

CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION

ALGLUCOSIDASE ALFA (Myozyme[®] – Genzyme Canada Inc.)

Description:

Alglucosidase alfa, the recombinant form of the human enzyme acid α -glucosidase, is approved for use in patients with Pompe disease, a rare disease characterized by acid α -glucosidase deficiency. Pompe disease manifests in three forms, infantile (<1 yr), juvenile (1-16 yrs), and late onset (> 16 yrs).

Dosage Forms:

50 mg vial for intravenous infusion. The recommended dose is 20 mg/kg administered every two weeks by intravenous infusion.

Recommendation:

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that alglucosidase alfa be listed in patients with infantile-onset Pompe disease, as demonstrated by onset of symptoms and confirmed cardiomyopathy within the first 12 months of life. The Committee further recommends that drug plans develop specific criteria for monitoring and stopping alglucosidase, in consultation with experts in the management of lysosomal storage diseases.

Reasons for the Recommendation:

1. Information from uncontrolled trials in patients with infantile-onset Pompe disease indicate that alglucosidase alfa significantly improves survival in comparison to historical controls who did not receive enzyme replacement therapy.
2. There is insufficient evidence to evaluate the effectiveness and safety of alglucosidase alfa in other forms of Pompe disease.

Summary of Committee Considerations:

The Committee considered a systematic review of clinical trials of alglucosidase alfa in patients with Pompe disease. Two open-label clinical trials in infantile-onset Pompe disease met the inclusion criteria for the systematic review.

One trial randomized 18 patients between two doses of alglucosidase alfa – 20 mg/kg vs 40 mg/kg, each given by intravenous infusion every two weeks. The mean age at diagnosis and treatment initiation were 3.7 months and 4.6 months, respectively. There was no apparent difference in the effectiveness of the two doses studied. All 18 patients survived to 12 months of age. The most recent information from this trial

reported that five patients have died, at ages ranging from 19.8 to 40.7 months. Two patients required invasive ventilation by 12 months of age and an additional seven patients required invasive ventilation by 15 to 30 months of age. The results of this study have been compared to a group of historical control patients (selected using the same eligibility criteria as patients treated with alglucosidase alfa in the trial) in which only one of 62 patients survived to the age of 18 months.

The other study was an uncontrolled trial of alglucosidase alfa 20 mg/kg given by intravenous infusion every two weeks in 21 patients. The mean age at diagnosis and treatment initiation was later in this study: 8.9 months and 15.7 months, respectively, though all patients had onset of symptoms by 12 months. Sixteen patients survived 12 months of treatment. Sixteen patients were ventilator-free at baseline; ten of these were ventilator-free at 12 months of therapy, two required ventilator support and four had died. In the subgroup of five patients who were receiving invasive ventilation at the initiation of treatment, one had died and four remained on invasive ventilation at 12 months of treatment, suggesting that alglucosidase alfa offers little improvement in the course of the disease for those patients already on invasive ventilation. The Committee considered other information from this study that the manufacturer has requested remain confidential pursuant to the Confidentiality Guidelines for the Common Drug Review.

Given the limited use of alglucosidase alfa to date, information on its safety is preliminary. The most commonly reported adverse events are hypersensitivity reactions, which can range in severity from mild to life-threatening, including anaphylaxis.

Alglucosidase alfa costs \$847 per 50 mg vial and the annual cost for patients between 5 – 10 kg ranges from \$44,000 to \$88,000.

Of Note:

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.
2. Using conventional criteria, alglucosidase alfa has not been shown to be cost-effective, though this, by itself, is only one of the factors that may be used in making a decision about funding. The Committee felt that funding was justified in a restricted group of patients given the rarity of infantile-onset Pompe disease and the evidence supporting a survival advantage with alglucosidase alfa therapy.

Background:

CEDAC provides formulary listing recommendations to publicly funded drug plans. Recommendations are based on an evidence-based review of the medication's effectiveness and safety and an assessment of its cost-effectiveness in comparison to other available treatment options. For example, if a new medication is more expensive than other treatments, the Committee considers whether any advantages of the new medication justify the higher price. If the recommendation is not to list a drug, the Committee has concerns regarding the balance between benefit and harm for the medication, and/or concerns about whether the medication provides good value for public drug plans.