Blue Cross Blue Shield Blue Care Network of Michigan

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Effective Date: 06/06/2024

Enzyme Replacement Therapy for Fabry Disease

Elfabrio® (pegunigalsidase alfa-iwxj)
Fabrazyme® (agalsidase beta)

HCPCS: Fabrazyme: J0180; Elfabrio: J2508

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Prescribed by or in consultation with a geneticist or metabolic specialist
   d. Confirmation of diagnosis as follows:
      i. Males: Serum assay of enzyme α- galactosidase showing decreased activity followed by genetic testing showing a mutation in the GLA gene
      ii. Females: Genetic testing showing a mutation in the GLA gene
   e. Initiation of therapy should begin as follows:
      i. Males with classic disease: At time of diagnosis
      ii. Females and males with atypical disease: Once patient is showing symptoms of Fabry's disease
   f. Trial and failure, intolerance, or contraindication to Fabrazyme
   g. Must not be using in combination or with any other enzyme replacement therapy or molecular chaperone for Fabry's disease
   h. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list and/or BCBSM/BCN's prior authorization and step therapy documents

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: 1 year at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Fabry's disease (FD) is autosomal recessive lysosomal storage disorder caused by a mutation on the GLA gene. It is characterized by lysosomal accumulation of undegraded glycosphingolipid due to a deficiency or insufficient activity of the enzyme α-galactosidase. Phenotypes vary from the "classic" phenotype, with pediatric onset and multi-organ involvement, to later-onset, a predominantly cardiac phenotype. While it was once thought females were asymptomatic carriers, it is now known they can develop a variety of symptoms later in life than their homozygous male counterparts. The most common symptoms include hearing loss, myocardial microvascular ischemia, dysrhythmias, hypertrophic cardiomyopathy, valvular insufficiency, gastrointestinal symptoms, hypohidrosis, temperature and exercise intolerance, dysregulation of vascular tone and autonomic functions, obstructive lung disease, progressive renal insufficiency leading to kidney failure, and increased risk of cerebrovascular accidents and myocardial infarctions.

- The American College of Medical Genetics 2011 guidelines state Fabry's disease is confirmed differently for males and females. Males should first be tested for reduced α-galactosidase activity in peripheral leukocytes or skin fibroblasts. If the enzyme activity test comes back with decreased activity, disease is then verified though genetic testing that shows the patient has a mutation of the GLA gene. Enzyme activity does not often correlate to disease symptoms or severity in heterozygous females. Therefore, when confirming disease in female patients, enzyme activity testing can be waived and genetic testing completed as the initial and only required diagnostic component.

- Enzyme replacement is the standard of care in FD. Fabrazyme is approved for patients age 2 years and older with Fabry's disease. Elfabrio is approved for adult patients with confirmed Fabry disease.

- There are no uniform recommendations as to when enzyme replacement therapy (ERT) should be started. Typically, males who present with classic disease should be started on prophylactic ERT at time of diagnosis even if they are not presenting with symptoms. Classic disease has little to no enzyme activity on serum assay (< 1% of the normal mean) with symptoms presenting as listed above. For female carriers and males with atypical disease, ERT should be held until patients become symptomatic. There is no data showing benefit of prophylactic therapy in these patients and some will not develop any disease manifestations.

- Fabrazyme, Elfabrio, and Galafold®, a pharmacological chaperone, have not been studied in any combination and there is no clinical data to support better patient outcomes with use of any of the drugs at the same time.

References:

1. Fabrazyme [prescribing information]. Cambridge, MA: Genzyme Corporation; March 2023.
2. Elfabrio [prescribing information]. Cary, NC: Chiesi USA, Inc.; May 2023.
3. Galafold [prescribing information]. Cranbury, NJ: Amicus Therapeutics U.S., Inc.; June 2023.
4. Lidove O, West ML, Pintos-Morell G, et al. Effects of enzyme replacement therapy in Fabry disease – a comprehensive review of the medical literature. Genet in Med. 2010 Nov; 12 (11): 668 - 79.
5. Wang RW, Bodamer OA, Watson MS, et al. Lysosomal storage diseases: diagnostic confirmation and management of presymptomatic individuals. Genetic Med. 2011 May; 13 (3): 457 – 84.
6. Laney DA, Bennett RL, Clarke V, et al. Fabry disease practice guidelines: recommendations of the national society of genetic counselors. J Gene Couns. 2013 Oct; 22 (5): 555 – 64.
7. Ortiz A, Germain DP, Desnick RJ, et al. Fabry disease revisited: management and treatment recommendations for adult patients. Molecular Gene Met. 2018 April; 123 (4): 416 – 27.
8. Hopkins RJ, Jefferies JL, Laney DA, et al. The management and treatment of children with fabry disease: a united states-based perspective. Molecular Gene Met. 2016 Feb; 117 (2): 104 – 13.
9. Eng CM, Germain DP, Banikazemi M, et al. Fabry disease: guidelines for the evaluation and management of multi-organ system involvement. Genet Med. 2006 Sept; 8 (9): 539 - 48.
10. Biegstraaten M, Arngrímsson R, Barbey F, at 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 - 46.
11. Wanner C, Arad M, Baron R, at al. European expert consensus statement on therapeutic goals in Fabry disease. Mole Gene Met. 2018 July; 124 (3): 189 – 203.

Policy History		
#	Date	Change Description
1.8	Effective Date: 06/06/2024	Annual review – no changes to the criteria at this time
1.7	Effective Date: 08/14/2023	UM medical management system update for BCNA and MAPPO for Elfabrio
1.6	Effective Date: 06/08/2023	Updated to include Elfabrio and changed the name from Fabrazyme to Enzyme Replacement Therapy for Fabry Disease UM medical management system update for BCN and BCBS for Elfabrio
1.5	Effective Date: 10/06/2022	Annual review – no changes to the criteria at this time
1.4	Effective Date: 10/07/2021	Annual review of policy. No changes were made to the criteria
1.3	Effective Date: 10/08/2020	New policy created for this disease state and class of drugs. The Enzyme Replacement Therapy policy will be retired
1.2	Effective Date: 07/05/2017	UM medical management system update for MAPPO and BCNA for Fabrazyme
1.1	Effective Date: 02/01/2015	UM medical management system update for BCN for Fabrazyme
1.0	Effective Date: 01/01/2015	UM medical management system update for BCBS for Fabrazyme

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*