# Medical Policy

**Healthcare Services Department**

| Policy Name | Policy Number | Scope |
|---|---|---|
| **Alglucosidase alfa (Lumizyme®), Avalglucosidase alfa-ngpt (Nexviazyme®), and Cipaglucosidase alfa-atga (Pombiliti®)** | MP-RX-FP-124-24 | ☒ MMM MA ☒ MMM Multihealth |

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

## Service Description

This document addresses the use of alglucosidase alfa (Lumizyme®), avalglucosidase alfa-ngpt (Nexviazyme®), and cipaglucosidase alfa-atga (Pombiliti®), hydrolytic lysosomal glycogen-specific enzymes approved by the Food and Drug Administration (FDA) for the treatment of patients with Pompe disease (GAA deficiency).

**Background Information**

This document addresses Lumizyme (alglucosidase alfa), avalglucosidase alfa-ngpt (Nexviazyme®), and cipaglucosidase alfa-atga (Pombiliti®) enzyme replacements used to treat Pompe disease. Pompe disease is a rare autosomal recessive disorder caused by a deficiency of acid alpha-glucosidase (GAA), an enzyme that degrades lysosomal glycogen.

Clinically, Pompe disease or glycogen storage disease type II (GSDII) presents as a wide spectrum ranging from the severe rapidly progressive infantile-onset form to a more slowly progressive late-onset form. The American College of Medical Genetics (ACMG) Work Group on Management of Pompe Disease (2006) developed algorithms to diagnose and manage both types of Pompe disease. The level of residual activity of the GAA enzyme drives Pompe disease severity and age of symptoms onset. GAA gene sequencing may be used to confirm a diagnosis or when there are discordant GAA enzyme activity studies (American Association of Neuromuscular and Electrodiagnostic Medicine [AANEM] 2009).

Lumizyme is the only alglucosidase alfa product indicated for use in the United States. Nexviazyme was approved August 2021 and is the only avalglucosidase alfa-ngpt product in the United States indicated for Pompe disease. Pombiliti was approved September 2023 to be used in combination with Opfolda (miglustat) capsules in individuals who are not improving on their current enzyme replacement therapy (ERT).

Lumizyme has a black box warning for the risk of anaphylaxis, hypersensitivity and immune-mediated reactions, and risk of cardiorespiratory failure in compromised patients with infantile-onset Pompe disease. Nexviazyme and Pombiliti also contain black box warnings for hypersensitivity reactions including anaphylaxis, infusion-associated reactions, and cardiorespiratory failure.

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In 2020, an update in the package label brings attention to the potential of those with infantile-onset Pompe disease should have a cross-reactive immunologic material (CRIM) assessment early in their disease course as CRIM status has been shown to be associated with immunogenicity and individuals' responses to enzyme replacement therapies.

**Approved Indications**

- Lumizyme® is approved by the FDA for the treatment of patients with Pompe disease.
- Nexviazyme® is approved by the FDA for the treatment of patients 1 year of age and older with late-onset Pompe disease (lysosomal acid alpha-glucosidase deficiency).
- Pombiliti® is approved by the FDA in combination with Opfolda, an enzyme stabilizer, for the treatment of adult patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) weighing ≥40 kg and who are not improving on their current enzyme replacement therapy (ERT).

**Other Uses**

N/A

**Applicable Codes**

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

| HCPCS | Description |
|---|---|
| J0221 | Injection, alglucosidase alfa, (Lumizyme), 10 mg |
| J0219 | Injection, avalglucosidase alfa-ngpt, 4 mg |
| J3490 | Unclassified drugs (when specified as [Pombiliti] (cipaglucosidase alfa-atga)) |
| J3590 | Unclassified biologics (when specified as [Pombiliti] (cipaglucosidase alfa-atga)) |
| S9357 | Home infusion therapy, enzyme replacement intravenous therapy, (e.g., Imiglucerase); administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem |

| ICD-10 | Description |
|---|---|
| E74.02 | Pompe disease |

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**Medical Necessity Guidelines**

