Drug Coverage Policy

Effective Date..... 07/15/2025
Coverage Policy Number IP0443
Policy Title..... Naglazyme

Enzyme Replacement Therapy – Naglazyme

- Naglazyme® (galsulfase intravenous infusion – BioMarin)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Naglazyme, a human *N*-acetylgalactosamine 4-sulfatase, is indicated for **Mucopolysaccharidosis type VI** (Maroteaux – Lamy syndrome [MPS VI]).[1] It is produced in a Chinese hamster ovary cell

line via recombinant DNA technology. The enzyme catalyzes the hydrolysis of the sulfate ester from the glycosaminoglycans, chondroitin 4-sulfate and dermatan sulfate. Naglazyme has been shown to improve walking and stair climbing capacity.

Disease Overview
MPS VI, or Maroteaux – Lamy syndrome, is a rare lysosomal storage disorder characterized by a deficiency of *N*-acetylgalactosamine 4-sulfatase (arylsulfatase B).[2,3] The enzyme deficiency results in the accumulation of partially hydrolyzed dermatan sulfate and chondroitin 4-sulfate in lysosomes leading to the signs and symptoms of the disease.[2,3] The onset, severity, and rate of progression of MPS VI is heterogeneous; however, most patients are severely affected with a rapidly progressive form.[3] Clinical manifestations include course facial features, short stature, kyphoscoliosis, joint stiffness, pulmonary insufficiency, cardiac disease, hepatosplenomegaly, corneal clouding, and hernias.[2,3] The definitive diagnosis of MPS VI is established by demonstrating deficient arylsulfatase B enzyme activity in leukocytes or fibroblasts, or by genetic testing.[2,3] Definitive treatment of MPS VI consists of either enzyme replacement therapy with Naglazyme or hematopoietic stem cell transplantation. Due to the morbidity and mortality associated with hematopoietic stem cell transplantation, this therapy is typically reserved for patients who are intolerant of or do not respond to enzyme replacement therapy.[2]

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of Naglazyme. Approval is recommended for those who meet the Criteria and Dosing for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Naglazyme as well as the monitoring required for adverse events and long-term efficacy, approval requires Naglazyme to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Naglazyme is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Mucopolysaccharidosis Type VI (Maroteaux – Lamy Syndrome).** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A)** The diagnosis is established by ONE of the following (i or ii):
     - **i.** Patient has a laboratory test demonstrating deficient *N*-acetylgalactosamine 4-sulfatase (arylsulfatase B) activity in leukocytes or fibroblasts; OR
     - **ii.** Patient has a molecular genetic test demonstrating biallelic pathogenic or likely pathogenic arylsulfatase B (*ARSB*) gene variants; AND
   - **B)** Naglazyme is prescribed by or in consultation with a geneticist, endocrinologist, a metabolic disorder sub-specialist, or a physician who specializes in the treatment of lysosomal storage disorders.

Dosing. Each dose must not exceed 1 mg/kg administered intravenously no more frequently than once weekly.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Naglazyme for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

Coding 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.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J1458	Injection, galsulfase, 1 mg

References

1. Naglazyme® intravenous infusion [prescribing information]. Novato, CA: BioMarin; April 2020.
2. Harmatz PR, Shediac R. Mucopolysaccharidosis VI: Pathophysiology, diagnosis and treatment. *Front Biosci*. 2017;22:385-406.
3. Vairo F, Federhen A, Baldo G, et al. Diagnostic and treatment strategies in mucopolysaccharidosis VI. *Appl Clin Genet*. 2015;8:245-255.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Updated** coverage policy title from *Galsulfase* to *Enzyme Replacement Therapy – Naglazyme.* **Mucopolysaccharidosis Type VI (Maroteaux – Lamy Syndrome):** **Added** dosing.	8/1/2024
Annual Revision	No criteria changes	07/15/2025

The policy effective date is in force until updated or retired.