Medical Policy Bulletin

Title:
Velmanase alfa (Lamzede)
Policy #:
MA08.147

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

Initial criteria
Velmanase alfa-tycv (Lamzede) is considered medically necessary and, therefore, covered for the treatment of non–central nervous system manifestations (e.g., skeletal abnormalities, myopathy, motor function disturbances, immunodeficiency) of alpha-mannosidosis (AM) in pediatric and adult individuals when all of the following criteria are met, including dosing and frequency:

- The individual is at least 3 years old
- Prescribed by or in consultation with a geneticist or metabolic specialist
- Diagnosis is confirmed by either of the following:
  - Confirmation of diagnosis by biochemical assay showing decreased alpha-mannosidase activity in white blood cells or skin fibroblasts less than 10 percent of normal values
  - Genotyping revealing two pathogenic mutations of the MAN2B1 gene
- Documented baseline age-appropriate values for one or more of the following:
  - 6-minute walk test (6-MWT)
  - 3-minute stair climb test (3-MSCT)
  - Pulmonary function tests (e.g., forced vital capacity [FVC]),
  - motor function (i.e., Bruininks-Oseretsky Test of Motor Proficiency [BOT-2])
- The individual does **not** have any of the following:
  - A history of a hematopoietic stem cell transplantation (HSCT) or bone marrow transplantation
  - The individual cannot walk without support
- Dosing and frequency: children, adolescents and adults dosing intravenous infusion: 1 mg/kg once every week

NOTE: For very young individuals in whom FVC or 6-MWT are not suitable for measuring, requests will be reviewed on a case-by-case basis.

Continuation criteria

- The individual continues to meet the initial criteria
- The individual 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-MWT
    - Stability or improvement in 3-MSCT
    - Stability or improvement in FVC (% predicted)
    - Stabilization or slowing in the rate of disease progression or clinical decline

EXPERIMENTAL/INVESTIGATIONAL

All other uses of velmanase alfa-tycv (Lamzede) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of velmanase alfa-tycv (Lamzede). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to, the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of velmanase alfa-tycv (Lamzede) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for velmanase alfa-tycv (Lamzede).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of velmanase alfa-tycv (Lamzede) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the company that supports this request.

Guidelines

There is no Medicare policy addressing this service; therefore, the Company policy is applicable.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable Evidence of Coverage, velmanase alfa-tycv (Lamzede) is covered under the medical benefits of the Company’s Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

Certain drugs are available through either the member's medical benefit (Part B benefit) or pharmacy benefit (Part D benefit), depending on how the drug is prescribed, dispensed, or administered. This medical policy only addresses

instances when velmanase alfa-tycv (Lamzede) is covered under a member's medical benefit (Part B benefit). It does not address instances when velmanase alfa-tycv (Lamzede) is covered under a member's pharmacy benefit (Part D benefit).

FOR MEDICARE ADVANTAGE POLICIES BASED ON COMMERCIAL POLICY IN WHICH THERE IS NO LCD, NCD, OR OTHER MEDICARE RESOURCE:

There is no Medicare coverage determination addressing velmanase alfa-tycv (Lamzede); therefore, the Company policy is applicable.

BLACK BOX WARNINGS

Refer to the specific manufacturer's prescribing information for any applicable Black Box Warnings.

TESTING

3-Minute Stair Climbing Test (3-MSCT)

The 3-MSCT is a physical test used to measure functional capacity and endurance. Individuals are asked to climb as many stairs as possible in 3 minutes; the result is often used to track disease progression or improvement in response to treatment.

6-Minute Walking Test (6-MWT)

The 6-MWT is a submaximal exercise test that measures aerobic capacity and endurance. The distance that an individual can quickly walk on a flat, hard surface in a period of 6 minutes is measured.

