be paid a per-pack fee of €3.69 + VAT for each item dispensed from the number of packs exceeding the ceiling of 1,500 items per year.
DPC ceilings	-
Drug substitutability	-
Mixed prescriptions	-
Medicines not available in the DPC channel/urgent prescriptions	-
Reference to "service pharmacy"	Active service 1. Screening for early diagnosis of colon-rectal cancer: • €3 incl. VAT per completed screening for the first 22,000 screenings on an annual basis 2. Flu vaccination campaign 2023 - 2024: • €100 +VAT one-off per pharmacy and €0.80 +VAT per vaccine dose delivered The pharmacist who provides the vaccination will be paid a VAT-free remuneration of €6.16. 3. Distribution of diabetic devices for self-monitoring in DPC mode: • €7.00 + VAT per order.
Piedmont	
Legal basis	*D.G.R. no. 1-7400 of 11 August 2023: transposition of the new remuneration rules on the DPC distribution of medicines defined as from 1 July 2023, providing for an experimental application until 31.12.23.DGR No n. 15-8046 of 29 December 2023 Extension of the experimental phase for a further period from 1 January 2024 to 30 June 2024, in order to allow for an appropriate assessment of the financial viability and appropriateness of the mechanism for remunerating the distribution of medicines in DPC mode.*
Agreement duration	01.07.2023 – 30.06.2024

continued

Table 8.1 - *continued*

Piedmont - *continued*	
Organisation of DPC distribution	The Piedmont region has identified a lead company (ASL of AT) that is responsible for the purchase and management of A-PHT drugs supplied in DPC. The ASTI Local Health Authority purchases drugs on the basis of tenders issued by SCR Piemonte. Medicines are received at the two identified lead intermediary distributors, who in turn distribute the stocks to the spoke warehouses, according to consumption. In pharmacies open to the public, there is no mini-stock of medicines and the order to wholesalers is placed when the prescription is received by the patient. The order from the pharmacies is placed through the GopenDPC platform, which manages the relevant operations.
Medicines/Criteria Attention for Distribution DPC	Excluded from the DPC distribution are drugs which, although classified in class A-PHT, are distributed exclusively by local health authorities: • growth factors • coagulation factors • combination buprenorphine + naloxone • methadone for drug addiction • liquid oxygen for long-term home oxygen therapy (OTD) • DAAs for the treatment of chronic hepatitis C • medicines for hypercholesterolaemia (Praluent and Repatha)
Remuneration per pack	Share including charges for intermediate and final distribution: • €5,00 + VAT; • €6,35 + VAT for subsidised rural pharmacies with NHS revenues <€387.342,67 • €7.25 + VAT for pharmacies with annual NHS revenues <€258.228,45
DPC ceilings	An average reference remuneration value of €5.39 + VAT is assumed. If, in the light of the verifications carried out by the Monitoring and Development Table, to be completed by 30 November of each year, deviations from the aforementioned value of €5.39 + VAT are recorded, the difference between this value and the actual value for the reference period will be charged to the Piedmont pharmacies that have distributed a number of packs exceeding the threshold of 4,500 units/year.
Drug substitutability	Dispensing of the drug awarded in the tender. In the case of a reasoned indication by the doctor of 'non-substitutability': • Active ingredients in a specific regional table: dispensing of the prescribed product in DPC without co-payment by the patient. The doctor is required to send the local health authority (of residence of the patient) a concise but comprehensive report justifying the prescription of the product other than the one awarded in the tender. Active ingredients not listed in a specific regional table: taking charge of the patient by the local health authority of residence and activation of direct distribution.
Mixed prescriptions	N.A.
Medicines not available in the DPC channel/urgent prescriptions	In the case of urgent prescriptions, on holidays, during evening and night on-call, on Saturday afternoons from 3 p.m. onwards, the pharmacy may also dispense a pack of the PHT medicines belonging to the classes listed below: • platelet aggregation inhibitors • low molecular weight heparins • insulin glargine/detemir • direct acting antiviral agents • atypical antipsychotics provided it is presented in the pharmacy: - a prescription from a doctor or GP or PLS (on which the indication of urgency is given) prescribed on a public holiday or pre-holiday or during the hours indicated above.

continued

Table 8.1 - *continued*

Piedmont - *continued*	
Reference to "service pharmacy"	Active service: **Front office: online activation service for accessing and using the ESF** (from January 2023) • training pharmacists: € 65/ farmacia Services purchased by the citizen: 1. activation upon consent/withdrawal of consultation € 1.00/each. 2. smartphone certification € 0.50/each. 3. proxy activation/deactivation € 1.00/each. **Prevention Serena-screening for colorectal cancer** (from March 2023) • Training pharmacists 80 €/ farmacia (già effettuata nel 2020) • IT platform € 10,000.00 4. Kit delivery € 3.60/each. (VAT included) 5. Intermediate distribution € 0.40 /cad (incl. VAT) **Flu and COVID-19 vaccinations:** Remuneration: - €9 administration of COVID-19 vaccine; - €6.16 administration of flu vaccine; **Telemedicine services (Cardiac Holter, Pressure Holter, ECG):** Cardiac Holter: € 62.00 blood pressure Holter : € 44.00 ECG: € 26,00- ' **Monitoring adherence to drug therapy in patients with hypertension';** - 10.00 € for each enrolment that led to the identification of non-target subjects; - 2.00 € for each subsequent measurement (max. 5/year).
Puglia	
Legal basis	DGR no. 610 of 19.04.2021, supplemented by D.G.R. no. 345 of 26.03.2024
Agreement duration	01.04.2024 – 30.11.2024
Organisation of DPC distribution	A lead company (the local health authority of Bari), to which the centralised management of the DPC has been delegated, buys the drugs on the basis of centralised tenders issued by the Regional Aggregator. The lead local health authority requests that the manufacturer deliver the DPC drugs to intermediate distributors in charge of storage and delivery to affiliated pharmacies.The lead Local Health Authority is responsible for keeping the list of products in DPC up-to-date.
Medicines/Criteria Attention for Distribution DPC	Exclusion from the regional list of: • drugs with treatment plan for cystic fibrosis, rare diseases, multiple sclerosis, AIDS • narcotic drugs • blood derivatives • ex-OSP2 reclassified by AIFA into A-PHT for which 'direct distribution' was envisaged
Remuneration per pack	Share including charges for intermediate and final distribution: • €5,50 + VAT; • €6,50 + VAT for subsidised rural pharmacies with NHS revenues <€450.000 and rural and urban pharmacies with NHS revenues <€300.000 Charge at the intermediate distributor: €1.10 + + VAT/package • with reference to the software used for the DPC of PHT drugs, the GO OPEN system is in use in the Apulia region, with charges borne entirely by Federfarma.
DPC ceilings	N.A.
Drug substitutability	Dispensing of the drug awarded in the tender. In the event of a reasoned indication by the doctor of 'non-substitutability', or a request for substitution by the user: • if the drug is 'patent expired', dispensation under agreement with the user sharing the difference from the price on the transparency list and any fixed fee per prescription expected. • if the drug is 'patent expired', user co-sharing of any fixed fee per prescription foreseen.

