European Medicines Agency

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QUESTIONS AND ANSWERS ON WITHDRAWAL OF THE MARKETING APPLICATION for XIMELAGATRAN ASTRAZENECA 36 MG FILM COATED TABLETS

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

On 14 February 2006, AstraZeneca officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Ximelagatran 36 mg film coated tablets, for the prevention of stroke and other thromboembolic complications associated with atrial fibrillation.

The withdrawal is part of a global withdrawal of all medicines containing ximelagatran or melegatran, and the impact of the withdrawal of medicines already on the market is being taken care of by the authorities in the countries where the medicines were marketed.
(*Link to the withdrawal EMEA press release*)

What is Ximelagatran 36 mg film coated tablets?
Ximelagatran 36 mg film coated tablets are reddish yellow tablets containing 36 mg of the active substance ximelagatran.

What was Ximelagatran 36 mg film coated tablets expected to be used for?
Ximelagatran 36 mg film coated tablets were to be used to prevent strokes and other complications due to excessive clotting in patients who suffer from atrial fibrillation (irregular contractions of the upper chambers of the heart).

How are Ximelagatran 36 mg film coated tablets expected to work?
Ximelagatran, the active substance in the medicine, is transformed in the body into the active form melagatran. Melagatran is an anti-coagulant medicine. It is an inhibitor of the formation of one of the enzymes in the blood, alpha-thrombin, that is involved in the coagulation (clotting) process, thus helping to prevent the complications due to excessive clotting (such as strokes) that can occur in patients with atrial fibrillation.

What documentation has been presented by the Company to support the application to the CHMP?
The effects of the medicine were first tested in experimental models before being studied in humans. The Company has submitted the results of studies where Ximelagatran 36 mg film coated tablets used twice daily for an average of 17 or 20 months, were compared to warfarin (another anti-coagulant medicine). The studies measured the number of complications due to excessive clotting that happened during the studies.

How far into the evaluation was the application when it was withdrawn?
The CHMP takes up to 210 days to evaluate a new application. Based on the review of the initial documentation, the CHMP prepares a list of questions (at day 120), which is sent to the Company. Once the Company has supplied responses to the questions, the CHMP reviews them and may, before give an opinion, ask any remaining questions (at day 180) to be answered by the Company in writing or during a hearing. Following CHMP opinion, it usually takes around 2 months to the European Commission to give a licence.

7 Westferry Circus, Canary Wharf, London E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 71 29
E-mail: mail@emea.eu.int http://www.emea.eu.int

The application was at Day 48 when the Company withdrew.

The CHMP was evaluating the initial documentation provided by the Company.

What was the recommendation of the CHMP at that time?
The CHMP was evaluating the initial documentation provided by the Company and had not made any recommendation yet.

What were the reasons given by the Company to withdraw the application?

(Link to the withdrawal letter).

What are the consequences of the withdrawal for patients undergoing clinical trials / compassionate use programmes with Ximelagatran 24 mg or 36 mg film coated tablets?
At the time of the withdrawal all ongoing clinical trials with ximelagatran were being stopped. Doctors involved in these trials have received information from AstraZeneca on what to do to close the trials, including how to change patients to alternative treatment. If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you. Patients must not stop treatment without consulting their doctor.