Prescribing Information: Myozyme® 50mg (alglucosidase alfa) powder for concentrate for solution for infusion

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

Presentation: Each vial contains 50mg of the active ingredient alglucosidase alfa. Following reconstitution each vial contains 5mg/ml alglucosidase alfa.

Indication: Myozyme is indicated for long-term enzyme replacement therapy (ERT) in patients with a confirmed diagnosis of Pompe disease (acid α-glucosidase deficiency). Myozyme is indicated in adults and paediatric patients of all ages.

Dosing and Administration: Myozyme treatment should be supervised by a physician experienced in the management of patients with Pompe disease or other inherited metabolic or neuromuscular diseases. The recommended dosage regimen for Myozyme is 20 mg/kg of body weight administered once every 2 weeks as an intravenous infusion. Infusions should be administered incrementally: it is recommended that the infusions begin at an initial rate of 1 mg/kg/hr and, if there are no signs of infusion associated reactions (IARs), are gradually increased by 2 mg/kg/hr every 30 minutes, until a maximum rate of 7 mg/kg/hr is reached. There is no evidence for special considerations when Myozyme is administered to children, adolescents, adults or elderly patients. The safety and efficacy of Myozyme in patients with renal or hepatic insufficiency have not been evaluated and no specific dosage regimen can be recommended for these patients. Before administration determine the number of vials to be reconstituted based on the individual patient's dose regimen (mg/kg) and remove the required vials from the refrigerator in order to allow them to reach room temperature (approx. 30 mins). Each vial of Myozyme is for single use only. *Refer to SmPC for full guidance on reconstitution of Myozyme.*

Contraindications: Life-threatening hypersensitivity to the active substance or to any of the excipients confirmed by re-challenge.

Warnings and Precautions: *Hypersensitivity/Anaphylactic reactions:* Serious and life-threatening anaphylactic reactions, including anaphylactic shock, have been reported in infantile and late onset patients during Myozyme infusions. Because of the potential for severe IARs, appropriate medical support measures, including cardiopulmonary resuscitation equipment should be readily available when Myozyme is administered and patients should be closely monitored. If severe hypersensitivity or anaphylactic reactions occur, immediate discontinuation of Myozyme infusion should be considered, and appropriate medical treatment should be initiated. *IARs:* Patients who have experienced IARs (and in particular anaphylactic reactions) should be treated with caution when re-administering Myozyme. Mild and transient effects may not require medical treatment or discontinuation of the infusion. Reduction of the infusion rate, and temporary interruption of the infusion, or pre-treatment, generally with oral antihistamine and/or antipyretics and/or corticosteroids, has effectively managed most reactions. *Immunogenicity:* In clinical studies, most patients are expected to develop IgG antibodies to rhGAA, typically within 3 months of starting treatment. Seroconversion is expected to occur in most patients treated with Myozyme. A tendency was observed for infantile onset patients treated with a higher dose (40mg/kg) to develop higher titers of antibodies. The probability of a poor outcome and of developing high and sustained antibody titres appears higher among CRIM-negative patients (Cross Reactive Immunological Material; negative patients in whom no endogenous GAA protein was detected by Western blot analysis and/or predicted based on genotype) than among CRIM-positive patients (patients in whom endogenous GAA protein was detected by Western blot analysis). However, high and sustained IgG antibody titres also occur in some CRIM-positive patients. Patients who experience hypersensitivity reactions may also be tested for IgE antibodies to alglucosidase alfa and other mediators of anaphylaxis. Immune-mediated reactions: Severe cutaneous reactions, possibly immune-mediated, have been reported with alglucosidase alfa, including ulcerative and necrotizing skin lesions. Nephrotic syndrome was observed in a few Pompe patients treated with alglucosidase alfa and who had high IgG antibody titres (≥102,400). In these patients renal biopsy showed immune complex deposition. Patients improved following treatment interruption. It is recommended to perform periodic urinalysis among patients with high IgG antibody titres. Immunomodulation: Immunogenicity data from clinical trials and published literature in CRIM-negative infantile-onset patients (IOPD) suggests that the administration of immune tolerance induction (ITI) regimen given to alglucosidase alfa naive patients (prophylactic ITI) may be effective in preventing or reducing the development of High Sustained Antibody Titer (HSAT) against alglucosidase alfa. Data from a small number of patients previously treated with HSAT, with or without inhibitory activity, showed limited ITI treatment effect. Better treatment responses were observed in younger patients with less advanced disease who received prophylactic ITI before development of HSAT, which suggests that early initiation of ITI can result in improved clinical outcomes. ITI regimens may need to be tailored to individual patient needs. Patients with Pompe disease are at risk of respiratory infections due to the progressive effects of the disease on the respiratory muscles. Treating patients with immunosuppressive agents may further increase the risk of developing severe respiratory infections and vigilance is recommended. Fatal and life-threatening respiratory infections have been observed in some of these patients. **Interactions:** No drug interaction studies have been carried out with Myozyme. Recombinant human protein, alglucosidase alfa is an unlikely candidate for cytochrome P450 mediated drug-drug interactions. Pregnancy and Lactation: Myozyme should not be used during pregnancy unless clearly necessary. Studies in animals have shown reproductive toxicity thus the potential risk for humans is unknown. Myozyme may be excreted in breast milk thus it is recommended to stop breastfeeding when Myozyme is used. Traceability: In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. **Adverse effects:** Infantile-onset Pompe Disease:. Serious infusion reactions including urticaria, rales, tachycardia, decreased oxygen saturation, bronchospasm, tachypnoea, periorbital oedema and hypertension have been reported. *Very common (≥1/10):* tachycardia, flushing, tachypnoea, cough, vomiting, urticaria, rash, pyrexia and decreased oxygen saturation. *Common (≥1/100 to <1/10):* agitation, tremor, cyanosis, hypertension, pallor, retching, nausea, erythema, rash maculopapular, rash macular, rash papular, pruritus, irritability, chills, increased heart rate, increased blood pressure and increased body temperature. Late-onset Pompe disease: Serious adverse reactions reported in 4 patients treated with Myozyme were: angioedema, chest discomfort, throat tightness, non-cardiac chest pain and supraventricular tachycardia. Reactions in 2 of these patients were IgE-mediated hypersensitivity reactions. *Common (≥1/100 to <1/10):* Hypersensitivity, dizziness, paraesthesia, headache, flushing, throat tightness, diarrhoea, vomiting, nausea, urticaria, rash papular, pruritus, hyperhidrosis, muscle spasms, muscle twitching, myalgia, pyrexia, chest discomfort, peripheral oedema, local swelling, fatigue, feeling hot and increased blood pressure. Please *consult the SPC for full details.*

Legal Category: POM. **List Price:** ***NI:*** £356.06 per vial. ***IE:*** Price on application. **Marketing Authorisation Number:** EU/1/06/333/001. **Marketing Authorisation Holder:** Genzyme Europe B.V. Paasheuvelweg 25, 1105 BP Amsterdam, The Netherlands. **For further information please contact:** ***NI:*** Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. uk-medicalinformation@sanofi.com. ***IE:*** Sanofi-Aventis Ireland Limited, 18 Riverwalk, Citywest Business Campus, Dublin 24, Ireland or contact IE-Medicalinformation@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