velmanase alfa-tycv (Lamzede®)

Policy # 00849
Original Effective Date: 09/11/2023
Current Effective Date: 09/11/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of velmanase alfa-tycv (Lamzede®)‡ for the treatment of alpha mannosidosis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for velmanase alfa-tycv (Lamzede) will be considered when the following criteria are met:

- Patient has a diagnosis of alpha mannosidosis (AM) confirmed by ONE of the following:
  - Enzyme assay demonstrating alpha mannosidase activity <10% of normal activity measured in peripheral blood leukocytes; OR
  - Genetic test demonstrating pathogenic mutations in the *MAN2B1* gene; AND
- Provider attests that the patient has the following signs and symptoms consistent with mild or moderate alpha mannosidosis:
  - Presence of muscle weakness, skeletal abnormalities, immunodeficiency with recurrent infections, or cardiac and/or pulmonary involvement; AND
  - Patient is able to walk without support; AND
  - Patient has absence of severe AM with rapid progression and central nervous system disease manifestations (e.g., hearing loss, ataxia, cognitive impairment); AND
    *(Note: These specific patient selection criteria are additional requirements for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient does NOT have a history of hematopoietic stem cell transplant or bone marrow transplant; AND

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*(Note: These specific patient selection criteria are additional requirements for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Dose will not exceed 1 mg/kg once weekly.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of velmanase alfa-tycv (Lamzede) when the patient does not have signs and symptoms consistent with mild to moderate alpha mannosidosis or when the patient has a history of hematopoietic stem cell transplant or bone marrow transplant to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of velmanase alfa-tycv (Lamzede) when the patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Lamzede is indicated for the treatment of non-central nervous system manifestations of alpha mannosidosis. It provides an exogenous source of alpha-mannosidase, the enzyme that has reduced activity in patients with alpha-mannosidosis. It is administered as a once weekly intravenous infusion at a dose of 1 mg/kg. The package insert contains a black box warning for hypersensitivity reactions including anaphylaxis that may occur following administration of the product.

Alpha mannosidosis (AM) is an ultra-rare, progressive lysosomal storage with variable severity that is caused by reduced activity in the alpha mannosidase enzyme due to mutation in the *MAN2B1* gene. This leads to accumulation of mannose-rich oligosaccharides intracellularly and can result in a variety of symptoms including immunodeficiency, hepatosplenomegaly, hearing impairment, impairment of mental function and speech, muscular weakness, joint abnormalities, ataxia, and distinctive facial features. Although there is considerable variability in symptoms, three general phenotypes have been described:

- Mild AM: recognized after 10 years of age; characterized by slow disease progression, muscle weakness, and absence of skeletal abnormalities
- Moderate AM: recognized before 10 years of age; characterized by slow disease progression that includes skeletal abnormalities and ataxia
- Severe AM: recognized in infancy; characterized by rapid disease progression and early death from central nervous system involvement.

Prior to the availability of Lamzede, the only disease modifying treatment for AM was hematopoietic stem cell transplant. However, this option is associated with significant complications that limit its widespread use.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Lamzede was approved in February 2023 for the treatment of non-central nervous system manifestations of alpha-mannosidosis in adult and pediatric patients.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy and safety of Lamzede in alpha mannosidosis were investigated in two trials.

Trial 1 was a phase 3 multicenter, randomized, double-blind, placebo-controlled, parallel group trial in adult and pediatric patients with alpha mannosidosis. The trial evaluated the efficacy of Lamzede over 52 weeks at a dose of 1 mg/kg given weekly as an intravenous infusion. A total of 25 patients were enrolled including 13 adults and 12 pediatric patients. All patients had alpha-mannosidase activity below 11% of normal at baseline. Fifteen patients received Lamzede and 10 patients received placebo. The efficacy results for the clinical endpoints assessed at 12 months, 3-minute stair climbing test (3MSCT), 6-minute walk test (6MWT), and forced vital capacity (FVC) favored the Lamzede group and were supported by a reduction in serum oligosaccharide concentration. For the

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3MSCT, the Lamzede group had a mean absolute change from baseline of 0.6 and the placebo had a mean absolute change of -2.4. For the 6MWT, patients in the Lamzede group had a mean absolute change from baseline of 4.4 compared to -4.6 in the placebo group. For the FVC, patients in the Lamzede group had a mean absolute change from baseline of 8.2 compared to 2.0 in the placebo group.

Trial 2 was a single arm trial in pediatric alpha-mannosidosis patients less than 6 years of age. All patients had alpha mannosidase activity below 10% of normal at baseline. The trial enrolled five patients ranging from 3.7 to 5.9 years of age. Patients received Lamzede 1 mg/kg as intravenous infusion once weekly for at least 24 months. The mean absolute and percentage changes from baseline for serum oligosaccharides at 24 months were -7.7 µmol/L and -65.8% respectively.

References

1. Lamzede [package insert]. Chiesi USA, Inc. Cary, North Carolina. Updated February 2023.
2. Lamzede New Drug Review. IPD Analytics. Updated March 2023.

Policy History

Original Effective Date: 09/11/2023
Current Effective Date: 09/11/2023
08/03/2023 Medical Policy Committee review
08/09/2023 Medical Policy Implementation Committee approval. New policy.
12/13/2023 Coding update
Next Scheduled Review Date: 08/2024

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2022 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J3490, J3590, C9399 Add code effective 01/01/2024: J0217
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety,

effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.