



Genzyme Therapeutics

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Date: April 2011

Dear Healthcare Professional,

RE: Cerezyme (imiglucerase) supply update

Over the last eighteen months the Gaucher community has experienced enormous disruption to the supply of Cerezyme. This, we all recognise, has impacted patients and the Gaucher community in many ways.

In the past few months we have seen considerable improvements in the supply of Cerezyme. In the UK and Ireland we are now in a position whereby patients can move back to receiving monthly deliveries of Cerezyme. We are working with the Homecare companies to manage the logistics of this process and hope over the next few weeks that all patients receiving Cerezyme can return to their previous delivery schedules.

For further information please contact Medical Information on ukmedinfo@genzyme.com or phone 01865-405-283.

Yours sincerely

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Date: April 2011

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Prescribing Information

Cerezyme® 200 U / 400 U, powder for concentrate for solution for infusion (imiglucerase).

Product composition: Each vial of Cerezyme contains 200 U or 400 U of imiglucerase, the recombinant form of human β -glucocerebrosidase, and the following excipients: mannitol, sodium citrate, citric acid monohydrate and polysorbate 80.

Indication: Cerezyme (imiglucerase) is indicated for use as long-term enzyme replacement therapy in patients with a confirmed diagnosis of non-neuronopathic (Type 1) or chronic neuronopathic (Type 3) Gaucher disease, who exhibit clinically significant non-neurological manifestations of the disease. The non-neurological manifestations of Gaucher disease include one or more of the following conditions:

- anaemia after exclusion of other causes, such as iron deficiency
- thrombocytopenia
- bone disease after exclusion of other causes, such as Vitamin D deficiency
- hepatomegaly or splenomegaly

Therapy should be supervised by physicians knowledgeable in the management of Gaucher disease.

Contraindications: Hypersensitivity to the active substance or to any of the excipients.

Dosage and administration: Due to the heterogeneity and the multi-system nature of Gaucher disease, dosage should be individualised for each patient based on a comprehensive evaluation of the clinical manifestations of the disease and individual treatment goals (see NCG Guidelines). A range of dosage regimens has proven effective towards some or all non-neurological manifestations. Initial doses of 60 U/kg of body weight once every 2 weeks have shown improvement in haematological and visceral parameters within 6 months of therapy, and continued use has either stopped progression of, or improved, bone disease. Administration of doses as low as 15 U/kg of body weight once every 2 weeks has been shown to improve haematological parameters and organomegaly, but not bone parameters. The usual frequency of infusion is once every 2 weeks; this is the frequency of infusion for which the most data are available.

The efficacy of Cerezyme on neurological symptoms of chronic neuronopathic Gaucher patients has not been established, and no special dosage regimen can be recommended for these manifestations.

Once individual patient response for all relevant clinical manifestations is well-established and stabilised, dosages may be adjusted for continued effective therapy, while continuing closely to monitor response parameters and patient well-being.

An infusion maintenance regimen once every 4 weeks (Q4) at the same cumulative dose as 2 weekly infusions (Q2) may be a therapeutic option for some adult patients with stable residual Gaucher disease type 1, but clinical data are limited.

Cerezyme should be reconstituted with Water for Injections and further diluted in 0.9% sodium chloride intravenous solution. The reconstituted and diluted preparation is administered by intravenous infusion over 1 to 2 hours. Alternatively, the appropriate dose of Cerezyme may be administered at a rate not exceeding 1 unit per kg body weight per minute. It is recommended to administer the diluted solution through an in-line low protein-binding 0.2 μ m filter to remove any protein particles. This will not lead to any loss of imiglucerase activity.

When infusions of Cerezyme have been well tolerated for several months, they may be undertaken at home at the discretion of the treating physician. Home infusion by the patient or caregiver requires appropriate training in infusion technique and maintenance of a treatment record by a qualified health care professional. If adverse events occur during an infusion, it must be stopped immediately and a healthcare professional informed. Subsequent infusions in a clinical setting may be needed at the discretion of the treating physician. Dose and infusion rate should not be changed without supervision by a health care professional.

Precautions:

Hypersensitivity: IgG antibodies to Cerezyme are formed in approximately 15% of the treated patients. Patients will rarely develop antibodies to Cerezyme after 12 months of therapy. Patients with antibodies to Cerezyme have a higher risk of hypersensitivity reactions. If a patient experiences a reaction suggestive of hypersensitivity, subsequent testing for imiglucerase antibodies is advised. Patients with an apparent decreased response to treatment should be monitored periodically for IgG imiglucerase antibodies.

Patients with antibodies to imiglucerase have a higher risk of hypersensitivity reactions. If a patient experiences hypersensitivity type reactions, testing for imiglucerase antibodies is advised. As with any intravenous protein product, severe allergic or anaphylactoid reactions are possible, but occur uncommonly. If these reactions occur, the Cerezyme infusion should be immediately discontinued and appropriate medical treatment initiated.

Patients who have developed antibodies or evidence of hypersensitivity to Ceredase (alglucerase) should be treated with caution when administering Cerezyme (imiglucerase).

Pulmonary hypertension: Pulmonary hypertension is a known complication of Gaucher disease. It has been observed both in patients receiving and not receiving enzyme replacement therapy. No causal relationship with enzyme replacement therapy has been established. Patients with respiratory symptoms should be evaluated for the presence of pulmonary hypertension.

Pregnancy and lactation: Limited experience from 150 pregnancy outcomes (primarily based on spontaneous reporting and literature review) is available suggesting that use of Cerezyme is beneficial to control the underlying Gaucher disease during pregnancy. Furthermore, the data indicate no foetal malformation due to Cerezyme, although the statistical power is low. Foetal death has been reported rarely, although it is not clear whether this is related to the use of Cerezyme or to the underlying Gaucher disease.

No animal studies have been carried out with respect to assessing the effects of Cerezyme on pregnancy, embryonic/foetal development, parturition and postnatal development. It is not known whether Cerezyme passes via the placenta to the developing foetus. In pregnant Gaucher patients and those intending to become pregnant, a risk-benefit treatment assessment is required for each pregnancy.

It is not known whether Cerezyme is excreted in human milk, however if so the enzyme is likely to be digested in the child's gastrointestinal tract. **(Please refer to section 4.6 of the Summary of product characteristics before prescribing)**

Undesirable effects: In approximately 3% of patients, symptoms suggestive of hypersensitivity have been noted, common: dyspnoea, coughing; pruritus, rash, urticaria/angioedema; uncommon: flushing, hypotension, chest discomfort, tachycardia, cyanosis, paraesthesia, backache. Additional uncommon adverse effects include: nausea, vomiting, abdominal cramping, diarrhoea, fatigue, headache, fever, rigors, dizziness, arthralgia, infusion/injection site reactions; rarely anaphylactoid reactions. (Please refer to SmPC for further information on Adverse Reactions)

Legal category: Prescription only medicine (POM).

List Price: Net price for a 200 Unit vial is £535.65 and for a 400 Unit vial is £1071.29

Marketing authorisation holder: Genzyme Europe B.V., Gooimeer 10, 1411 DD Naarden, The Netherlands
EU/1/97/053/001, EU/1/97/053/002, EU/1/97/053/003, EU/1/97/053/004, EU/1/97/053/005.

Further information is available from Genzyme Therapeutics, 4620 Kingsgate, Cascade Way, Oxford Business Park South, Oxford, OX4 2SU
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Adverse events should be reported. Reporting forms and information can be found at

www.yellowcard.gov.uk

Adverse events should also be reported to Genzyme Tel: +44(0)1865 405200