Corporate Medical Policy: Enzyme Replacement Therapy (ERT) for Lysosomal Storage Disorders **"Notification"** **POLICY EFFECTIVE OCTOBER 1, 2023**

Restricted Product(s):

- imiglucerase (Cerezyme®) intravenous infusion for administration by a healthcare professional
- taliglucerase alfa (Elelyso®) intravenous infusion for administration by a healthcare professional
- velaglucerase alfa (Vpriv®) intravenous infusion for administration by a healthcare professional
- sebelipase alfa (Kanuma®) intravenous infusion for administration by a healthcare professional
- pegunigalsidase alfa-iwxj (Elfabrio®) intravenous infusion for administration by a healthcare professional
- agalsidase beta (Fabrazyme®) intravenous infusion for administration by a healthcare professional
- alglucosidase alfa (Lumizyme®) intravenous infusion for administration by a healthcare professional
- avalglucosidase alfa-ngpt (Nexviazyme®) intravenous infusion for administration by a healthcare professional
- laronidase (Aldurazyme®) intravenous infusion for administration by a healthcare professional
- idursulfase (Elaprase®) intravenous infusion for administration by a healthcare professional
- vestronidase alfa-vjbk (Mepsevii®) intravenous infusion for administration by a healthcare professional
- galsulfase (Naglazyme®) intravenous infusion for administration by a healthcare professional
- elosulfase alfa (Vimizim®) intravenous infusion for administration by a healthcare professional
- cerliponase alfa (Brineura®) intraventricular infusion for administration by a healthcare professional
- olipudase alfa-rpcp (Xenpozyme®) intravenous infusion for administration by a healthcare professional
- velmanase alfa-tycv (Lamzede®) intravenous infusion for administration by a healthcare professional

FDA Approved Use:

- Imiglucerase (Cerezyme®)
  - For long-term ERT for adults and pediatric patients 2 years of age and older with a confirmed diagnosis of Type 1 Gaucher disease that results in one or more of the following conditions: anemia, thrombocytopenia, bone disease, hepatomegaly or splenomegaly
- Taliglucerase alfa (Elelyso®)
  - For treatment of patients 4 years of age and older with a confirmed diagnosis of Type 1 Gaucher disease
- Velaglucerase alfa (Vpriv®)
  - For long-term ERT for patients with Type 1 Gaucher disease

- Sebelipase alfa (Kanuma®)
  - For treatment of patients with a diagnosis of Lysosomal Acid Lipase (LAL) deficiency
- Pegunigalsidase alfa-iwxj (Elfabrio®)
  - For treatment of adults with confirmed Fabry disease
- Agalsidase beta (Fabrazyme®)
  - For treatment of adult and pediatric patients 2 years of age and older with confirmed Fabry disease
- Alglucosidase alfa (Lumizyme®)
  - For patients with Pompe disease (acid alpha-glucosidase [GAA] deficiency)
- Avalglucosidase alfa-ngpt (Nexviazyme®)
  - For patients 1 year of age and older with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency)
- Laronidase (Aldurazyme®)
  - For adult and pediatric patients with Hurler and Hurler-Scheie forms of Mucopolysaccharidosis I (MPS I), and for patients with the Scheie form who have moderate to severe symptoms
  - Limitations of use: Risks and benefits of treating mildly affected patients with the Scheie form have not been established; treatment has not been evaluated for effects on the central nervous system manifestations of the disorder
- Idursulfase (Elaprase®)
  - For patients with Hunter syndrome (Mucopolysaccharidosis II, MPS II)
  - Limitations of use: Safety and efficacy have not been established in pediatric patients less than 16 months of age
- Vestronidase alfa-vjbk (Mepsevii®)
  - For treatment of pediatric and adult patients with Mucopolysaccharidosis VII (MPS VII, Sly syndrome)
  - Limitations of use: The effect on central nervous system manifestations of MPS VII has not been determined
- Galsulfase (Naglazyme®)
  - For patients with Mucopolysaccharidosis VI (MPS VI; Maroteaux-Lamy syndrome)
- Elosulfase alfa (Vimizim®)
  - For patients with Mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome)
- Cerliponase alfa (Brineura®)
  - For slowing the loss of ambulation in symptomatic pediatric patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency
- Olipudase alfa-rpcp (Xenpozyme®)

