Prescribing Information: Nexviadyme (avalglucosidase alfa) 100 mg powder for concentrate for solution for infusion

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

Presentation: Each vial contains 100 mg of avalglucosidase alfa. After reconstitution, each vial contains a total extractable volume of 10.0 ml at a concentration of 10 mg of avalglucosidase alfa* per ml.

*Avalglucosidase alfa is a human acid α-glucosidase produced in Chinese hamster ovary cells (CHO) by recombinant DNA technology.

Indication: Nexviadyme is indicated for long-term enzyme replacement therapy for the treatment of patients with Pompe disease (acid α-glucosidase deficiency).

Dosage and Administration: Nexviadyme treatment should be supervised by a physician experienced in the management of patients with Pompe disease or other inherited metabolic or neuromuscular diseases. Patients may be pretreated with antihistamines, antipyretics and/or corticosteroids to prevent or reduce allergic reactions. The recommended dose of avalglucosidase alfa is 20 mg/kg of body weight administered once every 2 weeks. ***Dose modification for Infantile-Onset Pompe Disease (IOPD) patients:*** For IOPD patients who experience lack of improvement or insufficient response in cardiac, respiratory, and/or motor function while receiving 20 mg/kg, a dose increase to 40 mg/kg every other week should be considered in the absence of safety concerns (e.g., severe hypersensitivity, anaphylactic reactions, or risk of fluid overload). In patients who do not tolerate avalglucosidase alfa at 40 mg/kg every other week (e.g., severe hypersensitivity, anaphylactic reactions, or risk of fluid overload), consider decreasing the dose to 20 mg/kg every other week.

Special Populations: ***Elderly patients:*** No dose adjustment is required in patients >65 years. ***Hepatic impairment:*** The safety and efficacy of avalglucosidase alfa in patients with hepatic impairment have not been evaluated. ***Renal impairment:*** No dose adjustment is required in patients with mild renal impairment. The safety and efficacy of avalglucosidase alfa in patients with moderate or severe renal impairment have not been evaluated.

Paediatric population (patients 6 months of age and younger): The safety and efficacy of avalglucosidase alfa in children 6 months of age and younger have not yet been established. There are no data available in patients 6 months of age and younger.

Contraindications: Life-threatening hypersensitivity to the active substance or to any of the excipients.

Precautions and Warnings: ***Hypersensitivity reactions (including anaphylaxis):*** Hypersensitivity reactions, including anaphylaxis, have been reported in Nexviadyme-treated patients. Appropriate medical support measures, including cardiopulmonary resuscitation equipment especially for patients with cardiac hypertrophy and patients with significantly compromised respiratory function, should be readily available when Nexviadyme is administered. If severe hypersensitivity or anaphylaxis occur, Nexviadyme should be discontinued immediately, and appropriate medical treatment should be initiated. The risks and benefits of re-administering Nexviadyme following anaphylaxis or severe hypersensitivity reaction should be considered. ***Infusion associated reactions (IARs):*** In clinical studies, IARs were reported to occur at any time during and/or within a few hours after the infusion of

Nexviadyme and were more likely with higher infusion rates. Patients with an acute underlying illness at the time of Nexviadyme infusion appear to be at greater risk for IARs. Patients with advanced Pompe disease may have compromised cardiac and respiratory function, which may predispose them to a higher risk of severe complications from IARs. If severe IARs occur, immediate discontinuation of the administration of Nexviadyme should be considered and appropriate medical treatment should be initiated. The benefits and risks of re- administering Nexviadyme following severe IARs should be considered. ***Immunogenicity:*** Treatment emergent anti-drug antibodies (ADA) were reported in both treatment naïve (95%) and treatment experienced patients (49%). Adverse-event-driven immunologic testing, including IgG and IgE ADA, may be considered for patients who have risk for allergic reaction or previous anaphylactic reaction to alglucosidase alfa.

Risk of acute cardiorespiratory failure: Caution should be exercised when administering Nexviadyme to patients susceptible to fluid volume overload or patients with acute underlying respiratory illness or compromised cardiac and/or respiratory function for whom fluid restriction is indicated. These patients may be at risk of serious exacerbation of their cardiac or respiratory status during infusion. Appropriate medical support and monitoring measures should be readily available during Nexviadyme infusion. ***Cardiac arrhythmia and sudden death during general anaesthesia for central venous catheter placement.*** Cardiac arrhythmia, including ventricular fibrillation, ventricular tachycardia, and bradycardia, resulting in cardiac arrest or death, or requiring cardiac resuscitation or defibrillation, have been associated with the use of general anaesthesia in IOPD patients with cardiac hypertrophy.

Interactions: No interaction studies have been performed. Because it is a recombinant human protein, avalglucosidase alfa is an unlikely candidate for cytochrome P450 mediated drug-drug interactions. ***Fertility and Lactation:*** There are no available data on the use of Nexviadyme in pregnant women. The potential risk for humans is unknown. Nexviadyme should be used during pregnancy only if the potential benefits to the mother outweigh the potential risks, including those to the foetus. ***Breast-feeding:*** There are no available data on the presence of Nexviadyme in human milk or the effects of Nexviadyme on milk production or the breastfed infant. **Adverse Reactions**: ***Very common (≥1/10):*** Hypersensitivity. ***Common (≥1/100 to<1/10):*** Anaphylaxis, headache, dizziness, tremor, ocular hyperaemia, hypertension, cough, dyspnoea, nausea, diarrhoea, vomiting, lip swelling, swollen tongue, pruritus, rash, urticaria, erythema, palmer erythema, muscle spasms, myalgia, fatigue, chills, chest discomfort, pain, influenza like illness, infusion site pain, blood pressure increased, and oxygen saturation decreased. Prescribers should consult the SmPC in relation to other adverse reactions.

Marketing Authorisation Holder: Genzyme Europe B.V., Paasheuvelweg 25, 1105 BP Amsterdam, The Netherlands

Legal classification: Prescription only medicine

Date of last review: june 2022