SmartPA Criteria Proposal

Drug/Drug Class:	Lamzede Clinical Edit
First Implementation Date:	TBD
Proposed Date:	July 18, 2023
Prepared for:	MO HealthNet
Prepared by:	MO HealthNet/Conduent
Criteria Status:	☐Existing Criteria ☐Revision of Existing Criteria ☒New Criteria

Executive Summary

Purpose: Ensure appropriate utilization and control of Lamzede® (velmanase alfa-tycv).

Why Issue Selected: On February 16, 2023, the U.S. Food and Drug Administration (FDA) approved Lamzede® (velmanase alfa-tycv) for the treatment of non-central nervous system manifestations of alpha-mannosidosis (AM). The estimated prevalence of AM is approximately 1 in 500,000 to 1,000,000 people in the general population.

AM is a rare genetic lysosomal storage disorder characterized by a deficiency in alpha-mannosidase. Pathogenic variants in the *MAN2B1* gene cause alpha-mannosidosis, as this gene provides instructions for making the enzyme alpha-mannosidase. This enzyme works within liposomal cells to break down complex sugars, including oligosaccharides, which are important in the building of bones, cartilage, skin, and tendons. Without this enzyme-assisted breakdown, oligosaccharides will accumulate in the lysosomes causing cell malfunction and eventual death. Tissues and organs are damaged by the abnormal accumulation of oligosaccharides leading to the characteristic features of AM, including intellectual disability, muscle weakness, skeletal abnormalities, and ataxia. Severe forms of AM are rapidly progressive and can include all previously mentioned symptoms, plus hydrocephalus and hepatosplenomegaly.

Lamzede is a recombinant form of human alpha-mannosidase intended to provide or supplement natural alpha-mannosidase. This supplementation aids in oligosaccharide breakdown, thus preventing their accumulation in various tissues in the body. Prior to Lamzede's approval, traditional treatment of AM was supportive and mainly aimed at mitigating disease complications. Lamzede does not cross the blood brain barrier and is not expected to treat neurological manifestations of AM.

Due to the high cost and specific approved indication, MO HealthNet will impose clinical criteria to ensure appropriate utilization of Lamzede.

Program-Specific Information:

Drug	Cost per vial (WAC)	Cost per year (WAC) (based on 1mg/kg weekly dosing of a 70kg patient)
LAMZEDE 10 MG VIAL	$4,000	$1,456,000

Type of Criteria: ☐ **Increased risk of ADE** ☐ **Preferred Drug List**

	☒ **Appropriate Indications**	☒ **Clinical Edit**
Data Sources:	☐ **Only Administrative Databases**	☒ **Databases + Prescriber-Supplied**

Setting & Population

- Drug class for review: Lamzede® (velmanase alfa-tycv).
- Age range: All appropriate MO HealthNet participants

Approval Criteria

- Prescribed by or in consultation with a specialist in the treated disease state **AND**
- Documented diagnosis of AM confirmed by:
  - Molecular genetic testing revealing pathogenic variants of the MAN2B1 gene **OR**
  - Documentation of deficient acid alpha-mannosidase activity in leukocytes or other nucleated cells
- Participant is currently not pregnant
- Initial approval for one year

Continuation of Therapy:

- Documentation of clinical benefit of therapy, such as improvement in stair climbing, walking, or forced vital capacity from baseline
- Continued approval is for one year

Denial Criteria

- Therapy will be denied if all approval criteria are not met
- Participant has a history of haematopoietic stem cell transplantation (HSCT) or bone marrow transplant
- Participant cannot walk without support

Required Documentation

Laboratory Results:	**X**	Progress Notes:	**X**
MedWatch Form:		Other:	**X**

Disposition of Edit

Denial: Exception code “0682” (Clinical Edit)
Rule Type: CE

Default Approval Period

3 months

References

- Lamzede [package insert]. Cary, NC: Chiesi USA, Inc.; February 2023
- IPD Analytics. Endocrinology and Metabolic Agents: Other Lysosomal Storage Disorders. Accessed February 22, 2023.

- Hansen G, Berg T, Riise Stensland HM, et al. Intracellular transport of human lysosomal alpha-mannosidase and alpha-mannosidosis-related mutants. Biochem J. 2004 Jul 15;381(Pt 2):537-46.
- MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US); [updated 2020 Jun 24]. Alpha-mannosidosis; Accessed February 22, 2023. Available from: Alpha-mannosidosis: MedlinePlus Genetics
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- 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 41, 1215–1223 (2018). https://doi.org/10.1007/s10545-018-0185-0