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Coverage Policy Number **IP0563**

Velmanase

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for velmanase alfa-tycv intravenous infusion (**Lamzede**®).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Velmanase alfa-tycv (Lamzede) is considered medically necessary when the following are met:

Alpha-mannosidosis. Individual meets **ALL** of the following criteria:
- A. Documented diagnosis of alpha-mannosidosis supported by **ONE** of the following:
  - i. Alpha-mannosidase activity less than 10% of normal in blood leukocytes or fibroblasts
  - ii. Biallelic pathogenic variants in the *MAN2B1* gene in an individual with a documented family history of alpha-mannosidosis

B. Non-central nervous system disease manifestations are present (for example, progressive motor function disturbances, physical disability, hearing and speech impairment, skeletal abnormalities, and immune deficiency) or the individual is asymptomatic with a documented family history of symptomatic alpha-mannosidosis
C. Medication is prescribed by, or in consultation with, a geneticist, metabolic disorder sub-specialist, or a physician who specializes in the treatment of lysosomal storage disorders

Dosing. Up to 1 mg/kg (actual body weight) administered by intravenous infusion no more frequently than every week.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of velmanase alfa-tycv (Lamzede) is considered medically necessary for alpha-mannosidosis when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J3490	Unclassified drugs

Background

OVERVIEW
Lamzede, a recombinant human lysosomal alpha-mannosidase, is indicated for the treatment of **non-central nervous system manifestations of alpha-mannosidosis** in adult and pediatric patients.[1]

Disease Overview
Alpha-mannosidosis is an ultra-rare autosomal recessive lysosomal storage disease. It is estimated to occur in 1-2:1,000,000 live births.[2] Alpha-mannosidosis results from reduced activity of the lysosomal enzyme, alpha-mannosidase, which is caused by gene variants in Mannosidase Alpha Class 2B Member 1 (*MAN2B1*). This results in accumulation of mannose-rich oligosaccharides in various tissues, which leads to significant and diverse multi-systemic manifestations, such as progressive motor function disturbances and physical disability, hearing and speech impairment, intellectual disability, and immune deficiency. Lamzede is the first and only enzyme replacement therapy approved for alpha-mannosidosis in the United States. There are no other

therapies FDA approved for alpha-mannosidosis and treatment is targeted towards management of the various clinical manifestations of the disease. Hematopoietic stem cell transplantation (HSCT) has been used to prevent cognitive decline, preserve neurocognitive function, and prevent early death.[2-5] However, not all patients are eligible for HSCT and it is associated with risk of mortality and complications. Lamzede has been approved by the European Medicines Agency (EMA) in 2018.

Clinical Efficacy
The efficacy of Lamzede in adult and pediatric patients with alpha-mannosidosis was established in two pivotal studies (rhLAMAN-05 and rhLAMAN-08) and one non-pivotal trial (rhLAMAN-10).[2-5] Lamzede demonstrated a statistically significant clearance of serum oligosaccharides vs. placebo in the pivotal trials. Lamzede also demonstrated improvement in endurance, pulmonary function, motor proficiency testing and a decrease in serum immunoglobulins.

Dosing Information
The recommended dosage of Lamzede is 1 mg/kg (actual body weight) administered once every week as an intravenous infusion.[1] The total volume of infusion is determined by the patient's actual body weight and should be administered over a minimum of 60 minutes for patients weighing up to 49 kg. Patients weighing ≥ 50 kg should be infused at a maximum infusion rate of 25 mL/hour to control the protein load.

Safety
Lamzede has a Boxed Warning for hypersensitivity reactions, including anaphylaxis.[1] Other Warnings/Precautions for Lamzede include infusion-associated reactions and embryofetal toxicity. Pretreatment with antihistamines, antipyretics, and/or corticosteroids should be considered to reduce the risk of hypersensitivity and infusion-related reactions.

References

1. Lamzede® intravenous infusion [prescribing information]. Cary, NC: Chiesi USA; February 2023.
2. Borgwardt L, Guffon N, Amraoui Y, et al. Efficacy and safety of velmanase alfa in the treatment of patients with alpha-mannosidosis: results from the core and extension phase analysis of a phase III multicentre, double-blind, randomised, placebo-controlled trial. *J Inherit Metab Dis*. 2018; 41(6):1215-1223.
3. Data on file. Lamzede summary of studies evaluating safety and efficacy of velmanase alpha. Cheisi USA; received February 20, 2023.
4. Guffon N, Konstantopoulou V, Hennermann JB, et al. Long-term safety and efficacy of velmanase alpha (VA) treatment in children under 6 years of age with alpha-mannosidosis (AM). Presented at: 14th International Congress of Inborn Errors of Metabolism (ICIEM 2021); Sydney, Australia; November 21-23, 2021.
5. Lund A, Borgwardt L, Cattaneo F, et al. Comprehensive long-term efficacy and safety of recombinant human alpha-mannosidase (velmanase alfa) treatment in patients with alpha-mannosidosis. *J Inherit Metab Dis*. 2018; 41:1225-1233.

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