Medical Therapies for Enzyme Deficiencies (for Louisiana Only)
Retired April 1, 2026

Policy Number: CSLA2025D0052Y
Effective Date: October 1, 2025 – March 31, 2026

➲ Instructions for Use

Table of Contents **Page**

Application

This Medical Benefit Drug Policy only applies to the state of Louisiana.

Coverage Rationale

This policy refers to the following medical therapies for enzyme deficiency products:

- Aldurazyme® (laronidase)
- Elaprase® (idursulfase)
- Elfabrio® (pegunigalsidase alfa-iwxj)
- Fabrazyme® (agalsidase beta)
- Kanuma® (sebelipase alfa)
- Lamzede® (velmanase alfa-tycv)
- Lumizyme® (alglucosidase alfa)
- Mepsevii™ (vestronidase alfa-vjbk)
- Naglazyme® (galsulfase)
- Nexviazyme™ (avalglucosidase alfa-ngpt)
- Nulibry® (fosdenopterin)
- Pombiliti™ (cipaglucosidase alfa-atga)
- Revcovi™ (elapegademase-lvlr)
- Vimizim® (elosulfase alfa)
- Xenpozyme™ (olipudase alfa-rpcp)

Coverage for Aldurazyme, Elaprase, Mepsevii, Naglazyme, Nulibry, and Vimizim is contingent on state Medicaid clinical coverage criteria. Refer to the Louisiana Medicaid Preferred Drug List (PDL) / Non-Preferred Drug List (NPDL).

Coverage for Elfabrio, Fabrazyme, Kanuma, Lamzede, Lumizyme, Nexviazyme, Pombiliti, Revcovi, and Xenpozyme is contingent on criteria in the Drug-Specific Criteria section below.

Drug-Specific Criteria

Elfabrio® (pegunigalsidase alfa-iwxj) is proven for the treatment of adults with confirmed Fabry disease. Elfabrio is medically necessary when the following additional criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of Fabry disease as confirmed by **one** the following:
    - Absence or deficiency (< 5% of mean) of normal alpha-galactosidase A (α-Gal A) enzyme activity in leukocytes, dried blood spots, or serum analysis; **or**
    - Molecular genetic testing for deletion or mutations in the galactosidase alpha gene

    and
  - Presence of clinical signs and symptoms of the disease (e.g., acroparesthesias, angiokeratomas, whorls, anhidrosis/hypohidrosis, renal disease, exercise/heat/cold intolerance, etc.); **and**
  - Patient is **not** receiving Elfabrio in combination with another disease-modifying therapy used for the treatment of Fabry disease [e.g., Fabrazyme (agalsidase beta), Galafold (migalastat)]; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Patient has previously received treatment with pegunigalsidase alfa-iwxj therapy; **and**
  - Patient has experienced a positive clinical response to pegunigalsidase alfa-iwxj therapy (e.g., improved renal function, reduction in mean plasma GL-3 levels, decreased GL-3 inclusions, etc.); **and**
  - Patient is **not** receiving Elfabrio in combination with another disease-modifying therapy used for the treatment of Fabry disease [e.g., Fabrazyme (agalsidase beta), Galafold (migalastat)]; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Reauthorization will be for no more than 12 months

Fabrazyme (agalsidase beta) is medically necessary for the treatment of Fabry disease when the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of Fabry disease as confirmed by **one** the following:
    - Absence or deficiency (< 5% of mean) of normal alpha-galactosidase A (α-Gal A) enzyme activity in leukocytes, dried blood spots, or serum analysis; **or**
    - Molecular genetic testing for deletion or mutations in the galactosidase alpha gene

    and
  - Presence of clinical signs and symptoms of the disease (e.g., acroparesthesias, angiokeratomas, whorls, anhidrosis/hypohidrosis, renal disease, exercise/heat/cold intolerance, etc.); **and**
  - Patient is **not** receiving Fabrazyme in combination with another disease-modifying therapy used for the treatment of Fabry disease [e.g., Elfabrio (pegunigalsidase alfa-iwxj), Galafold (migalastat)]; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Patient has previously received treatment with agalsidase therapy; **and**
  - Patient has experienced a positive clinical response to agalsidase therapy (e.g., improved renal function, reduction in mean plasma GL-3 levels, decreased GL-3 inclusions, etc.); **and**
  - Patient is **not** receiving Fabrazyme in combination with another disease-modifying therapy used for the treatment of Fabry disease [e.g., Elfabrio (pegunigalsidase alfa-iwxj), Galafold (migalastat)]; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Reauthorization will be for no more than 12 months

Kanuma (sebelipase alfa) is medically necessary for the treatment of lysosomal acid lipase deficiency [LAL-D, Wolman disease (WD), cholesteryl ester disease (CESD)] when the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of lysosomal acid lipase deficiency [LAL-D, Wolman disease (WD), cholesteryl ester disease (CESD)] as confirmed by one the following:
    - Absence or deficiency lysosomal acid lipase activity by dried blood spot test; **or**
    - Molecular genetic testing for deletion or mutations in the lipase A, lysosomal acid type (LIPA) gene

    and
  - Presence of clinical signs and symptoms of the disease (e.g., abdominal distention, hepatosplenomegaly, liver fibrosis, ascites, etc.); **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization will be for no more than 12 months

- For **continuation of therapy**, **all** of the following:
  - Patient has previously received treatment with sebelipase therapy; **and**
  - Patient has experienced a positive clinical response to sebelipase therapy [e.g., improved disease symptoms, improvement of laboratory values (LFTs, cholesterol, triglycerides), etc.]; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Reauthorization will be for no more than 12 months

