15 November 2024
EMA/522805/2024

Updated advice to minimise risks of interaction between weight loss medicine Mysimba and opioids

Use of opioid medicines with Mysimba may lead to serious side effects

After re-examining its initial opinion, EMA recommends updating the advice aimed at minimising the risks of interaction between the weight loss medicine Mysimba (naltrexone/bupropion) and opioid-containing medicines (including painkillers such as morphine and codeine, other opioids used during surgery and certain medicines for cough, cold or diarrhoea).

Opioid medicines may not work effectively in patients taking Mysimba, because one of the active substances in Mysimba, naltrexone, blocks the effects of opioids. There is also a risk of rare but serious and potentially life-threatening reactions, such as seizures and serotonin syndrome (a potentially life-threatening condition that results from having too much serotonin in the body), in people taking Mysimba together with medicines for treating depression and opioids.

To minimise these risks, patients and healthcare professionals are reminded that Mysimba must not be used in people who are dependent on opioids, people receiving treatment with opioid agonists such as methadone or buprenorphine and people going through acute opioid withdrawal.

People using Mysimba will be given a patient card to be carried with them at all times. The card will remind them to inform their doctor, in case of surgery, that they are using Mysimba. This is because Mysimba should be stopped for a minimum of three days before starting treatment with opioids, which are often used to prevent pain and discomfort during surgery and medical procedures.

The product information for Mysimba is being updated to reflect these changes.

Information for patients

- The weight loss medicine Mysimba is known to block the effect of opioid medicines (including painkillers such as morphine and codeine, other opioids used during surgery and certain medicines for cough, cold or diarrhoea). This may also lead to an insufficient effect of opioid medicines used during and after surgery as part of anaesthesia and pain treatment.
- Each pack of Mysimba will include a patient card, which you should always carry with you. The card is a reminder to inform your doctor, in case of surgery, that you are using Mysimba. Your doctor may advise you to stop taking Mysimba for at least three days before the procedure.

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- Rare but serious side effects, including seizures and serotonin syndrome (a potentially life-threatening condition that results from having too much serotonin in the body), have also been reported in people taking Mysimba together with medicines for treating depression and opioid medicines.
- Because of the risk of these side effects, you must not use Mysimba if you are dependent on opioids, if you are taking certain opioids used to treat addiction such as methadone or buprenorphine or if you are going through acute withdrawal.

Information for healthcare professionals

- Insufficient intra- and post-operative opioid analgesia has been described in case reports and the literature in patients treated with Mysimba.
- Rare but serious and potentially life-threatening reactions such as seizures and serotonin syndrome have been observed after co-administration of Mysimba with a serotonergic agent (such as selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine re-uptake inhibitors (SNRIs)) and opioids.
- Mysimba must not be used in patients dependent on opioids, patients treated with opioid agonists used in opioid dependence (e.g. methadone, buprenorphine) or patients in acute opioid withdrawal. If opioid use is suspected, a test may be performed to ensure clearance of opioid medication before starting treatment with Mysimba.
- Patients must be warned against the concomitant use of opioids during treatment with Mysimba. If opioid use is required (e.g. due to a planned surgery), Mysimba should be stopped for a minimum of three days before starting opioid treatment.
- In case of emergency surgery in patients potentially treated with Mysimba, there is a risk that the effects of opioids may be reduced.

More about the medicine

Mysimba is a medicine used along with diet and exercise to help manage weight in adults who have obesity (have a body-mass index – BMI – of 30 or more) or who are overweight (have a BMI between 27 and 30) and have weight-related complications such as diabetes, abnormally high levels of fat in the blood or high blood pressure. Mysimba was granted marketing authorisation on 26 March 2015.

More information on Mysimba is available on the medicine's page.

More about the procedure

EMA's Pharmacovigilance and Risk Assessment Committee (PRAC) evaluated the risk of interaction between Mysimba and opioid medicines in the context of a periodic safety update report (PSUR) assessment. As an outcome of this assessment, the PRAC asked the company that markets Mysimba, Orexigen Therapeutics Ireland Limited, to submit a variation to the marketing authorisation of the medicine to address this risk. The PRAC and the Committee for Medicinal Products for Human Use (CHMP) could not reach an agreement with the company on appropriate risk minimisation measures. Therefore, at its July 2024 meeting, the CHMP issued an opinion refusing the variation.

In August 2024, the company marketing Mysimba requested a re-examination of EMA's opinion. During the re-examination, the PRAC re-assessed the available data and sought the advice of a group of experts including doctors specialised in anaesthesiology, obesity and pharmacology as well as family doctors and patient representatives. At the conclusion of the re-examination, the PRAC and the company agreed to implement some changes to the product information and to introduce a patient card as an additional measure to minimise the risks of interaction between Mysimba and opioid medicines.

The CHMP endorsed the PRAC recommendations and issued a positive opinion on the variation. The CHMP opinion will now be sent to the European Commission, which will issue a final decision applicable in all EU Member States in due course.