  - For treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients
- Velmanase alfa-tycv (Lamzede®)
  - For treatment of non-central nervous system manifestations of alpha-mannosidosis in adult and pediatric patients

Criteria for Medical Necessity:

Initial Criteria for Approval:

1. The patient has a diagnosis of **Type 1 Gaucher disease [medical record documentation required]**; **AND**
    a. The diagnosis has been confirmed by one of the following:
        i. A biochemical assay of beta-glucocerebrosidase activity (in leukocytes or skin fibroblasts) of less than 30% of normal values **[medical record documentation required]**; **OR**
        ii. Genetic testing demonstrating mutations in the glucocerebrosidase gene **[medical record documentation required]**; **AND**
    b. The request is for **imiglucerase (Cerezyme)**; **AND**
        i. The patient is 2 years of age or older; **AND**
        ii. The patient has one or more of the following conditions **[medical record documentation required]**:
            1. Anemia
            2. Thrombocytopenia
            3. Bone disease
            4. Hepatomegaly
            5. Splenomegaly; **OR**
    c. The request is for **velaglucerase alfa (Vpriv) or taliglucerase alfa (Elelyso)**; **AND**
        i. The patient is 4 years of age or older; **AND**
        ii. The patient has at least two of the following clinical signs and/or symptoms **[medical record documentation required]**:
            1. Hematologic abnormalities including anemia and thrombocytopenia
            2. Clinically significant hepatomegaly
            3. Clinically significant splenomegaly
            4. Radiologic evidence of skeletal disease; **OR**

2. The patient has a diagnosis of **Lysosomal Acid Lipase (LAL) Deficiency [medical record documentation required]**; **AND**

a. The request is for **sebelipase alfa (Kanuma)**; **AND**
b. The patient is 1 month of age or older; **AND**
c. The diagnosis has been confirmed by one of the following:
    i. A biochemical assay of lysosomal acid lipase (LAL) demonstrating deficient activity (in leukocytes or fibroblasts) per laboratory references **[medical record documentation required]**; **OR**
    ii. Genetic testing demonstrating biallelic pathogenic variants in the *LIPA* gene **[medical record documentation required]**; **OR**

3. The patient has a diagnosis of **Fabry Disease [medical record documentation required]**; **AND**
    a. The diagnosis has been confirmed by one of the following:
        i. For male patients, one of the following:
            1. A biochemical assay of alpha-galactosidase A (α-Gal A) in plasma, isolated leukocytes, and/or cultured cells demonstrating deficient activity (i.e., below the lower limit of normal) **[medical record documentation required]**; **OR**
            2. Genetic testing demonstrating pathogenic mutations in the *GLA* gene **[medical record documentation required]**; **OR**
        ii. For female patients: Genetic testing demonstrating pathogenic mutations in the *GLA* gene **[medical record documentation required]**; **AND**
    b. The patient has had baseline laboratory values obtained for plasma globotriaosylceramide (GL-3) and/or GL-3 inclusions, plasma or urinary globotriaosylceramide (Gb3/GL-3), or plasma globotriaosylsphingosine (lyso-Gb3) **[medical record documentation required]**; **AND**
    c. The prescriber is a specialist in the area of the patient's diagnosis (e.g., geneticist, metabolic specialist) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]**; **AND**
    d. The request is for **pegunigalsidase alfa-iwxj (Elfabrio)**; **AND**
        i. The patient is 18 years of age or older; **AND**
        ii. Elfabrio will NOT be used in combination with any other enzyme replacement therapy and any existing authorizations will be closed upon approval of Elfabrio; **AND**
        iii. Receipt of any requests for alternative drugs to treat Fabry disease (e.g., Fabrazyme, Galafold) will result in closure of the Elfabrio authorization; **OR**
    e. The request is for **agalsidase beta (Fabrazyme)**; **AND**
        i. The patient is 2 years of age or older; **AND**
        ii. Fabrazyme will NOT be used in combination with any other enzyme replacement therapy and any existing authorizations will be closed upon approval of Fabrazyme; **AND**

iii. Receipt of any requests for alternative drugs to treat Fabry disease (e.g., Elfabrio, Galafold) will result in closure of the Fabrazyme authorization; **OR**

