Effective Date **2/15/2024**
Next Review Date **2/15/2025**
Coverage Policy Number **IP0400**

Migalastat

Table of Contents

Overview 1
Medical Necessity Criteria 1
Reauthorization Criteria 2
Authorization Duration 2
Conditions Not Covered 2
Background 2
References 3

Related Coverage Resources

Pharmacogenetic Testing for Non-Cancer Indications – (0500)

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 migalastat (**Galafold**®).

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

Medical Necessity Criteria

Migalastat (Galafold) is considered medically necessary when the following are met:

Treatment of Fabry disease. Individual meets **ALL** of the following criteria:
- A. Age 18 years or older
- B. Diagnosis of Fabry disease confirmed by documentation of **ONE** of the following:
  - i. Male individual with a pathogenic, or likely pathogenic, amenable galactosidase alpha gene (*GLA*) variant based on in vitro assay data
  - ii. **BOTH** of the following:

a. Female individual with a pathogenic, or likely pathogenic, amenable galactosidase alpha gene (*GLA*) variant **OR** a male or female with an amenable *GLA* variant of uncertain significance (VUS) based on in vitro assay data
b. At least **ONE** of the following signs or symptoms of Fabry disease:
    1. Crises of severe pain in the extremities (acroparesthesia)
    2. Appearance of vascular cutaneous lesions (angiokeratomas)
    3. Sweating abnormalities (anhidrosis, hypohidrosis or hyperhidrosis)
    4. Albuminuria/proteinuria
    5. Renal failure
    6. Cardiomyopathy

C. Medication is prescribed by, or in consultation with, a medical geneticist, nephrologist or a physician who specializes in the treatment of Fabry disease

---

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

Continuation of migalastat (Galafold) is considered medically necessary for Fabry disease when the above medical necessity 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

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. **Concurrent use with Fabrazyme® (agalsidase beta intravenous infusion).** 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.[6] Galafold is not FDA approved for concurrent use with Fabrazyme.

2. **Concurrent Use with Elfabrio (pegunigalsidase alfa intravenous infusion).** Galafold has not been evaluated for use in combination with Elfabrio. It is not FDA approved for concurrent use with enzyme replacement therapy.

Background

OVERVIEW
Galafold, an oral alpha-galactosidase A (α-Gal) pharmacological chaperone, is indicated for the treatment of adults with a confirmed diagnosis of **Fabry disease** and an amenable galactosidase alpha gene (*GLA*) variant based on in vitro assay data.[1]

Disease Overview

Fabry disease is a rare inherited X-linked lysosomal storage disorder.[2-4] Absent or significantly reduced α-Gal activity leads to the accumulation of globotriaosylceramide (GL-3) in a wide variety of cells throughout the body. The accumulation of GL-3 leads to progressive multisystem disease, primarily impacting the kidney, heart, and nervous system.[3,4] Life expectancy in patients with Fabry disease is reduced; median survival is typically 50 to 55 years in men and 70 years in women.[2]

Currently, there have been more than 800 mutations to the gene encoding α-Gal identified.[5] About 60% are missense mutations resulting in single amino acid substitutions. Some of these mutated enzymes have activity levels similar to normal α-Gal; however, they have been found to be unstable and are retained in the endoplasmic reticulum.

References

1. Galafold® capsules [prescribing information]. Cranbury, NJ: Amicus Therapeutics; June 2023.
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. Benjamin ER, Della Valle MC, Wu X, et al. The Validation of Pharmacogenetics for the Identification of Fabry Patients to be Treated with Migalastat. *Genet Med*. 2017;19:430-438.
6. 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.