continued

Table 8.1 - *continued*

Puglia - *continued*	
Mixed prescriptions	Separate prescriptions for medicines DPC and under approved care regime.
Medicines not available in the DPC channel/urgent prescriptions	In case of unavailable medicines:branded drug unavailable: • equivalent generic dispensation in DPC; • generic unavailable: dispensing DPC branded drug; • if branded and generic drugs are unavailable: dispensation under agreement.
Reference to "service pharmacy"	Active service 1. Online activation of citizen access to the Electronic Health File (Fascicolo Sanitario Elettronico, FSE), for the completion of the which the following remuneration was established for pharmacies: • €5,00 + VAT for each FSE activated by urban pharmacies; • €5,50 + VAT for each FSE activated by rural pharmacies; This project ended in October 2020. 2. Administration of anti-COVID-19 vaccines through pharmacies, for the performance of which the following remuneration was established for pharmacies: • €6.00 (VAT exempt) per professional act + €4.50 for accessory charges, for the administration of a single dose of vaccine by subsidised rural pharmacies with SSN turnover <€450,000 • €6.00 (VAT exempt) per professional act + €4.00 for incidental charges, for the administration of a single dose of vaccine by all other pharmacies. Tale progettualità è attualmente in corso. The remaining projects included in the Regional Chronoprogramme of the Service Pharmacy are being defined by the Regional Commission on Service Pharmacy, in agreement with the Pharmacy Associations and the Professional Orders of Pharmacists of Apulia.
Sardinia	
Legal basis	DGR n. 20/69 of 30.06.2022
Agreement duration	7 July 2022 - 31 December 2024, extendable
Organisation of DPC distribution	A leading company (ARES) buys the drugs on the basis of tenders issued by the Regional Purchasing Centre of Sardinia. The manufacturer delivers the DPC drugs to intermediate distributors in charge of storage and delivery to affiliated pharmacies.
Medicines/Criteria Attention for Distribution DPC	Exclusion from the regional list of: • LMWH • teriparatide • ex-OSP2 reclassified by AIFA into A-PHT • FGM (Flash Glucose Monitoring) devices
Remuneration per pack	Share including charges for intermediate and final distribution: • €5.70 + VAT, urban and rural pharmacies not subsidised For subsidised rural pharmacies with NHS turnover <450.000,00: • €5,70 + VAT for drugs with pP ≤ €50,00 + VAT; • €8,60 + VAT for drugs with pP ≤ €50,00 + VAT; FGM €3 per quarterly delivery Kit (6 sensors, 6 packs of strips and 3 packs of lancets, strips and lancets provided free of charge by the company). The share of intermediate distribution is defined by separate agreement of the pharmacies with the intermediate distributors.
DPC ceilings	N.A.
Drug substitutability	Dispensing of the drug awarded in the tender. In the case of a reasoned indication by the doctor of 'non-substitutability' with approval of the pharmaceutical service: • if the drug is included in DPC list, dispensed in DPC; • in the event of a justified clinical impossibility for which the patient cannot take the drug in the DPC (e.g. ADR), the requested speciality can be dispensed through the pharmaceutical service of the local health authority to which the patient belongs In case of a replacement request by • the user:the user bears the full cost of the medicine.

continued

Table 8.1 - *continued*

Sardinia - *continued*	
Mixed prescriptions	N.A.
Medicines not available in the DPC channel/urgent prescriptions	If drug is unavailable/untraceable: dispensation under agreement
Reference to "service pharmacy"	Active service • ticket payment with PagoPA • TS-CNS activation to the citizen • service booking via CUP • printing and withdrawal of documents via FSE • information centre on RAS online health services • choice/withdrawal of GP, PLS Colorectal screening
Sicily	
Legal basis	D.A. n221 of 2021 D.D.G n46 of 2021
Agreement duration	01.04.2021 – 01.04.2024
Organisation of DPC distribution	The local authority of Palermo, identified as leader by D.D.G. 46/2021 of 27/01/2021, purchases drugs on the basis of tenders issued by the regional CUC (Centrale Unica di Committenza). In the case of expired tenders, the lead local authority negotiates privately with the supplier companies. The lead local health authority places the orders by allocating them to the 19 intermediary distributors located throughout the region and in charge of storage and delivery to the contracted private pharmacies.
Medicines/Criteria Attention for Distribution DPC	Exclusion from the regional list of: • ticagrelor • prasugrel • clopidogrel+ASA • denosumab • interferon beta 1a, interferon beta 1b and pegiterferon 1a • glatiramer acetate • pioglitazone+metmorphine
Remuneration per pack	Pharmacies' remuneration share: • €4,30 + VAT; • €6,60 + VAT for subsidised rural pharmacies with revenues <€450.000, for pharmacies with NHS revenues <€300.000 Remuneration share of the intermediate distributor: • €1,30 + VAT;
DPC ceilings	N.A.
Drug substitutability	Dispensing of the drug awarded in the tender. In the case of a reasoned indication by the doctor of 'non-substitutability': • if the drug is included in DPC list, dispensed in DPC; • if the drug is not included in the DPC, dispensing in agreement with the user sharing the difference from the tender price.
Mixed prescriptions	Separate prescriptions for medicines DPC and under approved care regime.
Medicines not available in the DPC channel/urgent prescriptions	N.A.
Reference to "service pharmacy"	Inactive service.

continued

Table 8.1 - *continued*

Tuscany	
Legal basis	Resolution No. 703 of 20.06.2022 Resolution No. 670 of 03.06.2024
Agreement duration	Resolution N.703 - 01.07.2022 – 30.06.2024 Resolution No. 670 of 30.06.2025
Organisation of DPC distribution	ESTAR tenders and buys the drugs. The supplying company delivers the DPC drugs to a lead distributor, one for each local health context, which stocks the drugs and distributes them to a series of satellite distributors (max. 4 for each local health authority) for delivery to the affiliated pharmacies.
Medicines/Criteria Attention for Distribution DPC	Inclusion in the regional list: - PHT drugs - Drugs DGRT no. 135/2002 - Supply of vaccines to the medical profession (GPs, Pediatricians) for administration as part of their outpatient activities (Resolution No. 703 of 20.06.2022) Exclusion from the regional list of: - medicines con PP < €13.50 - PHT drugs subject to exclusive direct distribution in Tuscany.
Remuneration per pack	Share including charges for intermediate and final distribution: €5,00 + VAT (medicines); €4,00 + VAT (vaccines); The remuneration is increased by: €0,50 + VAT to disadvantaged pharmacies referred to in Regional Law No 37/2004 €0,25 + VAT for subsidised rural pharmacies Pharmacies, at their own charge, pay wholesalers €1.10 + VAT per pack. – The distribution charges borne by the Lead and Satellite Warehouses are paid by public and private territorial pharmacies, according to private agreements. – The costs for the operation of the Information System are borne by the Region of Tuscany. There are no other charges.
DPC ceilings	N.A.
Drug substitutability	Dispensing of medicines under contract by Estar for 'per conto' distribution. For drugs that are not under contract, in the event of a reasoned indication by the doctor of 'non-substitutability', dispensing under the agreement is permitted in accordance with the rules therein, also for the purposes of cost-sharing by the patient. For microemulsified cyclosporine (exemption code 052), levetiracetam, tacrolimus, and topiramate, dispensing of the drug prescribed by the doctor is guaranteed and, if it is not available in the distribution channel 'per conto', dispensing under agreement is authorised without any cost-sharing charged to the patient.
Mixed prescriptions	Provision of separate prescriptions for DPC medicines under contract to Estar and all others dispensed under approved care regime.
Medicines not available in the DPC channel/urgent prescriptions	In the case of unavailable medicines or urgent prescriptions, dispensing under agreement.
Reference to "service pharmacy"	Active service • administration of anti-SARS-CoV-2 vaccines; remuneration of EUR 9.16 per any vaccination administered • administration of flu vaccines; remuneration of EUR 7.50 per any vaccination administered • CUP service, TS-CNS activation, access to the Electronic Health File (ESF): - €2.50 + VAT, urban and rural pharmacies not subsidisedIVA - €3.50 + VAT, subsidised rural pharmacies - €5.00 + VAT, disadvantaged pharmacies as per LR 37/2004 • Distribution 'per conto' of diabetic and supplementary care devices TN - €7.00 + VAT monthly requirement delivery, - Colorectal screening: ongoing activation - Choice/withdrawal GPs and Pediatricians: ongoing activation

