13 June 2014
EMA/348597/2014

European Medicines Agency starts review of ibuprofen medicines

Review to evaluate cardiovascular risk with high doses taken over long periods

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has started a review to evaluate the cardiovascular risks with systemic ibuprofen medicines (such as those taken by mouth but not topical medicines like creams and gels).

The cardiovascular risks being evaluated concern high-dose ibuprofen (2,400 mg per day) taken regularly for long periods. Ibuprofen is usually taken at lower doses and for short periods of time.

There is therefore no suggestion of a similar cardiovascular risk with ibuprofen as used by the overwhelming majority of patients. Ibuprofen is one of the most widely used medicines for pain and inflammation and has a well-known safety profile, particularly at usual doses.

Ibuprofen belongs to a class of medicines known as non-steroidal anti-inflammatory drugs (NSAIDs). The safety of these medicines including their cardiovascular risks has been under close review by the EMA and national regulatory authorities for many years. Data, in particular the results of a published analysis of clinical trial data, have suggested that the cardiovascular risk with diclofenac and high-dose ibuprofen (2,400 mg) may be similar to the known risk with COX-2 inhibitors (also of the NSAID class).[1] In 2013, the PRAC considered the available data relating to diclofenac and issued recommendations to minimise their risks. The PRAC is now considering the available data relating to high-dose ibuprofen.

The PRAC will also evaluate evidence on the interaction of ibuprofen with low-dose aspirin (taken to reduce the risk of heart attacks and strokes) to decide whether current advice to healthcare professionals is sufficient.

While the review is ongoing, patients should continue to use their medicines as per the instructions in the package leaflets or as directed by their doctor or pharmacist.

[1] Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. Coxib and traditional NSAID Trialists' (CNT) Collaboration. The Lancet, Volume 382, Issue 9894, Pages 769 - 779, 31 August 2013

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7129
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

More about the medicine

Ibuprofen is a painkiller and anti-inflammatory medicine. It 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.

Ibuprofen and dexibuprofen are currently available in the European Union (EU) in a number of different formulations. Most formulations are for systemic use, which are covered by the current review. Ibuprofen and dexibuprofen medicines have been authorised in the EU through national approval procedures and have been available for many years under a wide range of trade names. They are available on prescription and over the counter.

More about the procedure

The review of ibuprofen was initiated on 9 June 2014 at the request of the UK's medicines agency (MHRA), under Article 31 of Directive 2001/83/EC. It follows concerns that high doses of ibuprofen could have a similar cardiovascular risk to those of COX-2 inhibitors.

The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations. As ibuprofen medicines are all authorised nationally, the PRAC recommendation will be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a final position. The CMDh, a body representing EU Member States, is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.