

## Clinical Policy: Migalastat (Galafold)

Reference Number: PA.CP.PHAR.394

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[Revision Log](#)

### 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.*

It is the policy of health plans affiliated with PA Health & Wellness® 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;
2. Prescribed by or in consultation with a clinical geneticist;
3. 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:  
<http://www.fabrygenevariantsearch.com/hcp>;
  - c. Amicus Medical Information at 1-877-4AMICUS or [medinfousa@amicusrx.com](mailto:medinfousa@amicusrx.com);
4. Galafold is not prescribed concurrently with Fabrazyme;
5. Dose does not exceed 123 mg (1 capsule) every other day.

**Approval duration: 6 months**

##### B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

#### II. Continued Therapy

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
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 Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies.

**Approval duration: Duration of request or 6 months (whichever is less); or**

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

**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 – PA.CP.PMN.53 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: Treatment and Continuation of Therapy for Fabry Disease*

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.

- Similar to asymptomatic girls with classic mutations, non-classic/attenuated/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 compared with ERT continuation remain to be clarified 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 meets two criteria: 1) a relative increase of at least 20% compared to the pre-treatment alpha-Gal A activity, and 2) an 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 or has not been tested for in vitro amenability. For questions regarding the status of a mutation contact Amicus Medical Information at 1-877-4AMICUS or [medinfousa@amicusrx.com](mailto: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**

Capsules: 123 mg

**VII. References**

1. Galafold Prescribing Information. Cranbury, NJ: Amicus Therapeutics U.S., Inc., August 2018. Available at <https://www.amicusrx.com/pi/galafold.pdf>. Accessed August 23, 2018.
2. Fabrazyme Prescribing Information. Cambridge, MA: Genzyme Corporation; May 2010. Available at <http://www.fabrazyme.com>. Accessed August 23, 2018.
3. Ortiz A, Germain DP, Desnick RJ, et al. Fabry disease revisited: Management and treatment recommendations for adult patients. *Molecular Genetics and Metabolism*. 2018; 123: 416-427. DOI: 10.1016/j.ymgme.2018.02.014. PMID: 29530533.
4. 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
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