continued

Table 8.1 - *continued*

Province of Trento	
Legal basis	Resolution No. 1651 of 16.09.2022
Agreement duration	01.01.2023 – 31.12.2024
Organisation of DPC distribution	The Single Health Authority (APSS) buys drugs on the basis of tenders issued at provincial level or by joining multi-regional tenders. APSS requires the manufacturer to deliver the DPC drugs to intermediate distributors in charge of storage and delivery to affiliated pharmacies.
Medicines/Criteria Attention for Distribution DPC	PHT medicines with the following exclusions: • narcotics subject to charge and discharge register and oxygen • medicines for which the use of DPC is economically disadvantageous for the SSP compared to the AFC; • medicines which, for specific care (e.g. therapeutic monitoring) and organisational needs, are distributed directly by companies. Drugs not contained in the PHT may also be dispensed in DPC in order to ensure access to the drug when other distribution channels are disadvantageous or impractical.
Remuneration per pack	• Share paid to affiliated pharmacies including the share for intermediate and final distribution for each pack distributed: – Year 2023 - €5,60 + VAT; – Year 2024 - €5,30 + VAT; – The share of intermediate distribution is defined by separate agreement of the pharmacies with the intermediate distributors.
DPC ceilings	The quotas in the previous column are confirmed if a predefined number of packages delivered in the year is reached: 540,000 for 2023 and 590,000 for 2024. If this volume is not reached, the pharmacies will receive an adjustment for the difference between the fee and the fee for the previous year (fee year 2022: € 5.95 + VAT per pack).Note: for the year 2023, the quota paid to pharmacies (€ 5.60) is confirmed, without the need to make the above-mentioned adjustments, as the predefined cut-off value of packs supplied in the year (540,000) has been largely exceeded.
Drug substitutability	Dispensing of the drug awarded in the tender. In the case of a request for substitution by the user with an equivalent medicine in terms of active ingredient, dosage and packaging: • if the medicine is NOT patent-expired, dispensing in AFC with payment by the user of the full cost of the medicine • if the drug is off-patent, dispensing in AFC with payment by the user of the differential between the reference price and the public price The doctor's indication of 'non-substitutability' is not provided for in DPC.
Mixed prescriptions	Separate prescriptions for medicines DPC and under approved care regime.
Medicines not available in the DPC channel/urgent prescriptions	In the case of unavailable medicines or urgent prescriptions, procurement of the drug from hospital pharmacies (if available) and dispensing in DPC. Urgent prescriptions (date of dispensing coinciding with date of prescription) of valacyclovir can be dispensed by agreement.
Reference to "service pharmacy"	Inactive service.

continued

Table 8.1 - *continued*

Umbria	
Legal basis	Law no. 717 of 13.07.2022
Agreement duration	1/07/2022 - 31/12/2025
Organisation of DPC distribution	A lead company buys the drugs on the basis of tenders issued by the Regional Purchasing Centre. The lead local health authority require the manufacturer to deliver DPC drugs directly to a lead distributor. The latter stores the drugs purchased by local health authorities and distributes them to a series of satellite distributors. These make the delivery to pharmacies under agreement.
Medicines/Criteria Attention for Distribution DPC	Exclusion from the regional list of: • LMWH • ex-OSP2 reclassified by AIFA into A-PHT Exclusion from the regional list of drugs when the cost to the Regional Health System is higher than the supply under agreement.
Remuneration per pack	Share including charges for intermediate and final distribution: • €5.20 (excluding VAT) for the first year of the agreement, starting 1 July 2022; • €5.30 (excluding VAT) for the second year of the agreement; • €5.40 (excluding VAT) for the third year; For pharmacies with NHS revenue • < €450,000 the remuneration is increased by 10%.
DPC ceilings	N.A.
Drug substitutability	Dispensing of the drug awarded in the tender. In the event that the doctor includes a non-substitutability clause on the prescription, accompanied by a justification report giving adequate reasons why the patient needs to continue treatment with the same drug and is unable to switch to the medicinal product supplied by the local health authority, the drug may be dispensed under approved care regime in accordance with the current procedures (difference with reference price paid by the patient). In the event that the patient refuses the substitution, the requested medicine may be dispensed under approved care regime, but in that case the difference between the price of the drug and the tender price plus the ordinary pharmacies' surcharge remains at the patient's own expense. The local health authority will reimburse the pharmacy for the tender price plus the premium.
Mixed prescriptions	Separate prescriptions for medicines DPC and under approved care regime.
Medicines not available in the DPC channel/urgent prescriptions	For medicines reserved for the DPC, except in the case of a documented shortage in the regional distribution cycle (documentation in the management system attesting the 'shortage'); in this case, the pharmacist is however required to dispense the same pharmaceutical speciality as in the DPC and may only dispense one pack. This is without prejudice to the possibility of dispensing drugs not available in pharmacies, prescribed in an emergency by the Continuing Care Unit or Emergency Room. In that case, the pharmacist will send only one pack and will treat the prescription in the same way as the 'missing' one.

continued

Table 8.1 - *continued*

Umbria - *continued*	
Reference to "service pharmacy"	Active service • Booking service for specialist assistance (CUP) Remuneration: - up to 700,000 transactions €2.40 (excluding VAT) for the first year of the agreement, starting 1 July 2022; €2,45 + VAT for the second year €5.40 + VAT for the third year; - threshold of 700,000 transactions exceeded remuneration is decreased to: €1,45+VAT for the first year; €1,50+VAT for the second year; €1.55 + VAT for the third year. • Supporting Faecal Occult Blood Screening for the Prevention of Colorectal Cancer. Remuneration: € 3.00 for each sample delivered to the Single Screening Laboratory (LUS). This amount includes: - the fee for the intermediate distributor; - the provision of the IT platform for tracking samples; - the pharmacist's health promotion and education activities towards the population, in order to increase the population's adherence to the screening campaign. • Administration of COVID-19 vaccines and flu vaccines € 8 (this amount covers the professional act of the individual inoculation and the services strictly related to the vaccination, which include the material needed for the administration, the procedures for recording the data of the vaccinations carried out and the logistical operations connected with the DPC). The projects included in the Regional Chronoprogramme of the Experimentation of the Service Pharmacy, (State-Regions Agreement rep. deeds no. 167 of 17/10/2019 and Understanding Rep. Acts No. 41/CSR of 30/03/2022) have all been activated and include the following additional activities: - Monitoring drug therapy adherence in people with hypertension/BPCO/Diabetes - Cardiovascular Risk Screening Support - Telemedicine services (Holter Pulse, Cardiac Holter, ECG, auto-spirometry)
Valle d'Aosta	
Legal basis	DGR n1709 of 27.12.2021
Agreement duration	01.01.2022 – 31.12.2024
Organisation of DPC distribution	The Local Health Authority of Valle d'Aosta uses, for the purchase of most of the medicines of the DPC, the tender carried out by SCR Piemonte, under an agreement signed with the regional Central Unit for Purchasing.
Medicines/Criteria Attention for Distribution DPC	Inclusion in the regional list of EBPM
Remuneration per pack	Share including charges for intermediate and final distribution: €6.75 + VAT for pharmacies with annual NHS revenues <=€300,000 €5.75 + VAT for pharmacies with annual NHS revenues >€300,000
DPC ceilings	N.A.
Drug substitutability	Dispensing of the drug awarded in the tender. In the case of a reasoned indication by the doctor of 'non-substitutability': • dispensing in direct distribution, subject to in-depth study of the pharmaceutical sector In case of a replacement request by the user: • the user bears the full cost of the medicine.

continued

Table 8.1 - *continued*

Valle d'Aosta - *continued*	
Mixed prescriptions	Manageable if electronic prescriptions.
Medicines not available in the DPC channel/urgent prescriptions	In the case of unavailable medicines or urgent prescriptions, dispensing under agreement.
Reference to "service pharmacy"	Active service: 1.Distribution 'per conto' of diabetic medication (€5.5/access net of VAT). 2.Booking specialist visits and examinations (CUP) (€4.5/performance net of VAT). 3.Acquisition of consent for ESF consultation (€3.5/performance net of VAT). 4.Flu and anti-COVID vaccination (€7.16 /vaccination). 5.Performance of diagnostic tests with biological sample collection at nasal, salivary or oropharyngeal level (€15/tampon, limited to tests for SARS-CoV-2 antigen in cases provided for by the regional provisions in force)
Veneto	
Legal basis	DGR no. 629 of 14.05.2019 with addresses and remuneration for the definition of the DPC Agreement, DG Health and Social Affairs Area Decree No. 71 of 9.07.2019 approving the outline of the Regional Agreement for the DPC, DG Health and Social Affairs Area Decree no. 86 of 12.08.2020 updating the Guidelines for the Dispensing of Medicines in DPC
Agreement duration	01.08.2019 – 31.07.2023 renewed for a further 3 years (31.7.2026)
Organisation of DPC distribution	A lead company (Azienda Zero) buys the drugs on the basis of tenders issued by the region and asks the manufacturer to deliver the DPC drugs directly to the lead intermediate distributor in charge of storage and distribution to other distributors and further to pharmacies under agreement.
Medicines/Criteria Attention for Distribution DPC	Exclusion from the regional list of: • LMWH • ex-OSP2 reclassified by AIFA into A-PHT Exclusion from the regional list of: • narcotic drugs • oxygen • drugs subject to AIFA registers • drugs whose cost to the Regional Health System is higher than the supply under agreement.
Remuneration per pack	Total amount paid by the Region per pack: € 5.30+VAT/pack € 6.32+VAT/pack for subsidised rural pharmacies with NHS revenue <=€450,000.00 and for urban/rural pharmacies non subsidised • SSN ≤ €300,000.00
DPC ceilings	N.A.
Drug substitutability	Dispensing of the drug awarded in the tender. In the event of a reasoned indication by the doctor of 'non-substitutability' or a request for substitution by the user, dispensation in agreement with the user sharing the difference between the reimbursement price and the sale price. The non-acceptance of substitution by the user must be indicated in the prescription with an appropriate note and the signature of the user or family/caregiver confirming their choice.