4. The patient has a diagnosis of **Pompe disease [medical record documentation required]**; **AND**
    a. The diagnosis has been confirmed by one of the following:
        i. An enzyme assay measuring activity of the acid alpha-glucosidase (GAA) enzyme in the patient's body **[medical record documentation required]**; **OR**
        ii. Genetic testing demonstrating mutations in the *GAA* gene **[medical record documentation required]**; **AND**
    b. The request is for **alglucosidase alfa (Lumizyme)**; **OR**
    c. The request is for **avalglucosidase alfa-ngpt (Nexviazyme)**; **AND**
        i. The patient is 1 year of age or older; **AND**
        ii. The patient has a diagnosis of late-onset Pompe disease **[medical record documentation required]**; **OR**

5. The patient has a diagnosis of **Mucopolysaccharidosis type I (MPS I) [medical record documentation required]**; **AND**
    a. The request is for l**aronidase (Aldurazyme)**; **AND**
    b. The patient has Hurler and Hurler-Scheie forms of MPS I **[medical record documentation required]**; **OR**
    c. The patient has Scheie form of MPS I with moderate to severe symptoms **[medical record documentation required]**; **AND**
    d. The patient will receive antihistamines with or without antipyretics prior to infusion with the requested agent; **OR**

6. The patient has a diagnosis of **Mucopolysaccaridosis II (MPS II; Hunter Syndrome) [medical record documentation required]**; **AND**
    a. The request is for **idursulfase (Elaprase)**; **AND**
    b. The patient is 5 years of age and older; **AND**
        i. A baseline percent predicted forced vital capacity (FVC) and/or 6-minute walk test has been documented **[medical record documentation required]**; **OR**
    c. The patient is ≥ 16 months of age and < 5 years old; **AND**
        i. The patient is experiencing at least ONE somatic symptom (e.g., skeletal disease, liver and/or spleen enlargement) **[medical record documentation required]**; **AND**
        ii. A baseline spleen volume, liver volume, FVC and/or 6-minute walk test has been documented **[medical record documentation required]**; **OR**

7. The patient has a diagnosis of **Mucopolysaccharidosis VII (MPS VII; Sly Syndrome) [medical record documentation required]**; **AND**

a. The request is for **vestronidase alfa-vjbk (Mepsevii)**; **AND**
b. The diagnosis has been confirmed by BOTH of the following:
    i. Leukocyte or fibroblast glucuronidase enzyme assay or genetic testing **[medical record documentation required]**; **AND**
    ii. Elevated urinary glycosaminoglycan (uGAG) excretion at a minimum of 2-fold over the mean normal for age at start of therapy **[medical record documentation required]**; **AND**
c. The patient will receive antihistamines with or without antipyretics prior to infusion with the requested agent; **OR**

8. The patient has a diagnosis of **Mucopolysaccharidosis VI (MPS VI; Maroteaux-Lamy Syndrome) [medical record documentation required]**; **AND**
    a. The request is for **galsulfase (Naglazyme)**; **AND**
    b. The diagnosis has been confirmed by one of the following:
        i. A biochemical assay of N-acetylgalactosamine 4-sulfatase (arylsulfatase B, ASB) demonstrating deficient activity (in leukocytes or fibroblasts) per laboratory references **[medical record documentation required]**; **AND**
            1. Multiple sulfatase deficiencies have been ruled out (via assay of a second sulfatase) **[medical record documentation required]**; **AND**
            2. If fibroblasts are used, I-cell disease has been ruled out **[medical record documentation required]**; **OR**
        ii. Genetic testing demonstrating mutations in the *ARSB* gene **[medical record documentation required]**; **AND**
    c. The patient will receive antihistamines with or without antipyretics prior to infusion with the requested agent; **OR**