Forced Vital Capacity (FVC)

FVC is a measure of the amount of air an individual can exhale forcefully and quickly after taking a deep breath.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, velmanase alfa-tycv (Lamzede) is covered under the medical benefits of the Company's products when the medical necessity criteria including dosing and frequency requirements listed in this medical policy are met.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

On February 16, 2023, the FDA approved velmanase alfa-tycv (Lamzede), the first enzyme replacement therapy (ERT) approved in the United States for the treatment of non–central nervous system manifestations of alpha-mannosidosis (AM) in adult and pediatric individuals.

GERIATRIC USE

The safety and effectiveness of velmanase alfa-tycv (Lamzede) has not been established in individuals 65 years of age and older.

INDICATIONS AND USAGE

Velmanase alfa-tycv (Lamzede) is indicated for the treatment of non–central nervous system manifestations of AM in adult and pediatric patients.

Description

Alpha-mannosidosis (AM) is an ultra-rare, progressive genetic disorder characterized by a deficiency of the enzyme alpha-D-mannosidase. The estimated prevalence of AM is one in every 500,000 individuals worldwide. Symptoms vary widely in type and severity from one person to another, but may include recurrent infections, hearing impairment, impairment of mental function and speech, muscular weakness, joint abnormalities, ataxia, and distinctive facial

features. AM is caused by mutations of the MAN2B1 gene. This genetic mutation is inherited as an autosomal recessive trait.

AM is best thought of as a continuum of disease that is generally broken down into three forms: a mild, slowly progressive form (type 1); a moderate form (type 2); and a severe, often rapidly progressive and potentially life-threatening form (type 3).

AM belongs to a group of diseases known as the lysosomal storage disorders. Lysosomes are particles bound in membranes within cells that function as the primary digestive units. Enzymes within the lysosomes break down or digest particular nutrients, such as complex molecules composed of a sugar attached to a protein (glycoproteins). Low levels or inactivity of the alpha-mannosidase enzyme leads to the abnormal accumulation of compounds upstream in the metabolic pathway in the cells of affected individuals, with unwanted consequences.

Lamzede is the first and only FDA-approved treatment for AM. Lamzede does not cross the blood-brain barrier and therefore is not expected to treat the neurological aspects of the disease. Prior to the approval of Lamzede, treatment of AM was primarily symptomatic. Some individuals may benefit from allogeneic hematopoietic stem cell transplantation (HSCT). Those most likely to benefit from HSCT are younger individuals in whom significant complications have not yet developed.

The approval of Lamzede was based on a Phase 3, randomized, double-blind, placebo-controlled trial in 25 individuals 6 to 35 years of age (NCT01681953). Individuals treated with Lamzede performed better than those receiving placebo in outcomes such as the 3-minute stair climbing test, 6-minute walking test, and forced vital capacity.

Lamzede binds to extracellular mannose-6-phosphate receptors and is transported to lysosomes, where it provides an exogenous source of alpha-mannosidase. Alpha-mannosidase degrades mannose-containing oligosaccharides; lack of this enzyme leads to the accumulation of mannose-rich oligosaccharides in tissue, which causes clinical symptoms associated with AM lysosomal storage disease.

Lamzede is administered as a once-weekly intravenous infusion. Dosing of Lamzede is weight based; therefore, pricing may vary significantly for each individual.

OFF-LABEL INDICATIONS

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

References

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)

N/A

ICD - 10 Procedure Code Number(s)

N/A

ICD - 10 Diagnosis Code Number(s)

E77.1 Defects in glycoprotein degradation

HCPCS Level II Code Number(s)

J0217 Injection, velmanase alfa-tycv, 1 mg

Revenue Code Number(s)

N/A

Policy History

Revisions From MA08.147

03/28/2025	This policy has been reissued in accordance with the Company's annual review process.
05/07/2024	New policy #MA08.147 will become effective on 05/07/2024. The policy has been developed to communicate the Company’s coverage position for velmanase alfa-tycv (Lamzede) and is based on FDA labeling.

Version Effective Date:
05/07/2024
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05/07/2024
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03/28/2025