continued

Table 8.1 - *continued*

Veneto - *continued*	
Mixed prescriptions	Separate prescriptions for medicines DPC and under approved care regime. If there is an overlap, the user expresses a preference and will have to make a new prescription for the non-withdrawn drug.
Medicines not available in the DPC channel/urgent prescriptions	In the case of unavailable medicines, communication to the lead company, which is called upon to express an opinion on how to operate. In the absence of indications, dispensation under agreement with a short justification (e.g. missing in DPC). If Ex-OSP 2, live delivery and as a last resort by agreement. In the case of an urgent prescription, dispensation by agreement, with a note of the reason on the prescription and signature of the user or family member/caregiver.
Reference to "service pharmacy"	Active service Diabetes screening project unknown • € 10 (excl. VAT) project presentation and questionnaire completion • € 22 (excl. VAT) project illustration and questionnaire completion, glycaemic test proposal, explanation of results Drug therapy reconnaissance project after hospital discharge -AULSS no. 7 € 20 (excluding VAT) per card processed (the minimum number of cards to be processed during the enrolment period is 6) Unknown high blood pressure screening project * • € 15 (excl. VAT) per enrolled citizen Unknown high blood pressure screening project * • € 20 (excl. VAT) per citizen enrolled and subjected to lipid profile determination Monitoring adherence to drug therapy in patients with type 2 diabetes:* • € 40/patient (VAT excluded) for enrolment, first questionnaire and counselling, • € 20/patient (excl. VAT) follow-up questionnaire and counselling Monitoring adherence to drug therapy in COPD patients * • € 40/patient (VAT excluded) for enrolment, first questionnaire and counselling, • € 20/patient (excl. VAT) follow-up questionnaire and counselling Telemedicine • Telemedicine services general examination: € 20 (excluding VAT) per televisit* • Telemedicine services for specialist visits: €20 (excluding VAT) per TV, + €200 for pharmacies joining the project for the first time • Electrocardiogram (ECG)- Cardiac Holter- Holter pressure*: ECG: € 35 (excl. VAT) per enrolled citizen Cardiac Holter: € 59 (excl. VAT) per enrolled citizen Holter pressure: € 59 (excl. VAT) per enrolled citizen* for participation in at least two of these marked projects, pharmacies are entitled to a flat-rate fee of €180 as compensation for general expenses, including computer management. Supporting Faecal Occult Blood Screening for the Prevention of Colorectal Cancer. • € 4/sample delivered to the laboratory (excluding VAT) for subsidised rural pharmacies with SSN turnover ≤€450,000.00 and for non-subsidised urban/rural pharmacies with SSN turnover ≤€300,000.00, • € 3.85/sample delivered to the laboratory (excluding VAT) for all others; • both amounts are reduced by 50% if delivery takes place with a delay of up to 2 days after the maximum time for the Intermediary Distributor phase Vaccine administration for COVID-19: • € 10.66 + € 200 one-off payment upon achievement of 200 administrations/pharmacy; Flu vaccine administration 2023-2024 campaign: • €6.16 + €0.50 per inoculation, +€200 for new participating pharmacies or +€100 for pharmacies that had already participated in previous years, one-off payment upon reaching the target differentiated by type/turnover SSN pharmacies.

N.A.: the information could not be found

Service Pharmacy Update (year 2023)

According to the regional survey 2023, 17 regions declared to have activated the Service Pharmacy (PA Bolzano, Calabria, Campania, Emilia-Romagna, Friuli Venezia Giulia, Lazio, Liguria, Lombardy, Marche, Molise, Piedmont, Apulia, Sardinia, Tuscany, Umbria, Valle d'Aosta and Veneto).

According to the regional survey 2023, 17 regions declared to have activated the Service Pharmacy (PA Bolzano, Calabria, Campania, Emilia-Romagna, Friuli Venezia Giulia, Lazio, Liguria, Lombardy, Marche, Molise, Piedmont, Apulia, Sardinia, Tuscany, Umbria, Valle d'Aosta and Veneto). In addition to the most widespread activities, a group of regions reported the activation of new services by 2023. In particular, Emilia-Romagna has included among the services paid for by the National Health System structured interviews with patients suffering from chronic pathologies, to be recorded on a regional application, which includes the promotion and monitoring of adherence to therapy; pharmacological reconnaissance; the collection of suspected adverse reactions; and the assessment of the correct use of administration devices through patient training sessions. In addition, it provided for the involvement of pharmacies in telemonitoring paths in the field of cardiology. The Piedmont region has also indicated an increase in services available in pharmacies from 2023, including multiple telemedicine services (Holter pressure monitor, Holter heart monitor, ECG) and monitoring of medication adherence to therapy in patients with hypertension Similarly, the Umbria region has planned for 2023 the activation of a series of projects, including telemedicine services (blood pressure holter, cardiac holter, ECG, auto-spirometry), support for cardiovascular risk screening, and the monitoring of adherence to drug therapy in patients with hypertension, COPD and diabetes. Di particolare interesse è la regione Veneto che ha attivato un progetto di screening per il diabete non diagnosticato, che prevede l'illustrazione del progetto al paziente, la compilazione del questionario, la proposta di un prelievo di sangue capillare e la spiegazione di eventuali risultati.

Inter-regional differences also emerge in the remuneration of services. Take, for example, colorectal screening, for which there is a fee of EUR 2.40 per sample analysed in Friuli Venezia Giulia and a fee of EUR 3 per sample delivered to the Single Screening Laboratory (LUS) in Umbria. Similarly, the activation of the Fascicolo Sanitario Elettronico (Electronic Health File) costs EUR 2.50 in Tuscany (non-subsidised urban and rural areas) and EUR 5-5.50 in Apulia. In addition, some regions stated that they provide funding for the training of operators, in addition to remuneration for individual services (Piedmont and Liguria).

In conclusion, the analysis provides an update on the state of the art of DPC agreements in force across the country, identifying wide inter-regional variability on multiple aspects.

An update of this analysis will be necessary in the light of the Provisions to promote the provision of pharmacy services in the Budget Law 2024.