Lamzede (velmanase alfa-tycv) is proven and medically necessary for the treatment of alpha-mannosidosis when the following additional criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of alpha-mannosidosis confirmed by **one** of the following:
    - Absence or deficiency (< 10% of the lab specific normal mean) of alpha-Mannosidase enzyme activity; **or**
    - Molecular genetic testing for mutations in the MAN2B1 gene

    and
  - Presence of clinical signs and symptoms of the disease (e.g., hepatosplenomegaly, skeletal abnormalities, ataxia, intellectual disability, hearing loss); **and**
  - Lamzede (velmanase alfa-tycv) is not being used to treat central nervous system (CNS) manifestations of alpha-mannosidosis; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Patient has previously received treatment with Lamzede (velmanase alfa-tycv) therapy; **and**
  - Patient has experienced a positive clinical response to Lamzede (velmanase alfa-tycv) therapy (e.g., improved motor function, improved pulmonary function); **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Reauthorization will be for no more than 12 months

Lumizyme (alglucosidase alfa) is medically necessary for the treatment of Pompe disease when the following criteria are met:

- For **initial therapy**, **one** of the following:
  - **All** of the following for infantile-onset Pompe disease:
    - Diagnosis of infantile-onset Pompe disease as confirmed by **one** the following:
      - Absence or deficiency (< 1% of the lab specific normal mean) acid alpha-glucosidase deficiency (GAA) activity in skin fibroblasts; **or**
      - Molecular genetic testing for deletion or mutations in the GAA gene

      and
    - Presence of clinical signs and symptoms of the disease (e.g., cardiac hypertrophy, respiratory distress, skeletal muscle weakness, etc.); **and**
    - Patient is **not** receiving Lumizyme in combination with another disease-modifying enzyme therapy used for the treatment of Pompe disease [e.g., Nexviazyme (avalglucosidase alfa-ngpt), Pombiliti (cipaglucosidase alfa-atga)]; **and**
    - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
    - Initial authorization will be for no more than 12 months

    or
  - **All** of the following for late-onset (non-infantile) Pompe disease:
    - Diagnosis of late-onset Pompe disease as confirmed by **one** the following:
      - Absence or deficiency (< 40% of the lab specific normal mean) acid alpha-glucosidase deficiency (GAA) activity in lymphocytes, fibroblasts, or muscle; **or**
      - Molecular genetic testing for deletion or mutations in the GAA gene

      and
    - Presence of clinical signs and symptoms of the disease (e.g., cardiac hypertrophy, respiratory distress, skeletal muscle weakness, etc.); **and**
    - Patient is **not** receiving Lumizyme in combination with another disease-modifying enzyme therapy used for the treatment of Pompe disease [e.g., Nexviazyme (avalglucosidase alfa-ngpt), Pombiliti (cipaglucosidase alfa-atga)]; **and**
    - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
    - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Patient has previously received treatment with alglucosidase therapy; **and**

- Patient has experienced a positive clinical response to alglucosidase therapy (e.g., improved respiratory/cardiac function, improved endurance, etc.); **and**
- Patient is **not** receiving Lumizyme in combination with another disease-modifying enzyme therapy used for the treatment of Pompe disease [e.g., Nexviazyme (avalglucosidase alfa-ngpt), Pombiliti (cipaglucosidase alfa-atga)]; **and**
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Reauthorization will be for no more than 12 months

Nexviazyme (avalglucosidase alfa-ngpt) is medically necessary for the treatment of late-onset Pompe disease when the following additional criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of late-onset Pompe disease as confirmed by one the following:
    - Absence or deficiency (< 40% of the lab specific normal mean) acid alpha-glucosidase deficiency (GAA) activity in lymphocytes, fibroblasts, or muscle; **or**
    - Molecular genetic testing for deletion or mutations in the GAA gene

    and
  - Presence of clinical signs and symptoms of the disease (e.g., cardiac hypertrophy, respiratory distress, skeletal muscle weakness, etc.); **and**
  - Patient is **not** receiving Nexviazyme in combination with another disease-modifying enzyme therapy used for the treatment of Pompe disease [e.g., Lumizyme (alglucosidase alfa), Pombiliti (cipaglucosidase alfa-atga)]; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Patient has previously received treatment with avalglucosidase alfa-ngpt therapy; **and**
  - Patient has experienced a positive clinical response to avalglucosidase alfa-ngpt therapy (e.g., improved respiratory/cardiac function, improved endurance, etc.); **and**
  - Patient is **not** receiving Nexviazyme in combination with another disease-modifying enzyme therapy used for the treatment of Pompe disease [e.g., Lumizyme (alglucosidase alfa), Pombiliti (cipaglucosidase alfa-atga)]; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Reauthorization will be for no more than 12 months

Pombiliti (cipaglucosidase alfa-atga) is proven for the treatment of late-onset Pompe disease. Pombiliti is medically necessary when the following additional criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of late-onset Pompe disease as confirmed by **one** of the following:
    - Absence or deficiency (< 40% of the lab specific normal mean) acid alpha-glucosidase deficiency (GAA) activity in lymphocytes, fibroblasts, or muscle; **or**
    - Molecular genetic testing for deletion or mutations in the GAA gene

    and
  - Presence of clinical signs and symptoms of the disease (e.g., cardiac hypertrophy, respiratory distress, skeletal muscle weakness, etc.); **and**
  - Provider attests that the patient is not improving on their current enzyme replacement therapy (ERT) (e.g., Lumizyme, Nexviazyme) for the treatment of late-onset Pompe disease and this therapy will be stopped; **and**
  - Patient weighs ≥ 40kg; **and**
  - Prescribed in combination with oral Opfolda (miglustat); **and**
  - Patient is **not** receiving Pombiliti in combination with another disease-modifying enzyme therapy used for the treatment of Pompe disease [e.g., Lumizyme (alglucosidase alfa), Nexviazyme (avalglucosidase alfa-ngpt)]; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Patient has previously received treatment with Pombiliti therapy; **and**
  - Patient has experienced a positive clinical response to Pombiliti plus Opfolda therapy (e.g., improved respiratory/cardiac function, improved endurance, etc.); **and**
  - Continues to be prescribed in combination with Opfolda (miglustat); **and**
  - Patient is **not** receiving Pombiliti in combination with another disease-modifying enzyme therapy used for the treatment of Pompe disease [e.g., Lumizyme (alglucosidase alfa), Nexviazyme (avalglucosidase alfa-ngpt)]; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Reauthorization will be for no more than 12 months

