15th MAY 2007

FREQUENTLY ASKED QUESTIONS RELATING TO THE SUSPENSION OF MARKETING OF NIMESULIDE-CONTAINING MEDICINAL PRODUCTS FOR ORAL USE

1. What is nimesulide?

Nimesulide is a non-steroidal anti-inflammatory drug (NSAID) for the treatment of acute pain, primary dysmenorrhoea (period pains) and the symptomatic treatment of painful osteoarthritis. It is available only on prescription.

Nimesulide was first authorised in Ireland in February 1995.

2. What action did The Irish Medicines Board (IMB) take today?

The Irish Medicines Board [IMB] today announced the suspension of the marketing and sale of nimesulide-containing medicines for oral use, with immediate effect.

The products concerned are as follows:

Product Name	**Marketing Authorisation Number**
Aulin 100mg Tablets	**PA 294/18/1**
Aulin 100mg Granules	**PA 294/18/2**
Mesulid 100mg Granules	**PA 915/1/1**
Mesulid 100mg Tablets	**PA 915/1/2**
Mesine 100mg Tablets	**PA 281/111/1**
Aulin 100mg Tablets	**PPA 465/110/1**
Aulin 100 mg Granules	**PPA 1328/51/1**
Aulin 100 mg Tablets	**PPA 1328/51/2**

Please note this action does not apply to Aulin gel or Mesulid gel.

3. Why did the IMB take this action?

The IMB recently received six reports of liver failure that required transplantation after use of oral nimesulide, from the National Liver Transplant Unit at St Vincent's Hospital. Since nimesulide was first authorised in Ireland in 1995, a total of 53 liver-related adverse reaction reports have been received. This includes 9 cases of liver failure, 6 of which originated from the National Liver Transplant Unit. Three cases of liver failure resulted in a fatal outcome and the IMB is aware of one additional liver-related fatality.

After consideration of this cumulative information, the IMB has taken the decision that this medicine poses a significant safety concern, and, therefore, has suspended the marketing and sale in Ireland of nimesulide for oral use.

The IMB has notified the medicines authorities throughout Europe and has initiated a review of the safety of nimesulide-containing products.

4. What should I do if I am currently taking nimesulide?

The IMB advises you to stop taking nimesulide immediately and to contact your doctor to discuss alternative treatments and for further advice.

The IMB advises that you return any remaining packs (unused or partially used) to your pharmacist.

5. Can a pharmacist fill a prescription for nimesulide?

Following the suspension of marketing and sale of oral nimesulide-containing medicinal products it will not be possible to fill a prescription for nimesulide.

6. Will nimesulide be recalled?

The IMB has initiated a recall of oral nimesulide-containing medicinal products from patients, pharmacies, hospitals and wholesalers. The purpose of this recall is to remove all stocks of oral nimesulide from sale or use.

7. What side effects are known to occur with nimesulide?

The side effects known to occur with nimesulide are outlined in the product information. The following is the information contained in the Package Leaflet relating to possible side effects:

- Common (which may affect more than 1 person in 100): diarrhoea, sickness, vomiting, minor changes in blood tests for liver function.
- Uncommon (which may affect up to 1 person in 100): shortness of breath, dizziness, increased blood pressure, constipation, wind, stomach inflammation (gastritis), itching, rash, sweating, swelling (oedema).
- Rarely (which may affect less than 1 person in 1,000): anaemia, decrease in white cells in the blood, increase in certain white cells (eosinophils) in the blood, fluctuating blood pressure, discomfort passing urine or stoppage of urine, blood in the urine, increase in potassium in the blood, feelings of anxiety or nervousness, nightmares, blurring of vision, increased pulse rate, skin flushing, redness of the skin, skin inflammation (dermatitis), feeling generally unwell, tiredness.
- Very rarely (which may affect up to 1 person in 10,000): severe skin disorders (known as erythema multiforme, Stevens Johnson syndrome, toxic epidermal necrolysis); kidney failure or inflammation (nephritis); disorder of brain function (encephalopathy); decrease in platelets in the blood, bleeding under the skin or in other parts of the body; black stools due to bleeding; bleeding from stomach or bowel; duodenal or stomach ulcers and burst ulcers; hepatic inflammation (hepatitis), sometimes very severe; jaundice and stoppage of bile flow; allergies, including severe reactions with collapse and wheezing; asthma; decrease in body temperature; vertigo, headaches, sleepiness; stomach pain; indigestion; sore mouth; hives; swelling of the face and soft tissues.