Appendix 2

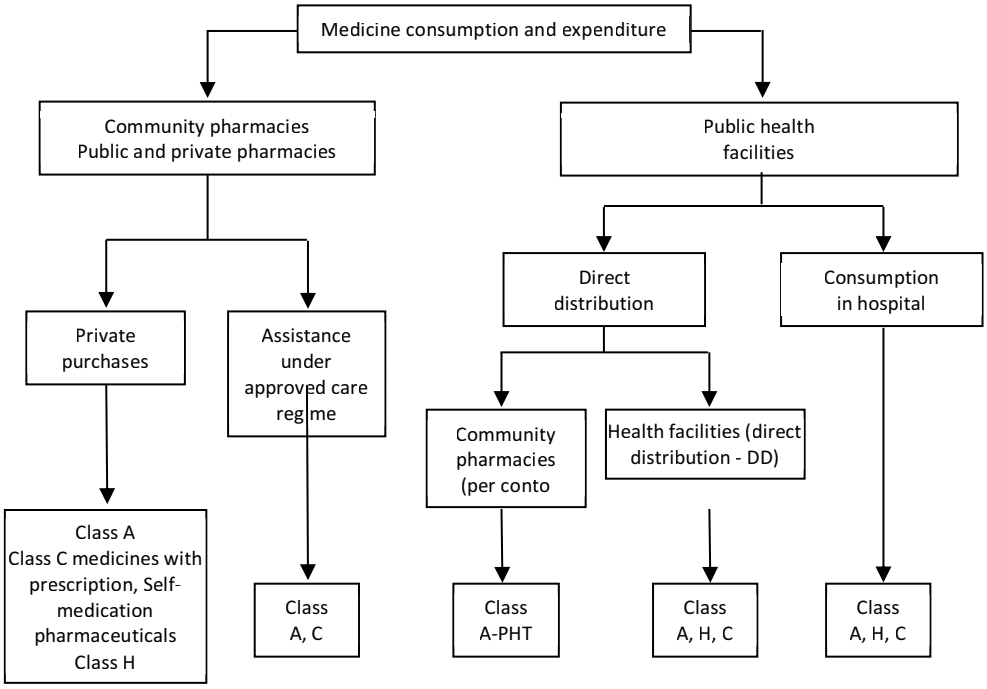
Data source and methods

BACK TO CONTENTS

1. Pharmaceutical consumption and expenditure data

The 2023 National Report on Medicines Use in Italy provides a summary of data on consumption and expenditure of medicines supplied by the National Health Service (NHS) under approved care regime (outpatient assistance), direct and per conto and hospital distribution (Figure 1.1). Moreover, this Report describes consumption and expenditure of Class C medicines purchased directly by the citizen, in addition to the private purchase of Class A-H medicines.

Figure 1.1 Summary of Report data



The description of medicine consumption made available by the Report is based on the analysis and integration of data collected through different information flows:

OsMed (National Observatory on the Use of Medicinals) flow. The information flow of pharmaceutical services provided through pharmacies (both public and private) affiliated with the NHS was established pursuant to Law 448/1998 and subsequent amendments, implemented by the Ministerial Decree No. 245/2004.1 [1] This flow records the data of the recipes collected by Federfarma (National Federation of Private Pharmacies affiliated with the NHS) and by Assofarm (Association of Public Pharmacies), that receive data from their provincial offices and subsequently aggregate them at regional level. The

[1] Art. 68, paragraph 7 of Law 23-12-1998, No. 448 as amended, implemented by Art. 18 of the Ministerial Decree 20-9-2004, No. 245 ("Regulation on the organisation and functioning of the Italian Medicines Agency, pursuant to Art. 48, paragraph 13, of Legislative Decree 30-9-2003, No. 269, converted into Law 24-11-2003, No. 326")

OsMed flow has a variable degree of completeness by geographical area and by month; the national data coverage in 2023 was generally 96.4% of expenditure. The share of missing expenditure and consumption was obtained by means of an expansion procedure, which uses as a reference value for pharmaceutical expenditure the data from the Summary Accounts Receipts (DCR), periodically updated by AIFA. In order to guarantee homogeneous comparisons between the Regions, the expansion procedure brings regional spending back to 100%, assuming that the distribution of missing data by specialty is not significantly different from the observed data and that the invariance of the retail price of the single medicinal package is guaranteed.

Purchase by public health facilities. The Decree of the Minister of Health of 15 July 2004 provided for the establishment, within the New Health Information System (NSIS), of the "Drug Traceability" flow, aimed at tracking the movement of medicines with Marketing Authorization (MA) in the national territory and/or abroad. This flow is fed by pharmaceutical companies and intermediate distribution and detects the packages handled along the distribution chain, up to the final supply points: pharmacies, hospitals, clinics, shops, etc. The data analysed in this Report refer to the purchase of medicines (in terms of both quantity and economic value) by public health facilities (i.e. non-agreed pharmaceutical assistance). Therefore, they relate to the supply of medicines by pharmaceutical companies to public health facilities (sell-in) which are subsequently used within the facilities themselves (i.e. sell-out of hospital consumption), or dispensed directly to the patient for their use also outside healthcare facilities (i.e. sell-out of direct and per conto distribution). Pursuant to Law 236/2016 (Budget Law 2017), Article 1, paragraph 398, the ceiling of hospital expenditure is calculated gross of the expenditure for Class A medicines in direct distribution and per conto distribution, therefore it was renamed "pharmaceutical expenditure ceiling for direct purchases". The data used for monitoring compliance with the expenditure ceiling are those collected from the Drug Traceability flow.

The rules of data transmission through the Drug Traceability flow provide for the daily transmission of data relating to the number of packs handled to the individual healthcare facility. However, since the sending of the economic value of the movements can also take place later than that of the movements, it is possible that the available data may include unexploited consumption.

Private purchase by the citizen. In addition to the medicines reimbursed by the NHS, local pharmacies also dispense Class A and Class C medicines purchased privately by citizens (with or without a prescription). The analysis of pharmaceutical consumption by the citizen is carried out using the data collected for Class C medicines through the Drug Traceability flow (established pursuant to the Decree of the Minister of Health of 15 July 2004), sent by the wholesalers to the central database of the Ministry of Health, concerning the drugs delivered to local pharmacies (sell-in). The private purchase of Class C medicines is derived by difference between what is purchased from pharmacies (sell-in), compared to what is paid by the NHS (sell-out, i.e. the OsMed flow), considering the citizen as a recipient. It should be noted that when analysing the consumptions related to a wide time span, any misalignment between sell-in and sell-out is minimised, consequent to the re-composition of the warehouse stocks of the pharmacy, which, on the contrary, could affect significantly on the single month.

Direct and *per conto* distribution. The information flow of pharmaceutical services carried out directly and *per conto* was established by the Decree of the Minister of Health of 31 July 2007 governing the New Health Information System (NSIS). This flow, fed by the Regions and the Autonomous Provinces of Trento and Bolzano, records the supply of medicines to be paid by the NHS to the assisted person, for consumption at his/her own home, an alternative to the traditional provision of the same at pharmacies, as well as those provided directly from health facilities pursuant to Law 405/2001, as amended. This flow includes pharmaceutical services provided on discharge from hospitalisation or after specialist examination, limited to the first complete therapeutic cycle, to chronic patients subject to therapeutic plans or taken care of by the facilities, in home care, residential or semi-residential (i.e. direct distribution), by the affiliated pharmacies, public or private, on behalf of the Local Health Authorities (i.e. per conto distribution). The survey is extended to the prescriptions of all medicines authorised for marketing in Italy and identified by the MA code, regardless of the class of supply paid by the NHS and the supply regime. However, in order to have a complete picture of the consumption and expenditure of medicines directly borne by the public structures of the National Health Service, the survey also includes foreign medicines not registered in Italy, medicines prepared in pharmacies on the basis of a medical prescription for a specific patient, "magistral formulae", and medicines prepared in pharmacies according to the indications of the European Pharmacopoeia or national Pharmacopoeias in force in the Member States of the European Union, "officinal formulae", which shall be directly provided to patients served by this pharmacy. For the purposes of this Report, analyses on pharmaceutical performance in direct or per conto distribution have been carried out with exclusive reference to medicines provided with MA, therefore it does not include preparations prepared extemporaneously in pharmacies. The data of this information flow was used for the periodic monitoring of the territorial pharmaceutical expenditure performed by AIFA, as well as for the calculation of the deviation from the ceiling of territorial pharmaceutical expenditure and the allocation of budgets to pharmaceutical companies. Starting from 2017, in accordance with Law 236/2016 (Budget Law 2017), Article 1, paragraph 399, the ceiling of local pharmaceutical expenditure, renamed "agreed pharmaceutical expenditure ceiling", is calculated net of direct and *per conto* distribution.

