European Medicines Agency

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Questions and answers on the withdrawal of the marketing authorisation application for Bosatria
mepolizumab

On 28 July 2009, Glaxo Group Limited officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Bosatria, for the treatment of adults with hypereosinophilic syndrome to reduce or eliminate the need for corticosteroid therapy and to reduce blood eosinophil counts.

What is Bosatria?
Bosatria is a powder that is made up into a solution for infusion (drip into a vein). It contains the active substance mepolizumab.

What was Bosatria expected to be used for?
Bosatria was expected to be used to treat adults with hypereosinophilic syndrome. This is a disease in which eosinophils (a type of white blood cell) start growing out of control, they accumulate in the tissues of many organs, and can cause damage to organs such as the heart, liver and lungs. Bosatria was expected to be used in patients who lack a gene called the 'FIP1L1-PDGRF fusion gene' to reduce or eliminate the need for the patients to be treated with corticosteroids (steroids used to treat the disease) and to reduce the level of eosinophils in the blood.
Bosatria was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 29 July 2004 for the treatment of hypereosinophilic syndrome.

How is Bosatria expected to work?
The active substance in Bosatria, mepolizumab, is a monoclonal antibody. A monoclonal antibody is an antibody (a type of protein) that has been designed to recognise and attach to a specific structure (called an antigen) that is found in the body. Mepolizumab has been designed to attach to a chemical messenger called interleukin 5 (IL-5), which is involved in the growth of eosinophils. By attaching to IL-5, mepolizumab was expected to reduce the accumulation of eosinophils in the blood, thereby relieving the symptoms of patients with hypereosinophilic syndrome.

What documentation did the company present to support its application to the CHMP?
The effects of Bosatria were first tested in experimental models before being studied in humans. In one main study involving 85 adults with hypereosinophilic syndrome, Bosatria was compared with placebo (a dummy treatment). All patients lacked the FIP1L1-PDGRF fusion gene and were receiving treatment with prednisone (a corticosteroid) that was helping to stabilise their symptoms. During the study the patients received either Bosatria or placebo while the amount of prednisone they received was gradually reduced. The main measure of effectiveness was the number of patients who could have their daily prednisone dose reduced to 10 mg or lower for a period of eight weeks.

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.

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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 two months for the European Commission to issue a decision on this opinion.

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 lists of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Bosatria could not have been approved for the treatment of adults with hypereosinophilic syndrome who lack the FIP1L1-PDGRF fusion gene, to reduce or eliminate the need for corticosteroid therapy and to reduce blood eosinophil counts.

What were the main concerns of the CHMP?
The CHMP was of the opinion that the main study did not provide sufficient evidence to show that Bosatria was effective in reducing the need for corticosteroid treatment. The CHMP was also concerned that the method used by the company to quantify the different forms of the active substance in the medicine was not appropriate. Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Bosatria did not outweigh its risks in the treatment of adults with hypereosinophilic syndrome who lack the FIP1L1-PDGRF fusion gene, to reduce or eliminate the need for corticosteroid therapy and to reduce blood eosinophil counts.

What were the reasons given by the company for withdrawing 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 in clinical trials or compassionate use programmes using Bosatria?
The company informed the CHMP that Bosatria will continue to be made available for patients in the open-label extension study and compassionate use programmes. 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.

The summary of opinion of the Committee for Orphan Medicinal Products for Bosatria is available here.