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EMA concludes review of weight management medicine Mysimba

Benefits continue to outweigh risks, with new risk minimisation measures and more information to be provided about long-term effect on the heart

EMA's human medicines committee (CHMP) has finalised its review of Mysimba (naltrexone / bupropion), a medicine used for weight management in adults with obesity or overweight. The review was prompted by concerns about a potential long-term cardiovascular risk (risk affecting the heart and blood circulation) with the medicine.

The CHMP has concluded that the benefits of Mysimba continue to outweigh its risks. However, the company must provide more information from an ongoing study on the medicine's cardiovascular effects in patients treated for longer than one year. New measures are also being implemented to minimise potential cardiovascular risks with long-term use.

At the time of Mysimba's authorisation, the CHMP noted uncertainties regarding the long-term effects of Mysimba on the cardiovascular system. To date, studies have shown that there is no cardiovascular safety concern when Mysimba is used for up to 12 months. However, the data available are not sufficient to fully determine the cardiovascular safety beyond this time.

The CHMP has agreed that an ongoing safety study with Mysimba in patients with obesity or overweight carried out by the company is appropriate to generate evidence about this risk in the long term. The results are expected in 2028, and the company must provide annual reports on the progress of the study. The CHMP has imposed this study as a condition to the marketing authorisation.

In addition, further measures will be implemented to minimise potential cardiovascular risks with long-term use. Treatment with Mysimba should be stopped after one year if weight loss of at least 5% of the initial body weight is not maintained. In addition, healthcare professionals should carry out a yearly assessment and discuss with their patients whether Mysimba remains beneficial for them, taking into account any changes to their cardiovascular risk and whether weight loss has been maintained.

During the review, the CHMP considered all available data in relation to the cardiovascular safety of Mysimba, including data from clinical studies and from clinical practice, as well as data from spontaneous reports of side effects and from the literature. Clinical and literature data in relation to the effectiveness of the medicine were also considered.

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The product information for Mysimba as well as a checklist for healthcare professionals will be updated to reflect the outcome of this review. A letter including the above recommendations will be sent in due course to healthcare professionals prescribing, dispensing or administering the medicine.

Information for patients

- A review of available data has concluded that the benefits of Mysimba, a medicine used for weight management, continue to outweigh its risks. However, the effects of treatment on the heart and blood vessels of patients treated for longer than one year have to be further investigated.
- A clinical study that will provide more information about the long-term effect of Mysimba on the heart is ongoing; results are expected in 2028.
- When starting treatment with Mysimba, your doctor will monitor weight loss and should stop treatment if you have not lost at least 5% of your initial body weight after 16 weeks. In addition, if weight loss of at least 5% of your initial body weight cannot be maintained after the first year of treatment, your healthcare professional will stop Mysimba and discuss alternative treatment options with you.
- Every year, your doctor should discuss with you whether Mysimba remains beneficial for you, taking into account any changes to your cardiovascular risk and whether weight loss has been maintained.
- If you are taking Mysimba and you have any questions or concerns, contact your doctor or pharmacist.

Information for healthcare professionals

- A review of available data has concluded that the benefits of Mysimba in its authorised indication continue to outweigh its risks. However, the cardiovascular safety of Mysimba in patients treated for longer than 12 months has not been fully determined and remains uncertain.
- An ongoing study (INFORMUS) proposed by the company will provide further information about this risk in the long term.
- The INFORMUS cardiovascular outcomes trial (NB-CVOT-3; a prospective, pragmatic randomised placebo-controlled study) is evaluating the long-term cardiovascular safety of Mysimba beyond the 12-month period; results are expected in 2028.
- Currently, treatment with Mysimba should be discontinued if there are concerns with the safety or tolerability of ongoing treatment, including concerns about increased blood pressure, or if patients have lost less than 5% of their initial body weight after 16 weeks. The need for continued treatment should be re-evaluated annually.
- To minimise potential cardiovascular risks with long-term use of Mysimba, the existing recommendations have now been clarified and reinforced:
  - treatment with Mysimba should be discontinued after one year if weight loss of at least 5% of the initial body weight is not maintained;
  - healthcare professionals should carry out an annual assessment and discuss with their patients whether Mysimba remains beneficial for them, taking into account any changes to the patient's cardiovascular risk and whether weight loss has been maintained.

- The product information, as well as the checklist for healthcare professionals, is being updated to reflect the above information.

A direct healthcare professional communication (DHPC) will be sent in due course to healthcare professionals prescribing, dispensing or administering the medicine. The DHPC will also be published on a dedicated page on the EMA website.

More about the medicine

Mysimba is a medicine used along with diet and exercise to help manage weight in adults who have obesity (with a body mass index - BMI - of 30 or more) or overweight (with 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. It was granted marketing authorisation on 26 March 2015.

More information about the medicine can be found on the EMA website.

More about the procedure

The review of Mysimba was initiated on 1 September 2023 at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004.

The review has been carried out by the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which has adopted the Agency's opinion. The CHMP opinion will now be forwarded to the European Commission, which will issue a final legally binding decision applicable in all EU Member States.