PRAC recommends updating advice on use of high-dose ibuprofen for systemic use

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Information on ibuprofen containing products

- Ibuprofen is a painkiller and anti-inflammatory medicine which works by blocking an enzyme called cyclo-oxygenase, which produces prostaglandins, substances that are involved in inflammation and pain. Ibuprofen is found in medicines used to treat pain, inflammation and fever.
- The usual dose for adults and children over 12 years of age is 200 to 400 mg, 3 or 4 times a day as needed.
- Ibuprofen is present in medicines as a mixture of two molecules that are enantiomers (mirror images of each other). Dexibuprofen, the active enantiomer, is sometimes available on its own and is therefore included in this review. A dose of 2,400 mg per day of ibuprofen is equivalent to 1,200 mg per day of dexibuprofen.
- Ibuprofen and dexibuprofen are currently available in the European Union (EU) in a number of different formulations. In Malta, there are no authorised medicinal products containing only dexibuprofen products but several exist with ibuprofen. A complete list of products can be extracted from www.medicinesauthority.gov.mt/medicinesdatabase

Information from the European Medicines Agency (EMA) about the safety concern

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has found that there is no increase in cardiovascular risk is seen with ibuprofen at doses up to 1,200 mg per day, which is the highest dose generally used for over-the-counter (OTC) preparations taken by mouth in Malta.

However, a small increase in the risk of cardiovascular problems, such as heart attacks and strokes, in patients taking high doses of ibuprofen (at or above 2,400 mg per day) has been confirmed. The review clarifies that the risk with high-dose ibuprofen is similar to the risk seen with some other non-steroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors and diclofenac.*[1] Therefore, high doses of ibuprofen (2,400 mg per day or higher) should be avoided in patients with serious underlying heart or

[1] Reviews carried out in 2005, 2006, and 2012 confirmed that NSAIDs as a class are associated with a small increase in the risk of arterial thromboembolic events (blood clots in the arteries) especially in patients with underlying heart or circulatory conditions or with certain cardiovascular risk factors, and particularly if used at high doses.

A class warning of this risk is already in place and the product information for all NSAIDs, including ibuprofen, recommends that these medicines be used at the lowest effective dose and for the shortest period of time necessary to control symptoms.

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circulatory conditions, such as heart failure, heart disease and circulatory problems or in those who have previously had a heart attack or stroke. A patient's risk factors (smoking, high blood pressure, diabetes and high blood cholesterol) for heart or circulatory conditions, before initiating long-term treatment with ibuprofen, particularly if high doses are required should be carefully considered prior to starting high dose treatment.

The PRAC also reviewed data on the interaction between ibuprofen and low-dose aspirin when the latter is taken to reduce the risk of heart attacks and strokes. The PRAC noted that ibuprofen has been shown in laboratory studies to reduce the anti-clotting effects of aspirin. However it remains uncertain whether long-term use of ibuprofen in clinical practice reduces the benefits of low-dose aspirin in preventing heart attacks and strokes. Occasional use of ibuprofen should not affect the benefits of low-dose aspirin.

The PRAC recommendations for ibuprofen and dexibuprofen have been sent the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a final position.

For more information please visit **www.ema.europa.eu**

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on ibuprofen containing medicines. Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form or online at **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Prof. John J Borg PhD (Bristol)
Post-licensing Director

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

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