Revcovi (elapegademase-lvlr) is medically necessary for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) when the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of ADA-SCID; **and**
  - Deficiency of adenosine deaminase is confirmed by **one** of the following:
    - Deficiency or absence of ADA in plasma, lysed erythrocytes, fibroblasts (cultured from amniotic fluid), or chorionic villus; **or**
    - Increase in deoxyadenosine triphosphate (dATP) levels in erythrocyte lysates compared to laboratory standard; **or**
    - Decrease in ATP concentration in erythrocytes; **or**
    - Molecular genetic confirmation of mutations in both alleles of the ADA1 gene; **or**
    - Positive screening by T cell receptor excision circles (TRECs)

    and
  - **One** of the following:
    - Patient is not a suitable candidate for hematopoietic cell transplantation (HCT); **or**
    - Patient has failed HCT; **or**
    - Patient is awaiting HCT

    and
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Patient has previously received treatment with elapegademase therapy; **and**
  - Patient has experienced a positive clinical response to elapegademase therapy (e.g., normalization of plasma ADA activity, erythrocyte dATP levels, improvement of disease symptoms, etc.); **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Reauthorization will be for no more than 12 months

Xenpozyme (olipudase alfa-rpcp) is medically necessary for the treatment of acid sphingomyelinase deficiency (ASMD) when all of the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of acid sphingomyelinase deficiency (ASMD) type A/B or B confirmed by **one** of the following:
    - Absence or deficiency of acid sphingomyelinase (ASM) enzyme activity; **or**
    - Molecular genetic testing for mutations in the SMPD1 gene

    and
  - Presence of clinical signs and symptoms of the disease (e.g., hepatosplenomegaly, elevated transaminases, mixed dyslipidemia, abnormal pulmonary function); **and**
  - Xenpozyme is not being used to treat central nervous system (CNS) manifestations of ASMD; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Patient has previously received treatment with olipudase alfa therapy; **and**
  - Patient has experienced a positive clinical response to olipudase alfa therapy (e.g., reduced spleen volume, reduced liver volume, improved liver transaminase levels, improved lipid profile, improved pulmonary function); **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Reauthorization will be for no more than 12 months

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

Elfabrio

HCPCS Code	Description
J2508	Injection, pegunigalsidase alfa-iwxj, 1 mg

Diagnosis Code	Description
E75.21	Fabry (-Anderson) disease

Fabrazyme

HCPCS Code	Description
J0180	Injection, agalsidase beta, 1 mg

Diagnosis Code	Description
E75.21	Fabry (-Anderson) disease

Kanuma

HCPCS Code	Description
J2840	Injection, sebelipase alfa, 1 mg

Diagnosis Code	Description
E75.5	Other lipid storage disorders

Lamzede

HCPCS Code	Description
J0217	Injection, velmanase alfa-tycv, 1 mg

Diagnosis Code	Description
E77.1	Defects in glycoprotein degradation

Lumizyme

HCPCS Code	Description
J0221	Injection, alglucosidase alfa, (Lumizyme), 10 mg

Diagnosis Code	Description
E74.02	Pompe disease

Nexviazyme

HCPCS Code	Description
J0219	Injection, avalglucosidase alfa-ngpt, 4 mg

Diagnosis Code	Description
E74.02	Pompe disease

Pombiliti

HCPCS Code	Description
J1203	Injection, cipaglucosidase alfa-atga, 5 mg

Diagnosis Code	Description
E74.02	Pompe disease

Revcovi

HCPCS Code	Description
J3590	Unclassified biologic

Diagnosis Code	Description
D81.31	Severe combined immunodeficiency due to adenosine deaminase deficiency

Xenpozyme

HCPCS Code	Description
J0218	Injection, olipudase alfa-rpcp, 1 mg

Diagnosis Code	Description
E75.241	Niemann-Pick disease type B; also applicable to ASMD type B & Chronic visceral acid sphingomyelinase deficiency
E75.244	Niemann-Pick disease type A/B; ASMD type A/B & Chronic neurovisceral acid sphingomyelinase deficiency

Background

Elfabrio (pegunigalsidase alfa-iwxj) **and Fabrazyme** (agalsidase beta) are a recombinant human α-galactosidase A enzymes. Fabry disease is caused by a deficiency of α-galactosidase A, a lyposomal enzyme that catalyzes the hydrolysis of globotriaosylceramide (GL-3) and other α-galactyl-terminated neutral glycosphingolipids, Elfabrio and Fabrazyme are intended to provide an exogenous source of α-galactosidase A and reduce accumulated Gb3 in Fabry disease patients.[11,35]

Kanuma (sebelipase alfa) is a recombinant human lysosomal acid lipase (rhLAL). Lysosomal acid lipase is a lysosomal glycoprotein enzyme that catalyzes the hydrolysis of cholesteryl esters to free cholesterol and fatty acids and the hydrolysis of triglycerides to glycerol and free fatty acids. Sebelipase alfa binds to cell surface receptors via glycans expressed on the protein and is subsequently internalized into lysosomes. Sebelipase alfa catalyzes the lysosomal hydrolysis of cholesteryl esters and triglycerides to free cholesterol, glycerol, and free fatty acids.[12]

