Effective Date **3/1/2024**
Next Review Date… **3/1/2025**
Coverage Policy Number **IP0570**

Pegunigalsidase Alfa

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Related Coverage Resources

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. 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

This policy supports medical necessity review for pegunigalsidase alfa intravenous infusion (**Elfabrio®**).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Pegunigalsidase alfa (Elfabrio) is considered medically necessary when the following are met:

Fabry Disease. Individual meets **ALL** of the following criteria:
- A. Age 18 years or older
- B. The diagnosis of Fabry disease is confirmed by documentation of **ONE** of the following:
  - i. Laboratory test demonstrating deficient α-galactosidase A activity in leukocytes or fibroblasts

ii. Molecular genetic test demonstrating a hemizygous pathogenic variant in the galactosidase alpha (*GLA*) gene

C. Medication 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

Dosing. Up to 1 mg/kg administered intravenously no more frequently than once every 2 weeks.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of pegunigalsidase alfa (Elfabrio) is considered medically necessary for the treatment of Fabry Disease when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

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:

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs
J3590	Unclassified biologics

Background

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.

References

1. Elfabrio® intravenous infusion [prescribing information]. Parma, Italy: Chiesi; May 2023.
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, Tukel T, Thiagarajan G, Sakuraba H, Ponzone A, Desnick RJ. 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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