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Policy Number: C21948-A

Nexviazyme (avalglucosidase alfa-ngpt)

PRODUCTS AFFECTED

Nexviazyme (avalglucosidase alfa-ngpt)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review.

A. POMPE DISEASE:
1. Documented diagnosis of late-onset Pompe disease (LOPD)
   AND
2. Documentation diagnosis was confirmed by ONE of the following: enzyme assay showing a deficiency of acid alpha-glucosidase (GAA) activity in the blood, skin, or muscle OR genetic testing showing a mutation in the GAA gene [DOCUMENTATION REQUIRED]

AND

3. Documentation of member's baseline percent-predicted forced vital capacity (FVC), baseline walking distance or 6-minute walk test (6MWT), or gastrointestinal symptoms [DOCUMENTATION REQUIRED]
   NOTE: 6MWT excluded for members at an age not able to walk
   AND
4. Prescriber attests Nexviazyme (avalglucosidase) will not be used concurrently with Lumizyme (alglucosidase)

CONTINUATION OF THERAPY:

A. POMPE DISEASE:

1. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
2. Documentation that member has demonstrated a beneficial response to therapy compared to pretreatment baseline as demonstrated by stabilization or improvement in FVC and/or 6MWT and signs/symptoms of the condition (e.g., gastrointestinal symptoms) [DOCUMENTATION REQUIRED]

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a metabolic specialist, endocrinologist, biochemical geneticist, or physician experienced in the management of Pompe disease [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

1 year of age and older

QUANTITY:

≥30 kg: 20 mg/kg (of actual body weight) every two weeks.
<30 kg: 40 mg/kg (of actual body weight) every two weeks.

PLACE OF ADMINISTRATION:

The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Nexviazyme (avalglucosidase alfa-ngpt)
For information on site of care, see
Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Intravenous

DRUG CLASS:

GAA Deficiency Treatment – Agents

FDA-APPROVED USES:

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

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX: None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Lysosomal acid alpha-glucosidase (GAA, also called acid maltase) deficiency (Pompe disease, formerly classified as glycogen storage disease type II [GSD II]) is an autosomal recessive disorder with considerable allelic heterogeneity. It is caused by mutations in the gene for lysosomal acid alpha-1,4- glucosidase. Deficiency of lysosomal GAA leads to accumulation of glycogen in lysosomes and cytoplasm, which results in tissue destruction.

- The infantile form (early onset) of GAA deficiency is characterized by cardiomyopathy and severe, generalized hypotonia. Most patients with this form die within the first year or two of life without treatment.
- The juvenile and adult form (late onset) is characterized by skeletal myopathy (usually in a limb-girdle distribution) and a protracted course leading to respiratory failure.
- Infantile-onset GAA deficiency should be suspected in infants with profound hypotonia and cardiac insufficiency. Juvenile or adult-onset GAA deficiency should be considered in patients with progressive weakness in a limb-girdle distribution. Supportive findings may include:
    - Electrocardiogram demonstrating short PR interval and giant QRS complexes in all leads, suggesting biventricular hypertrophy, although this is a nonspecific finding (infantile form).
    - Electromyogram demonstrating myopathic discharges, sometimes associated with abundant myotonic and complex repetitive discharges, most prominent in the paraspinal muscles (juvenile and adult form).
    - Elevated serum creatine kinase (all forms).
    - Demonstration of reduced GAA activity in a dried blood spot or leukocytes, followed by sequencing of the GAA gene, confirms the disease. Enzyme activity assays using skin fibroblasts or muscle tissue are alternatives to genetic testing to confirm the diagnosis.
- GAA deficiency is treated with enzyme replacement therapy (ERT), physical and occupational therapy, and supportive care (e.g., mechanical ventilation for respiratory failure).
- The advent of ERT has improved clinical outcomes and survival for both early- and late-onset GAA deficiency. However, patients on ERT may still develop gradual pelvic girdle muscle weakness. Additional complications may include fractures and sleep-disordered breathing
- The ERT provides an exogenous source of GAA and works by binding to mannose-6-phosphate (M6P) receptors on the cell surface via carbohydrate groups (including M6P) on the exogenous GAA molecule.
- Treatment with alglucosidase alfa has been demonstrated in the literature to reduce the risk of invasive ventilation, improve cardiac and skeletal muscle function, and prolong survival in patients with IOPD. In LOPD, alglucosidase alfa has been shown to improve muscle strength, mobility, and lung function.
- ERT is initiated immediately in patients who are diagnosed with IOPD. Patients with LOPD can be diagnosed long before symptoms begin through newborn screening or family testing, which raises the question of when it is appropriate to initiate ERT. While the guidelines, consensus statements, and literature recognize that there is not a gold-standard guideline that addresses this question, they all recommend initiating ERT after the onset of symptoms

Nexviazyme (avalglucosidase alfa-ngpt) is an ERT that is very similar to Lumizyme (alglucosidase alfa). Nexviazyme was designed with a 15-fold increase in M6P content compared to Lumizyme, which is intended to increase cellular uptake of the exogenous enzyme. However, the clinical implications of this altered M6P

content have not been established in clinical trials.

