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## QUESTIONS AND ANSWERS ON THE REVIEW OF NON-SELECTIVE NSAIDS

As part of its continuous monitoring of medicines, the European Medicines Agency (EMA) has reviewed cardiovascular safety data on non-selective NSAIDs. It has concluded that the overall benefit-risk balance of these medicines remains positive. No conclusion has yet been reached for the NSAID piroxicam, for which a review is still ongoing.

The EMA's Committee for Medicinal Products for Human Use (CHMP) recommended that doctors continue to prescribe, and patients continue to use, the lowest dose of NSAIDs for the shortest possible duration to control symptoms. They should base their choice of NSAID on the patient's underlying conditions and the safety profiles of the medicines.

### **What are non-selective NSAIDs?**

NSAIDs are non-steroidal anti-inflammatory drugs. They have been available on the market for many years and are important in the treatment of arthritis and other painful conditions.

There are many medicines in the NSAID class. Non-selective NSAIDs are so-called because they act on all types of the cyclo-oxygenase enzyme, including one type that is involved in the inflammation process.

### **Which non-selective NSAIDs have been looked at in this review?**

This review concentrated on the non-selective NSAIDs diclofenac, etodolac, ibuprofen, indomethacin, ketoprofen, ketorolac, meloxicam, nabumetone, naproxen, nimesulide and piroxicam.

### **Why did the CHMP review these medicines?**

In September 2006, the French national medicines agency, Agence française de sécurité sanitaire des produits de santé (Afssaps), asked the CHMP to give its opinion on the cardiovascular safety of NSAIDs in the context of their overall benefit-risk profile under an 'Article 5(3) procedure'. This procedure is described in Article 5(3) of Regulation (EC) No 726/2004 and results in a CHMP scientific opinion.

The procedure was triggered by new data and analyses identified as part of the close monitoring of this class of compounds by the EMA. This followed the conclusions of the CHMP's review of non-selective NSAIDs in October 2005 and of piroxicam, ketoprofen and ketorolac in September 2006. The new data stemmed from clinical and epidemiological studies and signalled a potentially increased thrombotic risk (such as heart attack and stroke) for non-selective NSAIDs, especially when used at high doses and in long-term treatment.

### **Which data has the CHMP reviewed?**

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 of diseases in the population) and information published in scientific journals. The data included information from the MEDAL programme (comprising of three long-term studies of the safety of a non-selective NSAID and a COX-2 inhibitor) and previous assessments of non-selective NSAIDs and COX-2 inhibitors.

### **What are the conclusions of the CHMP?**

Based on the information available, the CHMP concluded that:

- non-selective NSAIDs are important treatments for arthritis and other painful conditions,
- it cannot be excluded that non-selective NSAIDs may be associated with a small increase in the absolute risk for thrombotic events, especially when used at high doses for long-term treatment,
- the overall benefit-risk balance for non-selective NSAIDs remains favourable when used in accordance with the product information.

For the NSAID piroxicam, the balance of benefits and risks is still being assessed in a separate 'Article 31' referral procedure by the EMEA.

The Committee agreed that the information for prescribers should reflect current knowledge on the cardiovascular safety of the non-selective NSAIDs. It recommended that its Pharmacovigilance Working Party, a group that provides expert advice on the safety of medicines, consider whether, in light of the new data, there is a need for revision of the prescribing information for the medicines.

The CHMP also concluded that it will analyse the final results from the MEDAL programme when they become available. It will also explore possibilities for further studies to gain more information on the safety of non-selective NSAIDs.

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

Advice for patients and prescribers for NSAIDs remains as follows:

- Patients and prescribers should use NSAIDs as necessary at the lowest effective dose for the shortest possible duration to control symptoms.
- Doctors should continue to decide which NSAID to prescribe on the basis of the overall safety profiles of the medicines, as set out in the product information, as well as the patient's underlying conditions, including those affecting the gastrointestinal system (stomach and bowel), the cardiovascular system (heart and blood vessels) and the kidneys.
- Doctors should not switch patients from one NSAID to another without careful consideration of the overall safety profile of the medicines and the patient's underlying conditions and preferences. Patients should not switch between NSAIDs without talking to their doctor or pharmacist.

Patients who have concerns or questions should talk to their doctor or pharmacist.

For further information, see the [scientific opinion](#) adopted by the CHMP on 18 October 2006.