migalastat (Galafold®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO096

Description

Migalastat (Galafold) is a pharmacologic chaperone that binds to and stabilizes specific mutant forms of alfa-galactosidase, thereby facilitating proper trafficking of the enzyme to lysosomes and increasing enzyme activity.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
migalastat (Galafold)	123 mg capsule	Fabry disease	15 capsules/30 days

Initial Evaluation

I. Migalastat (Galafold) may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with an endocrinologist or a specialist in genetics; **AND**
   C. Medication will not be used in combination with Enzyme Replacement Therapy (ERT); **AND**
   D. A diagnosis of **Fabry disease** when the following are met:
      1. Documentation of a confirmed diagnosis with mutation of alpha-galactosidase A (alpha-Gal A) gene; **AND**
      2. Documentation that member has a mutation in the gene encoding galactosidase alpha gene (GLA) resulting in a mutant protein that would respond to migalastat (Galafold) (i.e. member has an **amenable** GLA variant); **AND**
      3. Documentation of the member's baseline value of GL-3 inclusions per kidney interstitial capillary; **AND**
      4. Member does not have an eGFR <30 mL/minute/1.73 m2 OR ESRD requiring dialysis; **AND**
      5. Member is ERT-naïve and is not a candidate for ERT (due to contraindication, etc.); **OR**
      6. Member is ERT-experienced and not able to continue ERT therapy

Renewal Evaluation

I. Member has not been established on therapy by the use of free samples, manufacturer coupons, or otherwise; **AND**
II. Member has received a previous prior authorization approval for this agent; **AND**
III. Member does not have an eGFR <30 mL/minute/1.73 m2 OR ESRD requiring dialysis; **AND**
IV. Evidence of disease response with treatment as defined by a 50% reduction in GL-3 inclusions per kidney interstitial capillary compared to pre-treatment baseline; **AND**
V. Documentation by chart notes of disease stability or improvement in clinical symptoms

Supporting Evidence

I. Safety and efficacy of migalastat (Galafold) has not been established in pediatric patients.
II. Eligible patients in the pivotal study (Study 011) had either never received ERT or had not received ERT for at least 6 months. Efficacy and safety of migalastat (Galafold) in combination with ERT is currently in early clinical trial stages.
III. Migalastat is only suitable for people with specific amenable mutations. Only mutations for which migalastat produced substantial increases in enzyme activity were judged amenable. Migalastat does not work in people with non-amenable mutations. Patients with non-amenable GLA variants within the clinical study had no change from baseline in the primary endpoint of number of GL-3 inclusions per kidney interstitial capillary. Per the package insert, consultation with a clinical genetics professional is strongly recommended in cases where the amenable GLA variant is of uncertain clinical significance or may be benign (not causing Fabry disease). Refer to the table in the package insert listing specific GLA gene variants that are amenable to treatment with migalastat (Galafold) or listed within the following search tool found at: http://www.fabrygenevariantsearch.com. Additionally, Fabrazyme (ERT) can be used in all variants of Fabry disease for the treatment of both adults and children. Migalastat (Galafold) is only indicated in the subset of adult patients with a confirmed amenable GLA mutation.
IV. The primary endpoint in Galafold trials was the percentage of patients who had a response (≥50% reduction in the number of globotriaosylceramide inclusions per kidney interstitial capillary) at 6 months. Baseline values are needed as this was the outcome measured used in clinical trials to assess treatment effect.
V. Use of migalastat (Galafold) is not recommended in patients with severe renal impairment (eGFR <30 mL/minute/1.73 m2) or with ESRD requiring dialysis, these patients were excluded from clinical trials.
VI. Migalastat (Galafold) has not been demonstrated in clinical trials to have a clinically meaningful benefit in patients with Fabry disease relative to placebo. While one trial concluded it has "comparable" effects on renal function relative to ERT, "comparable" was not well defined and

ERT also has limited evidence for efficacy in Fabry disease. The pivotal trial for migalastat (Galafold) failed to meet its primary endpoint and its outcome measure is of unknown significance as the relationship of GL-3 inclusion reduction to specific clinical manifestations of Fabry disease has not been established. Though ERT therapy also assessed GL-3 inclusion reduction and provides low quality evidence, Fabrazyme is not specific to amendable variants and can be used in all variants of Fabry disease for the treatment of both adults and children.

References

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5. Ortiz A, Germain DP, Desnick RJ et al. Fabry disease revisited: Management and treatment recommendations for adult patients. Mol Genet Metab. 2018;123:416-27.
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8. Germain DP, Hughes DA, Nicholls K, et al. Treatment of Fabry's Disease with the Pharmacologic Chaperone Migalastat. N Engl J Med. 2016;375(6):545-55.
9. Hughes DA, Nicholls K, Shankar SP, et al. Oral pharmacological chaperone migalastat compared with enzyme replacement therapy in Fabry disease: 18-month results from the randomised phase III ATTRACT study. J Med Genet. 2017;54(4):288-296.

Policy Implementation/Update:

Date Created	September 2018
Date Effective	November 2018
Last Updated	November 2019
Last Reviewed	09/2019

Action and Summary of Changes	Date
Specified mutation needed to have a genetically confirmed diagnosis. Added requirement for agent to be prescribed by or in consultation with an endocrinologist or a specialist in genetics.	11/2019