9. The patient has a diagnosis of **Mucopolysaccharidosis IVA (MPS IVA; Morquio A syndrome) [medical record documentation required]**; **AND**
    a. The request is for **elosulfase alfa (Vimizim)**; **AND**
    b. The patient is 5 years of age or older; **AND**
    c. The diagnosis has been confirmed by one of the following:
        i. Reduced N-acetylgalactosamine 6-sulfatase (GALNS) enzyme activity **[medical record documentation required]**; **OR**
        ii. Identification of biallelic variants in GALNS upon genetic testing **[medical record documentation required]**; **AND**
    d. The patient will receive antihistamines with or without antipyretics prior to infusion with the requested agent; **OR**

10. The patient has a diagnosis **Batten Disease (CLN2) [medical record documentation required]**; **AND**
    a. The request is for **cerliponase alfa (Brineura)**; **AND**
    b. The patient is 3 years of age or older; **AND**

c. The diagnosis has been confirmed by testing for deficiency of tripeptidyl peptidase 1 (TPP1) enzyme **[medical record documentation required]**; **AND**
d. The patient has been evaluated by or in consultation with a neurologist prior to starting treatment with the requested agent **[medical record documentation required]**; **OR**

11. The patient has a diagnosis of **acid sphingomyelinase deficiency (ASMD) type A/B OR type B [medical record documentation required]**; **AND**
    a. The request is for **olipudase alfa-rpcp (Xenpozyme)**; **AND**
    b. The patient has documented deficiency of acid sphingomyelinase as measured in peripheral leukocytes, cultured fibroblasts, or lymphocytes **[medical record documentation required]**; **AND**
        i. ONE of the following:
            1. The patient is less than 18 years of age; **AND**
                a. The patient has a spleen volume ≥ 5 multiple of normal (MN) measured by magnetic resonance imaging (MRI) **[medical record documentation required]**; **AND**
                b. The patient does NOT have acute or rapidly progressive neurological abnormalities **[medical record documentation required]**; **AND**
                c. The patient does NOT have a delay of gross motor skills **[medical record documentation required]**; **OR**
            2. The patient is 18 years of age or older; **AND**
                a. The patient has a spleen volume ≥ 6 multiple of normal (MN) measured by magnetic resonance imaging (MRI) **[medical record documentation required]**; **AND**
                b. The patient has a splenomegaly-related score (SRS) of ≥ 5 **[medical record documentation required]**; **AND**
                c. The patient has diffusing capacity of lung for carbon monoxide (DLCO) ≤ 70% of the predicted normal value **[medical record documentation required]**; **AND**
    c. The patient does NOT have any of the following medical conditions **[medical record documentation required]**:
        i. An active, serious, intercurrent illness
        ii. Active hepatitis B or hepatitis C infection
        iii. Infection with human immunodeficiency virus (HIV)
        iv. Cirrhosis determined by clinical evaluation
        v. Clinically significant arrhythmia, moderate or severe pulmonary hypertension or valvular dysfunction, or < 40% left ventricular ejection fraction by echocardiogram
        vi. Malignancy diagnosed within the previous 5 years other than non-melanoma skin cancer; **AND**
    d. The patient does NOT have any central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) **[medical record documentation required]**; **AND**

e. The patient has a platelet count ≥ 60 x 10^3/uL **[medical record documentation required]**; **AND**
f. The patient has an international normalized ratio (INR) < 1.5 **[medical record documentation required]**; **AND**
g. The patient has alanine aminotransferase (ALT) or aspartate aminotransferase (AST) < 250 IU/L or total bilirubin < 1.5mg/dL **[medical record documentation required]**; **AND**
h. The patient has NOT had a major organ transplant (bone marrow or liver) **[medical record documentation required]**; **AND**
i. The prescriber is a specialist in the area of the patient's diagnosis (e.g., geneticist, hepatologist, pulmonologist) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]**; **OR**