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

## Alglucosidase alfa (Lumizyme®), avalglucosidase alfa-ngpt (Nexviazyme®), and cipaglucosidase alfa-atga (Pombiliti®)

### A. Criteria For Initial Approval

I. Initial requests for Lumizyme (alglucosidase alfa) may be approved if the following criteria are met:

i. Individual has a diagnosis of infantile-onset Pompe disease as confirmed by all of the following (ACMG 2006):
   A. Documentation is provided that individual has acid alpha-glucosidase deficiency (GAA) activity in skin fibroblasts of less than 1% of the normal mean or by GAA gene sequencing (AANEM 2009); **AND**
   B. Individual has symptoms (for example respiratory and/or skeletal muscle weakness); **AND**
   C. Individual has evidence of hypertrophic cardiomyopathy;

   **OR**

ii. Individual has a diagnosis of non-infantile onset (late-onset) Pompe disease as confirmed by all of the following (ACMG 2006):
   A. Documentation is provided that individual has a GAA enzyme assay which shows reduced enzyme activity less than 40% of the lab specific normal mean value; **AND**
   B. Documentation is provided that individual has a second GAA enzyme activity assay in a separate sample (from purified lymphocytes, fibroblasts or muscle) or by GAA sequencing (AANEM 2009); **AND**
   C. Forced vital capacity (FVC) 30 – 79% of predicted value, and documentation is provided; **AND**
   D. Ability to walk 40 meters on a 6- minute walk test (assisted devices permitted), and documentation is provided; **AND**
   E. Muscle weakness in the lower extremities.

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II. Initial requests for Nexviazyme (avalglucosidase alfa-ngpt) may be approved if the following criteria are met:
   i. Individual has a diagnosis of non-infantile onset (late-onset) Pompe disease as confirmed by all the following (ACMG 2006):
      A. Documentation is provided that individual has a GAA enzyme assay which shows reduced enzyme activity less than 40% of the lab specific normal mean value; **AND**
      B. Documentation is provided that individual has a second GAA enzyme activity assay in a separate sample (from purified lymphocytes, fibroblasts or muscle) or by GAA sequencing (AANEM 2009); **AND**
      C. Forced vital capacity (FVC) 30 – 85% of predicted value, and documentation is provided; **AND**
      D. Ability to walk 40 meters on a 6- minute walk test (without assistive devices), and documentation is provided.

III. Initial requests for Pombiliti (cipaglucosidase alfa-atga) may be approved if the following criteria are met:
   i. Individual is 18 years of age or older; **AND**
   ii. Individual weighs 40 kg or more; **AND**
   iii. Individual has a diagnosis of non-infantile onset (late onset) Pompe disease as confirmed by all the following:
      A. Documentation is provided that individual has a GAA enzyme assay which shows reduced enzyme activity less than 40% of the lab specific normal mean value (ACMG 2006); **AND**
      B. Documentation is provided that individual has a second GAA enzyme activity assay in a separate sample (from purified lymphocytes, fibroblasts or muscle) or by GAA sequencing (AANEM 2009); **AND**
      C. Forced vital capacity (FVC) 30% or higher of predicted value (NCT03729362), and documentation is provided; **AND**
      D. Muscle weakness in the lower extremities; **AND**
      E. Individual is able to walk at least 75 meters on 2 (two) 6- minute walk tests (assisted devices permitted), and documentation is provided; **AND**
   iv. Individual is using in combination with Opfolda (miglustat); **AND**
   v. Documentation is provided that individual has tried alglucosidase or avalglucosidase alfa-ngpt without improvement.