Lamzede (velmanase alfa-tycv) is recombinant human lysosomal alpha-mannosidase. Velmanase alfa-tycv is produced by recombinant DNA technology in Chinese Hamster Ovary (CHO) cells. The amino acid sequence of the monomeric protein is identical to the naturally occurring human enzyme, alpha-mannosidase. Velmanase alfa-tycv has an approximate molecular weight of 130 kDa. Alpha-mannosidase catalyzes the degradation of accumulated mannose-containing oligosaccharides. The deficiency of alpha-mannosidase causes an intra-lysosomal accumulation of mannose-rich oligosaccharides in various tissues. Velmanase alfa-tycv provides an exogenous source of alphamannosidase. Velmanase alfa-tycv is internalized via binding to the mannose-6-phosphate receptor on the cell surface and transported into lysosomes where it is thought to exert enzyme activity.[33]

Lumizyme (alglucosidase alfa) is a hydrolytic lysosomal glycogen-specific enzyme encoded by the predominant of nine observed haplotypes of the human acid α-glucosidase (GAA) gene. Alglucosidase alfa is produced by recombinant DNA technology in a Chinese hamster ovary cell line. Alglucosidase alfa degrades glycogen by catalyzing the hydrolysis of α-1,4- and α-1,6- glycosidic linkages of lysosomal glycogen. Alglucosidase alfa provides an exogenous source of GAA. Binding to mannose-6-phosphate receptors on the cell surface has been shown to occur via carbohydrate groups on the GAA molecule, after which it is internalized and transported into lysosomes, where it undergoes proteolytic cleavage that results in increased enzymatic activity. It then exerts enzymatic activity in cleaving glycogen.[13]

Nexviazyme (avalglucosidase alfa-ngpt) is a recombinant hydrolytic lysosomal glycogen-specific human α-glucosidase enzyme that is conjugated with multiple synthetic bis-mannose-6-phosphate (M6P) and is produced in Chinese hamster ovary cells. M6P on avalglucosidase alfa-ngpt mediates the binding to M6P receptors on the cell surface that is then internalized and transported into lysosomes. It then undergoes proteolytic cleavage resulting in increased GAA enzymatic activity. This allows for avalglucosidase alfa-ngpt to exert enzymatic activity, thereby cleaving glycogen.

Pombiliti (cipaglucosidase alfa-atga) is a hydrolytic lysosomal glycogen-specific recombinant human α-glucosidase (rhGAA) enzyme derived from a Chinese Hamster Ovary (CHO) cell line using perfusion methodology, resulting in cellularly (CHO)-derived N-glycans. Cipaglucosidase alfa-atga provides an exogenous source of GAA. The bis-M6P on cipaglucosidase alfa-atga mediates binding to M6P receptors on the cell surface with high affinity. After binding, it is internalized and transported into lysosomes where it undergoes proteolytic cleavage and N-glycans trimming which are both required to yield the most mature and active form of GAA. Cipaglucosidase alfa-atga then exerts enzymatic activity in cleaving glycogen. Miglustat binds with, stabilizes, and reduces inactivation of cipaglucosidase alfa-atga in the blood after infusion.

Revcovi (elapegademase-lvlr) is a recombinant adenosine deaminase (rADA) based on bovine amino acid sequence, conjugated to monomethoxypolyethylene glycol (mPEG). rADA is manufactured in E.coli and is covalently conjugated to

mPEG with a succinimidyl carbamate linker to produce methoxypolyethylene glycol recombinant adenosine deaminase (SC-PEG rADA). The approximate molecular weight of elapegademase-lvlr (SC-PEG rADA) is 113 KDa.[24]

Vimizim (elosulfase alfa) is a purified human enzyme produced by recombinant DNA technology which provides exogenous N-acetylgalactosamine-6-sulfatase. The mannose-6-phosphate-terminated oligosaccharide chains of elosulfase alfa bind to mannose-6-phosphate receptors of lysosomal cells resulting in cellular uptake of elosulfase alfa and increased catabolism of KS and C6S.[1,5]

Xenpozyme (olipudase alfa) is a recombinant hydrolytic lysosomal human acid sphingomyelinase (ASM) enzyme designed to reduce sphingomyelin (SM) accumulation in the liver, spleen, and lung of patients with acid sphingomyelinase deficiency (ASMD). It provides exogenous ASM, replacing deficient or defective ASM caused by pathogenic variants in the sphingomyelin phosphodiesterase 1 gene (SMPD1). Olipudase alfa-rpcp is not expected to cross the blood-brain barrier or modulate the CNS manifestations of ASMD.[28]

Clinical Evidence

Proven

Elfabrio

The efficacy of pegunigalsidase alfa-iwxj was first established in an open-label dose-ranging study in adults diagnosed with Fabry disease.[35-36] Patients received pegunigalsidase alfa-iwxj at 0.2 mg/kg, 1 mg/kg, or 2 mg/kg given intravenously every other week for 52 weeks. The 0.2 mg/kg and 2 mg/kg dosage regimens are not approved and are not recommended. The trial enrolled 18 patients who were ERT-naïve or who had not received ERT for more than 26 weeks and had a negative test for anti-pegunigalsidase alfa-iwxj IgG antibodies prior to enrollment. Two patients in the 1 mg/kg treatment group discontinued the trial after their first infusion; one of them discontinued due to severe hypersensitivity reaction. The average number of Gb3 inclusions per renal peritubular capillary in renal biopsy specimens of patients was assessed by light microscopy using the quantitative Barisoni Lipid Inclusion Scoring System (BLISS). Evaluable renal biopsies were obtained at baseline and at 26 weeks of treatment in 14 of the 16 patients. The mean change from baseline to 26 weeks in the BLISS score was -3.1 (95% CI: -4.8, -1.4).

