**Prescribing Information: Fabrazyme (agalsidase beta) 5mg/ 35mg powder for concentrate for solution for infusion**

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

**Presentations:** Each vial contains 5mg or 35mg of agalsidase beta and excipients. Following reconstitution with water for injections each vial contains 5mg/ml agalsidase beta.

**Indication:** Fabrazyme is indicated in adults, children and adolescents aged 8 years and older, for long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency).

**Dosage and administration:** The 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 1mg/kg body weight administered once every 2 weeks as an intravenous infusion. Infusion of Fabrazyme at home may be considered for patients who are tolerating their infusions well. The decision to have a patient move to home infusion should be made after evaluation and recommendation by the treating physician. Patients experiencing adverse events during the home infusion need to immediately **stop the infusion process** and seek the attention of a healthcare professional. Subsequent infusions may need to occur in a clinical setting. Dose and infusion rate should remain constant while at home, and not be changed without supervision of a healthcare professional. Fabrazyme should be administered as an intravenous (IV) infusion. The initial IV infusion rate should be no more than 0.25 mg/min (15 mg/hour). The infusion rate may be slowed in the event of infusion-associated reactions. After patient tolerance is well established, the infusion rate may be increased in increments of 0.05 to 0.083 mg/min (increments of 3 to 5 mg/hr) with each subsequent infusion. In clinical trials with classic patients, the infusion rate was increased incrementally to reach a minimum duration of 2 hours. This was achieved after 8 initial infusions at 0.25 mg/min (15 mg/hr), without any IARs, change in infusion rate, or infusion interruption. A further decrease of infusion time to 1.5 hours was allowed for patients without new IARs during the last 10 infusions or reported serious adverse events within the last 5 infusions. Each rate increment of 0.083 mg/min (~5 mg/hr) was maintained for 3 consecutive infusions, without any new IARs, change in infusion rate, or infusion interruption, before subsequent rate increases. The number of vials should be determined to be reconstituted based on the individual patient's weight. Each vial of Fabrazyme 35 mg has to be reconstituted with 7.2 ml water for injections and each vial of Fabrazyme 5 mg has to be reconstituted with 1.1 ml water for injections. The reconstituted solution should be slowly injected directly into the 0.9% sodium chloride solution for injection (not in any remaining airspace) to a final concentration between 0.05 mg/ml and 0.7 mg/ml. The total volume of sodium chloride 0.9% solution for infusion (between 50 and 500 ml) should be determined based on the individual dose. For doses lower than 35 mg a minimum of 50 ml should be used, for doses 35 to 70 mg a minimum of 100 ml should be used, for doses 70 to 100 mg a minimum of 250 ml should be used and for doses greater than 100 mg only 500 ml should be used. It is recommended to administer the diluted solution through an in-line low protein-binding 0.2 µm filter. Fabrazyme must not be mixed with other medicinal products in the same infusion. **Special populations:** No dose adjustment is necessary for children 8-16 years. The safety and efficacy of Fabrazyme in children 0-7 years and in patients older than 65 years have not been established and no dosage regimen can presently be recommended in these patients. No dose adjustment is necessary for patients with renal insufficiency. Studies in patients with hepatic insufficiency have not been performed. For patients weighing < 30 kg, the maximum infusion rate should remain at 0.25 mg/min (15 mg/hr).

**Contraindications:** Life-threatening hypersensitivity (anaphylactic reaction) to the active substance or any of the excipients. **Warnings and Precautions:** *Immunogenicity:* The majority of patients are expected to develop IgG antibodies to agalsidase beta typically within 3 months of initiation of treatment. Over time, the majority of seropositive patients in clinical trials demonstrated either a downward trend in titres, tolerised or demonstrated a plateau. *Infusion-associated reactions (IAR):* Patients with antibodies to r-hαGAL have a greater potential to experience IARs. These patients should be treated with caution when re-administering agalsidase beta. Antibody status should be regularly monitored. In clinical trials, 67% of patients experienced at least one IAR. Patients experiencing mild or moderate infusion associated reactions 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. The frequency of these reactions decreased over time. Antibody status should be regularly monitored. *Hypersensitivity:* As with any intravenous protein product, allergic-type hypersensitivity reactions are possible. If severe allergic or anaphylactic-type reactions occur, immediate discontinuation of the administration of Fabrazyme should be considered and appropriate treatment be initiated. The current medical standards for emergency treatment are to be observed. *Patients with advanced renal disease:* The effect of Fabrazyme treatment on the kidneys may be limited in these patients. *Fertility, pregnancy and lactation:* There are limited data from the use of agalsidase beta in pregnant women or its potential effect on fertility. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicitiy. As precautionary measure, it is preferable to avoid the use of Fabrazyme during pregnancy. Agalsidase beta is excreted in human milk. The effect of agalsidase beta on newborns/infants is unknown. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Fabrazyme therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman. Studies have not been conducted to assess the potential effects of Fabrazyme on impairment of fertility. *Sodium:* This medicinal product contains less than 1 mmol sodium (23 mg) per vial that is to say essentially 'sodium-free'. **Interactions:** No interaction studies and no *in vitro* metabolism studies have been performed. 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.

**Adverse effects:** *Very Common (≥1/10):* Headache, paraesthesia, nausea, vomiting, chills, pyrexia, and feeling cold. *Common (≥1/100 to<1/10):* nasopharyngitis, dizziness, somnolence, hypoaesthesia, burning sensation, lethargy, syncope, lacrimation increased, 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 generalised, angioneurotic oedema, swelling face, rash maculopapular, 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. Prescribers should consult the SmPC in relation to other adverse reactions.

**Legal classification**: POM. **List Price NI:** £315.08. **IE:** price on application. **Marketing authorisation holder:** Sanofi B.V., Paasheuvelweg 25, 1105 BP Amsterdam, The Netherlands. **Marketing authorisation numbers:** Fabrazyme 5mg powder for concentrate for solution for infusion x 1 vial: EU/1/01/188/004. Fabrazyme 35mg powder for concentrate for solution for infusion x 1 vial: EU/1/01/188/001. **For more information please contact: NI:** Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. uk-medicalinformation@sanofi.com. **IE:** Sanofi, 18 Riverwalk, Citywest Business Campus, Dublin 24 or contact IEmedinfo@sanofi.com

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Adverse events should also be reported to the Sanofi drug safety department on Tel: 0800 0902 314. Alternatively, send via email to UK-drugsafety@sanofi.com
In Ireland: www.hpra.ie; email: medsafety@hpra.ie. Adverse events should also be reported to Sanofi Ireland Ltd. Tel: 01 403 5600. Alternatively, send via email to IEPharmacovigilance@sanofi.com