Purchase of medicines by health facilities not directly managed by the NHS, but subsequently reimbursed. In the information flow of pharmaceutical services carried out in direct or *per conto* distribution, the Regions and the Autonomous Provinces of Trento and Bolzano detect the delivery of medicines through the facilities not directly managed by the NHS. Such facilities provide for the purchase of medicines, subsequently reimbursed by the NHS as an excess over the rate reimbursed for the individual services provided ("extra-DRG").

Pharmaceutical prescriptions. The information flow for transmission of pharmaceutical prescriptions is provided by paragraph 5 of Art. 50 of the Decree Law of 30 September 2003, No. 269, converted, with modifications, by Law 24 November 2003, No. 326, as amended (Health Card). The provision of health services (local health authorities, hospitals, scientific institutions and hospitals, university clinics, public and private pharmacies, specialist outpatient clinics and other accredited facilities) have the obligation to transmit prescriptions charged to the NHS electronically to the Ministry of Economy and Finance (MEF). For the purpose of monitoring health expenditure, pursuant to the

aforementioned rule, the electronic transmission is requested of recipe data (and prescriptions) compliant with paragraph 2, Art. 50, commonly referred to as "red recipes", regardless of the content of the prescription and the medicine delivery method. This means that, in the case of prescription of medicines through "*per conto* distribution" mode or products related to supplementary assistance, reported on a "red recipe", the relative data are subject to the obligation of transmission, and incomplete, late or no transmission are sanctioned pursuant to Art. 50. The supply structures can also transmit recipes written on different models (white recipes, or modules not processed by the Health Card System, such as the tracing form) and recipes for the supply of pharmaceutical products in different ways: *per conto* distribution, direct distribution, additional home assistance and supplementary assistance. The data to be transmitted relate to the patient (fiscal code, Health Care Unit of residence, etc.), to the prescription (prescription identification code, Health Care Facility that processed it, etc.), to the services provided (product code, MA code, license number, amount, etc.) and to the prescriber (physician's code, specialization, etc.). In the case of pharmaceutical prescriptions, the transmission of prescription data by the dispensing facilities (by pharmacies open to the public) takes place within the 10th day of the month following the month in which the prescription is used (or according to the date submitted on the MEF website), also through professional associations and third parties identified by the facilities for this purpose.

For the purposes of this Report, the data flow has been used for analyses on the use of pharmaceuticals by age group and gender and for adherence and persistence analyses.. The data refer to all Italian Regions.

2. Classification systems

The drug classification system used in the Report is the one developed by the Oslo *Collaborating Centre for Drug Statistics Methodology* (http://www.whocc.no/) of the World Health Organisation (WHO), based on the ATC/DDD system (respectively: Anatomical-Therapeutic-Chemical category and Defined-Daily Dose). The ATC identifies a system for classifying the active ingredients of pharmaceuticals, grouping them in different categories on the basis of the apparatus/organ on which they exert their therapeutic action and according to their chemical and pharmacological properties. Each active ingredient is generally associated with a unique 5-level code; frequently the second, third and fourth levels are used to identify the pharmacological classes.
The defined-daily dose (DDD) represents the maintenance dose per day of therapy, in adult patients, related to the main therapeutic indication of the substance (therefore it is a standard unit and not the recommended dose for the single patient). The DDD is generally assigned to an active ingredient already classified with a specific ATC code. The number of DDD prescribed refers to 1000 inhabitants for each day of the time period in question (week, month, year, etc.). The DDD allows to aggregate the prescriptions regardless of the prescribed substance, the administration route, the number of dosage units and the dosage of the single package, and thus to make comparisons over time, between geographical areas and between therapeutic categories. The WHO annually provides for a revision of the ATC and DDD classification; consequently, it is likely that consumption and spending by category change over time, depending at least in part on these updating processes.
Ultimately, DDD was used in the analysis of drug consumption to parametrise the number of packages delivered to patients, according to the formula shown in section 4. In some specific analyses, a grouping of different ATC and/or active ingredients was applied, in order to analyse consumption patterns according to the therapeutic field. The list of pharmaceuticals for direct distribution is represented by the Direct Distribution Guide (PHT - Guide to continuity of hospital-local assistance) in force since November 2004.
For equivalent medicines, the “transparency lists” were used, published monthly by AIFA, relating to the year 2023.

3. National population and standardisation of the Regional population

Regional variability of pharmaceutical expenditure and consumption, although mainly influenced by the different prescribing attitudes of physicians and by the variable epidemiological profiles, is also partly dependent on demographic characteristics (composition by age and gender). Therefore, in order to optimise the comparability between the Regions, the resident population in each Region measured by the Italian National Institute of Statistics (ISTAT) was recalculated taking into account the statistical weights provided by the Programming Department of the Ministry of Health.

Table 3.1 Statistical weights provided the Programming Department of the Ministry of Health

Age group	0	1-4	5-14	15-44 Men	15-44 Women	45-64	65-74	> 74
Weight	1	0.969	0.695	0,693	0,771	2.104	4.176	4.29

The procedure followed for the calculation of the weighted population was as follows: the number of the composition was identified by age group and gender of each Region (data source: https://demo.istat.it/); the number in each class was then multiplied by the corresponding weight; then, the sum of the values thus obtained at regional level was re-proportioned to the Italian population of the reference year (In 2023: 58,850,717 inhabitants

The implementation of this process of population standardisation implies that a Region with an older population than the national average will have a higher weighted population than the resident population and vice versa. Table 3.2 shows the resident population measured by the Italian National Institute of Statistics (ISTAT) and the weighted population for the years 2022 and 2023.

Table 3.2 Resident population measured by ISTAT and weighted population for 2022 and 2023

Region	Resident population as at 1.1.2022	Resident population 2022	Resident population as at 1.1.2023	Resident population 2023	Δ % 23-22 Resident population	Δ % 23-22 Resident population
Piedmont	4,256,350	4,446,957	4,240,736	4,420,734	-0.4	-0.6
Valle d'Aosta	123,360	126,242	122,955	125,734	-0.3	-0.4
Lombardy	9,943,004	9,843,181	9,950,742	9,842,822	0.1	0.0
Province of Bolzano	532,616	493,887	533,267	493,770	0.1	0.0
Province of Trento	540,958	530,064	542,050	531,305	0.2	0.2
Veneto	4,847,745	4,878,348	4,838,253	4,869,730	-0.2	-0.2
Friuli Venezia Giulia	1,194,647	1,263,009	1,192,191	1,256,728	-0.2	-0.5
Liguria	1,509,227	1,652,840	1,502,624	1,637,237	-0.4	-0.9
Emilia Romagna	4,425,366	4,480,210	4,426,929	4,472,731	0.0	-0.2
Tuscany	3,663,191	3,819,443	3,651,152	3,798,841	-0.3	-0.5
Umbria	858,812	898,751	854,137	892,438	-0.5	-0.7
Marche	1,487,150	1,535,012	1,480,839	1,526,667	-0.4	-0.5
Lazio	5,714,882	5,650,670	5,707,112	5,650,197	-0.1	0.0
Abruzzo	1,275,950	1,302,441	1,269,860	1,295,770	-0.5	-0.5
Molise	292,150	303,997	289,840	301,298	-0.8	-0.9
Campania	5,624,420	5,218,547	5,592,175	5,204,193	-0.6	-0.3
Puglia	3,922,941	3,875,957	3,900,852	3,865,297	-0.6	-0.3
Basilicata	541,168	547,420	536,659	543,442	-0.8	-0.7
Calabria	1,855,454	1,819,026	1,841,300	1,808,515	-0.8	-0.6
Sicily	4,833,329	4,684,305	4,802,016	4,659,867	-0.6	-0.5
Sardinia	1,587,413	1,659,823	1,575,028	1,653,402	-0.8	-0.4
Italy	**59,030,133**	**59,030,133**	**58,850,717**	**58,850,717**	**-0.3**	**-0.3**
North	27,373,273	27,714,739	27,349,747	27,650,790	-0.1	-0.2
Centre	11,724,035	11,903,877	11,693,240	11,868,142	-0.3	-0.3
South and Islands	19,932,825	19,411,517	19,807,730	19,331,784	-0.6	-0.4

