Clinical Policy Title:	migalastat
Policy Number:	RxA.149
Drug(s) Applied:	Galafold®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
migalastat (Galafold®)	Fabry disease	123 mg PO every other day	123 mg every other day

Dosage Forms

- Capsules: 123 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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. 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: http://www.galafoldamenabilitytable.com/hcp;
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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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
Commercial: 12 months
Medicaid: 12 months

III. Appendices

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

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information
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.
- 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.

References

1. Galafold® Prescribing Information. Cranbury, NJ: Amicus Therapeutics U.S., Inc., February 02, 2021. Available at: https://www.amicusrx.com/pi/galafold.pdf. Accessed March 31, 2021.
2. Fabrazyme Prescribing Information. Cambridge, MA: Genzyme Corporation; May 2010. Available at: http://www.fabrazyme.com. Accessed March 31, 2021.
3. 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. Accessed March 31, 2021.
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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	1/2020	02/07/2020
Policy was reviewed: 1. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 2. References reviewed and	06/15/2020	09/14/2020

updated.		
Policy was reviewed: 1. Dosing frequency abbreviations expanded. 2. Clinical policy section standard verbiage was updated to include "The provision of provider samples…". 3. Continued therapy approval criteria II.A.1 was updated to "Member is currently receiving medication…". 4. References updated.	03/31/2021	06/10/2021