European Medicines Agency

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QUESTIONS AND ANSWERS ON WITHDRAWAL OF MARKETING APPLICATION
for
RETAANE

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

On 28 February 2006, Alcon Laboratories (U.K.) Limited. have officially notified the Committee for Medicinal Products for Human Use (CHMP) that they wish to withdraw their application for a marketing authorisation for Retaane, for the treatment of subfoveal choroidal neovascularisation (CNV) with classic component due to age-related macular degeneration (AMD).

What is Retaane?
Retaane is a suspension for injection onto the outer part of the eye ball. It contains 30 mg/ml of the active substance anecortave acetate.

What was Retaane expected to be used for?
Retaane was expected to be used to treat patients with the wet form of age-related macular degeneration. This disease affects the central part of the retina (called the macula), at the back of the eye and causes loss of vision. The wet form of the disease is caused by abnormal blood vessels under the retina and the macula, which may bleed and leak fluid. Retaane was expected to be used to stop or slow down the development of these new blood vessels (neovascularisation) in the eye.

How is Retaane expected to work?
Anecortave, the active substance in Retaane, is similar in structure to cortisol, a natural hormone in the body. It is able to stop or slow down the development of new blood vessels by interfering with the production of the proteins needed to build the vessels, and of the growth factors needed for the blood vessels to spread. Retaane was to be injected every 6 months directly into the space behind the eye, as a 'depot' injection (a type of injection where the medicine is prepared in such a way that it is absorbed by the body very slowly).

What documentation has been presented by the Company to support the application to the CHMP?
The effects of Retaane were first tested in experimental models before being studied in humans.
The two main clinical studies were carried out in patients aged between 51 and 96 years of age, and lasted up to two years. One compared Retaane at various strengths (3 mg, 15 mg or 30 mg) with a dummy treatment (placebo) in 128 patients. The second compared the effect of Retaane 15 mg to photodynamic therapy (the standard treatment for the wet form of AMD, where laser treatment is used to destroy the newly formed blood vessels) in 530 patients. The studies measured visual acuity (the results of an eye test) to see how the patients had responded to treatment.

How far into the evaluation was the application when it was withdrawn?
The application was at Day 180 when the Company withdrew. After the CHMP had assessed the responses from the Company to a list of questions, there were still unresolved outstanding issues.

The CHMP normally 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

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may, before giving an opinion, ask any remaining question(s) (at day 180). Following CHMP opinion, it usually takes around 2 months for the European Commission to give a licence.

What was the recommendation of the CHMP at that time?
Based on the review of the data submitted and the company's response to the CHMP list of questions at the time of the withdrawal, the CHMP had concerns and was of the provisional opinion that Retaane could not be approved for the treatment of subfoveal choroidal neovascularisation with classic component due to age-related macular degeneration.

What were the main concerns of the CHMP?
The CHMP had concerns that the effectiveness of Retaane was less than what they expected to see: Compared to placebo, Retaane has some effectiveness, but many patients were 'lost' (exited the study) before the end of the study; and this affects the reliability of the results. Compared to photodynamic therapy, Retaane was not as effective.

Therefore, at the time of the withdrawal, the CHMP's view was that the benefit had not been sufficiently demonstrated and did not outweigh the identified risks.

What were the reasons given by the Company to withdraw the application?
The letter from the Company notifying the EMEA of the withdrawal of Retaane is available here.

What are the consequences of the withdrawal for patients undergoing clinical trials / compassionate use programmes with Retaane?
The Company has informed the CHMP that there are clinical trials currently running in Europe. The Company plans to continue the two clinical trials in wet AMD patients, as well as the clinical trial in dry AMD patients at risk of developing wet AMD. The Company also plans to continue their compassionate use programme on a case-by-case basis. A compassionate use programme is a programme through which doctors can request a medicine for a specific disease for one of their patients before the medicine is fully authorised.
If you are in a clinical trial or compassionate use programme and need more information about your treatment, contact the doctor who is giving it to you.