12. The patient has a diagnosis of **alpha-mannosidosis (AM) [medical record documentation required]**; **AND**
    a. The request is for **velmanase alfa-tycv (Lamzede)**; **AND**
    b. The diagnosis has been confirmed by one of the following:
        i. An enzyme assay demonstrating alpha-mannosidase activity in leukocytes or fibroblasts below 10% of normal activity **[medical record documentation required]**; **OR**
        ii. Genetic testing demonstrating biallelic pathogenic variants in the *MAN2B1* gene **[medical record documentation required]**; **AND**
    c. The patient will be using the requested agent to treat non-central nervous system manifestations of AM (e.g., skeletal abnormalities, myopathy, motor function disturbances, immunodeficiency) **[medical record documentation required]**; **AND**
    d. The patient has signs and symptoms consistent with mild or moderate AM (e.g., absence of neurologic manifestations, ability to ambulate independently) **[medical record documentation required]**; **AND**
    e. The patient has NOT received an allogeneic hematopoietic stem cell transplant or bone marrow transplant **[medical record documentation required]**; **AND**
    f. The prescriber is a specialist in the area of the patient's diagnosis (e.g., geneticist, neurologist) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]**; **AND**

13. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
14. If the request is for Aldurazyme, Cerezyme, Elaprase, Elelyso, Elfabrio, Fabrazyme, Kanuma, Lamzede, Lumizyme, Mepsevii, Naglazyme, Nexviazyme, Vimizim, Vpriv, or Xenpozyme:
    a. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined below)*

Duration of Approval: 365 days (1 year)

Continuation Criteria for Approval:

1. The patient was approved through Blue Cross NC initial criteria for approval; **OR**
2. The patient would have met initial criteria for approval at the time they started therapy; **AND**
3. The patient has demonstrated clinical benefit since initiating therapy **[medical record documentation required]**; **OR**
4. The patient has experienced disease stabilization since initiating therapy **[medical record documentation required]**; **AND**
5. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
6. If the request is for Aldurazyme, Cerezyme, Elaprase, Elelyso, Elfabrio, Fabrazyme, Kanuma, Lamzede, Lumizyme, Mepsevii, Naglazyme, Nexviazyme, Vimizim, Vpriv, or Xenpozyme:
    a. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined below)*

Duration of Approval: 365 days (1 year)

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
imiglucerase (Cerezyme®) intravenous (IV) infusion	Type 1 Gaucher disease	IV: Dosage ranging from 2.5 U/kg 3 times weekly to 60 U/kg every 2 weeks	J1786	15,600
taliglucerase alfa (Elelyso®) intravenous (IV) infusion	Type 1 Gaucher disease	IV: 60 U/kg every other week	J3060	15,600
velaglucerase alfa (Vpriv®) intravenous (IV) infusion	Type 1 Gaucher disease	IV: 60 U/kg every other week	J3385	1,560

sebelipase alfa (Kanuma®) intravenous (IV) infusion	Lysosomal Acid Lipase (LAL) deficiency	Rapidly progressive LAL deficiency presenting in the first 6 months of life: 1 mg/kg IV once weekly; adjust up to 5 mg/kg once weekly based on clinical response Pediatric and adult patients: 1 mg/kg IV every other week; adjust up to 3 mg/kg every other week based on clinical response	J2840	7,800
pegunigalsidase alfa-iwxj (Elfabrio®) intravenous IV infusion	Fabry disease	IV: 1 mg/kg every two weeks	C9399** J3490** J3590**	2,600
agalsidase beta (Fabrazyme®) intravenous (IV) infusion	Fabry disease	IV: 1 mg/kg every two weeks	J0180	2,600
alglucosidase alfa (Lumizyme®) intravenous (IV) infusion	Pompe disease (GAA deficiency)	IV: 20 mg/kg every two weeks	J0221	5,200
avalglucosidase alfa-ngpt (Nexviazyme®) intravenous (IV) infusion	Late-onset Pompe disease (GAA deficiency)	IV: • ≥30 kg: 20 mg/kg every 2 weeks • <30 kg: 40 mg/kg every 2 weeks	J0219	13,000
laronidase (Aldurazyme®)	Mucopolysaccharidosis I	IV: 0.58 mg/kg once weekly	J1931	30,160