Additionally, pegunigalsidase alfa-iwxj was evaluated in a randomized, double-blind, and active-controlled study in 77 ERT-experienced adults diagnosed with Fabry disease.[35,37] Eligible patients were treated with agalsidase beta for at least one year prior to trial entry (mean duration of agalsidase beta treatment prior to enrollment was 5.7 years). Patients were randomized to receive pegunigalsidase alfa-iwxj or agalsidase beta every 2 weeks for 104 weeks. A total of 77 patients were randomized and received at least one dose of pegunigalsidase alfa-iwxj (n = 52, 68%) or agalsidase beta (n = 25, 32%). The primary endpoint was the annualized rate of change in estimated glomerular filtration rate (eGFR slope) assessed over 104 weeks. The estimated mean eGFR slope was -2.4 and -2.3 mL/min/1.73 m^2/year on Elfabrio and Fabrazyme respectively. The estimated treatment difference was -0.1 (95% CI: -2.3, 2.1) mL/min/1.73 m^2/year. The most common adverse reactions (≥ 15%) reported with pegunigalsidase alfa-iwxj were infusion associated reactions which occurred in 17 patients (32%); followed by, nasopharyngitis and headache each in 11 patients (21%); diarrhea in 10 patients (19%); fatigue and nausea each in 9 patients (17%); and back pain, pain in extremity, and sinusitis each in 8 patients (15%). One pegunigalsidase alfa-iwxj-treated patient experienced a severe hypersensitivity reaction during the first infusion and withdrew from the trial following a moderate hypersensitivity reaction during the second infusion. And one case of membranoproliferative glomerulonephritis with immune depositions in the kidney was reported in a pegunigalsidase alfa-iwxj-treated patient.

Fabrazyme

A multicenter, randomized, double-blind, placebo-controlled study was conducted to assess the efficacy of agalsidase beta to delay the onset of composite clinical outcome of renal, cardiovascular, and cerebrovascular events, and death in patients with advanced Fabry disease.[18] Patients (n = 82), were randomized (2:1 treatment-to-placebo) to receive either an intravenous infusion of agalsidase beta (1mg/kg) or placebo every 2 weeks for up to 35 months. The primary endpoint was the time to first clinical event (renal, cardiac, or cerebrovascular event, or death). Thirteen (42%) of the 31 patients in the placebo group, and 14 (27%) of the 51 patients in the agalsidase-beta group experienced clinical events. Primary intention-to-treat analysis that adjusted for an imbalance in baseline proteinuria showed that, compared with placebo, agalsidase beta delayed the time to first clinical event [hazard ratio, 0.47 (95% CI, 0.21 to 1.03); p = 0.06]. Secondary analyses of protocol-adherent patients showed similar results [hazard ratio, 0.39 (CI, 0.16 to 0.93); p = 0.034]. Ancillary subgroup analyses found larger treatment effects in patients with baseline estimated glomerular filtration rates greater than 55 mL/min per 1.73 m^2 [hazard ratio, 0.19 (CI, 0.05 to 0.82); p = 0.025] compared with 55 mL/min per 1.73 m^2 or less [hazard ratio, 0.85 (CI, 0.32 to 2.3); p = 0.75] (formal test for interaction, p = 0.09). Most treatment-related adverse events were mild or moderate infusion-associated reactions, reported by 55% of patients in the agalsidase-beta group and 23%

of patients in the placebo group. The authors concluded that therapy with agalsidase beta slowed the progression to the composite clinical outcome of renal, cardiac, and cerebrovascular complications and death compared with placebo in patients with advanced Fabry disease. The authors recommend therapeutic intervention before irreversible organ damage to provide greater clinical benefit.

Kanuma

Burton et al. conducted a phase 3 clinical trial to evaluate the safety and efficacy of enzyme-replacement therapy with sebelipase alfa.[19] This study was a multicenter, randomized, double-blind, placebo-controlled trial, enrolling 66 patients. Patients were randomized 1:1 to receive placebo (n = 30) or sebelipase alfa (n = 36) administered intravenously at 1mg/kg every other week. The placebo-controlled phase of the study was 20 weeks long, followed by an open-label treatment for all patients. The primary endpoint of the trial was the normalization of the alanine aminotransferase level. Secondary end points included additional disease-related assessments, safety, and side effects. Sebelipase alfa was associated with a significantly higher rate of normalization of the alanine aminotransferase level, (the primary end point) than was placebo (31% vs. 7%, p = 0.03). In addition, sebelipase alfa was associated with significant improvement in six consecutive secondary end points, as compared with placebo. The decrease from baseline in the mean alanine aminotransferase level was significantly greater in the sebelipase alfa group than in the placebo group (−58 U per liter vs. −7 U per liter, p < 0.001). Similar results were seen with respect to normalization of the aspartate aminotransferase level (42% vs. 3%, p < 0.001; mean reduction from baseline, −42 U per liter vs. −6 U per liter; p < 0.001). An additional analysis of reduction in the alanine aminotransferase level with the use of recently applied criteria in studies of nonalcoholic fatty liver disease showed a response rate of 67% with sebelipase alfa versus 7% with placebo. The sebelipase alfa group had significantly greater mean percentage decreases from baseline in the LDL cholesterol level (difference from the change with placebo, −22.2 percentage points; p < 0.001), the non-HDL cholesterol level (difference from placebo, −21.1 percentage points; p < 0.001), and the triglyceride level (difference from placebo, −14.4 percentage points; p = 0.04) and a significantly greater mean percentage increase in the HDL cholesterol level (difference from placebo, 19.9 percentage points; p < 0.001). The number of patients with adverse events was similar in the two groups; most events were mild and were considered by the investigator to be unrelated to treatment. Sebelipase alfa therapy resulted in a reduction in multiple disease-related hepatic and lipid abnormalities in children and adults with lysosomal acid lipase deficiency.

