Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review. Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 11/01/2022**
Policy Number: PA.CP.PHAR.394	**Effective Date: 01/2020** **Revision Date: 10/2022**
Policy Name: Migalastat (Galafold)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

4Q 2022 annual review: no significant changes; added requirement on continuation of therapy to document improvement on patient-specific clinical manifestations of Fabry disease, consistent with the previously P&T-approved approach for other Fabry disease therapies (e.g., Fabrazyme); references reviewed and updated.

Name of Authorized Individual (Please type or print): **Venkateswara R. Davuluri, MD**	**Signature of Authorized Individual:**

Clinical Policy: Migalastat (Galafold)

Reference Number: PA.CP.PHAR.394
Effective Date: 10/2018
Last Review Date: 10/2022

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 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 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 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 PA Health & 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 as evidenced by improvement in the individual member's Fabry disease manifestation profile *(see Appendix F for examples)*;
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 PA Health & 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: Fabry Disease Therapy Recommendations

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.
- 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.

Appendix F: Clinical Manifestations of Fabry Disease

The presenting symptoms and clinical course of Fabry disease can vary from one individual to another. As such, there is not one generally applicable set of clinical criteria that can be used to determine appropriateness of continuation of therapy. Some examples, however, of improvement in Fabry disease as a result of Fabrazyme therapy may include improvement in:

- Fabry disease signs such as pain in the extremities, hypohidrosis or anhidrosis, or angiokeratomas
- Diarrhea, abdominal pain, nausea, vomiting, and flank pain
- Renal function
- Neuropathic pain, heat and cold intolerance, vertigo and diplopia
- Fatigue
- Cornea verticillata

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., December 2021. Available at https://www.amicusrx.com/pi/galafold.pdf. Accessed August 24, 2022.
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.
4. Germain DP, Fouilhoux A, Decramer Stephane, et al. Consensus recommendations for diagnosis, management and treatment of Fabry disease in paediatric patients. Clinical Genetics. March 2019;96:107-17.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	10/2018	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019	
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; added age limit; references reviewed and updated.	07/2020	
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.	10/2021	
4Q 2022 annual review: no significant changes; added requirement on continuation of therapy to document improvement on patient-specific clinical manifestations of Fabry disease, consistent with the previously P&T-approved approach for other Fabry disease therapies (e.g., Fabrazyme); references reviewed and updated.	10/2022	