**Original Effective Date: 01/01/2019**
**Current Effective Date: 09/20/2023**
**Last P&T Approval/Version: 07/26/2023**
**Next Review Due By: 07/2024**
**Policy Number: C15445-A**

# Galafold (migalastat)

## PRODUCTS AFFECTED

Galafold (migalastat)

## 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:**
Fabry disease [E75.21 Fabry-Anderson disease]

**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.*

A. FABRY DISEASE:
1. (a) Diagnosis of classic Fabry disease with typical clinical manifestations confirmed by documented deficient α-galactosidase A (α-Gal A) enzyme activity in plasma, isolated leukocytes, and/or cultured

cells using alpha galactosidase A enzyme assay (Males with classic Fabry disease have less than 1% α-Gal A enzyme activity, Males with atypical Fabry disease have residual enzyme activity that is greater than 1% of normal) OR Molecular genetic testing that identifies aGLA mutation providing additional confirmation of the diagnosis [DOCUMENTATION REQUIRED]
OR
(b) Diagnosed as a carrier of Fabry disease with significant clinical manifestations, confirmed by documented decrease α-Gal A enzyme activity in plasma and/or isolated leukocytes [DOCUMENTATION REQUIRED]
AND

2. Documentation that member has at least ONE amenable galactosidase alpha (GLA) gene variant based on invitro assay data (see Appendix) [DOCUMENTATION REQUIRED]
   AND
3. Prescriber attests (or medical records support) that the member does not currently have severe renal impairment or end stage renal disease requiring dialysis
   AND
4. Documentation of member's baseline plasma globotriaosylceramide (GL3) level
   AND
5. Documentation of member's baseline clinical symptoms
   AND
6. Prescriber attests (or medical records support) that the member is not concurrently using enzyme replacement therapy (ERT) (Fabrazyme, Elfabrio)
   AND
7. Documentation of one of the following:
   a. Member is ERT naïve and is not a candidate for ERT
      OR
   b. Member is ERT experienced and not able to continue ERT due to non-responsiveness after 1 year of therapy, infusion reaction, antibody development, etc.

**CONTINUATION OF THERAPY:**

A. FABRY DISEASE:

1. Documentation of positive clinical response, or stabilization of disease, to Galafold therapy as documented by improvements in GL-3 and/or GL-3 inclusions compared to pre-treatment baseline, OR improvement in clinical symptoms
   AND
2. Prescriber attests to or clinical reviewer has found that member is not receiving Galafold in combination with Fabrazyme (agalsidase beta) or Elfabrio (pegunigalsidase alfa)
   AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

**DURATION OF APPROVAL:**

Initial authorization: 12 months, continuing authorization: 12 months

**PRESCRIBER REQUIREMENTS:**

Prescribed by, or in consultation with, a board-certified Nephrologist, Cardiologist, Neurologist, Endocrinologist, Clinical Geneticist, Clinical Biochemical Geneticist or physician experienced in the management of Fabry disease. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

**AGE RESTRICTIONS:**

18 years of age and older

**QUANTITY:**

123mg orally every other day, maximum 14 capsules/ 28 days

**PLACE OF ADMINISTRATION:**
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

## DRUG INFORMATION

**ROUTE OF ADMINISTRATION:**
Oral

**DRUG CLASS:**
Fabry disease agents

**FDA-APPROVED USES:**
Indicated for treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene (GLA) variant based on in vitro assay data.
This indication is approved under accelerated approval based on reduction in kidney interstitial capillary cell globotriaosylceramide (KIC GL-3) substrate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

**COMPENDIAL APPROVED OFF-LABELED USES:**
None

## APPENDIX

**APPENDIX:**
https://www.amicusrx.com/pi/galafold.pdf

Presence of at least one amenable GLA variant (mutation) may be confirmed by the following resources (Galafold prescribing information, 2022):

- Galafold Prescribing Information brochure (package insert; Section 12, Table 2); If aGLA variant is not listed in 'Table 2' of the Galafold Prescribing Information, it is either non-amenable (if tested) or has not been tested for in vitro amenability. If questions, contact Amicus Medical Information at 1- 877-4AMICUS or medinfousa@amicusrx.com
- Amicus Fabry GLA Gene Variant Search Tool: http://www.galafoldamenabilitytable.com/hcp

