Enzyme Replacement Therapy (ERT) for Fabry Disease:
Fabrazyme® (agalsidase beta), Elfabrio® (pegunigalsidase alfa-iwxj) (Intravenous)

Effective Date: 01/01/2021
Review Date: 12/21/2020, 04/22/2021, 02/24/2022, 1/19/2023, 1/1/2024, 2/14/2024, 65/41/2025

Scope: Medicaid, Commercial, Medicare

I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Max Units (per dose and over time) [HCPCS Unit]:

- Fabrazyme
  - 115 billable units every 14 days
- Elfabrio
  - 120 billable units every 14 days

III. Summary of Evidence

Fabrazyme (agalsidase) beta is indicated for the treatment of patients with confirmed Fabry disease, a rare lysosomal storage disorder caused by a-galactosidase A deficiency. In the pivotal 20-week, randomized, placebo-controlled study 1, 69% of patients treated with Fabrazyme achieved complete clearance of FL-3 inclusions from renal capillary endothelium compared to 0% in the placebo group ($p<0.001$). Additional reductions were seen in cardiac and skin tissue. In Study 2, a longer-term placebo-controlled trial of 82 Fabry patients, Fabrazyme treatment was associated with a lower incidence of clinically significant events (28%) compared to placebo (42%), with a hazard ratio of 0.57. In pediatric patients (Study 3), all 14 male participants achieved normalized plasma GL-3 by Week 24, and histological analysis confirmed clearance of GL-3 from skin capillary endothelium. Adverse events occurred primarily during infusions and included chills, fever, headache, paresthesia, rash, and nausea. Anaphylaxis and severe infusion reactions have been reported.

Elfabrio (pegunisgalsidase alfa-iwxj) is approved for the treatment of adult patients with confirmed Fabry disease, a lysosomal storage disorder caused by deficient alpha-galactosidase A activity. In Trial 1, a 52-week open-label study of 18 ERT-naïve or ERT-discontinued patients, Elfabrio 1 mg/kg IV every two weeks significantly reduced renal globotriaosylceramide (Gb3) accumulation. Among the 14 patients with evaluable biopsies, the mean reduction in Gb3 peritubular capillary inclusions (BLISS score) was a -3.1, including -4/7 in males and -1.0 in females. Trail 2 was a 104-week randomized, double-blind, active-controlled trial comparing Elfabrio to agalsidase beta in 77 ERT-experienced in patients. The primary endpoint was the annualized change in estimated glomerular filtration rate (eGFr). Elfabrio produced a mean eGFR slope of -2.4 mL/min/1.3m^2/year compared to -2.3

mL/min/1.73m^2/year with agalsidase beta, indicated comparable renal function stabilization. The most common adverse reactions (≥ 15%) reported in Trial were infusion-associated reactions (32%), nasopharyngitis (21%), headache (21%), diarrhea (195), fatigue (17%), and nausea (17%). Severe hypersensitivity reactions occurred in 3% of patients, particularly in those with pre-existing anti-drug antibodies (ADA).

IV. Initial Approval Criteria

Coverage is provided in the following conditions:

Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

- Member is at least 2 years of age if request is for Fabrazyme, OR member is at least 18 years of age if request is for Elfabrio; **AND**

Universal Criteria

- Medication is prescribed by or in consultation with a medical geneticist, nephrologist, or other physician who specializes in the treatment of Fabry disease; **AND**
- Must not be used in combination with migalastat or another ERT (i.e. Fabrazyme or Elfabrio); **AND**

Fabry Disease (alpha-galactosidase A deficiency) †

- Documented diagnosis of Fabry disease with biochemical/genetic confirmation by one of the following:
    - α-galactosidase A (α-Gal A) activity in plasma, isolated leukocytes, and/or cultured cells (males only); **OR**
    - Detection of pathogenic mutations in the *GLA* gene by molecular genetic testing; **AND**
- Patient has a baseline of one or more of the following:
    - Tissue globotriaosylceramide (Gb3/GL-3) inclusions
    - Plasma or urinary globotriaosylceramide (Gb_3/GL-3); or plasma globotriaosylsphingosine (lyso-Gb_3)
    - Clinical signs and/or symptoms of disease (e.g., dermatologic, gastrointestinal, pulmonary, vascular, renal, cardiac, neurologic manifestations); **AND**
- Member has had an inadequate response, intolerance or contraindication to Galafold (migalastat)*

***This only applies to Medicaid and Commercial Members**

† FDA approved indication(s)

V. Renewal Criteria [1]

Coverage can be renewed based on the following criteria:

- Member continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section IV; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: anaphylaxis and severe hypersensitivity reactions, severe infusion-associated reactions, glomerulonephritis, etc.; **AND**
    - Disease response with treatment as defined by a reduction or stabilization in one or more of the following, as compared to pre-treatment baseline:
        - Tissue GL-3 and/or GL-3 inclusions
        - plasma or urinary globotriaosylceramide (Gb_3/GL-3) or plasma globotriaosylsphingosine (lyso-Gb_3); **OR**
    - For Elfabrio requests, disease response with treatment as defined by an improvement or stabilization in the rate of decline of the estimated glomerular filtration rate (eGFR); OR
    - For Fabrazyme requests, disease response with treatment as defined by an improvement or stabilization of clinical signs and/or symptoms (e.g., dermatologic, gastrointestinal, pulmonary, vascular, renal, cardiac, neurologic manifestations)

VI. Dosage/Administration

Indication	Drug	Dose
Fabry Disease	Fabrazyme or Elfabrio	1 mg/kg of body weight infused every two weeks as an intravenous (IV) infusion.

VII. Billing Code/Availability Information

HCPCS code:

- J0180 – Injection, agalsidase beta, 1 mg; 1 billable unit = 1 mg
- J2508- Injection, pegunigalsidase alfa-iwxj, 1 mg; 1 billable unit= 1 mg

NDC:

- Fabrazyme 5 mg single-use vial for injection: 58468-0041-xx
- Fabrazyme 35 mg single-use vial for injection: 58468-0040-xx
- Elfabrio 20 mg/10 mL single-use vial for injection: 10122-0160-xx

VIII. References

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E75.21	Fabry (-Anderson) disease

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:

Enzyme Replacement Therapy for Fabry Disease: Fabrazyme and Elfabrio was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Enzyme Replacement Therapy for Fabry Disease: Fabrazyme and Elfabrio according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.