

## QUESTIONS AND ANSWERS ON THE REVIEW OF PIROXICAM

The European Medicines Agency (EMA) has recently completed a review of the safety of the non-steroidal anti-inflammatory drug (NSAID) piroxicam. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that piroxicam's benefits still outweigh its risks, but, based on safety grounds, only in certain, limited indications. In addition, the CHMP has concluded that piroxicam-containing medicines should no longer be used for the treatment of acute (short-term) pain and inflammation. The review was carried out under an 'Article 31' referral<sup>1</sup>.

As for all NSAIDs, piroxicam should always be used at the lowest dose for the shortest possible duration to control symptoms.

### What is piroxicam?

Piroxicam is a NSAID, a medicine used to treat inflammation. It has been available on the market for many years and has been used in the treatment of many painful conditions. Piroxicam is known as a non-selective NSAID because it acts on all types of the cyclo-oxygenase enzyme, including one type that is involved in the inflammatory process.

### Why was piroxicam reviewed?

The EMA reviewed the safety of non-selective NSAIDs in 2005 and 2006. It looked at the gastro-intestinal (stomach and bowel) and skin safety of the products, and then at their cardiovascular safety. During this process, piroxicam was singled out for special review because piroxicam-containing medicines are associated with more gastro-intestinal side effects and more serious skin reactions than other non-selective NSAIDs. Consequently, the European Commission asked the CHMP to carry out a full assessment of the benefit-risk balance of piroxicam.

### Which data has the CHMP reviewed?

In this review the CHMP has assessed information from previous reviews of safety data, as well as new data from clinical trials and epidemiological studies (studies of the causes and distribution of diseases in the population). It also looked at information published in scientific journals.

### What are the conclusions of the CHMP?

Based on the information available, the CHMP has concluded that:

- its use in the treatment of acute painful and inflammatory conditions should be abandoned,
- the use of piroxicam should be limited only to the symptomatic relief of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis,
- it should not be used as a first-line treatment,
- the dose of piroxicam should be limited to a maximum of 20 mg a day,
- its use should only be initiated by doctors who are experienced in treating chronic (long term) painful and inflammatory conditions.

In addition, the CHMP added some contraindications and strengthened warnings for piroxicam, to ensure that it is not used in patients who are at a higher risk of developing side effects.

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<sup>1</sup> Article 31 of Directive 2001/83/EC as amended, referral under Community interest.

### **What are the recommendations for patients?**

Patients who have been using piroxicam-containing medicines for the **short-term** treatment of acute pain or inflammation should not use it again. These patients will need to discuss with their doctor or pharmacist which medicine they can use in place of piroxicam.

The choice of an alternative medicine is likely to be based on the type of pain being treated.

Patients who are using piroxicam on a **long-term** basis to relieve the pain associated with chronic conditions should arrange to see the doctor who prescribed it to them, so that their treatment can be reviewed.

This review will allow the doctor to check that piroxicam is still the appropriate treatment for the patient's condition, and, if necessary, to determine which medicine should be used in place of piroxicam. It will also give the doctor the opportunity to consider prescribing another medicine to be taken along with piroxicam, to control the gastro-intestinal side effects. This only applies to patients who are not yet receiving such a medicine.

If the doctor decides to continue to prescribe piroxicam, patients should not take it with any other medicine of the same type. This includes acetylsalicylic acid (aspirin) when used for pain relief, as well as other NSAIDs that can be bought without a prescription ('over-the-counter').

These changes only apply to patients who are using piroxicam 'systemically' (when it is given as a treatment throughout the body) as tablets, capsules, injections or suppositories. Patients who use piroxicam 'topically' onto the skin can continue to use the medicine in the same way as before.

### **What are the recommendations for prescribers?**

Doctors should no longer prescribe piroxicam for the treatment of acute pain. This means that piroxicam can no longer be used for some conditions for which it was previously authorised<sup>2</sup>.

Doctors can still prescribe piroxicam for the symptomatic relief of pain and inflammation in patients suffering from:

- osteoarthritis,
- rheumatoid arthritis, or,
- ankylosing spondylitis,

but not as a first-line treatment.

- Only doctors who have experience in treating patients with inflammatory or degenerative rheumatic diseases will be able to initiate treatment with piroxicam. The first prescription should be for two weeks only, before treatment is reviewed.
- In any case, doctors should frequently review all patients receiving piroxicam.
- They should limit the prescription of piroxicam to a maximum of 20 mg a day.
- They should always consider prescribing piroxicam with a gastroprotective agent, such as misoprostol or a proton-pump inhibitor.
- They should not prescribe piroxicam to patients who are more likely to develop side effects, such as those with a history of gastro-intestinal disorders associated with bleeding, or those who have had skin reactions to other medicines.
- They should not prescribe piroxicam in association with any other NSAID or an anticoagulant.

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<sup>2</sup> Previously-authorized indications in the European Union vary from country to country and include: acute gout; primary dysmenorrhoea (period pain); post-operative pain; dental treatment and in the course of dental infection; the relief of fever and pain associated with acute upper respiratory tract inflammation; acute musculoskeletal disorders (such as bursitis and tendonitis); acute post-traumatic disorders; and radiculargia (pain due to nerve damage in the spine).