UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Enzyme Replacement Therapy – Elfabrio Utilization Management Medical Policy
- Elfabrio® (pegunigalsidase alfa intravenous infusion – Chiesi)

REVIEW DATE: 07/15/2026

OVERVIEW

Elfabrio, a PEGylated, crosslinked, chemically modified human alpha-galactosidase A (α -Gal A) enzyme, is indicated for the treatment of **Fabry disease** in adults.[1] The amino acid sequence of one subunit of Elfabrio consists of 405 amino acids, of which 398 amino acids are identical to human alpha-galactosidase A. Elfabrio catalyzes the breakdown of globotriaosylceramide (GL-3) and other α-galactyl-terminated neutral glycosphingolipids to ceramide and galactose and reduces the deposition of GL-3 in the capillary endothelium of the kidney and certain other cell types.

Disease Overview

Fabry disease is a rare inherited X-linked lysosomal storage disorder due to absent or significantly reduced α-Gal activity leading to the accumulation of GL-3 in a wide variety of cells throughout the body.[2-4] The accumulation of GL-3 leads to progressive multisystem disease, primarily impacting the kidney, heart, and nervous system.[3,4] Fabry disease can be divided into two phenotypes. A severe, classical phenotype that more commonly occurs in men without α-Gal activity, whereas a generally milder non-classical (late-onset) phenotype is found in men and women with some residual α-Gal activity.[2,3] Fabry disease is estimated to affect approximately 1 in 40,000 males and approximately 1 in 20,000 females. However, data from newborn screening programs suggest that the incidence of Fabry disease is generally underestimated and may equate to 1 per 3,100 live births, with late-onset phenotypes being more prevalent.[5] The diagnosis of Fabry disease can be confirmed in males by demonstrating a deficiency in α-Gal activity, and in all patients by identifying a Fabry disease-causing gene variant.[4] Long-term consequences of Fabry disease include hypertrophic cardiomyopathy, arrhythmias, renal failure, and stroke.[3] The kidney disease that occurs in Fabry disease is associated with progressive proteinuria and a decline in glomerular filtration rate, which over time, leads to end-stage renal disease requiring dialysis and ultimately, kidney transplantation.[2] Treatment with Elfabrio reduces the accumulation of GL-3 in the kidneys (and in other organs), with the goal of stopping or slowing the decline in kidney function.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Elfabrio. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Elfabrio as well as the monitoring required for adverse events and long-term efficacy, approval requires Elfabrio to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

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RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Elfabrio is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. **Fabry Disease.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** The patient is ≥ 18 years of age; AND
   - **B)** The diagnosis is established by ONE of the following (i or ii):
     - **i.** Patient has a laboratory test demonstrating deficient α-galactosidase A activity in leukocytes or fibroblasts; OR
     - **ii.** Patient has a molecular genetic test demonstrating a pathogenic variant in the galactosidase alpha *(GLA)* gene; AND
   - **C)** The medication is prescribed by or in consultation with a geneticist, endocrinologist, nephrologist, a metabolic disorder sub-specialist, or a physician who specializes in the treatment of lysosomal storage disorders.

   Dosing. Each dose must not exceed 1 mg/kg administered intravenously no more frequently than once every 2 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Elfabrio is not recommended in the following situations:

1. **Concurrent Use with Galafold (migalastat oral capsules).** Galafold has not been evaluated for use in combination with Elfabrio. It is not FDA approved for concurrent use with enzyme replacement therapy.

2. **Concurrent Use with Fabrazyme (agalsidase beta intravenous infusion).**

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Elfabrio® intravenous infusion [prescribing information]. Parma, Italy: Chiesi; May 2024.
2. Schiffmann R. Fabry Disease. *Handb Clin Neurol*. 2015;132:231-248.
3. Arends M, Wanner C, Hughes D, et al. Characterization of Classical and Nonclassical Fabry Disease: A Multinational Study. *J Am Soc Nephrol*. 2017;28:1631-1641.
4. Laney DA, Bennett RL, Clarke V, et al. Fabry Disease Practice Guidelines: Recommendations of the National Society of Genetic Counselors. *J Genet Counsel*. 2013;22:555-564.
5. Spada M, Pagliardini S, Yasuda M, et al. High incidence of later-onset Fabry disease revealed by newborn screening. *Am J Hum Genet*. 2006 Jul;79(1):31-40.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Fabry Disease**: For diagnosis confirmed by genetic testing, the term "mutation" was rephrased to "pathogenic variant."	07/03/2024
Annual Revision	No criteria changes.	07/02/2025
Annual Revision	**Fabry Disease**: Nephrologist was added amongst the specialists that can prescribe Elfabrio.	07/15/2026

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