Neighborhood Health Plan OF RHODE ISLAND™
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Lamzede® (velmanase alfa-tycv)
(Intravenous)

Effective Date: 05/01/2024
Dates Reviewed: 02/12/2024
Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

I. Length of Authorization

Coverage will be provided for six months initially and may be renewed for 6 months.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC unit]:

- Lamzede 10 mg as a lyophilized powder in a single-dose vial: 11 vials per 7 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 110 mg (110 units) every 7 days

III. Summary of Evidence

Lamzede (velmanase alfa-tycv) is indicated for the treatment of non–central nervous system manifestations of alpha-mannosidosis (AM) in adult and pediatric patients. AM affects 1 in every 500,000 to 1 in every 1 million individuals worldwide. It is an ultra-rare lysosomal storage disorder caused by deficient activity of the enzyme alpha-mannosidase from mutations in the MAN2B1 gene, resulting in intracellular accumulation of oligosaccharides, which is thought to contribute to the clinical manifestations of the disease. Symptoms vary in severity, but may include recurrent infections, hearing impairment, impairment of mental function and speech, muscular weakness, joint abnormalities, ataxia, and distinctive facial features. The trial that led to Lamzede's approval was a Phase 3 randomized, double-blind, placebo-controlled 52-week trial with 25 patients 6 to 35 years of age that demonstrated a statistical significant improvement in reduction in serum oligosaccharides (Lamzede -5.1 µmol/L vs. placebo -1.6 µmol/L, treatment difference -3.5 [95% CI: -4.4, -2.6]) and only a numerical improvement in the 3-minute stair climbing test (Lamzede 0.6 steps/min vs. placebo -2.4 steps/min, treatment difference 2.6 [95% CI: -3.8, 9.1]). The most common adverse reactions observed with Lamzede are hypersensitivity reactions (50%), infusion-associated reactions (50%), nasopharyngitis (66%), pyrexia (40%), headache (33%) and arthralgia (20%).

IV. Initial Approval Criteria [1-3]

Coverage is provided in the following conditions:

- Patient is between 3 and 35 years of age; **AND**
- The medication must be prescribed by or in consultation with a specialist familiar with the treatment of lysosomal storage disorders; **AND**
- Documented baseline serum oligosaccharides; **AND**

- Documented baseline age-appropriate values for one or more of the following have been obtained: 6-minute walk test (6-MWT), 3-minute stair climb test (3-MSCT), pulmonary function tests (e.g., forced vital capacity), motor function [i.e., Bruininks-Oseretsky Test of Motor Proficiency (BOT-2)], etc.; **AND**

  ***NOTE**: *For very young patients in which FVC or 6-MWT are not suitable for measuring, requests will be reviewed on a case-by case basis.*
- Patient has a definitive diagnosis of alpha-mannosidosis (AM) as confirmed by BOTH of the following:
  - Identification of deficient acid alpha-mannosidase enzyme activity in peripheral blood leukocytes or other nucleated cells such as fibroblasts of <10% of normal activity; **AND**
  - Identification of biallelic pathogenic variants in MAN2B1 by molecular genetic testing; **AND**
- Patient has signs and symptoms consistent with mild or moderate AM (e.g., absence of neurological manifestations, able to ambulate independently); **AND**
- Therapy will be used to treat non-central nervous system manifestations of alpha mannosidosis (e.g., myopathy, motor function disturbances, immunodeficiency, etc.); **AND**
- If patient is a female of reproductive potential, she has a confirmed negative pregnancy test; **AND**
- Coverage will not be provided in the following circumstances:
  - Patient cannot walk without support; **OR**
  - Patient has a history of a HSCT or bone marrow transplant; **OR**
  - Presence of known chromosomal abnormality and syndromes affecting psychomotor development, other than alpha-mannosidosis; **OR**
  - Total IgE >800 IU/ml; **AND**
- MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

V. Renewal Criteria [1-2]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the initial criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include anaphylaxis and severe allergic or infusion associated reactions, etc.; **AND**
- Patient has demonstrated a beneficial response to therapy or stabilization of disease compared to pretreatment age-appropriate baseline values in one or more of the following:
  - Stability or improvement in serum oligosaccharide concentration
  - Stability or improvement in 6-minute walking test (6-MWT)
  - Stability or improvement in 3-minute stair climbing test (3-MSCT)
  - Stability or improvement in forced vital capacity (FVC) (% predicted)
  - Stabilization or slowing in the rate of disease progression or clinical decline

VI. Dosage/Administration [1]

Indication	Dose
Alpha-mannosidosis	1 mg/kg (actual body weight) administered once every week as an intravenous infusion

VII. Billing Code/Availability Information

HCPCS Code:

- J0217 - Injection, velmanase alfa-tycv, 1 mg; 1 billable unit = 1 mg

NDC:

- Lamzede 10 mg as a lyophilized powder in a SDV for reconstitution: 10122-0180-xx

VIII. Investigational Use

All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

IX. References

1. Lamzede [package insert]. Cary, NC; Chiesi USA, Inc.; February 2023. Accessed January 2024.
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 Nov;41(6):1215-1223. doi: 10.1007/s10545-018-0185-0. Epub 2018 May 30.
3. Malm D, Nilssen Ø. Alpha-Mannosidosis. GeneReviews. https://www.ncbi.nlm.nih.gov/books/NBK1396/ (Accessed on January 22, 2024).

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E77.1	Defects in glycoprotein degradation

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:

Lamzede was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Lamzede according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.