European Medicines Agency

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Questions and answers on the shortages of Cerezyme and Fabrazyme

The European Medicines Agency has reviewed treatment recommendations from June 2009 on which patients should receive Cerezyme and Fabrazyme as a priority during the shortage of these two medicines over the next few months. The shortage, which is expected to last until the end of the year, is happening because of a problem in a factory where the active substances for the medicines are made.
The company has informed the Agency that the supply shortage of Cerezyme is more severe than it previously thought. Because of this, the Agency is now recommending the following:

- for Cerezyme, only patients at greatest need of treatment will receive Cerezyme but at a reduced dosage;
- for Fabrazyme, the recommendations given in June 2009 remain the same. They are ensuring that patients at greatest need of treatment continue to receive this medicine until the shortage is resolved.

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 found out 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.

In June 2009, in order to sanitise the production facilities and conduct an investigation to prevent the contamination from re-occurring, the company had to stop the production of new batches of Cerezyme and Fabrazyme for an extended period of time. As a result of the supply shortage of both medicines, the company, in agreement with the Agency, recommended some temporary changes to the way Cerezyme and Fabrazyme were prescribed and used.

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Although manufacturing is resuming, Genzyme has now informed the European Medicines Agency that the stocks of Cerezyme are lower than it said they were in June. Therefore the recommendations on the use of Cerezyme have had to be revised. These changes should be implemented immediately.

What are the recommendations while the shortages are ongoing?

Revised recommendations for Cerezyme

For Cerezyme, priority is given to infants, children and adolescents, and adults with severe, life-threatening disease progression:

- infants, children and adolescents should receive Cerezyme at a reduced dose or at a reduced infusion frequency. However, no patient should be treated at a dose lower than 15 units per kilogram body weight every two weeks, or alternative treatment should be considered.
- adult patients with severe, life-threatening disease progression should receive Cerezyme at a reduced dose or at a reduced infusion frequency. However, no patient should be treated at a dose lower than 15 U/kg every four weeks, or alternative treatment should be considered.

In adult patients without severe, life-threatening disease progression, alternative treatment such as miglustat should be considered or treatment should be interrupted. Adults who demonstrate progression to severe, life-threatening disease should re-initiate treatment with Cerezyme.

Recommendations for Fabrazyme

For Fabrazyme, as in June 2009, 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 treatment is suspended or 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 end of 2009 when the shortages are to be resolved.

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 or other treatment.

What are the recommendations for patients with Gaucher disease who receive Cerezyme?

- Young patients with the disease (infants, children and adolescents) and adult patients with severe, life-threatening disease progression should be contacted by their doctor to discuss their treatment options. While the shortages are ongoing, they may be treated at a different frequency and with a reduced dose.
- Adult patients without severe, life-threatening disease progression should be contacted by their doctor to discuss the possibility of switching to alternative treatments (e.g. miglustat) or suspending treatment.
- Patients who have any questions should speak to their doctor or pharmacist.

What are the recommendations for patients with Fabry disease who receive Fabrazyme?

- 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 prescribers on how to select patients for dose reduction, switch to alternative treatment or suspension of treatment, according to the new recommendations. Genzyme has informed the Agency that no changes to the June recommendations are required for Fabrazyme.

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

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