23 July 2010
EMA/463702/2010
Press Office

Press release

European Medicines Agency concludes review of modified-release oral opioids of the WHO level III scale for the management of pain

Benefits of most of these medicines outweigh risks; marketing authorisations of opioids using polymethacrylate-triethylcitrate controlled release systems should be suspended because of concerns over interaction with alcohol

The European Medicines Agency has finalised a review of modified-release oral opioids of the WHO level III scale for the management of pain. The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that the benefits of most of these medicines continue to outweigh their risks, but that the existing warnings on the interaction of these medicines with alcohol should be made consistent across the class.

However, for modified-release oral opioids that contain a polymethacrylate-triethylcitrate controlled-release system the Committee recommended suspension of the marketing authorisations, until the manufacturers have reformulated them so that they are more stable in alcohol.

Modified-release oral opioids of the WHO level III scale for the management of pain are strong painkillers used to treat pain that has not been controlled with other medicines. They release the active substance slowly, often over many hours, to reduce the number of times patients have to take the medicine every day. Included in the class are morphine and the related medicines oxycodone and hydromorphone.

These medicines were reviewed because of concerns that their controlled-release systems may be unstable in alcohol and that the active substance may be released too quickly when patients take them together with alcohol. This effect called 'dose dumping' could put patients at risk of exposure to large doses of the opioid, which may lead to serious side effects such as respiratory depression (an inhibition of breathing).

Based on the evaluation of the available data, the CHMP found that around half of the controlled-release systems tested interacted with alcohol, but that this effect was mild and would only have a minor effect on the release of the active substance.

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However, for opioids using a polymethacrylate-triethylcitrate controlled-release system, the CHMP found that there was a significant interaction with alcohol and that patients were at risk of dose dumping if they drink alcohol while taking them.

While the Committee noted that the current product information already contra-indicates drinking alcohol when using strong opioids, it also noted some studies which show that many patients with severe pain drink alcohol while they are being treated with opioids.

The CHMP therefore recommended the suspension of the marketing authorisation of these medicines until the marketing authorisation holders have developed a more alcohol-stable controlled-release system.

For all other modified-release oral opioids of the WHO level III scale for the management of pain the Committee concluded that the benefits outweigh the risks, but that the existing warnings in the product information on the potential interaction with alcohol, e.g. the increased sedative effects of opioids, should be made consistent across the whole class.

The CHMP's recommendations have been forwarded to the European Commission for the adoption of a binding decision.

Notes

1. More information about modified-release oral opioids of the WHO level III scale for the management of pain is available in the Questions and answers on the review of modified-release oral opioid medicines of the WHO level III scale for the management of pain.

2. The review of modified-release oral opioids of the WHO level III scale for the management of pain was initiated under Article 31 of Directive 2001/83/EC, as amended. This type of procedure may be initiated in specific cases where the interest of the Community is involved. The expression 'Community interest' has a broad meaning but it refers particularly to the interests of the public health in the Community, for example following concerns related to the quality, efficacy and/or safety of a medicinal product or new pharmacovigilance information.

3. For one of the medicines included in this review, Ethirfin (morphine sulphate), prolonged release capsules, from Ethypharm and associated names, the Committee carried out a parallel review under Article 29 (4) of Directive 2001/83/EC, as amended. The CHMP was asked to give a recommendation whether or not the marketing authorisation for Ethirfin could be renewed. Based on the review of the available data for Ethirfin, which also uses a polymethacrylate-triethylcitrate controlled release system and the outcome of its review of the modified-release oral opioids of the WHO level III scale for the management of pain, the CHMP recommended the renewal of the marketing authorisation, under the condition that the marketing authorisation holder develops a more stable controlled-release system. More information on Ethirfin is available in the Questions and answers on Ethirfin and associated names (morphine sulphate, prolonged-release capsules, 20, 60, 120 and 200 mg).

4. This press release, together with other information on the work of the European Medicines Agency, can be found on the Agency's website: www.ema.europa.eu

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