intravenous (IV) infusion				
idursulfase (Elaprase®) intravenous (IV) infusion	Mucopolysaccharidosis II	IV: 0.5 mg/kg once weekly	J1743	2,600
vestronidase alfa-vjbk (Mepsevii®) intravenous (IV) infusion	Mucopolysaccharidosis VII	IV: 4 mg/kg every two weeks	J3397	10,400
elosulfase alfa (Vimizim®) intravenous (IV) infusion	Mucopolysaccharidosis type IVA	IV: 2 mg/kg once weekly	J1322	10,400
galsulfase (Naglazyme®) intravenous (IV) infusion	Mucopolysaccharidosis VI	IV: 1 mg/kg once weekly	J1458	5,200
cerliponase alfa (Brineura®) intraventricular infusion	Batten Disease (CLN2)	IV: 300 mg every other week	J0567	7,800
olipudase alfa-rpcp (Xenpozyme®) intravenous (IV) infusion	Acid sphingomyelinase deficiency (ASMD)	Patients ≥ 18 years old: IV infusion every 2 weeks Week 0: 0.1 mg/kg Weeks 2-4: 0.3 mg/kg Weeks 6-8: 0.6 mg/kg	J0218	Patients ≥ 18 years old: 6,190

		Week 10: 1 mg/kg Week 12: 2 mg/kg Week 14: 3 mg/kg (Recommended maintenance dose) Patients < 18 years old: IV infusion every 2 weeks Week 0: 0.03 mg/kg Week 2: 0.1 mg/kg Weeks 4-6: 0.3 mg/kg Weeks 8-10: 0.6 mg/kg Week 12: 1 mg/kg Week 14: 2 mg/kg Week 16: 3 mg/kg (Recommended maintenance dose)		Patients < 18 years old: 5,893
velmanase alfa-tycv (Lamzede®) intravenous (IV) infusion	Alpha-mannosidosis (AM)	IV: 1 mg/kg once weekly	C9399** J3490** J3590**	5,200

***Maximum units allowed for duration of approval**
****Non-specific assigned HCPCS codes, must submit requested product NDC**

***Site of Care Medical Necessity Criteria [NOTE: Not applicable for cerliponase alfa (Brineura) requests]**

1. For requests for injection or infusion administration in an **inpatient setting**, the injection or infusion may be given if the above medical necessity criteria are met AND the inpatient admission is NOT for the sole purpose of administering the injection or infusion; **OR**
2. For requests for injection or infusion administration in an **outpatient hospital setting**, the injection or infusion may be given if the above medical necessity criteria are met AND ONE of the following must be met:

a. History of mild adverse events that have not been successfully managed through mild pre-medication (e.g., diphenhydramine, acetaminophen, steroids, fluids, etc.); **OR**
b. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity; **OR**
c. New to therapy, defined as initial injection or infusion OR less than 3 months since initial injection or infusion; **OR**
d. Re-initiation of therapy, defined as ONE of the following:
    i. First injection or infusion after 6 months of no injections or infusions for drugs with an approved dosing interval less than 6 months duration; **OR**
    ii. First injection or infusion after at least a 1-month gap in therapy outside of the approved dosing interval for drugs requiring every 6 months dosing duration; **OR**
e. Requirement of a change in the requested restricted product formulation; AND

3. If the Site of Care Medical Necessity Criteria in #1 or #2 above are not met, the injection or infusion will be administered in a home-based infusion or physician office setting with or without supervision by a certified healthcare professional.

References: all information referenced is from FDA package insert unless otherwise noted below.

