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# EMA advises about risks of using weight loss medicine Mysimba with opioids

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

Following a routine review of the safety of the weight loss medicine Mysimba (naltrexone/bupropion), EMA recommends strengthening existing advice to minimise the risks from interactions between Mysimba and opioid-containing medicines (including painkillers such as morphine and codeine, other opioids used during surgery, and certain medicines for cough, cold or diarrhoea).

In particular, EMA is advising that opioid painkillers may not work effectively in patients taking Mysimba, because one of the active substances in Mysimba, naltrexone, blocks the effects of opioids. If a patient requires opioid treatment while taking Mysimba, for example due to a planned surgery, they should therefore stop taking Mysimba for at least three days before treatment with opioid medicines starts.

Furthermore, EMA is informing patients and healthcare professionals about the 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 with opioids.

To minimise these risks, EMA recommends that Mysimba must not be used in people receiving treatment with opioid medicines. This is in addition to the existing contraindications stating that Mysimba must not be used in people who are dependent on long-term opioids, people receiving treatment with opioid agonist such as methadone, and people going through opioid withdrawal.

**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 lead to an insufficient effect of opioid medicines used during and after surgery as part of anaesthesia and pain treatment.
- Inform your doctor that you are using Mysimba in case of any planned surgery. Your doctor may advise you to stop taking Mysimba for at least three days before the procedure.
- 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 and opioid medicines.

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- Because of the risk of these side effects, you must not use Mysimba if you are receiving treatment with opioids, are dependent on opioids, are receiving opioids agonists such as methadone, or are going through acute opioid withdrawal.

**Information for healthcare professionals**

- Insufficient effects of opioids as part of anaesthesia and intra- or post-operative analgesia have been described in case reports and the literature in patients treated with Mysimba.
- Furthermore, rare but serious and potentially life-threatening reactions such as seizures and serotonin syndrome have been observed after co-administration of Mysimba and opioids.
- Mysimba must not be used in patients receiving opioid-containing medicines, patients currently dependent on opioids, patients treated with opioid agonists used in opioid dependence (e.g. methadone) or in patients in acute opioid withdrawal. If opioid use is suspected, a test should be performed to ensure clearance of opioid medication before starting treatment with Mysimba.
- Patients should 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.

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**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. However, both 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.

The company may request a re-examination within 15 days of receipt of the CHMP opinion.

EMA has provided this advice to patients and healthcare professionals pending the final outcome of this procedure.