Original Effective Date: 09/25/2024
Current Effective Date: 09/10/2025
Last P&T Approval/Version: 07/30/2025
Next Review Due By: 07/2026
Policy Number: C28288-A

Naglazyme (galsulfase)

PRODUCTS AFFECTED

Naglazyme (galsulfase)

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:
Mucopolysaccharidosis VI (MPS VI; Maroteaux-Lamy syndrome)

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. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. MUCOPOLYSACCHARIDOSIS VI (MPS VI; MAROTEAUX-LAMY SYNDROME):
   1. Documented diagnosis of Mucopolysaccharidosis VI (MPS VI; Maroteaux-Lamy syndrome) AND
   2. Documentation diagnosis confirmed by reduced fibroblast or leukocyte ARSB enzyme activity OR

Molecular genetic testing of ARSB [DOCUMENTATION REQUIRED]
AND

3. Documentation of baseline values for all of the following [DOCUMENTATION REQUIRED]:
   a. Urinary glycosaminoglycan (GAG) levels
      AND
   b. Member 6 years of age or older (ONE of the following): 6-minute walk test (6-MWT) and/or percent predicted Forced Vital Capacity (FVC)
      OR
      Member less than 6 years (ONE of the following): upper airway obstruction during sleep, cardiac status, growth velocity, mental development, FVC, hepatosplenomegaly, and/or 6-minute walk test

   AND
4. Documentation that member has at least ONE of the following symptoms of the disease: gait disturbance, growth deficiency, short stature, spinal abnormalities, chest abnormalities, joint abnormalities, respiratory compromise, cardiac valve abnormalities, muscular weakness, visual impairment, hearing loss, or dental abnormalities and oral health challenges

CONTINUATION OF THERAPY:

A. MUCOPOLYSACCHARIDOSIS VI (MPS VI; MAROTEAUX-LAMY SYNDROME):
   1. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity [e.g., hypersensitivity reactions, anaphylaxis, severe type III immune-mediated reactions (e.g., membranous glomerulonephritis)]
      AND
   2. Documentation of positive clinical response or disease stability compared to baseline (prior to therapy) as evidenced by [DOCUMENTATION REQUIRED]:
      a. Decreased urinary glycosaminoglycan (GAG) levels
         AND
      b. Members 6 years of age and older (ONE of the following): 6-minute walk test (6MWT) and/or percent predicted forced vital capacity (FVC)
         OR
         Members less than 6 years of age (ONE of the following): decreased hepatosplenomegaly, improvement in upper airway obstruction during sleep, cardiac status, growth velocity, mental development, FVC, and/or 6-minute walk test

DURATION OF APPROVAL:

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

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified geneticist, metabolic specialist, pediatric neurologist, pediatric developmentalist, endocrinologist, or a physician who specializes in the treatment of lysosomal storage disorders or physician experienced in the management of mucopolysaccharidoses (MPS). [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

3 months of age to 29 years of age

QUANTITY:

1 mg/kg once weekly

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 Naglazyme (galsulfase). 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:
Mucopolysaccharidosis VI (MPS VI) - Agent

FDA-APPROVED USES:
Indicated for patients with Mucopolysaccharidosis VI (MPS VI; Maroteaux-Lamy syndrome). Naglazyme has been shown to improve walking and stair-climbing capacity**.**

E76.29 Other mucopolysaccharidoses

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
The mucopolysaccharidoses (MPS) are inherited lysosomal storage disorders in which a deficiency of specific enzymes (depends on subtype) leads to the accumulation of mucopolysaccharides (glycosaminoglycans; GAGs). The accumulation of partially degraded GAG fragments in the lysosomes, results in permanent cellular dysfunction and clinical abnormalities which may manifest in various parts of the body. The symptoms and physical findings associated with MPS vary greatly depending on subtype and case. Common manifestations of MPS include central nervous system disease such as hydrocephalus or cervical spine myelopathy, cardiovascular and pulmonary disease, ophthalmologic disease, such as corneal clouding or retinal degeneration, hearing impairment, and musculoskeletal manifestations such as short stature, joint stiffness, or symptoms of peripheral nerve entrapment. There are seven types of MPS disorders which are differentiated by their clinical features and age of presentation and biochemically by their associated enzyme deficiency. MPS Type I has three subtypes, followed by MPS Types II, III, IV, VI, VII, and IX. MPS V (formerly Scheie syndrome) and MPS VIII are no longer acknowledged.

