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Questions and answers on the review of systemic medicines containing nimesulide

Outcome of a procedure under Article 31 of Directive 2001/83/EC as amended

The European Medicines Agency has completed a review of the safety and effectiveness of systemic medicines containing nimesulide (capsules, tablets, suppositories and powder or granules for oral suspension). The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that the benefits of nimesulide used systemically continue to outweigh its risks but that its use should be restricted to the treatment of acute pain and primary dysmenorrhoea. It issued a recommendation that it should no longer be used for the treatment of painful osteoarthritis.

What is nimesulide?

Nimesulide is a non-selective non-steroidal anti-inflammatory drug (NSAID). It has been used to treat:

- acute (short-term) pain,
- painful osteoarthritis (swelling in the joints) ,
- primary dysmenorrhoea (period pains).

Medicines containing nimesulide have been available since 1985 and are authorised in a number of Member States. They are only available with a prescription.

Systemic nimesulide medicines are available in the following Member States: Bulgaria, Czech Republic, Cyprus, France, Greece, Hungary, Italy, Latvia, Lithuania, Malta, Poland, Portugal, Romania, Slovakia and Slovenia. Nimesulide-containing medicines are authorised but not marketed in Austria and in Ireland.

Why was nimesulide reviewed?

Nimesulide was reviewed in 2007 because of concerns with liver injury. The review procedure was triggered by the decision of Ireland's medicines regulatory authority in May 2007 to suspend the marketing authorisation for systemic nimesulide-containing medicines, due to new information

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regarding cases of fulminant hepatic failure requiring liver transplantation.[1] The Committee concluded that the benefits of systemic formulations of nimesulide still outweigh their risks, provided that the use of these medicines is restricted to ensure that the risk of patients developing liver problems is kept to a minimum. To this effect the Committee recommended that treatment duration should be limited to a maximum of 15 days (packs were also limited to a two-week supply), that nimesulide should be restricted to second line treatment, and that doctors should be clearly informed of the risk. The CHMP also concluded that a fuller review of nimesulide was needed, that would look at all of the potential risks of the medicine, especially the risk of side effects affecting the stomach and the gut, which were outside the scope of the original review.

Consequently, on 19 January 2010, the European Commission asked the CHMP to carry out a full assessment of the benefit-risk balance of nimesulide and to issue an opinion on whether the marketing authorisations for systemic medicine containing nimesulide should be maintained, varied, suspended or withdrawn across the European Union.

Which data has the CHMP reviewed?

The Committee reviewed available post marketing data from spontaneous reports of side effects, individual study reports and epidemiological (population-based) studies. It also reviewed data from the published literature, including published clinical studies, reviews and overviews and combined analyses of results from various studies (pooled analyses and meta-analyses).

What are the conclusions of the CHMP?

The Committee noted that the studies looking into the effectiveness of nimesulide in acute pain relief have shown that it is as effective as other NSAID pain killers such as diclofenac, ibuprofen and naproxen.

In terms of safety, the Committee noted that nimesulide has the same risk of causing stomach and gut problems as other NSAIDs. To limit the risk of side effects affecting the liver, several restrictions have already been introduced in the past, including restriction to second line treatment, the use of lowest effective doses for the shortest possible duration, and a maximum duration of treatment for acute pain.

The CHMP concluded that nimesulide was associated with an increased risk of liver toxicity compared with other anti-inflammatory treatments. The CHMP is now recommending, as a further restriction, that systemic nimesulide should no longer be used for treating painful osteoarthritis. The Committee considered that the use of systemic nimesulide for the treatment of painful osteoarthritis, which is a chronic condition, will increase the risk of the medicines being used for long-term treatment with a consequent increase in the risk of liver injury.

What are the recommendations for patients and prescribers?

- Prescribers should no longer prescribe systemic nimesulide for treating painful osteoarthritis.
- Prescribers should review treatment of patients being treated for painful osteoarthritis with a view to choosing an appropriate alternative treatment.
- Nimesulide should only be used as a second choice, and only in the treatment of acute pain or dysmenorrhoea.

[1] Article 107 of Directive 2001/83/EC as amended. All information can be found on the Agency website under Regulatory > Human medicines > Referral procedures> Final decisions

- Patient currently receiving systemic nimesulide for painful osteoarthritis should consult their doctor in order to arrange alternative treatment.
- Patients who have any questions should speak to their doctor or pharmacist.

The European Commission issued a decision on 20 January 2012.