COMET trial
Nexviazyme (avalglucosidase alfa-ngpt) approval was based on data from the multicenter, randomized, double-blind a 49-week noninferiority phase 3 (NCT02782741), study between Nexviazyme and alglucosidase alfa (Lumizyme) which assessed the efficacy and safety of Nexviazyme in 100 treatment-naïve patients with late-onset Pompe disease. Patients were randomly assigned 1:1 to receive Nexviazyme (n=51) or alglucosidase alfa (n=49) administered as an intravenous infusion every 2 weeks. The primary endpoint was the change from baseline in percent predicted forced vital capacity (FVC) in an upright position. 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 alglucosidase alfa administered intravenously once every two weeks for49 weeks. The trial included an open-label, long-term, follow-up phase of up to 5 years, in which patients in the alglucosidase alfa 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 at diagnosis was 46.4 years old (range from 11 to 78), mean FVC (% predicted) at baseline was 62.1% (range from32 to 85%), and mean 6MWT at baseline was 388.9 meters (range from 118 to 630 meters).

Results showed that treatment with Nexviazyme met the primary endpoint achieving noninferiority to alglucosidase alfa with a 2.43% (95% CI, -0.13, 4.99) greater increase in FVC percent-predicted at week 49 (P =.0074); Nexviazyme did not achieve statistical superiority over alglucosidase alfa. Patients treated with Nexviazyme achieved a 30.0 meter (95% CI, 1.3-58.7) greater increase in the6-Minute Walk Test (key secondary endpoint) at week 49 compared with those treated with alglucosidase alfa.

Serious adverse reactions in the COMET trial occurred in 1 (2%) patient in the Nexviazyme arm and in 3 (6%) patients in the alglucosidase alfa arm. Infusion-associated reactions (IARs) occurred in 13 (25%) patients in the Nexviazyme arm and 16 (33%) patients in the alglucosidase alfa arm.
The most common adverse reactions for Nexviazyme (incidence greater than 5%) include headache, fatigue, diarrhea, nausea, arthralgia, dizziness, myalgia, pruritus, vomiting, dyspnea, erythema, paresthesia and urticaria.
An additional safety analysis was conducted on pooled data from 4 trials (mean exposure was 26 months). In this pooled analysis, a notable difference from the COMET trial safety data was a higher incidence of IARs, occurring in 34% of Nexviazyme-treated patients.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Nexviazyme (avalglucosidase alfa-ngpt) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Nexviazyme (avalglucosidase alfa-ngpt) include: No labeled contraindications.

OTHER SPECIAL CONSIDERATIONS:
FDA Label- Boxed Warning
Hypersensitivity reactions, including anaphylaxis
Patients treated with avalglucosidase alfa have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available during avalglucosidase alfa administration. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, avalglucosidase alfa should be discontinued immediately and appropriate medical treatment should be initiated. In patients with severe hypersensitivity reaction, a desensitization procedure to avalglucosidase alfa may be considered.
Infusion-associated reactions
Patients treated with avalglucosidase alfa have experienced severe infusion-associated reactions (IARs). If severe IARs occur, consider immediate discontinuation of avalglucosidase alfa, initiation of appropriate medical treatment, and the benefits and risks of readministering avalglucosidase alfa following severe IARs. Patients with an acute underlying illness at the time of avalglucosidase alfa infusion may be at

greater risk for IARs.
Patients with advanced Pompe disease may have compromised cardiac and respiratory function, which may predispose them to a higher risk of severe complications from IARs

Risk of acute cardiorespiratory failure in susceptible patients

Patients susceptible to fluid volume overload, or those with acute underlying respiratory illness or compromised cardiac or respiratory function for whom fluid restriction is indicated may be at risk of serious exacerbation of their cardiac or respiratory status during avalglucosidase alfa infusion. More frequent monitoring of vitals should be performed during avalglucosidase alfa infusion in such patients.

Prior to NEXVIAZYME administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids. Appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available during NEXVIAZYME administration.
Patients susceptible to fluid volume overload, or those with acute underlying respiratory illness or compromised cardiac or respiratory function for whom fluid restriction is indicated may be at risk of serious exacerbation of their cardiac or respiratory status during the NEXVIAZYME infusion. More frequent monitoring of vitals should be performed during NEXVIAZYME infusion in these patients. Some patients may require prolonged observation times.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J0219	Injection, avalglucosidase alfa-ngpt, 4 mg

AVAILABLE DOSAGE FORMS:
Nexviazyme SOLR 100MG single-dose vial

REFERENCES

1. Nexviazyme (avalglucosidase alfa) [prescribing information]. Cambridge, MA: Genzyme Corporation; April 2023.
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3. Cupler EJ, et al. Consensus treatment recommendations for late-onset Pompe disease. Muscle Nerve. 2012;45(3):319-333. doi:10.1002/mus.22329
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7. Wang RY, et al. ACMG Work Group on Diagnostic Confirmation of Lysosomal Storage Diseases. Lysosomal storage diseases: diagnostic confirmation and management of presymptomatic individuals. Genet Med. 2011;13(5):457- 484.doi:10.1097/GIM.0b013e318211a7e1

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q3 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Coding/Billing Information	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file