BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

GALAFOLD™ (migalastat) oral

This Pharmacy Coverage Guideline (PCG):

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope

- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Galafold (migalastat) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Pediatrician or Geneticist.

  2. Individual is 16 years of age or older.

  3. Individual has a confirmed diagnosis Fabry disease.

  4. The individual has received and completed **a baseline test** that shows presence of an amenable galactosidase alpha (*GLA*) gene variant determined to be either pathogenic or likely pathogenic as causing the disease.

5. Individual does not have severe renal impairment (eGFR less than 30 mL/min/1.73 m^2) or end-stage renal disease requiring dialysis.

Initial approval duration: 15 capsules per month for 6 months

- **Criteria for continuation of coverage (renewal request):** Galafold (migalastat) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy**):

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Pediatrician or Geneticist.

2. Individual's condition has responded while on therapy with response defined as **ONE** of the following:
    a. Achieved and maintains at least a 20% reduction in plasma globotriaosylsphingosine (lyso-GL_3) levels.
    b. Achieved and maintains at least a 20% reduction in urinary globotriaosylceramide (GL-3) levels.

3. Individual has been adherent with the medication.

Renewal duration: 15 capsules per month for 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Galafold (migalastat) 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. Treatment is indicated for patients with an amenable *GLA* variant that is interpreted by a clinical genetics professional as causing Fabry disease (pathogenic, likely pathogenic) in the clinical context of the patient. Consultation with a clinical genetics professional is strongly recommended in cases where the amenable *GLA* variant is of uncertain clinical significance (VUS, variant of uncertain significance) or may be benign (not causing Fabry disease)

Galafold (migalastat) is an alpha-galactosidase A (alpha-Gal A) pharmacologic chaperone that contains migalastat hydrochloride, an analogue of the terminal galactose of globotriaosylceramide (GL-3). It stabilizes certain mutant variants of alpha-galactosidase to increase enzyme trafficking to lysosomes. Migalastat reversibly binds to the active site of the alpha-Gal A protein (that is encoded by the galactosidase alpha gene, *GLA*). The *GLA* gene is deficient in Fabry's disease.

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Binding to the active site stabilizes alpha-Gal A allowing trafficking from the endoplasmic reticulum into the site of action, the lysosome, where migalastat dissociates from alpha-Gal A allowing it to break down glycosphingolipids GL-3 and globotriaosylsphingosine (lyso-Gb3). Certain *GLA* variants (mutations) causing Fabry's disease result in the production of abnormally folded and less stable forms of the alpha-Gal A protein which retains enzymatic activity. Those *GLA* variants, referred to as amenable variants, produce alpha-Gal A proteins that may be stabilized by migalastat thereby restoring their trafficking to lysosomes and their intralysosomal activity

Fabry's disease is an inherited disorder caused by the deficiency of an enzyme called alpha-galactosidase A or alpha-GAL. This enzyme is needed to metabolize lipids, fat-like substances that include oils, waxes, and fatty acids. A mutation in the gene that controls the alpha-GAL enzyme causes insufficient breakdown of lipids, which build up to harmful levels in the eyes, kidneys, autonomic nervous system, and cardiovascular system. Fabry's disease is also known as alpha-galactosidase A deficiency, Anderson-Fabry disease, angiokeratoma corporis diffusum, angiokeratoma diffuse, ceramide trihexosidase deficiency, and GLA deficiency.

Accumulation of GL-3 in different kidney cells has been recognized as an important marker of disease severity. Progressive decline in renal function is a major complication of Fabry's disease. In addition, patients with Fabry's disease have debilitating gastrointestinal symptoms. Cardiac complications are common and are the main cause of death in Fabry's disease.

The *GLA* gene is located on the X-chromosome. Fabry's disease is inherited as an X-linked disorder. Males are typically more severely affected than females. Females have a more variable course and may be asymptomatic or as severely affected as males. There are two major disease phenotypes: the type 1 "classic" and type 2 "later-onset" subtypes. Both lead to renal failure, and/or cardiac disease, and early death.

Resources:

Galafold (migalastat) product information, revised by Amicus Therapeutics US, LLC. 12-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 18, 2022.

Mauer M, Kopp JB, Wallace E. Fabry disease: Clinical features and diagnosis. In: UpToDate, Curhan GC, Glassock RJ, Lam AQ (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on August 12, 2021. Accessed July 21, 2022.

Mauer M, Wallace E . Fabry disease: Treatment and prognosis. In: UpToDate, Curhan GC, Glassock RJ, Lam AQ (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated July 08, 2022. Accessed July 21, 2022.