

## **Clinical Policy: Migalastat (Galafold)**

Reference Number: CP.PHAR.394

Effective Date: 09.11.18

Last Review Date: 11.21

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Migalastat (Galafold<sup>®</sup>) 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 Centene Corporation<sup>®</sup> 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  $\geq$  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](mailto:medinfousa@amicusrx.com);
5. Galafold is not prescribed concurrently with Fabrazyme<sup>®</sup>;
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 for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

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

1. Currently receiving medication via Centene benefit 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 Centene benefit and documentation supports positive response to therapy.

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

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
Fabry disease	123 mg PO QOD	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 Genetics 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
No significant changes; added HIM line of business per SDC.	02.01.19	
4Q 2019 annual review: no significant changes; references reviewed and updated.	08.25.19	11.19
4Q 2020 annual review: no significant changes; 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: no significant changes; 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; revised HIM.PHAR.21 to HIM.PA.154; 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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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