



avalglucosidase alfa-ngpt (Nexviazyme™)

Policy # 00771

Original Effective Date: 02/14/2022

Current Effective Date: 02/12/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider avalglucosidase alfa-ngpt (Nexviazyme™)† for the treatment of late onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for avalglucosidase alfa-ngpt (Nexviazyme) will be considered when the following criteria are met:

Initial

- Patient has a diagnosis of late onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) as evidenced by GAA enzyme deficiency from any tissue source and/or 2 confirmed GAA gene mutations; AND
Note: Late-onset disease (juvenile and adult presentations) is characterized by skeletal myopathy (i.e., progressive weakness in a limb-girdle distribution), protracted course, leading to respiratory failure. Supportive findings may include electromyographic (EMG) demonstrating myopathic discharges, sometimes abundant myotonic and complex repetitive discharges, most prominent in the paraspinal muscles, and elevated serum creatinine kinase.
- Patient is 1 year of age or older; AND
- Dosing is as follows:
 - ≥ 30 kg: 20 mg/kg of actual body weight every two weeks; OR
 - < 30 kg: 40 mg/kg of actual body weight every two weeks; AND

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- Patient has measurable signs of Pompe disease, such as impairment in pulmonary function or motor weakness; AND
*(Note: This specific criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient is able to ambulate at least 130 feet without stopping and without an assistive device; AND
*(Note: This specific criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met.)*
- Patient has a Forced Vital Capacity (FVC) $\geq 30\%$ predicted and $\leq 85\%$ predicted; AND
*(Note: This specific criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met.)*
- Patient is NOT using/planning to use alglucosidase alfa (Lumizyme[®])[†] concurrently with the requested medication; AND
- Patient does NOT require invasive ventilation; AND
*(Note: This specific criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met.)*
- Patient does NOT have Pompe-specific cardiac hypertrophy; AND
*(Note: This specific criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met.)*
- Patient has NOT failed therapy with alglucosidase alfa (Lumizyme); AND
*(Note: This specific criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met.)*
- Baseline percent predicted Forced Vital Capacity (FVC) and 6 minute walk test (6MWT) measurements are provided; AND
*(Note: This specific criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- There is clinical evidence or patient history that suggests the use of alglucosidase alfa (Lumizyme) will be ineffective or cause an adverse reaction to the patient.
*(Note: This specific criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

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Continuation

- Patient has received an initial authorization; AND
- Patient has responded to therapy as evidenced by an improvement or stabilization in percent predicted FVC and/or 6MWT; AND
*(Note: This specific criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Dosing is as follows:
 - ≥ 30 kg: 20 mg/kg of actual body weight every two weeks; OR
 - < 30 kg: 40 mg/kg of actual body weight every two weeks; AND
- Patient is able to ambulate at least 130 feet without stopping and without an assistive device; AND
*(Note: This specific criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met.)*
- Patient has a Forced Vital Capacity (FVC) $\geq 30\%$ predicted and $\leq 85\%$ predicted; AND
*(Note: This specific criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met.)*
- Patient is NOT using/planning to use alglucosidase alfa (Lumizyme) concurrently with the requested medication; AND
- Patient does NOT require invasive ventilation; AND
*(Note: This specific criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met.)*
- Patient does NOT have Pompe-specific cardiac hypertrophy.
*(Note: This specific criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of avalglucosidase alfa-ngpt (Nexviazyme) when any of the following criteria are NOT met to be **not medically necessary:****

- Patient has measurable signs of Pompe disease, such as impairment in pulmonary function or motor weakness
- Patient is able to ambulate at least 130 feet without stopping and without an assistive device
- Patient has a Forced Vital Capacity (FVC) $\geq 30\%$ predicted and $\leq 85\%$ predicted

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- Patient does NOT require invasive ventilation
- Patient does NOT have Pompe-specific cardiac hypertrophy
- Patient has NOT failed therapy with alglucosidase alfa (Lumizyme)
- Baseline percent predicted Forced Vital Capacity (FVC) and 6 minute walk test (6MWT) measurements are provided
- There is clinical evidence or patient history that suggests the use of alglucosidase alfa (Lumizyme) will be ineffective or cause an adverse reaction to the patient
- For continuation requests specifically: Patient has responded to therapy as evidenced by an improvement or stabilization in percent predicted FVC and/or 6MWT

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of avalglucosidase alfa-ngpt (Nexviazyme) when the patient selection criteria are not met (with the exception of those denoted as **not medically necessary****) to be **investigational**.*

Background/Overview

Nexviazyme is indicated for the treatment of patients 1 year of age and older with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency). Nexviazyme is given as an intravenous infusion. For patients weighing ≥ 30 kg, the recommended dosage is 20 mg/kg every two weeks. For patients weighing < 30 kg, the recommended dosage is 40 mg/kg every two weeks.