Lamzede

The efficacy of Lamzede was evaluated in a phase 3 multicenter, randomized, double-blinded, placebo-controlled, parallel group trial (rhLAMAN-05; NCT01681953) in adult and pediatric patients with alpha-mannosidosis. The trial evaluated the efficacy of Lamzede over 52 weeks at a dose of 1 mg/kg given weekly as an intravenous infusion. A total of 25 patients were enrolled (14 males, 11 females), including 13 adult patients (age range: ≥ 8 to 35 years; mean: 25 years) and 12 pediatric patients (age range: ≥ 6 to < 18 years; mean: 11 years); all patients were White. Ethnicity data were not collected. All patients had alphamannosidase activity below 11% of normal and in the range of 8 to 29 µmol/h/mg at baseline. All patients but one were naïve to Lamzede. Fifteen patients (8 adult and 7 pediatric) received Lamzede and 10 patients (5 adult and 5 pediatric) received placebo. All patients completed the trial. The efficacy results for the clinical endpoints assessed at 12 months, 3-minute stair climbing test (3MSCT), 6-minute walking test (6MWT) and forced vital capacity (FVC) (% predicted), favored the Lamzede group and were supported by a reduction in serum oligosaccharide concentration. At week 52, the mean relative change in serum oligosaccharide concentration was significantly greater with Lamzede than with placebo (-77.6% versus -24.1%, respectively; adjusted mean difference, -70.5%; p < 0.001). At week 52, there was no significant change in the 3MSCT from baseline with Lamzede compared to placebo (mean change, -1.1% versus -0.0%, respectively; adjusted mean difference, + 3; p = 0.648). In addition, a small increase in the secondary endpoint of change from baseline in 6MWT at week 52 was seen in the Lamzede group compared with a small decline in the placebo group; the difference was not significant. Five serious TEAEs were reported, one of which was considered related to Lamzede in a patient who received long-term ibuprofen who experienced acute renal failure; the patient recovered after Lamzede interruption and was able to restart therapy without incident. The single-center, open-label, long-term (up to 4 years) phase 3 rhLAMAN-10 trial (NCT02478840) assessed Lamzede in 33 patients (14 adults, 19 pediatrics) with confirmed alpha-mannosidosis who had previously participated in phase 1/2 and phase 3 trials. The coprimary endpoint of serum oligosaccharide level was significantly reduced in the overall population at 12 months (mean change, -72.7%; p < 0.001) which was reported through the last observation timepoint (mean change, -62.8%; p < 0.001). An improvement in the other coprimary endpoint of change from baseline in 3MSCT was also observed at 12 months (mean change, + 9.3%; p = 0.013) and continued through the last observation (mean change, + 13.8%; p = 0.004).

Lamzede was also investigated in a single arm trial (NCT02998879) in pediatric alpha-mannosidosis patients less than 6 years of age. All patients had alpha-mannosidase activity below 10% of normal at baseline. The trial enrolled five patients ranging from 3.7 to 5.9 years of age, with a mean age of 4.5 years. Four patients were White, race was not recorded for 1 patient; and 3 were male and 2 were female. Patients received Lamzede 1 mg/kg as intravenous infusion once weekly (4

patients for 24 months, 1 patient for 40 months). The mean (SD) absolute and percentage changes from Baseline for serum oligosaccharides at 24 months were -7.7 (4.27) µmol/L and -65.8% (23.1%) respectively.

Lumizyme

A randomized, double-blind, placebo-controlled, multicenter study was conducted to determine the safety and efficacy of alglucosidase alfa (GAA) for the treatment of late-onset Pompe's disease.[20] Ninety patients, 8 years of age or older, who were ambulatory, not dependent on invasive ventilation, were randomly assigned 2:1 to receive bi-weekly infusions of GAA (20mg/kg, n = 60) or placebo (n = 30). Co-primary efficacy end points were meters walked on the 6-minute walk test and percentage of the predicted FVC in the upright position. Secondary and tertiary efficacy end points included changes in the percentage of the predicted QMT leg score and QMT arm score, maximum inspiratory pressure, and maximum expiratory pressure. By 78 weeks, treatment with GAA had significantly increased both the distance walked on the 6-minute walk test and the percentage of the predicted FVC. The GAA group had a mean increase of 25.1 m on the 6-minute walk test (the average baseline was 332.2 m), whereas the placebo group had a decrease of 3.0 m (the average baseline was 317.9 m), for an estimated differential treatment effect of 28.1 m (p = 0.03). The estimated change in FVC, expressed as a percentage of each patient's predicted value, was an increase of 1.2 percentage points for the patients who received GAA and a decrease of 2.2 percentage points for the patients who received placebo, for an estimated treatment effect of 3.4 percentage points (p = 0.006). Patients in the two groups had similar frequencies of adverse events, serious adverse events, treatment-related adverse events, and infusion associated reactions. The authors concluded that, in this study population, treatment with alglucosidase alfa was associated with improved walking distance and stabilization of pulmonary function over an 18-month period.

