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Withdrawal of the marketing authorisation application for Efgratin (pegfilgrastim)

On 20 December 2018, Gedeon Richter Plc officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Efgratin, for reducing neutropenia.

What is Efgratin?

Efgratin is a medicine that contains the active substance pegfilgrastim, which stimulates the production of neutrophils (a type of white blood cell that fights infections). It was to be given by injection under the skin.

Efgratin was developed as a 'biosimilar' medicine. This means that Efgratin was intended to be highly similar to another biological medicine (the 'reference medicine') that is already authorised in the EU. The reference medicine for Efgratin is Neulasta. For more information on biosimilar medicines, see here.

What was Efgratin expected to be used for?

Efgratin was to be used in cancer patients to reduce neutropenia (low levels of neutrophils). Neutropenia is a side effect of certain cytotoxic (cell-killing) cancer treatments because the treatments also kill white blood cells. Efgratin was to be used to reduce the duration of neutropenia and the occurrence of febrile neutropenia (neutropenia with fever).

How does Efgratin work?

The active substance in Efgratin, pegfilgrastim, consists of filgrastim that has been 'pegylated' (attached to a chemical called polyethylene glycol). Filgrastim is very similar to a human protein called granulocyte-colony-stimulating factor (G-CSF). It encourages the bone marrow to produce more neutrophils and improves the patient's ability to fight off infections.

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Because filgrastim is pegylated, its removal from the body is slowed down, allowing the medicine to be given less often.

What did the company present to support its application?

The company presented results of two studies in healthy people designed to show that Efgratin is highly similar to its reference medicine Neulasta in terms of chemical structure, purity, the way it works and how the body handles the medicine. A further study in patients receiving cancer medicines compared the effectiveness of Efgratin and Neulasta. The safety of Efgratin was compared with that of Neulasta across different studies involving healthy people as well as patients with cancer.

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

The application was withdrawn after the CHMP had evaluated the initial documentation provided by the company and formulated a list of questions. The company had not yet responded to the questions at the time of the withdrawal.

What was the recommendation of the CHMP at that time?

Based on the review of the data, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Efgratin could not have been approved for reducing neutropenia. The CHMP was concerned about the validity of results from studies on how the body handles Efgratin compared with Neulasta. Moreover, information was not available on the possible formation in the body of antibodies against the active substance in Efgratin.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the company had not demonstrated that Efgratin was highly similar to Neulasta.

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

In its letter notifying the Agency of the withdrawal of the application, the company stated that it could not address the CHMP's concerns within the time allowed.

The withdrawal letter is available here.

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

The company informed the CHMP that there are no ongoing clinical trials or compassionate-use programmes for Efgratin.