Drug Coverage Policy

Effective Date..... 5/15/2026
Coverage Policy Number IP0406
Policy Title..... Fabrazyme

Enzyme Replacement Therapy – Fabrazyme

- Fabrazyme® (agalsidase intravenous infusion – Genzyme)

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

Fabrazyme, a human α-galactosidase A (α-Gal), is indicated for **Fabry disease**.[1] It is the same amino acid sequence as the native enzyme and is produced in Chinese hamster ovary cells via recombinant DNA technology. Fabrazyme catalyzes the breakdown of globotriaosylceramide (GL-3) and other α-galactyl-terminated neutral glycosphingolipids to ceramide and galactose and reduces the deposition of GL-3 in the capillary endothelium of the kidney and certain other cell types.

Disease Overview
Fabry disease is a rare inherited X-linked lysosomal storage disorder due to absent or significantly reduced α-Gal activity leading to the accumulation of GL-3 in a wide variety of cells throughout the body.[2-4] The accumulation of GL-3 leads to progressive multisystem disease, primarily impacting the kidney, heart, and nervous system.[3,4] The incidence of Fabry disease is estimated to be about 1:117,000 live male births.[2] Fabry disease can be divided into two phenotypes. A severe, classical phenotype typically occurs in men without α-Gal activity, whereas a generally milder non-classical phenotype is found in men and women with some residual α-Gal activity.[2,3] The diagnosis of Fabry disease can be confirmed in males by demonstrating a deficiency in α-Gal activity, and in all patients by identifying a Fabry disease causing gene mutation.[4] Long-term consequences of Fabry disease include hypertrophic cardiomyopathy, arrhythmias, renal failure, and stroke.[3] The kidney disease that occurs in Fabry disease is associated with progressive proteinuria and a decline in glomerular filtration rate, which over time, leads to end-stage renal disease requiring dialysis and ultimately, kidney transplantation.[2] Treatment with Fabrazyme reduces the accumulation of GL-3 in the kidney (and in other organs), with the goal of stopping or slowing the decline in kidney function.

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Policy Statement
Prior Authorization is required for benefit coverage of Fabrazyme. 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 Fabrazyme as well as the monitoring required for adverse events and long-term efficacy, approval requires Fabrazyme to be prescribed by or in consultation with a physician who specializes in the condition being treated.

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

FDA-Approved Indication

1. Fabry Disease. 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 α-galactosidase A activity in leukocytes or fibroblasts; OR
  - **ii.** Patient has a molecular genetic test demonstrating a pathogenic variant in the galactosidase alpha gene (GLA); AND
- **B)** Fabrazyme 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 every 2 weeks.

Conditions Not Covered

Fabrazyme for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent Use with Galafold® (migalastat oral capsules)**. One small study (n = 23) assessed a single dose of Galafold (150 mg or 450 mg) used concurrently with Fabrazyme or agalsidase alpha.[5] While a single dose of Galafold significantly increased α-Gal activity, the long-term safety and efficacy of concurrent use of Galafold and Fabrazyme has not been established. Galafold is not FDA approved for concurrent use with Fabrazyme.

2. **Concurrent Use with Elfabrio® (pegunigalsidase alfa intravenous infusion)**.

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
J0180	Injection, agalsidase beta, 1 mg

References

1. Fabrazyme® intravenous infusion [prescribing information]. Cambridge, MA: Genzyme; July 2024.
2. Schiffmann R. Fabry Disease. Handb Clin Neurol. 2015;132:231-248.
3. Arends M, Wanner C, Hughes D, et al. Characterization of Classical and Nonclassical Fabry Disease: A Multinational Study. J Am Soc Nephrol. 2017;28:1631-1641.
4. Laney DA, Bennett RL, Clarke V, et al. Fabry Disease Practice Guidelines: Recommendations of the National Society of Genetic Counselors. J Genet Counsel. 2013;22:555-564.
5. Warnock DG, Bichet DG, Holida M, et al. Oral Migalastat HCl Leads to Greater Systemic Exposure and Tissue Levels of Active α-Galactosidase A in Fabry Patients when Co-Administered with Infused Agalsidase. PLoS ONE. 2015;10: e0134341.

Revision Details

Summary of Changes	Review Date	Effective Date
Updated coverage policy title from *Agalsidase* to *Enzyme Replacment Therapy - Fabrazyme*. **<u>Fabry disease:</u>** **Added** dosing. **Removed** reauthorization criteria. **Added** Concurrent Use with Elfabrio as a condition not covered.	6/20/2024	8/1/2024
No criteria changes.	5/8/2025	7/15/2025
No criteria changes	4/23/2026	5/15/2026

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