European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

London, 23 March 2006
Doc.Ref. EMEA/CHMP/109088/2006

QUESTIONS AND ANSWERS ON RECOMMENDATION FOR REFUSAL OF MARKETING APPLICATION for ZELNORM

International Non-proprietary Name (INN): ***tegaserod***

On 15 December 2005 the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Zelnorm 6 mg tablets. Following request from the applicant, the CHMP re-examined the opinion and confirmed its previous view on 23 March 2006. Zelnorm aims to relieve the symptoms of irritable bowel syndrome with constipation in women. Zelnorm is approved outside the European Union for the treatment of irritable bowel syndrome and chronic constipation. The company who applied is Novartis Europharm Limited.

What is Zelnorm?
Zelnorm is a tablet to be swallowed. It contains 6 mg of the active ingredient tegaserod.

What was Zelnorm expected to be used for?
Zelnorm was expected to be used to relieve the symptoms of irritable bowel syndrome with constipation in women. These symptoms include pain or discomfort in the stomach or abdomen and a feeling of bloating.
Irritable bowel syndrome with constipation is a common disorder of the lower digestive system. It causes abnormal bowel function and makes the intestines more sensitive to normal stimulation, resulting in the above-mentioned symptoms.

How is Zelnorm expected to work?
Tegaserod, the active ingredient in Zelnorm, is a receptor agonist. It activates receptors in the body, known as 5-hydroxytryptamine (5HT) type 4 receptors. When these receptors are activated in the bowels, peristalsis that moves food along the bowels is stimulated. They also potentially reduce the sensitivity of the bowel. These effects are expected to relieve the symptoms described.

Which documentation has been presented by the Company to support the application to the CHMP?
The effects of Zelnorm were first tested in experimental models before being studied in humans.
The main study in humans was done in 2660 women aged 18 to 65 years, and with symptoms of irritable bowel syndrome with constipation. The study compared Zelnorm 6 mg to placebo (a dummy treatment). Treatments were double blinded (neither the patients nor the doctors knew which treatment had been given until the end of the study).
The study looked at the effectiveness of Zelnorm to relieve the overall symptoms of the disease and discomfort or pain in the stomach or abdomen.

Which were the major concerns, which lead to the refusal of the marketing authorisation by the CHMP?
The CHMP was concerned that the results of the study would not translate into real benefit to the patient treated to relieve the symptoms of this disorder in standard health care setting.
The CHMP was of the opinion that Zelnorm's benefits are not greater than its risks. Hence, the CHMP recommended that Zelnorm be refused marketing authorisation.

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What are the consequences of the refusal for patients undergoing clinical trials with Zelnorm?
No consequences for patients undergoing clinical trials have been identified by the CHMP.
If you are in a Zelnorm clinical trial for irritable bowel syndrome or any other indication under development and need more information about your treatment, contact the doctor who is giving it to you.