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Questions and answers

Withdrawal of the marketing authorisation application for Egrifta (tesamorelin)

On 21 June 2012, Ferrer Internacional, 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 Egrifta, for the treatment of excess abdominal fat in HIV patients with lipodystrophy.

What is Egrifta?

Egrifta is a medicine that contains the active substance tesamorelin. It was to be available as a powder to be made up into a solution for injection.

What was Egrifta expected to be used for?

Egrifta was expected to be used for the treatment of excess abdominal fat in HIV-infected patients with lipodystrophy, a condition that leads to changes in the distribution of body fat. Lipodystrophy is known to occur in some HIV-infected patients, where it leads to the loss of fat in certain areas of the body and sometimes to excessive accumulation of fat in the abdomen.

How is Egrifta expected to work?

The active substance in Egrifta, tesamorelin, is similar to 'human growth hormone-releasing factor' (GRF), a hormone in the body that stimulates the release of growth hormone. Growth hormone has been shown to play a role in regulating the formation and breakdown of fat tissue.

Tesamorelin is expected to act in a similar way to GRF, causing the release of growth hormone, which is then expected to increase the breakdown of fat in HIV patients with lipodystrophy, thereby reducing excess fat in the abdomen.

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What did the company present to support its application?

The company presented the results from two main studies involving 816 HIV patients with excessive accumulation of abdominal fat. The studies compared Egrifta with placebo (a dummy treatment), and the main measure of effectiveness was the change in abdominal fat after 26 weeks of treatment.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the documentation provided by the company and formulated lists of questions.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 responses to the CHMP lists of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Egrifta could not have been approved for the treatment of excess abdominal fat in HIV patients with lipodystrophy.

The CHMP was concerned about how Egrifta would be used in clinical practice as it would be difficult to differentiate excess abdominal fat due to lipodystrophy from excess fat due to obesity. The CHMP considered a suggestion by the company to restrict the medicine to patients with abdominal fat above a certain amount (defined as greater than 130 cm^2), but the evidence supporting the cut-off point was not considered to be sufficient.

In addition, although the main studies showed a reduction in abdominal fat with Egrifta, the reduction has not been shown to be clinically meaningful in terms of actual health benefits to patients. The relevance of the results was also questioned because the patients in the main studies were not representative of European HIV patients, who have a lower average body mass index (BMI) and smaller amounts of abdominal fats than the patients in the studies.

In terms of safety, the CHMP noted that there was an increase in the level of a protein called insulin-like growth factor 1 (IGF-1) in a considerable number of patients treated with Egrifta. High levels of IGF-1 may be associated with an increased risk of cancer and a potential worsening of diabetic eye disease, and the Committee considered this to be a major safety concern. In addition, no long-term safety data were provided, although treatment with Egrifta was expected to be long term.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Egrifta did not outweigh its risks.

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

In its official letter, the company stated that it decided to withdraw the application because the CHMP considered that the data provided did not allow the Committee to conclude on a positive benefit-risk balance.

The withdrawal letter is available here.

What consequences does this withdrawal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that there are no consequences for patients currently included in compassionate use programmes using Egrifta.

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