Corporate Medical Policy: Enzyme Replacement Therapy (ERT) for Lysosomal Storage Disorders

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
- 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

FDA Approved Use:

- Imiglucerase (Cerezyme®)
    - For long-term ERT for pediatric and adult patients 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
- 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)
- Vestronidase alfa-vjbk (Mepsevii™)
  - For treatment of pediatric and adult patients with Mucopolysaccharidosis VII (MPS VII, Sly syndrome)
- 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

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. 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 request is for **agalsidase beta (Fabrazyme)**; **AND**
    b. The patient is 2 years of age or older; **AND**
    c. 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**
    d. Receipt of any requests for alternative drugs to treat Fabry disease (e.g., 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**
    c. A baseline percent predicted forced vital capacity (FVC) and/or 6-minute walk test has been documented **[medical record documentation required]**; **OR**
    d. The patient is < 5 years old and ≥16 months of age; **AND**
    e. The patient is experiencing at least ONE somatic symptom (e.g., skeletal disease, liver and/or spleen enlargement) **[medical record documentation required]**; **AND**
    f. 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]**; **AND**

11. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
12. If the request is for Aldurazyme, Cerezyme, Elaprase, Elelyso, Fabrazyme, Kanuma, Lumizyme, Mepsevii, Naglazyme, Nexviazyme, Vimizim, or Vpriv:
    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, Fabrazyme, Kanuma, Lumizyme, Mepsevii, Naglazyme, Nexviazyme, Vimizim, or Vpriv:
    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: Up to 60 U/kg every 2 weeks	J1786	14196
Taliglucerase alfa (Elelyso®)	Type 1 Gaucher disease	IV: 60 U/kg every other week	J3060	14196

intravenous (IV) infusion				
Velaglucerase Alfa (Vpriv®) intravenous (IV) infusion	Type 1 Gaucher disease	IV: 60 U/kg every other week	J3385	1420
Sebelipase alfa (Kanuma®) intravenous (IV) infusion	Lysosomal Acid Lipase (LAL) deficiency	Rapidly progressive LAL Deficiency presenting in first 6 months of life: 1 mg/kg IV once weekly; adjust up to 3 mg/kg weekly Pediatric and adult patients: 1 mg/kg IV every other week	J2840	14196
Agalsidase beta (Fabrazyme®) intravenous (IV) infusion	Fabry disease	IV: 1 mg/kg every two weeks	J0180	2366
Alglucosidase alfa (Lumizyme®) intravenous (IV) infusion	Pompe disease (GAA deficiency)	IV: 20 mg/kg every two weeks	J0221	4732
Avalglucosidase alfa-ngpt (Nexviazyme™) intravenous (IV) infusion	Pompe disease (GAA deficiency)	IV: • ≥30 kg: 20 mg/kg every 2 weeks • <30 kg: 40 mg/kg every 2 weeks	C9085 J3490** J3590**	46800
Laronidase (Aldurazyme®) intravenous (IV) infusion	Mucopolysaccharidosis I	IV: 0.58 mg/kg once weekly	J1931	2756
Idursulfase (Elaprase®) intravenous (IV) infusion	Mucopolysaccharidosis II	IV: 0.5 mg/kg once weekly	J1743	1183
Vestronidase alfa-vjbk (Mepsevii™) intravenous (IV) infusion	Mucopolysaccharidosis VII	IV: 4 mg/kg every two weeks	J3397	9464
Elosulfase alfa (Vimizim®) intravenous (IV) infusion	Mucopolysaccharidosis type IVA	IV: 2 mg/kg once weekly	J1322	9464
Galsulfase (Naglazyme®) intravenous (IV) infusion	Mucopolysaccharidosis VI	IV: 1 mg/kg once weekly	J1458	4732
Cerliponase alfa (Brineura®) intraventricular infusion	Batten Disease (CLN2)	IV: 300 mg every other week	J0567	7800

***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.

Policy Implementation/Update Information:

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.

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