1. Muenzer J, Beck M, Eng CM, et al. Long-term, open-labeled extension study of idursulfase in the treatment of Hunter syndrome. *Genet Med*. 2011;13(2):95-101.
2. Muenzer J, Beck M, Giugliani R, et al. Idursulfase treatment of Hunter syndrome in children younger than 6 years: results from the Hunter Outcome Survey. *Genet Med*. 2011;13(2):102-109.
3. Scarpa M, Almássy Z, Beck M, et al. Mucopolysaccharidosis type II: European recommendations for the diagnosis and multidisciplinary management of a rare disease. *Orphanet J Rare Dis*. 2011;6:72.
4. Valayannopoulos V, Malinova V, Honzík T, et al. Sebelipase alfa over 52 weeks reduces serum transaminases, liver volume and improves serum lipids in patients with lysosomal acid lipase deficiency. J Hepatol. 2014;61(5):1135-1142.
5. Diaz, G.A., Jones, S.A., Scarpa, M. *et al*. One-year results of a clinical trial of olipudase alfa enzyme replacement therapy in pediatric patients with acid sphingomyelinase deficiency. *Genet Med* 23, 1543-1550 (2021).
6. Wasserstein, M., Lachmann, R., Hollak, C. et al. A randomized, placebo-controlled clinical trial evaluating olipudase alfa enzyme replacement therapy for chronic acid sphingomyelinase deficiency (ASMD) in adults: one-year results. *Genet Med.* 2022.
7. Laney DA, Bennett RL, Clarke V, et al. Fabry disease practice guidelines: recommendations of the National Society of Genetic Counselors. *J Genet Couns.* 2013;22(5):555-564.

8. Schiffmann R, Goker-Aplan O, Holida M, et al. Pegunigalsidase alfa, a novel PEGylated enzyme replacement therapy for Fabry disease, provides sustained plasma concentrations and favorable pharmacodynamics: a 1-year phase 1/2 clinical trial. *J Inherit Metab Dis*. 2019 May;42(3):534-544.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q1 annually.

October 2023: Criteria change: For Fabrazyme: Added diagnostic requirements for Fabry disease; required baseline laboratory values for plasma globotriaosylceramide (GL-3) and/or GL-3 inclusions, plasma or urinary globotriaosylceramide (Gb3/GL-3), or plasma globotriaosylsphingosine (lyso-Gb3); and specialist requirement. **Policy notification given 8/2/2023 for effective date 10/1/2023**.
July 2023: Criteria change: Added newly approved Elfabrio to policy for treatment of adults with confirmed Fabry disease, added drug to SOC criteria and associated dosing and maximum units to FDA label reference table. Updated maximum units to all drugs within policy for clarity according to FDA label. Updated formatting throughout policy for clarity with no change to intent.
May 2023: Criteria change: Added newly approved Lamzede to policy for treatment of non-central nervous system manifestations of alpha-mannosidosis in adult and pediatric patients, added drug to SOC criteria and associated dosing and maximum units to FDA label reference table. Updated formatting of Xenpozyme criteria for clarity with no change to intent.
April 2023: Coding update: Added HCPCS code J0218 for Xenpozyme to doing reference table effective 4/1/2023; deleted C9399, J3490, and J3590 termed 3/31/2023.
September 2022: Criteria change: Added newly approved Xenpozyme to policy for treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients, added drug to SOC criteria and associated dosing and maximum units to FDA label reference table.
March 2022: Coding update: Added HCPCS code J0219 to dosing reference table for Nexviazyme effective 4/1/2022, deleted C9085, J3490, J3590
January 2022: Coding update: Added HCPCS code C9085 to dosing reference table for Nexviazyme effective 1/1/2022, deleted C9399 termed 12/31/2021. Blue Cross NC Pharmacy and Therapeutics Committee 12/21/2021.
November 2021: Criteria change: Added newly approved Nexviazyme to policy for treatment of late-onset Pompe disease in patients 1 year or older, added drug to SOC criteria and associated dosing and maximum units to FDA label reference table; updated Pompe disease criteria to include genetic testing as option for diagnosis confirmation.
June 2021: Criteria change: Added age requirement for Fabrazyme and Vimizim per FDA label; site of care requirements applicable to all requested agents except Brinuera. Blue Cross NC Pharmacy and Therapeutics Committee 6/29/2021.

June 2021: Criteria change: Added baseline assessment parameters and expansion of age to less than 5 years and ≥16 months of age to Elaprase criteria; added maximum units; medical policy formatting change. **Policy notification given 4/16/2021 for effective date 6/16/2021**.
*Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy.