RX.PA.034.MPC Specialty Enzymes
Lumizyme, Fabrazyme, Elfabrio, Pombiliti & Opfolda, Nexviazyme, Galafold

The purpose of this policy is to define the prior authorization process for the following specialty enzymes: Lumizyme (alglucosidase alfa), Fabrazyme (agalsidase beta), Elfabrio (pegunigalsidase alfa-iwxj), Pombiliti (cipaglucosidase alfa-atga) and Opfolda (miglustat), Nexviazyme (avalglucosidase alfa); Galafold (migalastat)

- Lumizyme (alglucosidase alfa) is indicated for patients with Pompe disease. Lumizyme consists of the human enzyme acid alpha-glucosidase (GAA) and is intended for intravenous infusion.
- Fabrazyme (agalsidase beta) is a recombinant human enzyme indicated for use in patients with Fabry disease. Agalsidase beta (Fabrazyme) reduces globotriasylceramide (GL-3) deposition in capillary endothelium of the kidney and certain other cell types.
- Elfabrio (pegunigalsidase alfa-iwxj) is indicated for the treatment of adults with confirmed Fabry disease.
- Galafold (migalastat) is an alpha-galactosidase A (alpha-Gal A) pharmacological chaperone indicated for the treatment of adults with a confirmed diagnosis of Fabry disease.
- Pombiliti (cipaglucosidase alfa-atga) and Opfolda (miglustat) are indicated as a two-component therapy for patients with late onset Pompe disease weighing $\geq$ 40 kg and are not improving on their current enzyme replacement therapy.
- **Nexviazyme (avalglucosidase alfa)** is indicated for the treatment of Pompe disease, late onset.

DEFINITIONS

Mucopolysaccharidosis I – a rare, autosomal recessive genetic disease caused by a defect in the gene coding for the lysosomal enzyme alpha-L-iduronidase resulting in inability to produce sufficient amounts of the enzyme

Hunter Syndrome – a serious progressive genetic disorder caused by a deficiency or absence of the lysosomal enzyme (iduronate-2-sulfatase) required for the degradation of glycosaminoglycans (GAG) resulting in accumulation of GAG in cells throughout the body. Hunter Syndrome affects males almost exclusively.

Mucopolysaccharidosis VI – a progressive lysosomal storage disorder caused by a deficiency in the arylsulfatase B enzyme causing retention of glycosaminoglycans leading to multisystemic organ damage.

Pompe Disease – A genetic absence or deficiency of acid alpha-glucosidase (GAA) resulting in build-up of glycogen in the cardiac and skeletal muscles, and in hepatic tissue. This results in the development of cardiomyopathy, progressive muscle weakness, and impairment of respiratory function.

Fabry Disease – a rare genetic disorder caused by a defect in the gene for the lysosomal enzyme alpha-galactosidase resulting in inability or diminished ability to catabolize certain lipids. These lipids then accumulate in many cell-types throughout the body.

Globotriasylceramide – a type of glycolipid compound that accumulates in blood vessel walls of people with Fabry disease

PROCEDURE

A. Initial Authorization Criteria:

Must meet all of the criteria listed below under each respective drug.

Lumizyme (alglucosidase alfa)

- Must be prescribed by or in consultation with a physician who specializes in the treatment of inherited metabolic disorders or a neurologist
- Must have a documented confirmed diagnosis of alpha glucosidase deficiency (Pompe disease)
    - Diagnosis must be confirmed through GAA enzyme assay (from blood, skin fibroblasts, lymphocytes, or muscle) and/or identification of GAA gene mutation
- Member must have clinical signs and symptoms of Pompe disease such as cardiac hypertrophy, respiratory distress, skeletal muscle weakness, etc.
- Must have documentation of baseline factors for the following:
    - Percent predicted forced vital capacity (FVC)
    - 6-minute walk test
        - Note: 6 minute walk test is excluded for members at an age not able to walk
- Dosage must not exceed 20mg per kg body weight administered every 2 weeks
- Must not be used in combination with other enzyme replacement therapies (Pombiliti, Nexviazyme, etc.)

Pombiliti (cipaglucosidase alfa-atga) and Opfolda (miglustat)

- Must be ≥ 18 years of age with a body weight of ≥ 40kg
- Must have a documented confirmed diagnosis of alpha glucosidase deficiency (Pompe disease)
    - Diagnosis must be confirmed through GAA enzyme assay (from blood, skin fibroblasts, lymphocytes, or muscle) and/or identification of GAA gene mutation
- Member must have clinical signs and symptoms of Pompe disease such as cardiac hypertrophy, respiratory distress, skeletal muscle weakness, etc.
- Must have a documented trial and failure, intolerance to, or contraindication to Nexviazyme
- Must have documentation of baseline factors for the following:
    - Percent predicted forced vital capacity (FVC)
    - 6-minute walk test
        - Note: 6 minute walk test is excluded for members at an age not able to walk
- Must be prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of inherited metabolic disorders
- Provider attests that Pombiliti will be used in combination with Opfolda
- Must not be used in combination with other enzyme replacement therapies (Lumizyme, Nexviazyme, etc.)

Nexviazyme (avalglucosidase alfa)

- Must be age 1 year or older
- Must be prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of inherited metabolic disorders
- Must have a documented confirmed diagnosis of alpha glucosidase deficiency (Pompe disease)
    - Diagnosis must be confirmed through GAA enzyme assay (from blood, skin fibroblasts, lymphocytes, or muscle) and/or identification of GAA gene mutation
- Member must have clinical signs and symptoms of Pompe disease such as cardiac hypertrophy, respiratory distress, skeletal muscle weakness, etc.
- Nexviazyme must not be used in combination with other enzyme replacement therapies (i.e. alglucosidase-alfa, etc.)
- Member must not be susceptible to fluid volume overload, have acute underlying respiratory illness, or have compromised cardiac or respiratory function
- Must have documentation of baseline factors for the following:
    - Percent predicted forced vital capacity (FVC)
    - 6-minute walk test
        - Note: 6 minute walk test is excluded for members at an age not able to walk

Fabrazyme (agalsidase beta) and Galafold (migalastat)

- Must be prescribed by or in consultation with a provider who specializes in the treatment of inherited metabolic disorders or a neurologist
- Member is at least 2 years of age or older
- Must have a documented diagnosis of Fabry disease confirmed by one of the following:
  - Genetic test confirming mutation of galactosidase alpha (GLA) gene
  - Biopsy of tissue or organ (such as kidney) showing intracellular globotriaosylceramide (Gb3) inclusion
  - Male members only may also have their diagnosis confirmed by an Alpha-galactosidase A (alpha-Gal A) enzyme activity <3%
- Fabrazyme (agalsidase beta) and Galafold (migalastat) must not be used together or in combination with other enzyme replacement therapies for Fabry's disease
- Dosage must not exceed 1mg per kg body weight administered every 2 weeks

Elfabrio (pegunigalsidase alfa-iwxj)

- Member is at least 18 years of age or older
- Must be prescribed by or in consultation with a provider who specializes in the treatment of inherited metabolic disorders or a neurologist
- Must have a documented diagnosis of Fabry disease confirmed by one of the following:
  - Genetic test confirming mutation of galactosidase alpha (GLA) gene
  - Biopsy of tissue or organ (such as kidney) showing intracellular globotriaosylceramide (Gb3) inclusion
  - Male members only may also have their diagnosis confirmed by an Alpha-galactosidase A (alpha-Gal A) enzyme activity <3%
- Member must have documentation of at least one or more symptoms:
  - Pain in the extremities (acroparesthesias); OR
  - Cutaneous vascular lesions (angiokeratomas)
  - Corneal verticillata (whorls)
  - Decreased sweating (anhidrosis or hypohidrosis)
  - Personal or family history of exercise, heat, or cold intolerance
- Must not be used in combination with Galafold (migalastat), Fabrazyme (agalsidase beta), or other enzyme replacement therapies for Fabry's disease
- Dosage must not exceed 1mg per kg (actual body weight) administered every 2 weeks
- Must have documented baseline values of at least one of the following:
  - Globotriaosylceramide (Gb3) concentration in urine > 1.5 times upper normal limit
  - Plasma globotriaosylceramide (GL3) level
  - Plasma globotriaosphingosine (lyso-Gb3) level

B. Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc) listed in the FDA approved labeling.

C. Lumizyme, Fabrazyme, Galafold, Elfabrio, Opfolda and Pombiliti, Nexviazyme will be considered investigational or experimental for any other use and will not be covered.

D. <u>Reauthorization Criteria:</u>

All prior authorization renewals are reviewed on an annual basis to determine the Medical Necessity for continuation of therapy.

- **MPC Renewal:**
  - Must be prescribed by or in consultation with a provider who specializes in the treatment of inherited metabolic disorders or a neurologist
  - Documentation of a clinical response of the member's condition which has stabilized or improved based upon the prescriber's assessment
  - For alpha glucosidase deficiency (Pompe disease), must provide documentation of an improvement in percent predicted FVC and/or 6 minute walk test compared to baseline
    - Note: 6 minute walk test is excluded for members at an age not able to walk

- **Renewal from Previous Insurer:**
  - Members who have received prior approval (from insurer other than MPC), or have been receiving medication samples, should be considered under criterion A (Initial Authorization Criteria).
  - Must be prescribed by or in consultation with a provider who specializes in the treatment of inherited metabolic disorders or a neurologist
  - Provider has a documented clinical response of the member's condition which has stabilized or improved based upon the prescriber's assessment
  - For alpha glucosidase deficiency (Pompe disease), must provide documentation of an improvement in percent predicted FVC and/or 6 minute walk test compared to baseline
    - Note: 6 minute walk test is excluded for members at an age not able to walk

<u>Limitations:</u>

Length of Authorization (if above criteria met)	
Initial Authorization	Up to 6 months
Reauthorization	Up to 12 months

If the established criteria are not met, the request is referred to a Medical Director for review.

Codes: J Code(s)

Code	Description
J0180	Injection, agalsidase beta, 1 mg
J0221	Injection, alglucosidase alfa, (lumizyme), 10 mg
J3590	Unclassified biologic
J0219	Injection, avalglucosidase alfa-ngpt, 4 mg
J2508	Injection, pegunigalsidase alfa-iwxj, 1 mg

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5. American Association of Neuromuscular & Electrodiagnostic Medicine. Diagnostic criteria for late-onset (childhood and adult) Pompe disease. Muscle Nerve 2009;40:149-160
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10. Elfabrio [package insert]. Chiesi USA, Inc. Cary NC, May 2023.
11. Nexviazyme (avalglucosidase alfa) [prescribing information]. Cambridge, MA: Genzyme Corporation; August 2021
12. 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

REVIEW HISTORY

DESCRIPTION OF REVIEW / REVISION	DATE APPROVED
Annual Review	*02/2026*
Annual Review	*02/2025*
Selected Review *Addition of criteria requirements for Opfolda & Pombiliti* *Addition of criteria requirements for Nexviazyme*	*02/2024*
Annual Review *Change in Non-MPC renewal to renewal from previous insurer*	*02/2024*
Selected Review *Addition of criteria requirements for Elfabrio* (pegunigalsidase alfa-iwxj)	*09/2023*

Annual review	*02/2023*
Selected Revision *Addition of MPC vs Non-MPC Renewal Criteria and expanded initial review criteria*	*08/2022*
Annual review	*02/2022*
Addition of dosing requirements and off-label restrictions	*12/2021*
P&T Review	*11/2020*