Pompe disease, also known as lysosomal acid alpha-glucosidase (GAA) deficiency, is an autosomal recessive disorder which leads to an accumulation of glycogen in lysosomes and cytoplasm. This ultimately leads to tissue destruction. There are two type of GAA deficiency: infantile onset and late onset. Infantile onset typically presents within the first few months of life and is characterized by cardiomyopathy and hypotonia. Late onset may present at any age and is characterized by skeletal myopathy and eventual respiratory failure without cardiomyopathy. Prior to Nexviazyme's FDA approval, Lumizyme was the only product on the market for the treatment of Pompe disease. Lumizyme carries approval for both the infantile and late onset varieties of Pompe disease, while

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Nexviazyme only carries approval for late onset Pompe disease. Given that this condition results from a genetic disorder, which ultimately leads to an enzyme deficiency, Nexviazyme and Lumizyme focus on replacing the missing enzyme. These two products are structurally and mechanistically similar and contain the same enzyme needed for replacement in Pompe Disease. Clinical trials comparing Nexviazyme and Lumizyme in late onset Pompe disease showed non-inferiority and non-superiority of Nexviazyme as compared to Lumizyme. Safety is also considered similar between the two products. Given that safety and efficacy are similar, Lumizyme is a more economical choice for use in therapy due to its longevity in the marketplace which impacts cost factors in a very complex pharmaceutical pricing system. Although Nexviazyme may be marketed as “cost parity” to Lumizyme, it is not due to the complexities of the pricing system of pharmaceutical products.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Nexviazyme is indicated for the treatment of patients 1 year of age and older with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency).

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Study 1 was a randomized, double-blinded, multinational, multicenter trial comparing the efficacy and safety of Nexviazyme to Lumizyme in 100 treatment-naïve patients with late onset Pompe Disease (LOPD). Patients were randomized in a 1:1 ratio based on baseline forced vital capacity (FVC), gender, age, and country to receive 20 mg/kg of Nexviazyme or Lumizyme administered intravenously once every two weeks for 49 weeks. The trial included an open-label, long-term, follow-up phase of up to 5 years, in which patients in the Lumizyme arm were switched to Nexviazyme treatment. Of the 100 randomized patients, 52 were males, the baseline median age was 49 years old (range from 16 to 78), median baseline weight was 76.4 kg (range from 38 to 139 kg), median length of time since diagnosis was 6.9 months (range from 0.3 to 328.4 months), mean age

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at diagnosis was 46.4 years old (range from 11 to 78), mean forced vital capacity (FVC, measured as % predicted) at baseline was 62.1% (range from 32 to 85%), and mean 6 minute walk test (6MWT) at baseline was 388.9 meters (range from 118 to 630 meters). The primary endpoint of Study 1 was the change in FVC (% predicted) in the upright position from baseline to Week 49. At Week 49, the least squares (LS) mean change in FVC (% predicted) for patients treated with Nexviazyme and Lumizyme was 2.9% and 0.5%, respectively. The estimated treatment difference was 2.4% (95% CI: -0.1, 5.0) favoring Nexviazyme. However, it should be clearly noted that there was a noninferiority margin of 1.1% ($p=0.0074$). Statistical superiority of Nexviazyme over Lumizyme was not achieved ($p=0.06$).

References

1. Nexviazyme [package insert]. Genzyme Corporation. Cambridge, Massachusetts. Updated August 2021.
2. Lysosomal acid alpha-glucosidase deficiency (Pompe disease, glycogen storage disease II, acid maltase deficiency). UpToDate. Updated September 2021.
3. Nexviazyme New Drug Review. IPD Analytics. August 2021.

Policy History

Original Effective Date: 02/14/2022

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01/06/2022 Medical Policy Committee review

01/12/2022 Medical Policy Implementation Committee approval. New policy.

03/21/2022 Coding update

01/05/2023 Medical Policy Committee review

01/11/2023 Medical Policy Implementation Committee approval. No change to coverage.

01/04/2024 Medical Policy Committee review

01/10/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 01/2025

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Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)†, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No Codes
HCPCS	J0219, J3490, J3590, C9399
ICD-10 Diagnosis	E74.02

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into

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standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

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