European Medicines Agency

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Questions and answers on the withdrawal of the marketing application for Vekacia

International non-proprietary name (INN): ***ciclosporin***

On 14 November 2008, Novagali Pharma S.A. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Vekacia, for the treatment of vernal keratoconjunctivitis. Vekacia was designated as an orphan medicinal product on 6 April 2006.

What is Vekacia?
Vekacia is a medicine that contains ciclosporin. It was to be available as eye drops.

What was Vekacia expected to be used for?
Vekacia was expected to be used to treat vernal keratoconjunctivitis. This is inflammation of the conjunctiva (the membrane that lines the eyelid) and the cornea (the transparent layer in front of the pupil), which is caused by allergy. Vernal keratoconjunctivitis is a long-term disease that mainly affects young boys living in warm, dry climates such as Mediterranean countries. 'Vernal' means that it usually occurs in the spring. The disease can lead to loss of vision.

How is Vekacia expected to work?
The active substance in Vekacia, ciclosporin, is an immunosuppressant. This means that it reduces the activity of the immune system (the body's natural defences). Ciclosporin has been used since the mid-1980s to help prevent rejection in transplant patients (when the immune system attacks the transplanted organ). In patients with vernal keratoconjunctivitis, ciclosporin given as eye drops was expected to suppress the local immune reactions that trigger inflammation in the conjunctiva and cornea.

What documentation did the company present to support its application to the CHMP?
Because ciclosporin has been used for many years, the applicant presented data on experimental models from the scientific literature.
To support the use of Vekacia in vernal keratoconjunctivitis, the company presented the results of one study in 118 children (over the age of four years) and adolescents. The patients were treated with Vekacia at a concentration of 0.05% (0.5 mg ciclosporin per millilitre) or of 0.1% (1 mg/ml), or with placebo (dummy eye drops). In this case this was the 'vehicle' (the same eye drops but without ciclosporin). The main measure of effectiveness chosen was the change in the symptoms of the disease after four weeks, as scored by the doctor. Symptoms that were looked at included: burning, itching, pain, sticky eyelids, the sensation of a foreign body in the eyes or photophobia (oversensitivity of the eyes to light).

How far into the evaluation was the application when it was withdrawn?
The application was at day 175 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

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giving an opinion, ask any remaining questions at day 180. Following the CHMP's opinion, it usually takes around two 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 Vekacia could not have been approved for the treatment of vernal keratoconjunctivitis.

What were the main concerns of the CHMP?
The CHMP had concerns that the effectiveness of Vekacia had not been shown when compared to the vehicle. The Committee's concerns related to the way the study was designed, in terms of the choice of the patients treated, how symptoms were measured and the way the study's results were analysed. The Committee also noted that the long-term effectiveness of the medicine had not been investigated. Therefore, at the time of the withdrawal, the CHMP's view was that a benefit of Vekacia 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 Vekacia?
The company informed the CHMP that there are no clinical trials or compassionate use programmes with Vekacia in Europe.