4. Indicators and measures of use of medicines

Analysis of the main expenditure components

The analysis is based on disaggregated data on pharmaceutical expenditure and DDDs in the current and previous years. These data are combined according to the following formula:

$$IV = \frac{S^{23}}{S^{22}} = \frac{\sum_i q_i^{23}}{\sum_i q_i^{22}} \times \frac{\sum_i p_i^{23} q_i^{22}}{\sum_i p_i^{22} q_i^{22}} \times \frac{\frac{\sum_i p_i^{22} q_i^{22}}{\sum_i q_i^{22}}}{\frac{\sum_i p_i^{23} q_i^{22}}{\sum_i q_i^{22}}}$$

Quantity effect | Price effect | Mix effect

where:

"i" varies in the "field" constituted by the packages present on the market (also for zero sale)

IV = index of variation in expenditure between 2023 and 2022

S_{23} = pharmaceutical expenditure in 2023

S_{22} = pharmaceutical expenditure in 2022

qi_{23} = quantity sold in 2023 of the pack "i" (expressed in DDD)

qi_{22} = quantity sold in 2022 of the pack "i" (expressed in DDD)

pi_{23} = average price in 2023 of the single DDD with the pack "i"

pi_{22} = average price in 2022 of the single DDD with the pack "i"

This indicator consists of three factors:

- the first factor (quantity effect) relates to variation in the quantities of pharmaceuticals consumed;
- the second factor (price effect) concerns changes in the price of pharmaceuticals;
- the third factor (mix effect) describes if in the current year (considering current prices) more expensive medicinal products are consumed, compared to the previous year. If the factor is greater than 1, high-price pharmaceuticals are mostly consumed; vice versa, if this factor is less than 1, medicines with lower prices are mostly consumed in the current year.

In the analysis of the mix effect of a year, the use of DDDs avoids the introduction of bias induced by changing the packaging of some products available in the previous year with a different number of DDDs per item.

This type of analysis partially records the effect due to the introduction of medicines belonging to categories for which therapeutic alternatives were previously absent. In this case an increase is expected in the total number of DDD prescribed, while the analysis does not apply

to either price changes or the mix effect. The aforementioned limits do not concern the case of admission to the reimbursement of new molecules of therapeutic groups, for which other reimbursable medicines were already available, because the analysis highlights both possible variations in the overall prescription volume and shifts in the type of prescriptions.

When reading the results, it should be taken into account that:

- the indices of variation were expressed as percentage changes;
- the deviation (%) of pharmaceutical expenditure does not exactly coincide with the sum of the three deviations calculated (quantity, prices, mix), since it is the result of a product.

Temporal dynamics of the prices of Class A-NHS, of Class C medicines with prescription and of medicines purchased by healthcare facilities

The data used for the analysis of price dynamics refer to the consumption of Class A-NHS medicines, of Class C mediciness with prescription, of medicines purchased by public health facilities, collected and processed by OsMed. Prices relating to a single specialty are obtained as the ratio between the expenditure values (in euros) and the quantities sold (both in terms of DDD and packaging). Starting from the prices relating to single specialties, the Weighted Average Prices (PMP) were calculated for each month, for which the weights consist of either the number of DDD or the number of packages, according to the following formula:

$$PMP_i = \frac{\sum_{j=1}^{n} p_j^i q_j^i}{\sum_{j=1}^{n} q_j^i}$$

where:

n = is the number of specialties marketed in the month "i"

p_j^i = is the price of a DDD (or of a package) of the product "j" in the month "i"

q_j^i = is the number of DDDs (or of the packages) of the specialities "j" sold in the month "i"

The monthly temporal dynamics of prices is analysed in Section 1. The growth value of the weighted average price per DDD in this analysis is different from the one calculated in the breakdown of the variation in pharmaceutical expenditure (price effect component). In the monthly price trend the index used takes into account all specialties marketed at that time; the price index used to break down the variation in expenditure is instead constructed using only the DDD relating to the specialties present in the period with which the comparison is made (previous year) and, therefore, does not take into account the new specialties marketed in the current year.

Herfindahl-Hirschman Index (HHI): it is defined as the sum of the squares of the market shares. The index assumes values ranging between 0 and 1, where the maximum value corresponds to a situation of complete monopoly, while very low values are obtained in markets

in which there is a large number of competing agents, each of which holds a small market share. In order to be able to make comparisons taking into account the differences in formulation between the originator and biosimilars, the calculations were made on the defined daily doses (DDD) of each medicine in order to obtain a standardised daily dose.

Definitions of the indicators

Coefficient of variation % (CV%): allows to evaluate the dispersion of the values around the mean regardless of the unit of measurement and is calculated according to the formula:

$$CV = \frac{DS}{average} \times 100$$

Packs per 1000 inhabitants (or children): average number of medicine packs consumed by 1000 inhabitants (or children) during the period

$$\frac{\text{N. total number of packs consumed in the period}}{\text{N. inhabitants (or children)}} \times 1000$$

Packs per user: average number of drug packs consumed by each user (subject with at least one prescription in the period)

$$\frac{\text{N. total number of packs consumed in the period}}{\text{N. of users}} \times 1000$$

Average DDD cost: indicates the average cost of a DDD (or a day of therapy). It is calculated as the ratio between total expenditure and the total number of doses consumed.

Average cost per user: indicates the average expenditure per user. It is calculated as the ratio between the total DDD consumed and the total number of subjects who received at least one prescription during the period of time.

DDD/1000 inhabitants per day: average number of doses of medicine consumed daily by 1000 inhabitants (or users).
For example, for the calculation of the DDD/1000 inhabitants of a given active ingredient, the value is obtained as follows:

$$\frac{\text{Total number of DDD consumed in the period}}{\text{No. of subjects} \times \text{No. of days in the period}} \times 1000$$

DDD per user: it is an indicator of the average number of days of therapy. It is calculated as the ratio between the total DDD consumed and the total number of subjects who received at least one prescription during a period of time (users in the period).

DDD per user = (no. DDD consumed in the period/users in the period)

Incidence of use: the ratio of new drug users to the reference population over a specified period of time

I = (new users in the period / reference population) x 100 (or x 1,000)

Compound Annual Growth Rate (CAGR): is calculated through the n^{th} root of the overall percentage rate where n is the number of years of the period considered.

Therefore:

$$CAGR = \left(\frac{x_f}{x_{ii}}\right)^{\left(\frac{1}{n}\right)} - 1$$

where x_f represents the indicator calculated in the final period, xi represents the indicator calculated in the initial period and n represents the number of years considered.

Median: in relation to an orderly distribution of values in a population (DDD, per capita expenditure) the median represents the value which divides the population into two equal parts.

The prevalence of medicine use: is the ratio between the number of subjects who received at least one prescription and the reference population (potential users) in a specific period of time:

P = (no. users / population) x 100 (or x 1000 inhabitants, etc.)

Quartiles: values dividing the ordered distribution (expenditure, DDD, ...) into four parts of equal frequency.

- The first quartile is the value including 25% of data (25th percentile);
- the second quartile is the value including 50% of data (50th percentile), thus corresponding to the median;
- the third quartile is the value which includes 75% of data (75th percentile).

The *interquartile range* (IQR) is the interval between the 25th and 75th percentile and represents the central range in which 50% of the data lies.

% deviation from average: the % deviation from average of the Region i, with reference to an indicator x (per capita expenditure, DDD/1000 inhabitants per day, etc.), is constructed as:

$$\frac{x_i - Media}{Media} \times 100$$

where x_i represents the indicator calculated in the Region *i* and *Media* (Average) represents the average of the indicator calculated for all Regions.

Gross expenditure: pharmaceutical expenditure calculated as the sum of the quantities sold multiplied by the retail price.

Net expenditure: expenditure actually borne by the NHS (share of gross pharmaceutical expenditure). Therefore, the legal discounts and the shareholdings paid by the citizen are not considered.

Per capita expenditure: represents the average expenditure on pharmaceuticals per recipient. It is calculated as total expenditure (gross or net) divided by the weighted population.

