Protocol for Fabry Disease Products
Approved January 2020

Fabrazyme® (agalsidase beta)
Galafold® (migalastat)

Background:
Fabry disease is a rare genetic disorder caused by mutations in the alpha-galactosidase A (GLA) gene located on the X-chromosome. It results from a buildup of fat called globotriaosylceramide (GL-3) in blood vessels, kidneys, the heart, the nerves, and other organs. Patients with Fabry disease can develop slowly progressive kidney disease, cardiac hypertrophy, arrhythmias, stroke and early death.

Fabrazyme *provides an exogenous source of alpha-galactosidase A, which is deficient in patients with Fabry disease. It catalyzes the hydrolysis of glycosphingolipids, including GL-3, which can accumulate in various body tissues of patients with Fabry disease.*

Galafold *is an alpha-galactosidase A (alpha-Gal A) "pharmacological chaperone" that reversibly binds to the active site of the alpha-galactosidase A protein (encoded by the GLA), which is deficient in Fabry disease.*

Criteria for approval:

1. Patient has a diagnosis of Fabry disease confirmed by **one** of the following:
   a. Documentation of complete deficiency or ≤ 5% of mean normal alpha-galactosidase A (α- GAL A) enzyme activity in leukocytes, dried blood spots, or serum (plasma) analysis; **OR**
   b. Documented galactosidase alpha mutation by gene sequencing; **AND**
2. Patient has one or more clinical/physical features associated with Fabry disease, such as:
   a. Intermittent episodes of burning pain in the extremities (acroparesthesias)
   b. Cutaneous vascular lesions (angiokeratomas)
   c. Diminished perspiration (hypo- or anhidrosis)
   d. Characteristic corneal and lenticular opacities
   e. Chronic kidney disease (CKD) and/or proteinuria of unknown etiology
3. Medication is prescribed by or in consultation with a specialist in genetic disorders

For Fabrazyme:
a. Patient is 8 years or older
b. Patient is not receiving Galafold

For Galafold:
a. Patient is an adult
b. Patient has an amenable galactosidase alpha gene (GLA) variant based on in vitro assay data
c. Patient does not have severe renal impairment or end-stage renal disease requiring dialysis
d. Patient is not receiving Fabrazyme

4. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, or national guidelines.

Initial Approval Duration: 6 months

Continuation of therapy:

1. There is a positive clinical response to therapy
2. Patient has been adherent with the medication
3. Routine lab tests to include ALL of the following:
   a. Complete Blood Count (CBC)
   b. Estimated glomerular filtration Rate (eGFR)
   c. Urinalysis, urinary protein-to-creatinine ration, or albumin-to-creatinine ratio
   d. Basic metabolic panel (BMP)

Renewal Approval Duration: 6 months

References:

1. Fabrazyme [package insert]. Genzyme Corporation. Cambridge, MA 02142. December 2018
2. Galafold [package insert]. Amicus Therapeutics U.S., Inc. Cranbury, NJ 08512. August 2018
3. R.J. Hopkin, et al., The management and treatment of children with Fabry disease: A United States-based perspective, Molecular Genetics and Metabolism. (2015), http://dx.doi.org/10.1016/j.ymgme.2015.10.007
4. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier 2016. Updated periodically
5. Biegstraaten M, Arngrímsson R, et al. Recommendations for initiation and cessation of enzyme replacement therapy in patients with Fabry disease: the European Fabry Working Group consensus document. Orphanet J Rare Dis. 2015 Mar 27;10:36. From: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4383065/pdf/13023_2015_Article_253.pdf Accessed: October 29, 2019.
6. Mauer, M., Kopp, J.,B., Schiffmann, R., Fabry Disease: Clinical features and diagnosis. (2019). UpToDate. In AQ Lam (Ed.), Retrieved from: https://www.uptodate.com/contents/fabry-disease-treatment-and-prognosis Accessed: October 29, 2019.