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**B. Criteria For Continuation of Therapy**

i. MMM considers continuation of **alglucosidase alfa (Lumizyme®)** therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) if the following criteria are met:
   A. Individuals are using Lumizyme for the treatment of infantile-onset Pompe disease; **OR**
   B. Individuals with non-infantile onset (late-onset) Pompe disease are responding to therapy (including improvement, stabilization, or slowing of disease progression).

ii. MMM considers continuation of **avalglucosidase alfa-ngpt (Nexviazyme®)** therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) if the following criteria are met:
   A. Individuals with non-infantile onset (late-onset) Pompe disease are responding to therapy (including improvement, stabilization, or slowing of disease progression).

iii. MMM considers continuation of **cipaglucosidase alfa-atga (Pombiliti®)** therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) if the following criteria are met:
   A. Individuals with non-infantile onset (late-onset) Pompe disease are responding to therapy (including improvement, stabilization, or slowing of disease progression); **AND**
   B. Individual is using in combination with Opfolda (miglustat).

**C. Authorization Duration**

i. Initial Approval Duration: Up to 12 months
ii. Reauthorization Approval Duration: Up to 12 months

D. **Conditions Not Covered**

*Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):*

Lumizyme (alglucosidase alfa) may not be approved for the following:

i. In combination with Nexviazyme (avalglucosidase alfa); **OR**
ii. In combination with Pombiliti; **OR**
iii. When the above criteria are not met and for all other indications.

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Nexviazyme (avalglucosidase alfa-ngpt) may not be approved for the following:

i. In combination with Lumizyme (alglucosidase alfa); **OR**
ii. In combination with Pombiliti; **OR**
iii. When the above criteria are not met and for all other indications.

Requests for Pombiliti (cipaglucosidase alfa-atga) may not be approved for the following:

i. Individual is using in combination with Nexviazyme; **OR**
ii. Individual is using in combination with Lumizyme; **OR**
iii. When the above criteria are not met and for all other indications.

## Limits or Restrictions

A. Therapeutic Alternatives

*The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.*

i. N/A

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B. Quantity Limitations

*Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.*

| Drug | Recommended Dosing Schedule |
|---|---|
| **Alglucosidase alfa (Lumizyme®)** | 20 mg/kg IV every 2 weeks |
| **Avalglucosidase alfa-ngpt (Nexviazyme®)** | For patients weighing:<br>• ≥30 kg, the recommended dosage is 20 mg/kg (of actual body weight) every two weeks.<br>• <30 kg, the recommended dosage is 40 mg/kg (of actual body weight) every two weeks. |
| **Cipaglucosidase alfa-atga (Pombiliti®)** | 20 mg/kg IV every 2 weeks |
| **Exceptions** | |
| None | |

## Reference Information

1. American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM). Pompe. Available at: https://www.aanem.org/Patients/Disorders/Pompe. Accessed on August 5, 2022.
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4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2023. URL: http://www.clinicalpharmacology.com. Updated periodically.
5. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically.
6. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
7. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
8. Lumizyme [Package insert], Cambridge, MA. Genzyme Corporation; 2022.

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9. Nexviazyme [Package insert], Cambridge, MA. Genzyme Corporation; 2021.
10. Opfolda [Package insert], Philadelphia, PA. Amicus Therapeutics US, LLC; 2023.
11. Pombiliti [Package insert], Philadelphia, PA. Amicus Therapeutics US, LLC; 2023.
12. Schoser B, Roberts M, Byrne BJ, et al. Safety and efficacy of cipaglucosidase alfa plus miglustat versus alglucosidase alfa plus placebo in late-onset Pompe disease (PROPEL): an international, randomised, double-blind, parallel-group, phase 3 trial. *Lancet Neurol*. 2021;20(12):1027-1037. doi:10.1016/S1474-4422(21)00331-8

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.



## Policy History

| Revision Type | Summary of Changes | P&T Approval Date | UM/CMPC Approval Date |
|---|---|---|---|
| Policy Inception | Elevance Health's Medical Policy adoption | N/A | 6/28/2024 |

Revised: 04/10/2024