NOTE: Based on available published data, the GLA variant c.937G>T, (p.(D313Y)) is considered benign (not causing Fabry disease). Consultation with a clinical genetics professional is strongly recommended in patients with Fabry disease who have this GLA variant as additional evaluations may be indicated. (Galafold prescribing information, 2022)

## BACKGROUND AND OTHER CONSIDERATIONS

**BACKGROUND:**
Fabry disease is an X-linked lysosomal storage disorder caused by mutations in the GLA gene leading to deficient α- galactosidase A activity, glycosphingolipid accumulation, and life- threatening complications. Phenotypes vary from the "classic" phenotype, with pediatric onset and multi- organ involvement, to later-onset, a predominantly cardiac phenotype.
Manifestations are diverse in female members in part due to variations in residual enzyme activity and X chromosome inactivation patterns. Enzyme replacement therapy (ERT) and adjunctive treatments can provide significant clinical benefit.
However, much of the current literature reports outcomes after late initiation of ERT, once substantial organ damage has already occurred. Updated monitoring and treatment guidelines for pediatric

patients with Fabry disease have recently been published. Expert physician panels were convened to develop updated, specific guidelines for adult patients. Management of adult patients depends on 1) a personalized approach to care, reflecting the natural history of the specific disease phenotype; 2) comprehensive evaluation of disease involvement prior to ERT initiation; 3) early ERT initiation; 4) thorough routine monitoring for evidence of organ involvement in non- classic asymptomatic patients and response to therapy in treated patients; 5) use of adjuvant treatments for specific disease manifestations; and 6) management by an experienced multidisciplinary team.

**CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:**

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

**OTHER SPECIAL CONSIDERATIONS:**

The recommended dosage regimen of GALAFOLD is 123 mg orally once every other day at the same time of day. Do not take GALAFOLD on 2 consecutive days. If a dose is missed entirely for the day, take the missed dose of GALAFOLD only if it is within 12 hours of the normal time that the dose should have been taken. If more than 12 hours have passed, resume taking GALAFOLD at the next planned dosing day and time, according to the every-other-day dosing schedule

## CODING/BILLING 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*

| HCPCS CODE | DESCRIPTION |
|---|---|
| NA | |

**AVAILABLE DOSAGE FORMS**:

Galafold CAPS 123 mg (14 capsules per wallet pack for 28-day supply)

## REFERENCES


1. Galafold™ capsules [prescribing information]. Philadelphia, PA Amicus Therapeutics U.S., Inc.: December 2022.
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. Biegstraaten M, Arngrimsson R, Barbey F, et al. Recommendations for Initiation and Cessation of Enzyme Replacement Therapy in Patients with Fabry Disease: The European Fabry Working Group Consensus Document. Orphanet J Rare Dis. 2015; 10:36 DOI10.1186/s13023- 015-0253
7. 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.
8. 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.

doi:10.1371/journal.pone.0134341.
9. Ortiz, A., Germain, D. P., Desnick, R. J., Politei, J., Mauer, M., Burlina, A., … Wilcox, W. R. (2018). Fabry disease revisited: Management and treatment recommendations for adult patients. Molecular Genetics and Metabolism, 123(4), 416–427. https://doi.org/10.1016/j.ymgme.2018.02.014
10. Henderson, N., Berry, L., & Laney, D. A. (2020). Fabry Disease practice resource: Focused revision. Journal of Genetic Counseling, 29(5), 715–717. https://doi.org/10.1002/jgc4.1318

| SUMMARY OF REVIEW/REVISIONS | DATE |
|---|---|
| REVISION- Notable revisions:<br>Diagnosis<br>Required medical Information<br>Continuation of Therapy<br>Quantity<br>FDA-Approved Uses<br>Background<br>Other Special Considerations<br>Available Dosage Forms<br>References | Q3 2023 |
| REVISION- Notable revisions:<br>Required Medical Information<br>Prescriber Requirements<br>Contraindications/Exclusions/Discontinuation<br>References | Quarter 3 2022 |
| Q2 2022 Established tracking in new format | Historical changes on file |
| | |