Galafold (migalastat) Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date 06-01-2025

Date of Origin

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Galafold® (migalastat) Capsule	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

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Fabry Disease	Fabry disease, also called Anderson-Fabry disease, is a rare X-linked lysosomal storage disorder caused by pathogenic mutations in the *GLA* (galactosidase alpha) gene, resulting in functional deficiency of the enzyme alpha-galactosidase A (alpha-Gal A).(4) Markedly reduced, or absent, activity of alpha-Gal A results in progressive accumulation of glycolipids, primarily globotriaosylceramide (GL-3, Gb3), within lysosomes in multiple cell types throughout the body.(4,5) This includes those particularly relevant to disease pathology (e.g., vascular endothelial cells, podocytes, cardiomyocytes, arterial smooth muscle cells) and other cell types in the kidneys, nervous system, and other organs.(5,6) Although some *GLA* variants do not appear to cause disease, more than a thousand disease-causing *GLA* variants have been identified. The severity of symptoms may vary among individuals depending upon the specific *GLA* mutation within their family. In general, mutations that result in little to no alpha-Gal A activity cause the classic Fabry phenotype, and those mutations that result in residual alpha-Gal A activity cause the atypical later-onset phenotype.(4,5) The "classic" form of Fabry disease is the most severe clinical phenotype and occurs predominantly in males. These patients are characterized by absent or severely reduced alpha-Gal A activity, with childhood or adolescent onset of symptoms including severe neuropathic or limb pain, abdominal pain, telangiectasias and angiokeratomas, corneal opacities, renal involvement that may progress to end-stage renal disease (ESRD), and hearing loss, with cardiac and cerebrovascular involvement occurring by adulthood. The spectrum of disease severity in heterozygous female patients ranges from asymptomatic to a severe phenotype resembling the male "classic" phenotype and is, in part, dependent on the mutation and the X chromosome inactivation (Lyonization) profile. The prevalence of signs and symptoms at any given age is lower in females, though increasing age will result in development of cardiac and cerebrovascular involvement.(5,6) Fabry disease should be suspected in patients with a family history of Fabry disease or those who present with the clinical manifestations or laboratory abnormalities associated with the disease. The diagnosis is typically confirmed by biochemical and/or molecular genetic testing, with the latter approach being the final determinant.(5) An initial evaluation includes baseline documentation of renal function (e.g., proteinuria,

	glomerular filtration rate [GFR]), cardiac function (e.g., left ventricular hypertrophy, conduction defects, mitral and/or aortic valve abnormalities), ophthalmological signs (e.g., corneal verticillate, subcapsular cataracts, conjunctival and/or retinal vasculopathy), peripheral nerve symptoms (e.g., neuropathic pain, heat and/or cold intolerance, impaired sweat function), and gastrointestinal involvement (e.g., nausea, vomiting, abdominal pain, diarrhea, constipation).(5,6) After a thorough clinical evaluation, mutational analysis of the *GLA* gene is the gold-standard assay to confirm the diagnosis of Fabry disease in males and females. For male patients suspected of having Fabry disease, an initial measurement of alpha-Gal A activity (in leukocytes, plasma, fibroblasts, or dried blood spots [DBS]) may be performed. However, the alpha-Gal A activity assay is not definitive confirmation of Fabry disease, since the assay will identify less than 50% of female carriers. Additionally, for patients with residual alpha-Gal A activity on assay (3-35%), genetic testing for a pathogenic *GLA* gene will confirm the Fabry disease diagnosis, and establish the patient's amenability to treatment with chaperone therapy.(5) There is no cure for Fabry disease. Available Fabry-specific therapies include intravenous enzyme replacement therapy (ERT) and pharmacologic chaperone therapy. ERT with Fabrazyme (agalsidase beta) or Elfabrio (pegunigalsidase alfa) focuses on replacing the missing or deficient enzyme (alpha-Gal A). Galafold (migalastat, an oral capsule) is approved as first-line therapy in patients with amenable *GLA* gene variants.(4,6) Migalastat is a pharmacologic chaperone that binds to and stabilizes specific (amenable) mutant forms of alpha-Gal A, thereby facilitating proper trafficking of the enzyme to lysosomes. Once in the lysosome, migalastat dissociates from alpha-Gal A allowing it to then catabolize accumulated glycolipids.(1,4) Certain *GLA* mutations causing Fabry disease result in the production of abnormally folded and less stable forms of the alpha-Gal A protein which retain residual enzymatic activity. These *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.(1) A complete list of amenable variants is available in the Galafold prescribing information or a specific variant can be verified as amenable at http://www.galafoldamenabilitytable.com/hcp. Patients on ERT or migalastat should have a clinical evaluation every 6-12 months. Renal function, cardiac function, ophthalmological signs, peripheral nerve symptoms, and gastrointestinal involvement should all be assessed to monitor disease manifestations, disease severity, and/or side effects of therapy.(5)
Efficacy	Study AT1001-011 (NCT00925301) included a 6-month randomized, double-blind, placebo-controlled phase followed by a 6-month open-label treatment phase and a 12-month open-label extension phase. A total of 67 patients with Fabry disease who were naïve to migalastat and enzyme replacement therapy (ERT) or who were previously treated with ERT and had been off ERT for at least 6 months were randomized in a 1:1 ratio to receive migalastat every other day or placebo for the first 6 months. In the second 6 months, all patients were treated with migalastat. At 6 months, patients treated with migalastat had lower plasma globotriaosylceramide (GL-3, Gb3) levels compared with placebo. No changes in these parameters occurred in patients with non-amenable GLA mutations.(1) A second trial, 18-month, randomized, active-controlled, with 57 adults, compared migalastat with ERT in patients who were previously treated with ERT. Primary objective was to assess renal function and secondary endpoints of cardiovascular and patient-reported outcomes. At 18 months, migalastat and ERT had comparable effects on kidney function. Left ventricular mass index decreased from baseline in patients on migalastat but did not change significantly in those on ERT.(3)
Safety	Migalastat has no FDA labeled contraindications for use.(1)

