



Drug Coverage Policy

Effective Date.....9/1/2025

Coverage Policy Number IP0570

Policy Title.....Elfabrio

Enzyme Replacement Therapy – Elfabrio

- Elfabrio® (pegunigalsidase alfa intravenous infusion – Chiesi)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

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 mutation.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 kidney (and in other organs), with the goal of stopping or slowing the decline in kidney function.

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for benefit coverage of Elfabrio. 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.

Elfabrio is considered medically necessary when the following are met:

FDA-Approved Indication

- 1. Fabry Disease.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
 - A)** The patient is $\geq$ 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)** Elfabrio is prescribed by or in consultation with a geneticist, endocrinologist, a metabolic disorder sub-specialist, or a physician who specializes in the treatment of lysosomal storage disorders.

Conditions Not Covered

Elfabrio for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

- 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).**

Coding Information

- 1) This list of codes may not be all-inclusive.
- 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPSC Codes	Description
J2508	Injection, pegunigalsidase alfa-iwxj, 1 mg

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.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	Update coverage policy title from <i>Pegunigalsidase Alfa</i> to <i>Enzyme Replacement Therapy – Elfabrio</i> . Removed the language <i>hemizygous</i> from criterion B.ii (term that describes having two identical versions of the same gene).	9/1/2024
Annual Revision	No criteria changes.	9/1/2025

The policy effective date is in force until updated or retired.

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