Abbreviated Prescribing Information

Fabrazyme® 35mg / Fabrazyme® 5mg (agalsidase beta), powder for concentrate for solution for infusion.
Product composition: Each vial contains a nominal value of 35 mg or 5 mg of agalsidase beta. After reconstitution with water for injections, each vial of Fabrazyme contains 5 mg/ml of agalsidase beta. The reconstituted solution must be diluted further. List of excipients: mannitol, sodium phosphate monobasic monohydrate, and sodium phosphate dibasic heptahydrate.
Indication: Fabrazyme is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency). Fabrazyme is indicated in adults, children and adolescents aged 8 years and older.
Dosage and administration: Fabrazyme treatment should be supervised by a physician experienced in the management of patients with Fabry disease or other inherited metabolic diseases. The recommended dose of Fabrazyme is 1 mg/kg body weight administered once every 2 weeks as an intravenous infusion.
The initial infusion rate should be no more than 0.25 mg/min (15 mg/hour) to minimise the potential occurrence of infusion-associated reactions (IARs). After patient tolerance is established, the infusion rate may be increased gradually with subsequent infusions. Infusion of Fabrazyme at home may be considered for patients who are tolerating their infusions well, after evaluation and recommendation by the treating physician.
Special populations: No dose adjustment is necessary for patients with renal insufficiency. Studies in patients with hepatic insufficiency have not been performed. The safety and efficacy of Fabrazyme in children aged 0 to 7 years have not yet been established. No recommendations on posology can be made in children aged 5-7 years based on currently available data. No data are available in children aged 0-4 years. No dose adjustment is necessary for children 8-16 years. Safety and efficacy of Fabrazyme in patients older than 65 years have not been established and no dosage regimen can presently be recommended.
Contraindications: Life threatening hypersensitivity (anaphylactic reaction) to the active substance or to any of the excipients (see product composition).
Special warnings and precautions for use: Since agalsidase beta is a recombinant protein, the development of IgG antibodies is expected in patients with little or no residual enzyme activity. The majority of patients developed IgG antibodies to agalsidase beta, typically within 3 months of the first infusion of Fabrazyme. Over time, the majority of seropositive patients in clinical trials demonstrated either a downward trend in titers (40% of patients), tolerised (14%) or demonstrated a plateau (35%).
Patients with antibodies to agalsidase beta have a greater potential to experience IARs, which are defined as any related adverse event occurring on the infusion day. Antibody status should be regularly monitored. In clinical trials, 67% of the patients experienced at least one IAR. The frequency of IARs decreased over time. Patients experiencing mild or moderate IARs when treated with agalsidase beta during clinical trials have continued therapy after a reduction in the infusion rate (~0.15 mg/min; 10 mg/hr) and/or pre-treatment with antihistamines, paracetamol, ibuprofen and/or corticosteroids.
As with any intravenous protein medicinal product, allergic-type hypersensitivity reactions are possible. A small number of patients have experienced reactions suggestive of immediate (Type I) hypersensitivity. If severe allergic or anaphylactic-type reactions occur, immediate discontinuation of the administration of Fabrazyme should be considered and appropriate treatment initiated. The current medical standards for emergency treatment are to be observed.
The effect of Fabrazyme treatment on the kidneys may be limited in patients with advanced renal disease.
This medicine contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially 'sodium-free'.
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.
Interactions: No interaction studies and no *in vitro* metabolism studies have been performed. Based on its metabolism, agalsidase beta is an unlikely candidate for cytochrome P450 mediated drug-drug interactions. Fabrazyme should not be administered with chloroquine, amiodarone, benoquin or gentamycin due to a theoretical risk of inhibition of intra-cellular α-galactosidase A activity.
Fertility, pregnancy and lactation: There are no adequate data from the use of agalsidase beta in pregnant women. Fabrazyme should not be used during pregnancy unless clearly necessary. Agalsidase beta may be excreted in milk. Because there are no data available on effects in neonates exposed to agalsidase beta via breast milk, it is recommended to stop breast-feeding when Fabrazyme is used. Studies have not been conducted to assess the potential effects of Fabrazyme on impairment of fertility.
Effects on ability to drive and use machines: Fabrazyme may have a minor influence on the ability to drive or use machines on the day of Fabrazyme administration because dizziness, somnolence, vertigo and syncope may occur.

Undesirable Effects
The very common (≥/=10%) and common (≥/=1% to <10%) adverse reactions reported from clinical trials with a total of 168 patients treated with Fabrazyme at a dose of 1mg/kg every 2 weeks for a minimum of one

infusion up to a maximum of 5 years are listed below. Adverse reactions were mostly mild to moderate in severity:

Very common (≥10%): headache, paraesthesia, nausea, vomiting, chills, pyrexia, feeling cold.

Common (≥1% to <10%): nasopharyngitis, dizziness, somnolence, hypoaesthesia, burning sensation, lethargy, syncope, increased lacrimation, tinnitus, vertigo, tachycardia, palpitations, bradycardia, flushing, hypertension, pallor, hypotension, hot flush, dyspnoea, nasal congestion, throat tightness, wheezing, cough, dyspnoea exacerbated, abdominal pain, abdominal pain upper, abdominal discomfort, stomach discomfort, hypoaesthesia oral, diarrhoea, pruritus, urticaria, rash, erythema, pruritus generalized, angioneurotic oedema, swelling face, rash maculo-papular, pain in extremity, myalgia, back pain, muscle spasms, arthralgia, muscle tightness, musculoskeletal stiffness, fatigue, chest discomfort, feeling hot, oedema peripheral, pain, asthenia, chest pain, face oedema, hyperthermia. Consult the SmPC for full list of reported undesirable events.

Limited information from clinical trials suggests the safety profile of Fabrazyme treatment in paediatric patients ages 5-7, treated with either 0.5mg/kg every 2 weeks or 1.0mg/kg every 4 weeks is similar to that of patients (above the age of 7) treated at 1.0 mg/kg every 2 weeks.

Health care professionals are asked to report any suspected adverse reactions via their national reporting system.

LEGAL CLASSIFICATION: POM (Prescription Only Medicine).

Marketing authorisation holder: Genzyme Europe B.V., Paasheuvelweg 25, 1105 BP Amsterdam, The Netherlands**. Date of last review: December 2020**

Abbreviated Prescribing Information based on the EU SmPC as of October 2020.

Before prescribing the product always refer to your full local prescribing information as this information may vary from country to country.