Effective Date: 08/30/2023
Current Effective Date: 08/30/2023
Last P&T Approval/Version: 07/26/2023
Next Review Due By: 07/2024
Policy Number: C25436-A

Lamzede (velmanase alfa-tycv)

PRODUCTS AFFECTED

Lamzede (velmanase alfa-tycv)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Alpha-Mannosidosis (AM)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review.

A. ALPHA-MANNOSIDOSIS (AM)
   1. Documentation of diagnosis of alpha-mannosidosis
      AND
   2. Documentation diagnosis was confirmed by deficiency of alpha-mannosidase enzyme activity as measured in peripheral blood leukocytes or fibroblasts OR genetic testing of MAN2B1 gene [DOCUMENTATION REQUIRED]

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NOTE: Peripheral blood leukocytes or fibroblasts assessment of Alpha-Mannosidosis (AM) activity of less than 10% of control sample demonstrates deficiency.
AND

3. Documentation of member's therapeutic goals based on their individual non-neurologic baseline symptoms (e.g., stabilization & motor function [e.g., 3-minute stair climb test, 6-minute walk test, etc.], serum oligosaccharide levels, pulmonary function [e.g., FVC, etc.], overall health and quality of life)
   AND
4. Documentation that Lamzede (velmanase alfa-tycv) is not being used to treat neurologic manifestations, if present
   AND
5. Documentation that member does not have a history of hematopoietic stem cell transplant (HSCT) or bone marrow transplant.
   AND
6. FOR WOMEN OF CHILDBEARING POTENTIAL: Prescriber attests member is not pregnant AND member will be counseled on the use of effective contraception.

CONTINUATION OF THERAPY:

A. ALPHA-MANNOSIDOSIS (AM):
   1. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity, including severe hypersensitivity reactions (i.e., anaphylaxis).
      AND
   2. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms (improvement of stabilization in motor function [e.g., 3-minute stair climb test, 6-minute walk test, etc.], pulmonary function [e.g., FVC, etc.], reduction in frequency of infections, reduction in oligosaccharide levels)

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified geneticist, metabolic specialist, endocrinologist or physician experienced in the management of Alpha-Mannosidosis or enzyme deficiency disorders. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

No restriction

QUANTITY:

1mg/kg (actual body weight) once weekly
See appendix for infusion rate

PLACE OF ADMINISTRATION:

The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-inpatient hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Intravenous

DRUG CLASS:

HIGH RISK ALERT

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FDA-APPROVED USES:
Indicated for the treatment of non-central nervous system manifestations of alpha-mannosidosis in adult and pediatric patients.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Infusion Rate:
< 50kg (actual body weight): Administer total volume over 60 minutes
≥ 50kg (actual body weight): Maximum infusion rate of 25mL/hour

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Alpha-Mannosidosis (AM) is a rare autosomal recessive lysosomal storage disorder characterized by a deficiency in alpha-Mannosidase, caused by mutations of the MAN2B1 gene. The deficiency of alpha-Mannosidase leads to an intra-lysosomal accumulation of mannose rich-oligosaccharides in various tissues, causing impaired cellular function and apoptosis. Lamzede (velmanase alfa-tycv) provides an exogenous form of alpha-Mannosidase. Lamzede (velmanse alfa-tycv) does not cross the blood-brain barrier and is not expected to modulate CNS manifestations of Alpha-Mannosidosis. The prevalence of alpha-mannosidosis (AM) is 1 to 2 per 1 million live births worldwide. Symptoms vary widely in type and severity but may include recurrent infections, hepatosplenomegaly, hearing impairment, impairment of mental function and speech, muscular weakness, joint abnormalities, ataxia and distinctive facial features. There is not a clearly established relationship between genotype and severity of disease; however, significant phenotypic variability represents a spectrum of disease categorized into 3 types (mild, moderate and severe). Severe AM is generally recognized in infancy and characterized by rapid disease progression and a short life expectancy. Moderate AM is generally recognized before 10 years of age and mild recognized after 10 years of age, but both have a slower disease progression. Therefore, alpha-mannosidosis is largely a disease of pediatric and young adult patients due to shorter life expectancy. Clinical trials of Lamzede did not include patients 65 years of age and older but did not specifically exclude them.
Lamzede is the first and only enzyme replacement therapy FDA approved for the treatment of Alpha-Mannosidosis (AM). Prior to the approval of Lamzede (velmanase alfa-tycv), treatment was primarily symptomatic and supportive care. Allogeneic hematopoietic stem cell transplantation (HSCT) is indicated for very select younger patients with less significant complications.

