European Medicines Agency

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

International non-proprietary name (INN): ***hyaluronidase (ovine)***

On 25 April 2007, ISTA Pharma Limited officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Vitragan, for the treatment of vitreous haemorrhage.

What is Vitragan?
Vitragan is a powder containing the active substance hyaluronidase (ovine). It was to be made up into a solution for injection into the eye.

What was Vitragan expected to be used for?
Vitragan was expected to be used to treat vitreous haemorrhage (bleeding into the vitreous humour, the jelly-like fluid in the central chamber of the eye) in adults. This was intended to improve vision and to help doctors in their diagnosis of underlying problems in the retina (the light-sensitive surface at the back of the eye).

How is Vitragan expected to work?
The active substance in Vitragan, hyaluronidase (ovine), is an enzyme extracted from sheep. It is expected to work by breaking down a molecule in the vitreous humour called hyaluronic acid. When the acid is broken down, the vitreous humour turns from a jelly into a liquid, allowing cells to move more freely through the vitreous humour. This was expected to allow phagocytes (specialised 'scavenger' cells of the immune system) to clear away any blood clots from the vitreous humour.

What documentation did the company present to support its application to the CHMP?
The effects of Vitragan were first tested in experimental models before being studied in humans. The company also presented the results of two main studies involving 1,306 patients with vitreous haemorrhage, where the effects of a single injection of Vitragan were compared with those of placebo (a dummy treatment). The main measure of effectiveness was the improvement in vision three months after the injection, assessed using a standard letter chart.

How far into the evaluation was the application when it was withdrawn?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 some unresolved issues outstanding. 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.

What was the recommendation of the CHMP at that time?
Based on the review of the data and the company's response to the CHMP list of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Vitragan could not have been approved for the treatment of vitreous haemorrhage.

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What were the main concerns of the CHMP?
The CHMP had concerns over the benefits of Vitragan, since the main studies had not shown convincingly that it was more effective than available options for managing vitreous haemorrhage. The Committee was also concerned over the safety of the medicine and the consistency of the medicine between batches.
Therefore, at the time of the withdrawal, the CHMP's view was that a benefit of Vitragan 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 or compassionate use programmes with Vitragan?
The company informed the CHMP that there are currently no clinical trials or compassionate use programmes with Vitragan.