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PRAC starts review of topiramate use in pregnancy and women of childbearing potential

EMA's safety committee (PRAC) has started a review of topiramate and the risk of neurodevelopmental disorders in children whose mothers were taking topiramate during pregnancy. Topiramate is a medicine used in the EU for the treatment of epilepsy, prevention of migraine and, in some countries, in combination with phentermine for body weight reduction.

Use of topiramate in pregnant women is known to increase the risk of birth defects. Women with epilepsy who are being treated with topiramate for their seizures are advised to avoid becoming pregnant, and to consult their doctor for advice if they wish to become pregnant. Topiramate must not be used to prevent migraine or control body weight in pregnant women and in women of childbearing potential (women able to have children) who are not using highly effective birth control methods (contraception).

The review was triggered by a recent study[1] which suggested a possible increase in the risk of neurodevelopmental disorders, in particular autism spectrum disorders and intellectual disability, in children whose mothers were taking topiramate during pregnancy.

The study was based on data from several Nordic registries (Denmark, Finland, Iceland, Norway and Sweden), and included information from more than 24,000 children exposed to at least one anti-epileptic medicine before birth. Of these children, 471 were exposed to topiramate alone, including 246 children born to mothers who had epilepsy.

The PRAC started reviewing the study results as part of a safety signal assessment in July 2022. The committee will now conduct an in-depth review of the available data on the benefits and risks of topiramate use in pregnant women and women of childbearing potential in the approved indications. The committee will look in particular at the current risk minimisation measures and consider the need for additional measures to minimise the risks of topiramate use in these women.

While the review is ongoing, topiramate should continue to be used according to the authorised product information. Women should discuss any questions or concerns about their topiramate treatment with their doctor or pharmacist. Patients should not stop antiepileptic treatment before speaking with their doctor.

[1] Bjørk M, Zoega H, Leinonen MK, et al. Association of Prenatal Exposure to Antiseizure Medication With Risk of Autism and Intellectual Disability. JAMA Neurol. Published online May 31, 2022. doi:10.1001/jamaneurol.2022.1269.

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Following this review, the PRAC will give its recommendation as to whether marketing authorisations of topiramate-containing products should be maintained, varied, suspended or revoked.

EMA will communicate the PRAC's recommendation once the review has concluded.

More about the medicine

Topiramate is used on its own or together with other medicines to prevent epileptic seizures. The medicine is also used to prevent migraine headaches and, in some EU countries, for weight reduction in fixed-dose combination with phentermine.

Topiramate is available in the European Union (EU) under various trade names, including Topamax, Topimax, Epitomax, and several generic medicines. In some EU countries topiramate is available in combination with phentermine as Qsiva.

More about the procedure

The review of topiramate has been initiated at the request of the French medicine agency, under Article 31 of Directive 2001/83/EC. This is related to a safety signal review that started in July 2022 and concluded this month.

The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations. As topiramate-containing medicines are all authorised nationally, the PRAC recommendations will be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a position. The CMDh is a body representing EU Member States as well as Iceland, Liechtenstein and Norway. It is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.