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(IN REPLY PLEASE QUOTE THIS FILE REF.)

DEPARTMENT OF HEALTH
DRUG OFFICE
DRUG INFORMATION AND
IMPORT/EXPORT CONTROL DIVISION
Suites 2002-05, 20/F, AIA Kowloon Tower
Landmark East, 100 How Ming Street
Kwun Tong, Kowloon, Hong Kong

31 March 2025

Dear Healthcare Professionals,

EMA concludes review of weight management medicine Mysimba (naltrexone / bupropion) – Benefits continue to outweigh risks, with new risk minimisation measures and more information to be provided about long-term effect on the heart

Your attention is drawn to the European Medicines Agency's (EMA) announcement that its Committee for Medicinal Products for Human Use (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.

In the European Union, 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 by the EMA in due course to healthcare professionals prescribing, dispensing or administering the medicine.

Healthcare professionals are advised that:

- 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 by the EMA:
  - 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.

Please refer to the following website in EMA for details:
https://www.ema.europa.eu/en/news/ema-concludes-review-weight-management-medicine-mysimba

In Hong Kong, Mysimba is a registered pharmaceutical product under the name Contrave Prolonged-release Tablets 8mg/90mg (HK-66934), a prescription-only medicine and is the only registered pharmaceutical product containing naltrexone and bupropion. So far, the Department of Health (DH) has not received any case of adverse drug reaction related to naltrexone alone and naltrexone/bupropion combination. The DH has received 5 cases of adverse drug reactions with bupropion alone, of which 2 cases were reported as increased blood pressure and heart rate; but none of these cases were related to the combination use of naltrexone/bupropion.

Related news of Mysimba was previously issued by EMA, and was posted on the Drug Office website on 27 Jul 2024 and 16 Nov 2024. In light of above EMA's latest announcement, the matter will also be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Please note that this letter serves as a means for the DH to communicate important new safety information about registered pharmaceutical products with healthcare professionals in Hong Kong and is not intended to serve as guidelines or to replace professional clinical judgement. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Clinical Trials and Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Vincent CHIANG)
for Assistant Director (Drug)