Clinical Policy: Migalastat (Galafold)

Reference Number: ERX.SPA.289
Effective Date: 12.01.18
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Migalastat (Galafold®) is an alpha-galactosidase A (alpha-Gal A) pharmacological chaperone.

FDA Approved Indication(s)
Galafold 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.

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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Galafold is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Fabry Disease (must meet all)**:**

1. Diagnosis of Fabry disease confirmed by one of the following (a or b):
   a. Enzyme assay demonstrating a deficiency of alpha-galactosidase activity;
   b. DNA testing;
2. Prescribed by or in consultation with a clinical geneticist, cardiologist, nephrologist, neurologist, lysosomal disease specialist, or Fabry disease specialist;
3. Age ≥ 18 years;
4. Presence of at least one amenable GLA variant (mutation) as confirmed by one of the following resources (a, b or c):
   a. Galafold Prescribing Information brochure (package insert; Section 12, Table 2);
   b. Amicus Fabry GLA Gene Variant Search Tool: https://www.galafoldamenabilitytable.com/?validated=1&language=et;
   c. Amicus Medical Information at 1-877-4AMICUS or medinfousa@amicusrx.com;
5. Galafold is not prescribed concurrently with Fabrazyme®;
6. Dose does not exceed 123 mg (1 capsule) every other day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Fabry Disease (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 123 mg (1 capsule) every other day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;

B. Amenable GLA variants (mutations) associated with benign phenotypes (i.e., phenotypes known not to cause Fabry disease), including the following GLA mutation: c.937G>T, (p.(D313Y)).

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

alpha-Gal A: alpha-galactosidase A
ERT: enzyme replacement therapy
FDA: Food and Drug Administration
GLA: galactosidase alpha gene
KIC GL-3: kidney interstitial capillary cell globotriaosylceramide

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: Fabry Disease Therapy Recommendations[3,4]

Hopkin, et al. 2016 pediatric guidelines and Ortiz, et al. 2018 adult guidelines outline the following treatment recommendations:

- Treatment initiation:
  - Enzyme replacement therapy (ERT) should begin if symptomatic regardless of age or sex.
  - If asymptomatic and with a “classic” mutation, ERT should begin around age 8 to 10 years in boys; for girls treatment should begin around the same age if assessment indicates injury to major organs.
  - Non-classic, attenuated, or late-onset variants, or those identified through family or newborn screening programs, should be treated once assessment indicates injury to major organs.
- Treatment discontinuation:
  - Because the clinical consequences of treatment cessation versus ERT continuation remain unclear no recommendations are made in regard to when and if treatment should ever be discontinued.

Appendix E: In Vitro Amenability Assay

- The proprietary Amicus in vitro assay (HEK-293 assay) categorizes a GLA variant as “amenable” if the resultant mutant alpha-Gal A activity (measured in the cell lysates) meets two criteria: 1) relative increase of at least 20% compared to the pre-treatment alpha-Gal A activity, and 2) absolute increase of at least 3% of the wild-type (normal) alpha-Gal A activity.

- If a GLA variant does not appear 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.
- The in vitro assay does not test whether a GLA variant causes Fabry disease.
  - Consequently, whether a certain amenable GLA variant in a patient with Fabry disease is disease-causing or not should be determined by the prescribing physician (in consultation with a clinical genetics professional, if needed) prior to treatment initiation.
  - 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Fabry disease	123 mg PO every other day	123 mg QOD

VI. Product Availability

Capsule: 123 mg

VII. References

1. Galafold Prescribing Information. Cranbury, NJ: Amicus Therapeutics U.S., Inc., February 2021. Available at https://www.amicusrx.com/pi/galafold.pdf. Accessed August 16, 2021.
2. Ortiz A, Germain DP, Desnick RJ, et al. Fabry disease revisited: Management and treatment recommendations for adult patients. Molecular Genertics and Metabolism. 2018; 123: 416-427. DOI: 10.1016/j.ymgme.2018.02.014. PMID: 29530533.
3. Hopkin RJ, Jefferies JL, Laney DA, et al. on behalf of the Fabry Pediatric Expert Panel. The management and treatment of children with Fabry disease: A United States-based perspective. Molecular Genetics and Metabolism. February 2016; 117(2): 104-113. https://doi.org/10.1016/j.ymgme.2015.10.007.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	09.11.18	11.18
4Q 2019 annual review: no significant changes; references reviewed and updated.	09.10.19	11.19
4Q 2020 annual review: added requirement for enzyme or genetic testing to confirm Fabry disease diagnosis, consistent with the previously P&T-approved approach for Fabry disease diagnosis confirmation for Fabrazyme; revised link to GLA mutation search tool; references reviewed and updated.	07.21.20	11.20
4Q 2021 annual review: added other specialist types who might be involved in a Fabry patient's care, in line with the previously P&T-approved approach to specialists in Fabry disease; references reviewed and updated.	08.16.21	11.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional

medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.