# Clinical Policy: Migalastat (Galafold)

Reference Number: CP.PHAR.394
Effective Date: 09.11.18
Last Review Date: 11.23
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®) 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® 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® or Elfabrio®;
6. Dose does not exceed any of the following (a and b):
   a. 123 mg every other day;
   b. 1 capsule every other day.

**Approval duration: 6 months**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
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. Galafold is not prescribed concurrently with Fabrazyme® or Elfabrio®;
4. If request is for a dose increase, new dose does not exceed any of the following (a and b):
   a. 123 mg every other day;
   b. 1 capsule every other day.

**Approval duration: 12 months**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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.

*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 every other day |

## VI. Product Availability

Capsule: 123 mg

## VII. References

1. Galafold Prescribing Information. Cranbury, NJ: Amicus Therapeutics U.S., Inc., June 2023. Available at https://www.amicusrx.com/pi/galafold.pdf. Accessed June 30, 2023.
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.
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 |
|---|---|---|
| 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 |
| 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. Template changes applied to other diagnoses/indications and continued therapy section. | 08.24.22 | 11.22 |
| 4Q 2023 annual review: no significant changes; added exclusion against concomitant use of Galafold with Elfabrio to the Initial Approval Criteria section, since Elfabrio is now FDA-approved; added exclusion against concomitant use with either Fabrazyme or Elfabrio to the Continued Therapy section; references reviewed and updated. | 08.14.23 | 11.23 |

**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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**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.