

Questions and answers on the shortages of Cerezyme and Fabrazyme

The European Medicines Agency has recommended which patients should receive Cerezyme and Fabrazyme as a priority during the expected shortage of these two medicines over the next few months. The shortage is happening because of a problem in the factory where the active substances for the medicines are made. The recommendation is intended to ensure that the patients at greatest need of treatment continue to receive these medicines while the company solves its supply problems.

Updated treatment recommendations for Cerezyme are available [here](#).

What are Cerezyme and Fabrazyme?

Cerezyme and Fabrazyme are medicines that are used in two rare, inherited, life-threatening diseases in which patients have a lack of an enzyme involved in the breakdown of fatty substances in the body:

- Cerezyme is used in patients with Gaucher disease, a disease in which patients do not have enough of an enzyme called alglucerase. Cerezyme contains imiglucerase, which is a copy of the natural enzyme;
- Fabrazyme is used in patients with Fabry disease, a disease in which patients do not have enough of an enzyme called alpha-galactosidase A. Fabrazyme contains agalsidase beta, which is a copy of the natural enzyme.

In both medicines, the replacement enzyme is made by a method known as 'recombinant DNA technology': the enzymes are made by cells that have received genes (DNA) that makes them able to produce the enzymes. The cells are grown in special tanks called 'bioreactors' over a three- to four-month process, and the enzyme is extracted from the culture at regular intervals during the process.

Cerezyme has been authorised since November 1997 and Fabrazyme since August 2001. Both medicines are marketed in all Member States of the European Union.

What is the problem with Cerezyme and Fabrazyme?

Earlier this year, Genzyme, the company that makes Cerezyme and Fabrazyme, became aware of reduced yields from the bioreactors used to produce Cerezyme and Fabrazyme at their production site in Allston Landing in the United States of America. The company have found that the bioreactors were contaminated with a virus (a calicivirus of the type Vesivirus 2117). This virus is not known to cause disease in humans, but it can attack the cells used to produce these medicines.

The contamination has an impact on cell growth, affecting the quantity, but not the quality, of the enzymes produced by the cells. All batches prepared using enzymes produced prior to the contamination being detected have been tested and the Agency has confirmed that they are suitable for release onto the market.

The company has now shut down the factory so that it can be sanitised. While this is ongoing, Genzyme cannot make any new batches of Cerezyme or Fabrazyme. Existing stocks are expected to run out as early as August 2009 for Cerezyme, and by October 2009 for Fabrazyme. To ensure that these stocks last as long as possible while the company resolves its manufacturing problems, the company, in agreement with the European Medicines Agency, is recommending some temporary changes to the way Cerezyme and Fabrazyme are prescribed and used. These changes should be implemented immediately.

What are the recommendations while the shortages are ongoing?

- ***Cerezyme***

For Cerezyme, priority is given to infants, children and adolescents, and adults with active disease progression. These patients can continue to receive Cerezyme at the standard dose schedule of one infusion every two weeks.

However, adult patients without clinical evidence of active disease progression should receive Cerezyme at a reduced dose (half a dose once every two weeks) or at a reduced infusion frequency (once a month at their current dose).

- ***Fabrazyme***

For Fabrazyme, priority is given to children and adolescents, and adult male patients, who should continue to receive Fabrazyme as one infusion every two weeks.

However, adult female patients, in whom the disease is less severe, may receive Fabrazyme at a reduced dose.

All patients will be closely monitored while they are receiving reduced doses of Cerezyme or Fabrazyme. Reporting of side effects will continue as normal, with doctors recording the batch numbers of the medicines in each patient's records.

These changes will need to continue until the shortages are resolved, by the end of the year at the latest.

What are the recommendations for prescribers?

- Doctors who look after patients with Gaucher or Fabry disease should be aware of the shortages, and should consider which patients should be switched to the reduced dose.

What are the recommendations for patients with Gaucher disease?

- There are no consequences for young patients with the disease (infants, children and adolescents) or for adult patients with active disease.
- Adult patients with Gaucher disease whose disease is not currently active should be contacted by their doctor to discuss their treatment options. While the shortages are ongoing, they may be treated at the same frequency (every two weeks) but with a reduced dose, or they may be asked to come to the clinic only once a month.
- Patients who have any questions should speak to their doctor or pharmacist.

What are the recommendations for patients with Fabry disease?

- There are no consequences for young patients with the disease (infants, children and adolescents) or for adult male patients.
- Adult female patients with Fabry disease should be contacted by their doctor to discuss their treatment options. While the shortages are ongoing, they may be treated at the same frequency (every two weeks) but with a reduced dose.
- Patients who have any questions should speak to their doctor or pharmacist.

What will happen next?

Genzyme is sending specific communications to all Cerezyme and Fabrazyme prescribers to ensure that they have full details on how to select patients for dose reduction.

Genzyme has also informed the CHMP that these stock-sparing measures will have no impact on the supplies to ongoing clinical trials.

While the company is sanitising its factory, it is also investigating in depth, at the request of the Agency, the reasons why the contamination arose. The company will keep the Agency informed of its findings.

The European Medicines Agency will update this document as new information becomes available.