PRIOR AUTHORIZATION POLICY

POLICY: Fabry Disease – Galafold Prior Authorization Policy
- Galaford® (migalastat capsules – Amicus Therapeutics, Inc.)

REVIEW DATE: 09/30/2020

OVERVIEW

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.[1] Certain GLA variants produce abnormally folded and less stable forms of the α-galactosidase A (α-GAL) enzyme, however the enzyme still retains activity. Galafold is a pharmacologic chaperone which binds to the active site of α-GAL, which stabilizes the enzyme and allows it to be trafficked from the endoplasmic reticulum to lysosomes. In the lysosome, Galafold dissociates from the enzyme allowing it to exert its pharmacologic activity.

Disease Overview

Fabry disease is a rare inherited X-linked lysosomal storage disorder due to absent or significantly reduced α-Gal activity leading to the accumulation of globotriaosylceramide (GL-3) in a wide variety of cells throughout the body.[2-4] The accumulation of GL-3 leads to progressive multisystem disease, primarily impacting the kidney, heart, and nervous system.[3,4] Life expectancy in patients with Fabry disease is reduced, median survival is typically 50 to 55 years in men and 70 years in women.[2]

The disease can be divided into two phenotypes, a severe, classical phenotype typically found in men without α-Gal activity, and a generally milder non-classical phenotype in men and women with some residual α-Gal activity.[2,3] Classical Fabry disease symptoms often seen at presentation include neuropathic pain, cornea verticillata, and angiokeratoma,[3] and can occur in males as young as 6 to 8 years of age and at 9 years of age in females.[4] Long–term consequences of Fabry disease include hypertrophic cardiomyopathy, arrhythmias, renal failure, and stroke.[3] Individuals with some residual α-Gal activity typically develop non-classical Fabry disease, which has a later onset, variable disease course, is typically less severe and may affect a single organ, most commonly the heart.[2,3] Despite Fabry disease being an X–linked disorder, women often have Fabry disease signs and symptoms, however they typically have less severe disease than men.

Currently, there have been more than 800 mutations to the gene encoding α-Gal identified and about 60% are missense mutations resulting in single amino acid substitutions.[5] Some of these mutated enzymes have activity levels similar to normal α-Gal however they have been found to be unstable and are retained in the endoplasmic reticulum.

Guidelines

Current Fabry disease treatment guidelines either do not mention Galafold as a treatment option or discuss it as an investigational agent.[6,7]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Galafold. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Galafold as well as the monitoring required for adverse events and long-

term efficacy, initial approval requires Galafold to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Galafold is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Fabry Disease.** Approve for 3 years if the patient meets the following criteria (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has an amenable galactosidase alpha gene (GLA) variant based on *in vitro* assay data; AND
   - **C)** The medication is prescribed by or in consultation with a geneticist, nephrologist, or a physician who specializes in the treatment of Fabry disease.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Galafold is not recommended in the following situations:

1. **Concurrent Use with Fabrazyme.** One small study (n = 23) assessed a single dose of Galafold (150 mg or 450 mg) used concurrently with Fabrazyme or agalsidase alpha. While a single dose of Galafold significantly increased α-GAL activity, the long-term safety and efficacy of concurrent use of Galafold and Fabrazyme has not been established.[8] Galafold is not FDA approved for concurrent use with Fabrazyme.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Galafold® capsules [prescribing information]. Cranbury, NJ: Amicus Therapeutics U.S., Inc.: June 2019.
2. Schiffmann R. Fabry Disease. *Handb Clin Neurol*. 2015;132:231-248.
3. Arends M, Wanner C, Hughes D, et al. Characterization of Classical and Nonclassical Fabry Disease: A Multinational Study. *J Am Soc Nephrol*. 2017;28:1631-1641.
4. Laney DA, Bennett RL, Clarke V, et al. Fabry Disease Practice Guidelines: Recommendations of the National Society of Genetic Counselors. *J Genet Counsel*. 2013;22:555-564.
5. Benjamin ER, Della Valle MC, Wu X, et al. The Validation of Pharmacogenetics for the Identification of Fabry Patients to be Treated with Migalastat. *Genet Med*. 2017;19:430-438.
6. Biegstraaten M, Arngrimsson R, Barbey F, et al. Recommendations for Initiation and Cessation of Enzyme Replacement Therapy in Patients with Fabry Disease: The European Fabry Working Group Consensus Document. *Orphanet J Rare Dis*. 2015;10:36 DOI 10.1186/s13023-015-0253-6.
7. Laney DA, Bennett RL, Clarke V, et al. Fabry Disease Practice Guidelines: Recommendations of the National Society of Genetic Counselors. *J Genet Counsel*. 2013;22:555-564.
8. Warnock DG, Bichet DG, Holida M, et al. Oral Migalastat HCl Leads to Greater Systemic Exposure and Tissue Levels of Active α-Galactosidase A in Fabry Patients when Co-Administered with Infused Agalsidase. *PLoS ONE*. 2015;10: e0134341. doi:10.1371/journal.pone.0134341.