27 January 2017
EMA/47326/2017
EMEA/H/C/004211

**Questions and answers**

# Withdrawal of the marketing authorisation application for Zioxtenzo (pegfilgrastim)

On 18 January 2017, Sandoz GmbH officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Zioxtenzo, intended for treating neutropenia in patients taking cancer treatments.

## What is Zioxtenzo?

Zioxtenzo is a medicine that contains the active substance pegfilgrastim. It was to be available as a solution for injection under the skin.

Zioxtenzo was developed as a 'biosimilar' medicine. This means that it was intended to be highly similar to a biological medicine (the 'reference medicine') already authorised in the European Union. The reference medicine for Zioxtenzo is Neulasta. For more information on biosimilar medicines, see the question-and-answer document here.

## What was Zioxtenzo expected to be used for?

Zioxtenzo was to be used in cancer patients to treat neutropenia (low levels of neutrophils, a type of white blood cell that helps fight infection).

Neutropenia is a side effect of certain cytotoxic (cell-killing) cancer treatments and can lead to development of serious infections. Zioxtenzo was to be used to reduce the duration of neutropenia and the occurrence of febrile neutropenia (neutropenia with fever).

## How does Zioxtenzo work?

The active substance in Zioxtenzo, pegfilgrastim, consists of filgrastim that has been 'pegylated' (attached to a chemical called polyethylene glycol). Filgrastim is very similar to a human protein called

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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.

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 studies designed to show that Zioxtenzo 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. In addition, two studies in patients receiving cancer medicines compared the safety and effectiveness of Zioxtenzo and Neulasta.

## How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the initial documentation provided by the company and formulated a list of questions.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 two main concerns and was of the provisional opinion that Zioxtenzo could not have been approved as a biosimilar of Neulasta.

One concern was that study results were not able to show that the concentrations of pegfilgrastim in blood were the same after taking Zioxtenzo and Neulasta. The other concern was the lack of a certificate of Good Manufacturing Practice (GMP) for the medicine's manufacturing site. An inspection of the site will therefore be needed before the medicine can be approved.

At the time of the withdrawal, the company had not demonstrated that Zioxtenzo is highly similar to Neulasta and an inspection to confirm that it was being manufactured according to GMP standards had not yet taken place.

## 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 would not be able to provide the additional data required by the CHMP within the timeframe allowed for the procedure. The withdrawal letter is available here.

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

The company informed the CHMP that there is no impact of the withdrawal of Zioxtenzo on ongoing clinical trials and there are no compassionate use programmes for Zioxtenzo.