European Medicines Agency

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QUESTIONS AND ANSWERS ON THE WITHDRAWAL OF THE MARKETING APPLICATION
for
RETISERT

International non-proprietary name (INN): ***fluocinolone acetonide***

On 16 July 2007, Bausch & Lomb Ireland officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for RETISERT, for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye. RETISERT was designated an orphan medicinal product on 7 March 2005.

What is RETISERT?
RETISERT is an intravitreal implant (inserted into the vitreous humour, the jelly-like fluid in the central chamber of the eye). It contains the active substance fluocinolone acetonide, which is released slowly by the implant over a period of around three years.

What was RETISERT expected to be used for?
RETISERT was expected to be used to treat chronic (persistent) non-infectious uveitis affecting the posterior (rear) part of the eye. This is inflammation within the eye, which is not caused by an infection, but which affects areas including the retina (the light-sensitive layer at the back of the eye), and the choroid (the layer below the retina that contains blood vessels).

How is RETISERT expected to work?
The active substance in RETISERT, fluocinolone acetonide, is a synthetic corticosteroid. It acts like corticosteroids (a family of naturally occurring hormones) by dampening down the activity of the immune system and reducing inflammation. This anti-inflammatory activity was expected to reduce the symptoms of uveitis.

What documentation did the company present to support its application to the CHMP?
The effects of RETISERT were first tested in experimental models before being studied in humans. RETISERT was studied in one main study involving 146 patients who had had non-infectious uveitis affecting the posterior part of one or both eyes for at least a year, and had been treated with corticosteroids or immunosuppressant medicines for at least a month. The effects of RETISERT, implanted into the more severely affected eye, were compared to those of standard care (the use of corticosteroids or immunosuppressant medicines affecting the whole body). The main measure of effectiveness was the time taken until the disease came back. The study was still ongoing at the time of assessment, but was designed to last a total of three years.

How far into the evaluation was the application when it was withdrawn?
The application was at day 120 when the company withdrew. The CHMP had formulated a list of questions to be answered by the company, but the company had not yet responded to the questions. 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 may, before giving an opinion, ask any remaining questions at day 180. Following the CHMP's opinion, it usually takes around 2 months for the European Commission to grant a licence.

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What was the recommendation of the CHMP at that time?
Based on the review of the data, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that RETISERT could not have been approved for the treatment of chronic non-infectious uveitis.

What were the main concerns of the CHMP?
The CHMP was concerned that a benefit of RETISERT had not been demonstrated based on the two year results presented in the application, since the patients receiving RETISERT in the main study did not have a longer time until their disease came back than those taking standard care. In addition, the Committee did not consider the main measure of effectiveness to be appropriate for this type of study. The use of RETISERT was also linked to side effects, including eye pain, increased pressure within the eyeball and cataracts, which led to vision problems in some patients. There were also concerns over the quality of the medicine.
Therefore, at the time of the withdrawal, the CHMP's view was that a benefit of RETISERT had not been sufficiently demonstrated and any benefits 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 the application is available here.

What are the consequences of the withdrawal for patients undergoing clinical trials with RETISERT?
The company informed the CHMP that there are no clinical trials with RETISERT ongoing in Europe.