Effective Date **9/15/2023**
Next Review Date… **9/15/2024**
Coverage Policy Number **IP0406**

Agalsidase

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Related Coverage Resources

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. 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

This policy supports medical necessity review for agalsidase intravenous infusion (**Fabrazyme®**).

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

Medical Necessity Criteria

Agalsidase (Fabrazyme) is considered medically necessary when the following are met:

1. **Fabry Disease.** Individual meets **BOTH** of the following criteria (A and B):
    A. Documented diagnosis of Fabry disease confirmed by **ONE** of the following (i or ii):
        i. Individual has a laboratory test demonstrating deficient α-galactosidase A activity in leukocytes or fibroblasts
        ii. Confirmation of a hemizygous pathogenic variant in the *GLA* gene

B. The medication is prescribed by or in consultation with a medical geneticist, endocrinologist, a metabolic disorder sub-specialist, or a physician who specializes in the treatment of lysosomal storage disorders

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.

Reauthorization Criteria

Agalsidase (Fabrazyme) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Agalsidase (Fabrazyme) is considered experimental, investigational or unproven for **ANY** other use including the following (this list may not be all inclusive):

1. **Concurrent Use with Galafold® (migalastat).** One small study (n = 23) assessed a single dose of Galafold (150 mg or 450 mg) used concurrently with Fabrazyme or agalsidase alpha. 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.[5] Galafold is not FDA approved for concurrent use with Fabrazyme.

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

Background

OVERVIEW
Fabrazyme, a human α-galactosidase A (α-Gal), is indicated for use in patients with **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.

References

1. Fabrazyme® intravenous infusion [prescribing information]. Cambridge, MA: Genzyme; March 2021.
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.