RX.PA.062.CCH SPECIALTY ENZYME REPLACEMENT THERAPY (ERT)

The purpose of this policy is to define the prior authorization process for Elfabrio (pegunigalsidase alfa-iwxj), Fabrazyme (agalsidase beta), Lamzede (velmanase alfa-tycv), Lumizyme (alglucosidase alfa), and Nexviazyme (avalglucosidase).

- Elfabrio (pegunigalsidase alfa-iwxj) is indicated for the treatment of adults with confirmed Fabry disease.
- Fabrazyme (agalsidase beta) is indicated for the treatment of adult and pediatric patients 2 years of age and older with confirmed Fabry disease.
- Lamzede (velmanase alfa-tycv) is indicated for the treatment of non-central nervous system manifestations of alpha-mannosidosis in adult and pediatric patients.
- Lumizyme (alglucosidase alfa) is indicated for patients with Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency).
- Nexviazyme (avalglucosidase) is indicated for the treatment of patients 1 year of age and older with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency).
- Xenpozyme (olipudase alfa-rpcp) is indicated for the treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in pediatric and adult patients.

POLICY

It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, and approval by the Medical Policy Committee.

The drugs, Elfabrio, Fabrazyme, Lamzede, Lumizyme, Nexviazyme, and Xenpozyme are subject to the prior authorization process.

PROCEDURE

Initial Authorization Criteria:

Must meet all the criteria listed below:

Elfabrio (pegunigalsidase alfa-iwxj) and Fabrazyme (agalsidase beta)

- Must be at least:
  - 2 years of age or older (Fabrazyme)
  - 18 years of age or older (Elfabrio)
- Must be prescribed by or in consultation with a neurologist or a provider who specializes in the treatment of inherited metabolic disorders
- Must have a documented diagnosis of Fabry disease confirmed by ONE of the following:
  - Mutation in the galactosidase alpha (*GLA*) gene confirmed by genetic testing
  - Intracellular globotriaosylceramide (Gb3) inclusion confirmed by a biopsy of tissue or organ (such as kidney)
  - *MALES ONLY:* leukocyte alpha- galactosidase A (alpha-Gal A) enzyme activity <3%
- Must not be used in combination with Galafold (migalastat) or other enzyme replacement therapies for Fabry's disease
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

Lamzede (velmanase alfa-tycv)

- Must be prescribed by or in consultation with a neurologist or a provider who specializes in the treatment of inherited metabolic disorders
- Must have a documented diagnosis of alpha mannosidosis confirmed by:
  - Alpha-mannosidase activity < 10% of normal activity in blood leukocytes or fibroblasts **OR**
  - Molecular genetic testing revealing biallelic MAN2B1 gene mutation
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling
- Must have documentation or attestation from the provider for all the following:
  - Lamzede is being used to treat non-central nervous system (CNS) disease manifestations (e.g., skeletal abnormalities, myopathy, motor function disturbances, immunodeficiency)
  - The member does NOT have a history of hematopoietic stem cell transplant (HSCT)
  - *Female sex assigned at birth only:* The member is not pregnant AND the member has been counseled on the effective use of contraception
- Must have documentation of the following age-appropriate baseline labs/tests:
  - Serum oligosaccharide concentration
  - 6-minute walking test (6-MWT)
  - 3-minute stair climbing test (3-MSCT)
  - Predicted forced vital capacity (FVC)

Lumizyme (alglucosidase alfa) and Nexviazyme (avalglucosidase)

- Must be age 1 year or older (applies to Nexviazyme *only*)
- Must be prescribed by or in consultation with a neurologist or a provider who specializes in the treatment of inherited metabolic disorders
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling
- Must have a diagnosis of alpha glucosidase deficiency (Pompe disease) confirmed through GAA enzyme assay (from blood, skin fibroblasts, lymphocytes, or muscle) and/or identification of GAA gene mutation

Xenpozyme (olipudase alfa-rpcp)

- Must have a diagnosis of acid sphingomyelinase deficiency (ASMD) type A/B, or B (also known as Niemann-Pick disease)
- Must have documentation of the following:
    - Genetic testing showing a mutation of the SMPD1 gene
    - Deficiency of the acid sphingomyelinase enzyme activity of <10%
- Must be prescribed by, or in consultation with, a geneticist, pulmonologist, hepatologist or metabolic specialist
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc) listed in the FDA approved labeling
- Must have documentation of all the following baseline measures:
    - Spleen volume
    - Liver volume
    - Height Z-scores (pediatrics only)
    - Platelet count
    - Percent predicted diffusion capacity of the lungs for carbon monoxide (DLCO) or, if pediatric members, other age-appropriate pulmonary function testing
- Must have documentation or an attestation from the provider on all the following:
    - Xenpozyme is not being used to treat neurologic (i.e., CNS) manifestations
    - For women of child-bearing potential, that member is currently not pregnant and will be counseled on the use of effective contraception
    - Baseline transaminase (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) levels will be collected within 1 month prior to treatment initiation

Reauthorization Criteria:

All prior authorization renewals are reviewed on an annual basis to determine the Medical Necessity for continuation of therapy. Authorization may be extended at 1-year intervals based upon the following:

Elfabrio and Fabrazyme

- Must have updated chart documentation from the prescriber that the member's condition has improved or stabilized based upon the prescriber's assessment while on therapy
- The member has been adherent to >50% of infusions during the last authorization
- The member does NOT have life-threatening or severe infusion reactions that do not respond to prophylaxis
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc) listed in the FDA approved labeling

Lamzede

- Must have updated chart documentation from the prescriber that the member's condition has improved or stabilized based upon meeting ONE of the following when compared to age-appropriate baseline values:
    - Stability or improvement in serum oligosaccharide concentration
    - Stability or improvement in 6-minute walking test (6-MWT)
    - Stability or improvement in 3-minute stair climbing test (3-MSCT)
    - Stability or improvement in forced vital capacity (FVC) (% predicted)
    - Stability or improvement in other symptoms of disease (e.g., reduction in frequency of infection)
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc) listed in the FDA approved labeling

Lumizyme and Nexviazyme

- Must have updated chart documentation from the prescriber that the member's condition has improved or stabilized based upon the prescriber's assessment while on therapy
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc) listed in the FDA approved labeling

Xenpozyme

- Must have updated chart documentation from the prescriber showing a positive clinical response or stabilization in disease, as determined by a positive change in at least one or more of the member's baseline values:
    - Improvement in diffuse capacity of the lung for carbon monoxide (DLCO) (or other pulmonary function tests depending on age)

  - Increased platelet count
  - Reduction in spleen volume
  - Reduction in liver volume
  - Improvement in height Z-scores (pediatric members only)
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc) listed in the FDA approved labeling

Limitations:

Length of Authorization (if above criteria met)	
Initial Authorization	Up to 1 year
Reauthorization	Same as initial

If the established criteria are not met, the request is referred to a Medical Director for review, if required for the plan and level of request.

Codes:

CPT Codes / HCPCS Codes / ICD-10 Codes		
Code	Brand	Description
J0180	Fabrazyme	Injection, agalsidase beta, 1 mg
J0217	Lamzede	Injection, velmanase alfa-tycv, 1 mg
J0218	Xenpozyme	Injection, olipudase alfa-rpcp, 1mg
J0219	Nexviazyme	Injection, avalglucosidase alfa-ngpt, 4 mg
J0221	Lumizyme	Injection, alglucosidase alfa, (lumizyme), 10 mg.
J2508	Elfabrio	Injection, pegunigalsidase alfa-iwxj, 1 mg

References:

1. Nexviazyme (avalglucosidase alfa) [prescribing information]. Cambridge, MA: Genzyme Corporation; August 2021
2. van der Ploeg AT, Kruijshaar ME, Toscano A, et al; European Pompe Consortium. European consensus for starting and stopping enzyme replacement therapy in adult patients with Pompe disease: a 10-year experience. Eur J Neurol. 2017;24(6):768-e31. doi:10.1111/ene.13285
3. Fabrazyme (agalsidase beta) [prescribing information]. Cambridge, MA: Genzyme Corporation; February 2024.
4. Hopkin RJ, Jefferies JL, Laney DA, et al. The management and treatment of children with Fabry disease: A United States-based perspective. Mol Genet Metab. 2016;117(2):104-113.
5. 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. 2018;41(6):1215-1223. doi:10.1007/s10545-018-0185-0 [PubMed 29846843]
6. Guffon N, Konstantopoulou V, Hennermann JB, et al. 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. J Inherit Metab Dis. 2023;46(4):705-719. doi:10.1002/jimd.12602 [PubMed 36849760]
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9. Bernat J, Holida M, Goker-Alpan O, et al. Tolerability and infusion duration of pegunigalsidase alfa in patients with Fabry Disease: Data from 5 completed clinical trials. Poster presented at: 7th Update on Fabry Disease; May 29-31, 2022; Würzberg, Germany.
10. Elfabrio (pegunigalsidase alfa) [prescribing information]. Cary, NC: Chiesi USA; May 2023.
11. Xenpozyme [package insert]. Cambridge, MA: Genzyme Corporation.; December 2023.
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13. Wasserstein M, Lachmann R, Hollak C, et al. A randomized, placebo-controlled clinical trial evaluating olipudase alfa enzyme replacement therapy for chronic acid sphingomyelinase deficiency (ASMD) in adults: one-year results. Genet Med. 2022;24(7):1425-1436. doi:10.1016/j.gim.2022.03.021 [PubMed 35471153]

Revision History

DESCRIPTION OF REVIEW / REVISION	DATE APPROVED
Initial review	05/2023
Addition of Elfabrio, Fabrazyme, Lamzede, Lumizyme, & Xenpozyme Renamed policy to “Specialty Enzyme Replacement Therapy” from “Nexviazyme”	XX/XX

Record Retention

Records Retention for Evolent Health documents, regardless of medium, are provided within the Evolent Health records retention policy and as indicated in CORP.028.E Records Retention Policy and Procedure.

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