Nexviazyme

The efficacy and safety of avalglucosidase alfa-ngpt for the treatment of late onset Pompe disease was evaluated in a randomized, double-blinded, multinational, multicenter trial (NCT02782741). Efficacy and safety was compared to alglucosidase alfa. 100 treatment-naïve patients were randomized in a 1:1 ratio, based on forced vital capacity (FVC), age, gender, and country, to receive 20 mg/kg of avalglucosidase alfa-ngpt or alglucosidase alfa administered once every two weeks for 49 weeks. The trial included an open label, long-term, follow-up of up to 5 years, in which patients were switched to avalglucosidase alfa-ngpt treatment. The primary endpoint was the change in FVC (% predicted) in the upright position from baseline to week 49. Secondary endpoint was the change in total walking distance in 6 minutes (6-minute walk test) from baseline to week 49. At week 49, the least squares (LS) mean change in FVC was 2.9% (avalglucosidase alfa-ngpt) and 0.5% (alglucosidase alfa), with an estimated treatment difference of 2.4% (95% CI: -0.1, 5) favoring avalglucosidase alfa-ngpt [non-inferiority margin of 1.1% (p = 0.0074), statistical superiority was not achieved (p = 0.06)]. Secondary endpoint had an estimated treatment difference of 30 meters (95% CI: 1.3, 58.7) favoring avalglucosidase alfa-ngpt (p = 0.04).[27]

Pombiliti

The safety and efficacy of cipaglucosidase alfa-atga was evaluated in a randomized, double-blind, active-controlled, international, multi-center clinical trial (NCT#03729362) in patients ≥ 18 years old diagnosed with LOPD. Patients were randomized 2:1 to receive cipaglucosidase alfa-atga (20 mg/kg by intravenous infusion) in combination with miglustat (260 mg orally for those ≥ 50 kg or 195 mg orally for those ≥ 40 kg to < 50 kg) or a non-U.S.-approved alglucosidase alfa product with placebo every other week for 52 weeks. The efficacy population included a total of 123 patients of whom 95 (77%) had received prior treatment with U.S.-approved alglucosidase alfa or a non-U.S.-approved alglucosidase alfa product (ERT-experienced) and 28 (23%) were ERT-naïve. More than two thirds (n = 64, 67%) of ERT-experienced patients had been on ERT treatment for more than 5 years prior to entering Trial 1 (mean of 7.4 years). Key efficacy endpoints included assessment of sitting FVC (% predicted) and 6MWD.

Patients treated with cipaglucosidase alfa-atga in combination with miglustat showed a mean change in sitting FVC from baseline at Week 52 of -1.1% as compared with patients treated with a non-U.S.-approved alglucosidase alfa product with placebo of -3.3%; the estimated treatment difference was 2.3% (95% CI: 0.02, 4.62). The ERT-experienced patients treated with cipaglucosidase alfa-atga in combination with miglustat showed a numerically favorable change in sitting FVC from baseline at Week 52 patients treated with cipaglucosidase alfa-atga in combination with miglustat walked on average 21 meters farther from baseline as compared to those treated with a non-U.S.-approved alglucosidase alfa product with placebo who walked 8 meters farther from baseline; the estimated treatment difference was 14 meters (95% CI: -1, 28). The ERT-experienced patients treated with cipaglucosidase alfa-atga in combination with miglustat showed a numerically favorable change in 6MWD from baseline at Week 52.

Revcovi

The safety and efficacy of elapegademase-lvlr was evaluated in a phase 3, open-label, multicenter, single-arm, one-way crossover study. The study consisted of three phases: Adagen Lead-in Phase (minimum of 3 weeks), the Revcovi

Treatment Phase (weeks 1 through 21), and followed by the Revcovi Maintenance Phase. The efficacy endpoints evaluated included trough dAXP level, trough plasma ADA activity and immune status. Five of six patients reached the 21-week endpoint of the Treatment Phase. These patients (except for one value in a patient at Treatment Week 47) had erythrocyte dAXP concentration equal to or below 0.02 mmol/L. These patients had trough plasma ADA activity equal to or above 15 mmol/hr/L at 88/89 time points and maintained metabolic detoxification for at least 2 years under Revcovi treatment. Patients achieved through plasma ADA activity above 30 mmol/hr/L by week 5, except for one patient who achieved this level at week 1. The mean trough plasma ADA activity for patients receiving Revcovi at a normalized dose of 0.2 mg/kg/week were 34.3 ±6.6 mmol/hr/L. The same patients had a mean trough plasma ADA activity of 14.2 ±5.1 mmol/hr/L when treated with Adagen at a normalized dose of 30 U/kg/week during the Lead-in Phase of the study. For these three patients who completed the primary endpoint or 21 weeks of treatment and received Revcovi for over 135 weeks, a positive trend between high trough plasma ADA activity and increased total lymphocyte counts was observed.[24]

Another study to evaluate the safety, efficacy, and PK of Revcovi in patients with ADA-SCID included two phases, and evaluation and dose maintenance period. A total of four patients were enrolled in the study: two patients, who were on Adagen treatment within 4 weeks before entering the study, received a first dose of Revcovi that was calculated to be equivalent their prior Adagen dose. One patient, who did not receive Adagen within four weeks prior to entering the study. Over the dose adjustment phase of the study, the dose was titrated to meet criteria for dAXP level (equal to or below 0.02 mmol/L) and adequate trough ADA activity. The fourth patient was dosed with Revcovi at 0.4 mg/kg weekly for 16 weeks. All four of the patients in Study 2 achieved and maintained detoxification throughout their participation in the Treatment Phase of 21 weeks. Serum ADA activity increased after administering REVCOVI for all four patients, with three patients achieving activity level over 15 mmol/hr/L during the Dose Maintenance Period. Total lymphocyte counts and B-/T-/NK-lymphocyte subset counts for three patients increased from screening to Day 15 during dose adjustment and were stable or increasing during the Maintenance Period.[24]

Xenpozyme

The efficacy of Xenpozyme for the treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) has been evaluated in 3 trials in patients with ASMD.[28]

