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Withdrawal of application for the marketing authorisation of Lutholaz (pegfilgrastim)

YES Pharmaceutical Development Services GmbH withdrew its application for a marketing authorisation of Lutholaz for use in cancer patients to reduce the duration of neutropenia (low levels of neutrophils, a type of white blood cell) and prevent febrile neutropenia (neutropenia accompanied by fever due to an infection). Neutropenia is a common side effect of cancer chemotherapy and can leave patients vulnerable to infections.

The company withdrew the application on 19 July 2023.

What is Lutholaz and what was it intended to be used for?

Lutholaz was developed as a medicine to reduce the duration of neutropenia and prevent febrile neutropenia in adults with cancer. The medicine was not intended for use in patients with the blood cancer chronic myeloid leukaemia or with myelodysplastic syndromes (conditions in which large numbers of abnormal blood cells are produced, which can develop into leukaemia).

Lutholaz contains the active substance pegfilgrastim and was to be available as a pre-filled syringe containing a solution for injection under the skin, given as a single dose.

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

How does Lutholaz work?

The active substance in Lutholaz and Neulasta, pegfilgrastim, consists of filgrastim, which is very similar to a human protein called granulocyte colony stimulating factor (G-CSF). Filgrastim works by encouraging the bone marrow to produce more white blood cells, increasing white blood cell counts and so treating neutropenia and helping the body fight infection.

Filgrastim has been available in other medicines in the European Union for a number of years. In Lutholaz and Neulasta, filgrastim has been 'pegylated' (attached to a chemical called polyethylene glycol). This slows down the removal of filgrastim from the body, allowing the medicine to be given less often.

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What did the company present to support its application?

The company presented results from laboratory studies that investigated whether the active substance in Lutholaz is highly similar to that in Neulasta in terms of structure, purity and biological activity.

The company also presented results from a study involving 150 healthy volunteers investigating whether Lutholaz and Neulasta produce similar levels of the active substance in the body and have a similar effect on the number of neutrophils in the blood.

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

The application was withdrawn after the European Medicines Agency had evaluated the information from the company and prepared questions for the company. The company had not responded to the last round of questions at the time of the withdrawal.

What did the Agency recommend at that time?

Based on the review of the data at the time of the withdrawal, the Agency had some concerns and its provisional opinion was that Lutholaz could not have been authorised for the reduction of neutropenia and prevention of febrile neutropenia in patients with cancer.

The Agency had concerns relating to the quality of the medicine as EU certification to show that the active substance is manufactured according to EU good manufacturing practice (GMP) by the manufacturer had not been provided following an inspection carried out by an authority in the EU.

Therefore, at the time of the withdrawal, the Agency's opinion was that the company had not provided enough data to support the application for Lutholaz.

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 Agency's concern regarding the EU GMP certification of one of the manufacturing sites involved within the required time limit.

Does this withdrawal affect patients in clinical trials?

The company informed the Agency that there are no ongoing clinical trials with Lutholaz.

If you have taken part in a clinical trial and need more information about your treatment, speak with your clinical trial doctor.