REFERENCES

Number	Reference
1	Galafold prescribing information. Amicus Therapeutics US, Inc. October 2024.
2	Reference no longer used.
3	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 randomized phase III ATTRACT study. J Med Genet. 2017;54:288-296.
4	Germain DP, Nicholls K, Giugliani R, et al. Efficacy of the pharmacologic chaperone migalastat in a subset of male patients with the classic phenotype of Fabry disease and migalastat-amenable variants: Data from the phase 3 randomized, multicenter, double-blind clinical trial and extension study. Genet Med. 2019 Feb;21(9):1987-1997.
5	Ortiz A, Germain DP, Desnick RJ, et al. Fabry disease revisited: Management and treatment recommendations for adult patients. Mol Genet Metab. 2018 Apr;123(4):416-427.
6	Ganesh J, et al. Fabry Disease. National Organization for Rare Disorders (NORD): Rare Disease Database. 2019. Available at: https://rarediseases.org/rare-diseases/fabry-disease/.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Galafold	migalastat hcl cap	123 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Galafold	Migalastat HCl Cap 123 MG (Base Equivalent)	123 MG	14	Capsules	28	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Galafold	migalastat hcl cap	123 MG	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Galafold	Migalastat HCl Cap 123 MG (Base Equivalent)	123 MG	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** Galafold 1. The patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR** 2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR** B. BOTH of the following: 1. The patient has a diagnosis of Fabry disease AND BOTH of the following: A. The diagnosis was confirmed by mutation in the galactosidase alpha (*GLA*) gene **AND** B. The patient has a confirmed amenable *GLA* variant based on in vitro assay data (a complete list of amenable variants is available in the Galafold prescribing information, or a specific variant can be verified as amenable at http://www.galafoldamenabilitytable.com/hcp) **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist, geneticist, nephrologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 3. The patient will NOT be using the requested agent in combination with enzyme replacement therapy (ERT) (e.g., Elfabrio, Fabrazyme) for the requested indication **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 6 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist, geneticist, nephrologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient will NOT be using the requested agent in combination with enzyme replacement therapy (ERT) (e.g., Elfabrio, Fabrazyme) for the requested indication **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent

Module	Clinical Criteria for Approval
	Length of Approval: 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Universal QL	**Quantity limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following: A. BOTH of the following: 1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **OR** B. BOTH of the following: 1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 2. There is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **Length of Approval:** up to 12 months