Trial 1 was a randomized, double-blinded, placebo-controlled, repeat-dose trial in 31 adult patients with ASMD (clinical diagnosis consistent with ASMD type B and A/B). Patients received either Xenpozyme or placebo. Key efficacy endpoints included assessment of % predicted diffusion capacity of the lungs for carbon monoxide (DLco), spleen volume, liver volume, and platelet count. At week 52, an increase of 20.9% in the mean percent change in % predicted DLco was observed in the Xenpozyme-treated patients compared to the placebo-treated patients ($p = 0.0003$). A reduction in spleen volume of 39.4% was observed in the Xenpozyme-treated patients compared to the placebo-treated patients ($p < 0.0001$). A 24.7% decrease in mean liver volume and a 15.6% increase in mean platelet count were also noted in the Xenpozyme-treated patients compared to the placebo-treated patients at week 52 ($p < 0.0001$ and $p = 0.0280$, respectively).[28,31]

Trial 2 was an open-label, repeated-dose trial of Xenpozyme in 8 pediatric patients aged < 18 years with a clinical diagnosis consistent with ASMD type B and A/B. Exploratory efficacy endpoints related to organomegaly, pulmonary and liver functions, and linear growth were evaluated at week 52. Treatment with Xenpozyme resulted in improvements in mean percent change in % predicted DLco, spleen and liver volumes, platelet counts, and linear growth progression (as measured by height Z-scores) at week 52 as compared to baseline. Refer to the drug label for full results.[28,32]

Additionally, the 8 pediatric patients 2 to < 12 years of age from Trial 2 continued treatment in an open label long term trial (Trial 3) and were treated with Xenpozyme for 2.5 to 3.2 years. Efficacy analyses showed continued improvements in the 3 patients evaluated for % predicted DLco, 6 patients evaluated for platelet counts, and all 8 patients evaluated for spleen and liver volumes, compared to baseline, during the additional 6 months extension. In addition, the height Z-score increased by 1.3 from baseline when evaluated through 24 months of Xenpozyme treatment.[28]

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Elfabrio (pegunigalsidase alfa-iwxj) is indicated for the treatment of adults with confirmed with Fabry disease. Elfabrio reduces globotriaosylceramide (GL-3) accumulation in blood vessel walls of the kidneys, heart, and cerebrovascular system.[35]

Fabrazyme (agalsidase beta) is indicated for use in patients with Fabry disease. Fabrazyme reduces globotriaosylceramide (GL-3) deposition in capillary endothelium of the kidney and certain other cell types.[11]

Kanuma is indicated for the treatment of patients with a diagnosis of Lysosomal Acid Lipase (LAL) deficiency.[12]

Lamzede (velmanase alfa-tycv) is recombinant human lysosomal alpha-mannosidase indicated for the treatment of non-central nervous system manifestations of alpha-mannosidosis in adult and pediatric patients.[33]

Lumizyme (alglucosidase alfa) is a hydrolytic lysosomal glycogen-specific enzyme indicated for patients with Pompe disease (acid α-glucosidase (GAA) deficiency).[13]

Nexviazyme (avalglucosidase alfa-ngpt) is indicated for the treatment of patients 1 year of age and older with late-onset Pompe disease [lysosomal acid alpha-glucosidase (GAA) deficiency].[27]

Pombiliti (cipaglucosidase alfa-atga) is indicated, in combination with Opfold (miglustat), an enzyme stabilizer, for the treatment of adult patients with late-onset Pompe disease [lysosomal acid alpha-glucosidase (GAA) deficiency] weighing ≥ 40 kg and who are not improving on their current enzyme replacement therapy (ERT).

Revcovi (elapegademase-lvlr) is indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.[24]

Xenpozyme (olipudase alfa) is indicated for the treatment of non-central nervous system (non-CNS) manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients.[28]

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Policy History/Revision Information

Date	Summary of Changes
04/01/2026	• Retired policy; Louisiana plan membership disenrolled on Apr. 1, 2026
10/01/2025	**Coverage Rationale** • Replaced language indicating "coverage for Aldurazyme, Elaprase, Mepsevii, Naglazyme, Nulibry, and Vimizim is contingent on *criteria in the Drug-Specific Criteria section [of the policy]*" with "coverage for Aldurazyme, Elaprase, Mepsevii, Naglazyme, Nulibry, and Vimizim is contingent on *state Medicaid clinical coverage criteria; refer to the Louisiana Medicaid Preferred Drug List (PDL)/Non-Preferred Drug List (NPDL)*" • Removed coverage guidelines for Aldurazyme, Elaprase, Mepsevii, Naglazyme, Nulibry, and Vimizim • Revised coverage criteria for: ***Elfabrio*** and ***Fabrazyme*** ○ Added criterion requiring the patient is not receiving Elfabrio/Fabrazyme in combination with another disease-modifying therapy used for the treatment of Fabry disease ***Lumizyme***, ***Nexviazyme***, and ***Pombiliti*** ○ Added criterion requiring the patient is not receiving Lumizyme/Nexviazyme/Pombiliti in combination with another disease-modifying enzyme therapy used for the treatment of Pompe disease **Applicable Codes** • Added HCPCS codes J0217 and J2508 • Removed HCPCS codes C9399, J1322, J1458, J1743, J1931, J3397, and J3490 • Removed ICD-10 diagnosis codes E72.10, E72.19, E76.01, E76.02, E76.03, E76.1, E76.210, and E76.29 ***Elfabrio, Lamzede,*** and ***Nulibry*** • Removed HCPCS code J3590 **Supporting Information**

Date	Summary of Changes
	• Updated *Background*, *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information • Archived previous policy version CSLA2024D0052X

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

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