Single prescription users: percentage of subjects with only one prescription in the period compared to total users

$$\frac{\text{Users with 1 prescription}}{\text{total users}} \times 1000$$

5. Indicators of adherence and persistence

The administrative database of prescriptions of Class A medicines dispensed on the national territory was employed to monitor the use of medicinal products for chronic therapies (so-called "art.50 flow"/Health Card provided for by article 50, paragraph 5, of Law Decree no. 269 dated 30 September 2003 converted with amendments into Law no. 326 dated 24 November 2003, as amended). In particular, the analysis of repeated prescriptions allowed to estimate adherence and persistence to treatment for such chronic therapies.
An analysis on new users – aged at least 45 years – was conducted, considering a one-year follow-up. In detail, new users were defined as individuals who received a prescription for drugs belonging to the therapeutic category in question in the period between 01/10/2022 and 31/12/2022 and who did not receive prescriptions for medicines belonging to the same category in the previous months starting from 01/10/2022. The year 2023 was therefore used for the follow-up of the subjects enrolled in 2022, in addition, new users who did not receive at least one medical prescription for any medicine in the last quarter of 2023 were excluded from the analysis, proxy of the status in life of the patient.
Adherence was assessed through the Medication Possession Ratio (MPR) indicator, defined as the ratio between the number of dispensed therapy days (calculated on the basis of DDD) and the number of days in the time interval between the beginning of the first and the theoretical conclusion of the last prescription, as supplied during the follow-up period; in formula:

$$MPR = \frac{number\ of\ therapy\ days}{interval\ between\ first\ and\ last\ prescription\ (plus\ days\ last\ prescription)}\ x\ 100$$

Low adherence to treatment is defined as therapeutic coverage lower than 40% in the observation period, whereas high adherence is defined as therapeutic coverage higher than or equal to 80% in the observation period (1).

Persistence is defined as "the time between the beginning and the interruption of a prescribed pharmacological treatment" and is a dynamic measure that describes the maintenance of the therapeutic regime over time, which is assumed to also include any gap periods between prescriptions, provided that this gap does not exceed an a priori fixed number of days, in this discussion equal to 60 days. Therefore, a subject who started pharmaceutical treatment on date *t*0 was defined as "persistent" to treatment after x days from the start of the same treatment if he took the medicine without interruption until day (*t*0 + *x*); consequently, an interruption occurs if, between the theoretical end (calculated on the basis of the DDD) of one prescription and the beginning of the next one or the end of the follow-up, a time gap greater than 60 days is observed. (2-4)

If a subject received a prescription before the theoretical end of the previous prescription, the prescription in question was considered sequential, so its start date was postponed to the day after the theoretical end of the previous prescription. Persistence at 12 months was estimated through the Kaplan-Meier analysis; the subjects were "censored" if at the end of the follow-up period they were still in therapy (persistent) or within the time gap between subsequent prescriptions that defines the maintenance of the therapeutic regime.

Before the computation of adherence and persistence, it was necessary to carry out a series of data systematisation procedures. In particular, if a subject received multiple prescriptions, relating to different medicines, on the same date, only the prescription with the longest duration was considered. Also, if a subject received a prescription for a period of time that was entirely within the therapeutic coverage of a previous prescription, that prescription was not considered. For both the assessment of adherence and persistence, only subjects with at least 2 prescriptions were considered.

The results obtained were stratified by gender, age groups (45-54, 55-64, 65-74, 75-84, 84+) and geographical distribution (North: Piedmont, Valle d'Aosta, Liguria, Lombardy, A.P. of Trento and A.P. of Bolzano, Veneto, Friuli Venezia Giulia, Emilia Romagna; Centre: Tuscany, Umbria, Marche, Lazio; South and Islands: Abruzzo, Molise, Campania, Puglia, Basilicata, Calabria, Sicily, Sardinia). Finally, in order to assess the trend over time, the synthetic values obtained from 2019 to 2023 and the percentage variations of the adherence and persistence indicators compared to the previous year were reported.

For each therapeutic class considered, the analyses carried out included only those Regions in which the proportion of medicines provided under the territorial assistance regime (under agreemenet and per conto distribution) was equal to or greater than 85% of the total (also including direct distribution, Health Ministry Decree of 31 July 2007 regulating the New Health Information System [NSIS] and Law 405/2001 and subsequent amendments).

Only for the categories of antihypertensives and hypolipidemic drugs was an in-depth study carried out considering a 4-year follow-up (divided into 12, 24, 36 and 48 months) and consequently the cohort of new users detected in the last quarter of 2019 and followed until the end of 2023. New users are subjects who received a first prescription in the period 01/10/2019-31/12/2019, not treated in the previous months starting from 01/01/2019 and followed up for 4 years.

Medicinal products and therapeutic classes considered

1. **Antidepressant medicines:**
   – Antidepressants (ATC: N06A)
2. **Lipid-lowering medicines:**
   – Hydroxymethylglutaryl-CoA reductase inhibitors (C10AA)
   – Fibrates (C10AB)
   – Omega-3 triglycerides (C10AX06)
   – Ezetimibe (C10AX09)
   – Lipid modifying agents, associations (C10B)
3. **Antiosteoporosis medicines:**
   – Raloxifene (ATC: G03XC01)
   – Bazedoxifene (ATC: G03XC02)
   – Bisphosphonates alone (ATC: M05BA)
   – Bisphosphonates in combination (ATC: M05BB)
   – Teriparatide (ATC: H05AA02)
   – Strontium ranelate (ATC M05BX03)
4. **Antihypertensives:**
   – Antihypertensives (ATC: C02A; C02C)
   – Diuretics (ATC: C03)
   – Beta blockers (ATC: C07)
   – Calcium channel blockers (ATC: C08)
   – Medicines for the renin-angiotensin system (ATC: C09)
5. **Medicines for benign prostatic hypertrophy (ATC: G04C)**
6. **Anticoagulant Medicines:**
   – Direct thrombin inhibitors (ATC: B01AE*)
   – Direct Xa factor inhibitors (ATC: B01AF*)
   – Vitamin K antagonists (ATC: B01AA*)
7. **Antiplatelet medicines:**
   – Clopidogrel (ATC: B01AC04)
   – Ticlopidine (ATC: B01AC05)
   – Acetylsalicylic acid (ATC: B01AC06)
   – Prasugrel (ATC: B01AC22)
   – Ticagrelor (ATC: B01AC24)
   – Clopidogrel/ACETYLSALICYLIC acid (ATC: B01AC30)
   – Esomeprazole/acetylsalicylic acid (ATC: B01AC56)
8. **Antidiabetic medicines (ATC: A10*)**
9. **Drugs for Obstructive Airway Diseases (ATC: R03*)**

References

1. Borghi C, Cicero AFG. Aderenza e persistenza in terapia. Giornale Italiano di Farmacoeconomia e Farmacoutilizzazione 2008; 1(2): 5-13.
2. Choi YJ, Ah YM, Kong J, et al. Implication of different initial beta blockers on treatment persis- tence: atenolol vs new-generation beta blocker, a population-based study. Cardiovasc Ther 2016; 34(4): 268-75.
3. Mazzaglia G. Brignoli O, Caputi AP, Claudio Cricelli C. Aderenza e persistenza: due elementi chiave per la determinazione dell'efficacia terapeutica in usual care. Farmacoeconomia e percorsi tera- peutici 2011; 12 (Suppl 2).
4. Santoni L, Dall'Asta G, Spampinato A, et al. Aderenza e persistenza alla terapia con statine: analisi di farmacoutilizzazione a partire dai database amministrativi di cinque ASL italiane. Giornale Italiano di Farmacoeconomia e Farmacoutilizzazione 2009; 2(1): 5-16.

METHODOLOGICAL NOTE

Comparing the different editions of the Report, it should be considered that in drawing up the National Reports, updating operations are systematically carried out on the information recorded in the OsMed datawarehouse, and that may lead to slight differences in the values (expenditure, consumption, exposure) published in previous national Reports. Such updating activities may derive, for example, from the definition of new DDDs by the WHO, from the clarification of previously unavailable data (for example updated population data), from checks carried out on the basis of new data flows.
The data used in this report, acquired through the New Health Information System (NSIS) of the Ministry of Health, are updated as of 23 April 2024 and, therefore, do not take into account any further revisions by companies and Regions. The data presented are for information purposes only and are not useful for the purposes of AIFA's administrative procedures.