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PRAC recommends restricting the use of flupirtine-containing medicines

Committee also recommends weekly monitoring of patients' liver function

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has concluded its review of flupirtine-containing medicines and recommended restrictions in their use. The Committee recommended that oral flupirtine medicines and suppositories should only be used to treat acute (short-term) pain in adults who cannot use other painkillers (such as NSAIDs and weak opioids) and that treatment should not exceed two weeks.

In addition, patients should have their liver function monitored after each full week of treatment and treatment should be stopped if there are signs of liver problems. The PRAC also recommended that flupirtine must not be used in patients with pre-existing liver disease or suffering from alcohol abuse as well as in patients taking other medicines that cause liver problems.

The PRAC's recommendations follow concerns raised by the German medicines regulatory agency, the Federal Institute for Drugs and Medical Devices (BfArM), about reports of liver problems in patients taking flupirtine. The problems ranged from cases of high levels of liver enzymes in the blood to liver failure cases, some of which were fatal or resulted in liver transplantation. BfArm was also concerned about the lack of data on the use of the medicine in treating chronic (long-term) pain.

The PRAC agreed that while there were data from studies of flupirtine in treating acute pain, the data on long-term pain were less convincing. The Committee noted the lack of sufficient data on the benefits of flupirtine when used for longer than 4 weeks.

With regard to liver safety, the PRAC noted that the duration of treatment seemed to be relevant to the occurrence of liver problems and that no cases of liver failure or liver transplantation were reported for patients who took the medicine for 2 weeks or less.

Considering the data on the benefits in acute pain, as well as the data on the occurrence of liver problems, the PRAC concluded that the proposed restrictions and regular liver monitoring were required to ensure that the benefits of flupirtine outweigh their risks.

The PRAC recommendation will be considered by the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) at its meeting on 24-26 June 2013. Patients who have any questions should speak to their doctor or pharmacist.

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More about the medicine

Flupirtine is a non-opioid painkiller that has been used to treat acute and chronic pain, such as pain associated with muscle tension, cancer pain, menstrual (period) pain and pain following orthopaedic surgery or injuries.

Flupirtine-containing medicines have been authorised since the 1980s and are currently available in the following EU Member States: Bulgaria, Estonia, Germany, Hungary, Italy, Latvia, Lithuania, Poland, Portugal, Romania and Slovakia.

Flupirtine is available as 100 mg immediate-release capsules, 400 mg extended-release tablets, 75 mg and 150 mg suppositories and as a solution for injection (100 mg). The 100 mg immediate-release capsules are available in the 11 EU Member States listed above. The other dosages and pharmaceutical forms are only available in Germany.

Flupirtine was first introduced as an alternative painkiller to opioids and non-steroidal anti-inflammatory drugs (NSAIDs). Subsequently, multiple other actions such as muscle relaxation were identified. Flupirtine works as a 'selective neuronal-potassium-channel opener'. This means that it opens specific pores on the surface of nerve cells called potassium channels. The opening of these channels reduces the excessive electrical activity that leads to many pain states.

More about the procedure

The review of flupirtine-containing medicines was initiated in March 2013 at the request of Germany, under Article 107i of Directive 2001/83/EC. It followed the procedural steps laid out in Article 107i of Directive 2001/83, also known as the urgent Union procedure.

As the review only covers nationally authorised medicines, the PRAC recommendation will now be forwarded to the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a final position. The CMDh is a medicines regulatory body representing the EU Member States.

If the CMDh position is agreed by consensus, the agreement will be directly implemented by the Member States where the medicines are authorised. Should the CMDh position be adopted by majority vote, the CMDh position will be sent to the European Commission, for the adoption of an EU-wide legally binding decision.

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