Most people taking nimesulide will not develop any serious side-effects. However liver damage is a rare but serious side effect associated with the use of oral nimesulide.

8. Is liver damage known to occur with oral nimesulide?

Liver damage is a rare but serious adverse effect known to occur with oral nimesulide and the product information contained the following warnings regarding this risk.

Nimesulide should not be used in patients with:

history of hepatotoxic reactions to nimesulide.
hepatic impairment.

Special warnings and special precautions for use of nimesulide:

The risk of undesirable effects may be reduced by using nimesulide for the shortest possible duration. Treatment should be discontinued if no benefit is seen.

Rarely nimesulide has been reported to be associated with serious hepatic reactions, including very rare fatal cases. Patients who experience symptoms compatible with hepatic injury during treatment with nimesulide (e.g. anorexia, nausea, vomiting, abdominal pain, fatigue, dark urine) or patients who develop abnormal liver function tests should have treatment discontinued. These patients should not be rechallenged with nimesulide. Liver damage, in most cases reversible, has been reported following short exposure to the drug.

Concomitant administration with known hepatotoxic drugs, and alcohol abuse must be avoided during treatment with nimesulide, since either may increase the risk of hepatic reactions.

During therapy with nimesulide patients should be advised to refrain from other analgesics. Simultaneous use of different NSAIDs is not recommended.

Elderly patients are particularly susceptible to the adverse effects of NSAIDs, including gastrointestinal haemorrhage and perforation, impaired renal, cardiac and hepatic function. Therefore, appropriate clinical monitoring is advisable.

In addition, the IMB has previously issued advice to healthcare professionals regarding the risk of liver damage with oral nimesulide via the IMB Drug Safety Newsletter (July 1999, July 2002, July 2003, July 2004).

9. Has the safety of nimesulide been reviewed before?

The safety of nimesulide was assessed by the EU's scientific committee (Committee for Human Medicinal Products, CHMP) in April 2002. The CHMP concluded that the benefit/risk profile of nimesulide was positive subject to changes to the recommended conditions for use. This conclusion was endorsed by the European Commission who published their legally binding decision in April 2004 and the product information was subsequently changed to contraindicate its use in patients with hepatic impairment and to include warnings about the risk of hepatitis, fulminant hepatitis (including fatal cases), jaundice and cholestasis (see response to Q8) and to limit the oral dose to a maximum of 200 mg daily.

10. Are other NSAIDs associated with a risk of liver damage?

Liver damage is a rare side effect of non-steroidal anti-inflammatory drugs (NSAIDs), however, the frequency and severity varies from one NSAID to another.

11. Are there any other risks associated with use of NSAIDs?

All medicines, including NSAIDs, carry risks associated with their use. Details of known side effects for individual medicines are outlined in the product information.

12. How can I report a side effect with nimesulide?

The IMB encourages anyone who has experienced an adverse reaction to nimesulide to report this to their doctor, who can then notify the IMB, as well as considering any alternative treatments that you may need.

Your doctor can report an adverse reaction in two ways:

- Visit www.imb.ie, down load an adverse report form, fill it in and send it to the IMB Pharmacovigilance Department.
- Contact the Pharmacovigilance Department in the IMB on 01-676 4971.

13. Where is nimesulide marketed?

The marketing authorisation holder has confirmed that nimesulide is currently marketed in more than 50 countries world-wide, particularly in Europe and South America. In the EU, nimesulide is authorised in 17 Member States: Austria, Belgium, Bulgaria, Czech Republic, France, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Poland, Portugal, Romania, Slovakia and Slovenia. The first launch was in Italy in 1985.

The marketing authorisation holder has also confirmed that they have never submitted an application for a marketing authorisation in the UK, USA, Denmark or Sweden.

14. Where can I get more information?

To find out more about nimesulide from the IMB:

- Visit www.imb.ie

- Call the information helpline at Freephone: 1 800 251 054 or 01 6343555