Pharmacy Policy Bulletin

Title:	Fabry Disease Agents
Policy #:	Rx.01.212

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for migalastat **(Galafold ™)** as provided under the member's prescription drug benefit.

Description:

Fabry Disease is a rare, inherited metabolic disorder characterized by enzyme deficiencies and the resultant accumulation of toxic materials within the lysosomes of cells. It is caused by a mutation in the alpha-Gal A gene located on the X-chromosome. The deficiency of the lysosomal alpha-galactosidse A (alpha-Gal A), which catalyzes the breakdown of globotriaosylceramide (Gb3), leads to accumulation of Gb3 and glycosphingolipids globotriaosylceramide (GL-3) in cells. Certain GLA variants (mutations) causing Fabry Disease result in the production of abnormally folded and less table forms of the alpha-Gal A protein which, however, retain enzymatic activity. Those variants are referred to as amendable variants. Clinical manifestation of Fabry Disease may include severe neuropathic or limb pain; telangiectasias and angiokeratomas; gastrointestinal (GI) symptoms; ocular manifestations; renal manifestations including proteinuria and renal insufficiency; and heat, cold, and exercise intolerance. Eventual progression of microvascular disease of the kidneys, heart, and brain contribute to increased mortality.

Migalastat (Galafold™) is an alpha-galactosidase A (alpha-Gal A) pharmacological chaperone that reversibly binds to the active site of the alpha-galactosidase A (alpha-Gal A) protein (encoded by the galactosidase alpha gene, *GLA*), which is deficient in Fabryl Disease. This binding stabilizes alpha-Gal A allowing its trafficking from the endoplasmic reticulum into the lysosome where it exerts its action. In the lysosome, at a lower pH and at a higher concentration of relevant substrates, migalastat dissociates from alpha-Gal A allowing it to break down the glycosphingolipids globotriaosylceramide (GL-3) and globotriaosylspingosine (lyso-Gb3).

Migalastat (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.

Policy:

INITIAL CRITERIA: Galafold™ (migalastat) is approved when all of the following are met:

1. Diagnosis of Fabry disease; and
2. Member is 16 years of age or older; and
3. Member has an amenable galactosidase alpha gene (GLA) variant (per FDA labeling information) based on in vitro assay data.

Initial Authorization: 6 months

REAUTHORIZATION CRITERIA: Galafold™ (migalastat) is re-approved when there is documentation of positive clinical response to therapy

Reauthorization: 2 years

Black Box Warning as shown in the drug Prescribing Information:

N/A

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Galafold™ (migalastat) [prescribing information]. Cranbury, NJ. Amicus Therapeutics U.S., Inc. February 2021. Available at: https://www.amicusrx.com/pi/galafold.pdf. Accessed March 25, 2021.

Mauer M, Kopp JB. Fabry disease: treatment. UpToDate Web site. Updated September 5, 2019. www.uptodate.com. Accessed March 25, 2021.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Galafold™	migalastat

Cross References:

Off-Label Use Rx.01.33

Policy Version Number:	4.00
P&T Approval Date:	March 18, 2021
Policy Effective Date:	July 01, 2021
Next Required Review Date:	March 18, 2022