EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Questions and answers

Withdrawal of the marketing authorisation application for IXinity (trenonacog alfa)

On 13 June 2013, Cangene Europe Ltd. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for IXinity, for the treatment and prevention of bleeding in patients with haemophilia B.

What is IXinity?

IXinity is a medicine that contains the active substance trenonacog alfa (recombinant human factor IX). It was expected to be available as a powder and solvent to make up a solution for injection (500, 1,000 and 1,500 units).

What was IXinity expected to be used for?

IXinity was expected to be used to prevent and treat bleeding episodes in patients at least 12 years of age with haemophilia B (an inherited bleeding disorder caused by lack of factor IX).

How is IXinity expected to work?

Patients with haemophilia B do not have sufficient levels of factor IX, a protein in the blood that helps it to clot normally. This causes problems with blood clotting, leading to bleeding into the joints, muscles and internal organs. The active substance in IXinity, trenonacog alfa, is a form of human factor IX that replaces the missing factor IX in the blood, temporarily controlling the bleeding disorder.

The active substance in IXinity is produced by a method known as 'recombinant DNA technology': it is made by cells into which a gene (DNA) has been introduced that makes them able to produce the clotting factor.

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What did the company present to support its application?

The company presented the results of studies involving 42 patients with moderate or severe haemophilia B who were given IXinity for treatment or prevention of bleeding, including some patients undergoing surgery. Effectiveness was measured by the patients' assessment of how well bleeding was controlled, and by the number of bleeding episodes that occurred while receiving the medicine.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the documentation provided by the company and formulated lists of questions. After the CHMP had assessed the company's responses to the last round of questions, there were still some unresolved issues.

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 IXinity could not have been approved for the prevention and treatment of bleeding episodes in patients with haemophilia B.

Although the studies had shown evidence of the effectiveness of IXinity, they had also revealed that patients developed an unexpectedly high level of antibodies against proteins from the cells used to make IXinity, which were also present in the medicine. The company refined the manufacturing process for IXinity to remove these proteins, but it was not clear if the refined medicine would act in the same way as the original product in the studies, and the CHMP recommended further study in patients.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that based on the currently available data the balance of the benefit and risks of the refined IXinity product was negative.

What were the reasons given by the company for withdrawing the application?

In its letter notifying the Agency of the withdrawal of application, the company stated that its decision to withdraw the application was based on the fact that the additional data required to address the CHMP's concerns could not be made available within the regulatory timeframe. The company expressed its intention to re-apply for marketing authorisation once the data were available.

The withdrawal letter is available here.

What consequences does this withdrawal have for patients in clinical trials?

The company informed the CHMP that patients currently included in clinical trials would continue to receive IXinity and would be switched to the refined product once revised rules for the conduct of the trials had been approved.

If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.