Myozyme (Alglucosidase Alfa) - Abbreviated Prescribing Information

Presentation: Myozyme 50 mg powder for concentrate for solution for infusion. Each vial contains 50mg of the active ingredient alglucosidase alfa, which is a recombinant form of human acid α-glucosidase, and the following excipients: mannitol, sodium dihydrogen phosphate monohydrate, disodium phosphate heptahydrate and polysorbate 80. Following reconstitution with water for injections 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..

Dose and Administration: The recommended dose regimen of alglucosidase alfa is 20 mg/kg of body weight administered once every 2 weeks. Patient response to treatment should be routinely evaluated based on a comprehensive evaluation of all clinical manifestations of the disease. Paediatric and older people There is no evidence for special considerations when Myozyme is administered to paediatric patients of all ages or older people.
Patients with renal and hepatic impairment the safety and efficacy of Myozyme in patients with renal or hepatic impairment have not been evaluated and no specific dose regimen can be recommended for these patients.

Contraindications: Life threatening hypersensitivity (anaphylactic reaction) to the active substance or to any of the excipients listed, when rechallenge was unsuccessful.

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 infusion associated reactions, 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.
Infusion Associated Reactions: 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, 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. Thus 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 titres 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; patients in whom no endogenous GAA protein was detected by Western blot analysis) 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 hypersensitivitiy 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 patient's renal biopsy showed immune complex deposition. Patients improved following treatment interruption. It is therefore recommended to perform periodic urinalysis among patients with high IgG antibody titres.
Immunomodulation: Patients with Pompe disease are at risk of respiratory infections due to the progressive effects of the disease on the respiratory muscles. Fatal and life-threatening respiratory infections have been observed in some of these patients. Therefore, treating patients with Pompe disease with immunosuppressive agents may further increase the risk of developing severe respiratory infections and vigilance is recommended.

Interactions: No drug interaction studies have been carried out with Myozyme. Because it is a recombinant human protein, alglucosidase alfa is an unlikely candidate for cytochrome P450 mediated-drug interactions.

Fertility, pregnancy and lactation: Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown. Myozyme should not be used during pregnancy unless clearly necessary. Myozyme may be excreted in breast milk. Because there are no data available on effects in neonates exposed to Myozyme via breast milk, it is recommended to stop breast-feeding when Myozyme is used. There are no clinical data on the effects of alglucosidase alfa on fertility. Preclinical data did not reveal any significant adverse findings.

Undesirable Effects:
Infantile-onset Pompe disease in clinical trials, 39 infantile-onset patients were treated with Myozyme for more than three years (168 weeks with a median of 121 weeks; see section 5.1). Adverse reactions reported in at least 2 patients are listed in Table 1 by System Organ Class. Adverse reactions were mostly mild to moderate in intensity and almost all occurred during the infusion or during the 2 hours following the infusion (infusion associated reactions, IARs). Serious infusion reactions including urticaria, rales, tachycardia decreased oxygen saturation, bronchospasm, tachypnea, periorbital edema and hypertension have been reported.
Late-onset Pompe disease In a placebo-controlled study lasting 78 weeks, 90 patients with late-onset Pompe disease, aged 10 to 70 years were treated with Myozyme or placebo randomized in a 2:1 ratio. overall, the numbers of patients experiencing adverse reactions and serious adverse reactions were comparable between the two groups. The most common adverse reactions observed were IARs. Slightly more patients in the Myozyme group than in the placebo group experienced IARs (28% versus 23%). The majority of these reactions were non-serious, mild to moderate in intensity and resolved spontaneously. Adverse reactions reported in at least 2 patients. 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.
Marketing Authorisation Holder: Genzyme Europe B.V., Paasheuvelweg 25, 1105 BP Amsterdam, The Netherlands

Legal classification: Prescription only medicine
Abbreviated Prescribing Information based on the EU SmPC as of May 2019.
Before prescribing always refer to your full local prescribing information as this information may vary from country to country

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