BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**9/20/2018**
LAST REVIEW DATE:	**8/19/2021**
LAST CRITERIA REVISION DATE:	**8/19/2021**
ARCHIVE DATE:	

GALAFOLD™ (migalastat) oral

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Galafold (migalastat) is considered ***medically necessary*** and will be approved when **ALL** of 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. A confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene (GLA) variant based on in vitro assay data

  4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     a. Presence of an amenable galactosidase alpha (*GLA*) gene variant determined to be either pathogenic or likely pathogenic as causing the disease

  5. Will not be used in an individual with 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** of the following criteria are met:

  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
     a. Response is defined as **ONE** of the following:
        i. Achieved and maintains at least a 20% reduction in plasma globotriaosylsphingosine (lyso-GL_3) levels
        ii. 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

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- 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 a Non-cancer Medications**

  2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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.

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.

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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. 02-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on July 17, 2021.

Mauer M, Kopp JB. 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. Accessed on July 17, 2021.

Mauer M, Kopp JB. Fabry disease: Treatment and prognosis. In: UpToDate, Curhan GC, Glassock RJ, Lam AQ (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on July 17, 2021.