European Medicines Agency

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QUESTIONS AND ANSWERS ON THE RECOMMENDATION TO WITHDRAW THE MARKETING AUTHORISATIONS FOR LUMIRACOXIB-CONTAINING MEDICINES

The European Medicines Agency (EMEA) has completed a review of the safety of medicines containing lumiracoxib. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that the benefits of these medicines no longer outweigh their risks, and that all marketing authorisations should be withdrawn (revoked) throughout Europe.

What is lumiracoxib?
Lumiracoxib is a non-steroidal anti-inflammatory drug (NSAID) that belongs to the group 'COX-2 inhibitors'. It blocks an enzyme called cyclooxygenase-2 (COX-2), which is involved in the inflammation process. Lumiracoxib is used to relieve the signs of inflammation (pain, swelling and stiffness) in patients who have osteoarthritis of the knee or the hip (a disease in which the protective cartilage in the joints is worn down).

Tablets containing 100 mg lumiracoxib have been available in a number of European Union (EU) countries since 2005. They have been available in Austria, Belgium, Cyprus, Germany, Hungary, Malta, Portugal, Sweden and the United Kingdom (UK) under the trade names Prexige, Stellige, Hirzia and Frexocel.

Why was lumiracoxib reviewed?
On 15 November 2007, the CHMP started a review of lumiracoxib's safety, following an assessment by the UK medicines regulatory authority of reports of liver problems in patients taking the medicine. Looking at worldwide reports in patients receiving lumiracoxib at various doses (often higher than those authorised in the EU), the authority noted that the effects were sometimes severe enough to result in liver failure or even death.

As required by Article 107 of Directive 2001/83/EC as amended, the UK authority informed the CHMP so that the Committee could consider whether the marketing authorisations for all lumiracoxib-containing medicines should be maintained, changed, suspended or revoked across the European Union (EU).

On the basis of their findings, the UK authority concluded that the benefits of lumiracoxib no longer outweighed its risks. Therefore, on 19 November 2007, the UK authority suspended the marketing authorisation for Prexige. In the following week, the regulatory authorities in Germany, Cyprus and Belgium followed the action taken by the UK, and also took the decision to suspend the marketing authorisations for lumiracoxib in their markets.

Which data has the CHMP reviewed?
The CHMP looked at available information on the safety of lumiracoxib, particularly on side effects affecting the liver, as supplied by the companies that market lumiracoxib-containing medicines in the EU.

Because the safety of all COX-2 inhibitors including lumiracoxib was reviewed by the CHMP in 2004 and 2005, the CHMP took data that they had previously considered into account. The CHMP also considered the 'urgent safety restriction' carried out in August 2007, which had resulted in new contraindications in patients with existing liver disease or who had previously experienced medicine-

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related liver problems, strengthened warnings to doctors on the potential liver problems linked to lumiracoxib, and information on the need to monitor liver function before and during treatment.

What are the conclusions of the CHMP?
The CHMP concluded that there is a risk of liver injury in patients taking lumiracoxib, and that problems might occur after short-term treatment. Up until 15 November 2007, there were 74 cases of serious liver problems, 19 of which were serious and linked to the use of the 100-mg dose (the dose approved in the EU).

The CHMP noted that the risk of liver problems with lumiracoxib may be reduced by limiting the use of the medicine to the short term. However, this was considered unrealistic for osteoarthritis, which is a long-term condition and for which alternative treatments are available.

The Committee concluded that the benefit-risk balance of lumiracoxib-containing medicines is negative. Therefore, the Committee recommended that the marketing authorisations of medicines containing lumiracoxib be revoked in all EU markets.

What are the recommendations for patients and prescribers?
- Patients who are currently taking lumiracoxib and have signs of possible problems with their liver should see their doctor immediately. The signs to watch out for are: feeling sick; vomiting; loss of appetite; tiredness; stomach pains; dark urine; itching; or yellowing of the skin.
- Patients who are currently taking lumiracoxib and who are feeling well should make an appointment to see their doctor as soon as is convenient, so that the doctor can change their prescription.
- Doctors should stop prescribing lumiracoxib. Alternative treatments should be used as appropriate, based on each patient's symptoms and individual risk profile.

A European Commission Decision on this opinion will be issued in due course.