MPS VI or Maroteaux-Lamy Syndrome is caused by mutations in the N-acetyl- galactosamine-4- sulfatase (ARSB) gene. This enzyme deficiency results in the accumulation of dermatan sulfate and chondroitin 4-sulfate GAGs.

The goal of therapy is to reduce the accumulation of the toxic GAGs to prevent disease progression. The primary mechanism of action for therapy involves replacing the missing or defective GAG with a genetically engineered enzyme (ERT). The primary goals of therapy are to improve pulmonary symptoms and progression of symptoms and enhancement in the overall health and quality of life. Galsulfase is the first pharmacotherapy available for MPS IV and the first ERT designed to target the underlying cause of the syndrome.

Galsulfase is a hydrolytic lysosomal GAG-specific enzymes. Galsulfase provides exogenous N-acetyl-galactosamine-4-sulfatase (ARSB) in adults and pediatric patients 3 months and older with MPS VI. Galsulfase is a purified human enzyme that is produced by recombinant DNA technology in a Chinese hamster ovary line. Galsulfase (N-acetylgalactosamine 4-sulfatase; ARSB) is a lysosomal enzyme that catalyzes the cleavage of the sulfate ester from terminal-ARSB residues of GAG, chondroitin 4- sulfate and dermatan sulfate.

Prior to the approval of ERT for the treatment of MPS VI, the only alternatives were palliative or supportive care, which does not treat the underlying cause of the disease so it continued to progress. In consideration of the unmet need for the treatment of MPS VI, the benefits of ERT for patients with MPS VI outweigh the known risks since there are no clinical alternatives to galsulfase for ERT in patients with MPS VI.

Galsulfase is reasonably safe with consideration of the seriousness of the disorder though this therapy is associated with development of NAbs and infusions reactions. The studies reviewed support the efficacy of the recombinant enzyme; however, efficacy was established based primarily on subjective tests of endurance and effort (% predicted FVC and 6- MWT are subjective tests which depend on the effort and motivation of the individual patient, which may be difficult to control in younger children) and long-term outcomes have not been established. The journal of Genetics and Molecular Biology and Orphanet Journal of Rare Diseases recommend initiating treatment as soon as the diagnosis has been confirmed by an enzyme activity test.

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

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
J1458	Injection, Galsulfase, 1mg

AVAILABLE DOSAGE FORMS:
Naglazyme SOLN 1MG/ML single-dose vial

REFERENCES

1. Naglazyme (galsulfase) injection, for intravenous use [prescribing information]. Novato, CA: BioMarin

Pharmaceutical Inc.; September 2024.
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3. Hendriksz CJ, Berger KI, Lampe C, et al. Health-related quality of life in mucopolysaccharidosis: looking beyond biomedical issues. Orphanet J Rare Dis. 2016 Aug 26;11(1):119.
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6. Giugliani R, Federhen A, Rojas MV, et al. Mucopolysaccharidosis I, II, VI: Brief review and guidelines for treatment. Genet Mol Biol. 2010 Oct;33(4):589-604.
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10. Harmatz, P. R., Garcia, P., Guffon, N., Randolph, L. M., Shediac, R., Braunlin, E., Lachman, R. S., & Decker, C. (2014). Galsulfase (Naglazyme®) therapy in infants with mucopolysaccharidosis VI. Journal of inherited metabolic disease, 37(2), 277–287. https://doi.org/10.1007/s10545-013-9654-7

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Quantity References	Q3 2025
NEW CRITERIA CREATION From retired Enzyme Replacement Therapy for Lysosomal Storage Disorders (MPS I, VI) [Aldurazyme, Naglazyme] C9997-A	Q3 2024
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Prescriber Requirements Quantity FDA-Approved Uses	Q3 2023
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Prescriber Requirements Contraindications/Exclusions/Discontinuation References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file