Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 04/10/2025

Lamzede® (velmanase alfa-tycv)

HCPCS: J0217

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Prescribed by or in consultation with a geneticist or metabolic specialist
   d. Confirmation of diagnosis by biochemical assay showing decreased alpha-mannosidase activity in white blood cells or skin fibroblasts less than 10% of normal AND genotyping revealing two pathogenic mutations of the MAN2B1 gene
   e. Must not have a history of hematopoietic stem cell transplant (HSCT)
   f. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: One year at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

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Background Information:

- Alpha-mannosidosis is an ultra-rare genetic lysosomal storage disorder that begins in childhood and progresses through adulthood. It is caused by a mutation on the MAN2B1 gene resulting in a deficiency of alpha-mannosidase and the body not being able to breakdown α-mannosyl rich N-linked oligosaccharides. The prevalence is estimated to be 1 in every 500,000 people in the general population.

- The symptoms, progression and severity of alpha-mannosidosis vary widely from one person to another, including between siblings who share the same mutation. Alpha-mannosidosis represents a spectrum or continuum of disease and is highly individualized. The disorder is generally broken down into three separate subtypes: mild (type 1), moderate (type 2), and severe (type 3).

    - The mild form may not be evident until the teen years and progresses slowly. Symptoms typically include muscle weakness and skeletal abnormalities are usually not present. A person with type 1 may have normal cognitive and physical development, however, even this later-onset form may be accompanied by mild to moderate intellectual disability. In some cases, the clinical progression of the disease appears to slow down or stop as the affected individual grows beyond school age.

    - In the moderate form of the disorder, signs of skeletal abnormalities and muscle weakness may appear before ten years of age and progress slowly. Type 2 also may be characterized by distinctive facial features including widely spaced or unevenly developed teeth, macroglossia, prominent forehead, flattened nasal bridge, and prognathism. Abnormalities affecting the eyes may include strabismus, opacity of the cornea, and farsightedness. Ataxia may develop by the age of 20-30.

    - The severe form begins within the first year of life. In most cases, infants appear normal at birth, but the condition grows progressively worse. Type 3 alpha-mannosidosis is characterized by rapid progression of intellectual disability, hydrocephalus, progressive ataxia, hepatosplenomegaly, skeletal abnormalities, and coarse facial features.

- The 2019 diagnostic algorithm for the recognition of alpha-mannosidosis in pediatric and adult patients states analysis of oligosaccharides in urine can be considered as an initial screening procedure. An abnormal result in the measurement of the biomarker is to be considered suggestive of the disease but not sufficient for a definite diagnosis. The determination of enzymatic activity is considered the first choice for screening. Alpha-mannosidosis is confirmed when patients have a biochemical assay showing decreased alpha-mannosidase activity in white blood cells or skin fibroblasts less than 10% of normal and genotyping revealing two pathogenic mutations of the MAN2B1 gene.

- Lamzede is an enzyme replacement therapy for the treatment of non-central nervous system manifestations of alpha-mannosidosis in adult and pediatric patients. Prior to Lamzede's approval, therapy was supportive and focused on preventing emerging complications, such as, hydrocephalus, otitis media, hearing loss, dental caries, joint symptoms, and kyphoscoliosis. There are studies regarding the use of HSCT in patients with outcomes reported as variable with mixed reports on the neurocognitive impact of the therapy. In 2004, results were published for four patients, aged 3 to 23 years, who had undergone HSCT, suggesting that intellectual function in these patients stabilized with improvement in adaptive skills and verbal memory function. Transplant-related complications are more frequent and severe in older patients, which means HSCT is more of an option in the first years of life making early identification of affected patients critical. Lamzede has not been studied in patients who have undergone a HSCT.

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References:

1. Lamzede [prescribing information]. Cary, NC: Chiesi USA, Inc.; February 2023.
2. Lund AM, Borgwardt L, Cattane 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 Nov; 41 (6): 1225 – 33.
3. National Organization of Rare Diseases. Alpha-mannosidosis. 2018. Available at: https://rarediseases.org/rare-diseases/alpha-mannosidosis/. Accessed on February 20, 2023.
4. Guffon N, Tylki-Szymanska A, Borgwardt L, et al. Recognition of alpha-mannosidosis in pediatric and adult patients: presentation of a diagnostic algorithm from an international working group. Mole Gen & Metab. 2019; 126: 470 – 4.
5. Chiesi. Discover alpha mannosidosis. 2022. Available at: https://www.alphamannosidosis.com/en/for-healthcare-professionals/disease-information/disease-progression/. Accessed on February 20, 2023.
6. Grewal SS, Shapiro EG, Krivit W, et al. Effective treatment of alpha-mannosidosis by allogeneic hematopoietic stem cell transplantation. J Pediatr. 2004; 144: 569 – 73.

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<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.5</td><td>Effective Date: 04/10/2025</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.4</td><td>Effective Date: 04/11/2024</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.3</td><td>Effective Date: 05/01/2023</td><td>UM medical management system update for MAPPO and BCNA
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<tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr>
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<tr><td>BCN</td><td>Yes</td></tr>
<tr><td>MAPPO</td><td>Yes</td></tr>
<tr><td>BCNA</td><td>Yes</td></tr>
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<tr><td>1.2</td><td>Effective Date: 04/06/2023</td><td>New policy</td></tr>
<tr><td>1.1</td><td>Effective Date: 03/09/2023</td><td>UM medical management system update for BCBS and BCN
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

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