Malta, 4th August 2010
Circular No. P10/2010

Dear Healthcare Professional,

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

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. There are no formulations in Malta that contain this modified release system.

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.

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.

1. The Medicines Authority has participated in the discussions held at the EMA and is in agreement with the full **press release** issued by the EMA, attached here for your perusal. A **question-and-answer** document with more information about the outcome of this assessment is also available.

Healthcare professionals are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

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