The FDA approval of Lamzede (velmanase alfa-tycv) was based on 2 clinical trials. The phase 3 rhLAMAN-05 trial evaluated the efficacy of Lamzede (velmanase alfa-tycv) over 52 weeks at a dose of 1mg/kg given weekly as an intravenous infusion. A total of 25 patients were enrolled ages 6 to 35 years old with documented alpha-mannosidase activity below 11% of normal and in the range of 8 to 29 µmol/h/mg at baseline. Efficacy assessments included the 3-minute stair climb test, reduction in serum oligosaccharides, 6-minute walking test and forced vital capacity. All endpoints numerically favored the Lamzede (velmanase alfa-tycv) group with a statistically significant reduction in serum oligosaccharides. The most common adverse reactions reported in rhLAMAN-05 (incidence >20%) were hypersensitivity reactions, nasopharyngitis, pyrexia, headache, and arthralgia.
The phase 2 rhLAMAN-08 trial was a single-arm study of 5 pediatric patients <6 years of age that included patients with alpha-mannosidase activity below 10% of normal at baseline. Patients received Lamzede (velmanase alfa-tycv) 1mg/kg once weekly (4 patients for 24 months, 1 patient for 40 months).

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At 24 months of Lamzede (velmanase alfa-tycv) treatment there was a reduction in serum oligosaccharides from baseline. Adverse reactions that occurred in at least 2 of 5 patients in the rhLAMAN-08 trial included cough, otitis media, rhinitis conjunctivitis, fall, ligament sprain, oropharyngeal pain, face swelling and upper respiratory tract infections.

Hypersensitivity reactions were reported in 50% of treated patients, including 5% who experienced anaphylaxis. A higher incidence of hypersensitivity reactions occurred in Lamzede (vemanase alfa-tycv) treated pediatric patients (58%) compared to adult patients (36%). Lamzede (velmanase alfa-tycv) has a black box warning for severe hypersensitivity reactions. Infusion-associated reactions (IARs) were reported in 50% of treated patients. Infusion associated reactions (including anaphylaxis and severe hypersensitivity reactions) occurred in a higher incidence in Lamzede (velmanase alfa-tycv) treated patients who developed anti-drug antibodies. The most frequent symptoms of IARs that occurred in >10% of the population were pyrexia, chills, erythema, vomiting, cough, urticaria, rash and conjunctivitis. Similar symptoms were observed in adult and pediatric populations. Prior to Lamzede (velmanase alfa-tycv) administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids to reduce the risk of hypersensitivity and infusion-associated reactions.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Lamzede (velmanase alfa-tycv) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Lamzede (velmase alfa-tycv) include: No labeled contraindications.

OTHER SPECIAL CONSIDERATIONS:
Lamzede (velmanase alfa-tvcv) has a black box warning for severe hypersensitivity reactions. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue Lamzede immediately and initiate appropriate medical treatment. Consider the risks and benefits of re-administering Lamzede following severe hypersensitivity reactions (including anaphylaxis).

There is a risk of embryo-fetal malformations associated with Lamzede (velmanse alfa-tycv). For females of reproductive potential, verify that the patient is not pregnant prior to initiating treatment. Advise females of reproductive potential to use effective contraception during treatment and for 14 days after the last dose of Lamzede (velmanse alfa-tycv).

Lamzede (velmanase alfa-tycv) should be stored refrigerated (2º C to 8º C) in the original carton to protect from light. Reconstituted vials may be stored refrigerated for up to 24 hours (including infusion time) and must be infused within 10 hours after removal from refrigeration.

If one or more doses are missed, restart the treatment as soon as possible, as long as it is at least 3 days from the next scheduled dose.

CODING/BILLING INFORMATION

Note: 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

HCPCS CODE	DESCRIPTION
J3590	Unclassified biologics (Lamzede)

AVAILABLE DOSAGE FORMS:
Lamzede solution (reconstituted) 10MG single dose vial

HIGH RISK ALERT

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REFERENCES

1. Lamzede (velmanase alfa-tycv) for injection [prescribing information]. Parma, Italy: Chiesi Farmaceutici S.p.A.; February 2023.
2. Borgwardt, L., Guffon, N., Amraoui, Y., Dali, C. I., De Meirleir, L., Gil-Campos, M., . . . Lund, A. M. (2018, May 30). 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. Journal of Inherited Metabolic Disease, 41(6), 1215-1223. doi:10.1007/s10545-018-0185-0
3. Guffon, N., Konstantopoulou, V., Hennermann, J. B., Muschol, N., Bruno, I., Tummolo, A., . . . Lund, A. (2023). Long-term safety and efficacy of Velmanase Alfa Treatment in children under 6 years of age with alpha-mannosidosis: A phase 2, open label, Multicenter study. *Journal of Inherited Metabolic Disease,* 1-15. doi:10.1002/jimd.12602
4. Malm, D. (2023, January 12). *Alpha-Mannosidosis – symptoms, causes, treatment: Nord.* National Organization for Rare Disorders. https://rarediseases.org/rare-diseases/alpha-mannosidosis/#disease-overview-main
5. National Institutes of Health. (2023, February). *Alpha-Mannosidosis – about the disease.* Genetic and Rare Diseases Information Center. https://rarediseases.info.nih.gov/diseases/6968/alpha-mannosidosis

SUMMARY OF REVIEW/REVISIONS	DATE
New Criteria	Q3 2023

HIGH RISK ALERT

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