



Nonprofit corporations and independent licensees
of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

RETIRED

Effective Date: 10/08/2020

Enzyme Replacement Therapy

Adagen® (pegademase bovine)
Aldurazyme® (laronidase)
Brineura® (cerliponase alfa)
Cerezyme® (imiglucerase)
Elaprase® (idursulfase)
Elelyso® (taliglucerase)
Fabrazyme® (agalsidase beta)
Kanuma® (sebelipase alfa)
Lumizyme® (alglucosidase alfa)
Mepsevii™ (vestronidase alfa-vjbk)
Myozyme® (alglucosidase alfa)
Naglazyme® (galsulfase)
Revcovi™ (elapegademase-lvlr)
Strensiq® (asfotase alfa)
Vimizim® (elosulfase alfa)
Vpriv® (velaglucerase alfa)

FDA approval: See Table 1

HPCPS: See Table 1

Benefit: Medical and Pharmacy - See Table 1

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. Type 1 Gaucher (*Cerezyme, Elelyso, Vpriv*)
 - i. Diagnosis must be made by or in consultation with a geneticist or metabolic specialist
 - ii. Diagnosis of Type 1 Gaucher disease confirmed by one of the following:
 - 1. Biochemical assay of glucocerebrosidase activity in WBCs or skin fibroblasts is less than or equal to 30% of normal activity (Note: laboratory normals may vary)
 - OR
 - 2. Genotyping revealing two pathogenic mutations of the glucocerebrosidase gene
 - iii. Symptomatic manifestations of the disease are present, such as anemia, thrombocytopenia, bone disease, hepatomegaly or splenomegaly

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

- iv. Patient has experienced treatment failure or intolerance to the preferred product
- b. Mucopolysaccharidosis (MPS)
 - i. Diagnosis must be made by or in consultation with a geneticist or metabolic specialist
 - ii. Baseline disease status must be documented
 - iii. MPS I (*Aldurazyme*)
 - 1. Diagnosis of Hurler and Hurler-Scheie forms of MPS I OR Scheie form who have moderate to severe symptoms (see Appendix 1)
 - 2. Diagnosis must be confirmed by serum assays showing enzyme deficiency of alpha-L-iduronidase AND urinary glycosaminoglycan (GAG), dermatan sulfate or heparin sulfate
 - iv. MPS II (*Elaprase*)
 - 1. Diagnosis of Hunter's Syndrome (MPS II)
 - 2. Diagnosis must be confirmed by serum assays of enzyme deficiency of iduronate sulfatase AND urinary GAG, dermatan sulfate or heparin sulfate
 - v. MPS IVA (*Vimizim*)
 - 1. 5 years of age or older AND
 - 2. Diagnosis of MPS IVA (Morquio A syndrome)
 - 3. Diagnosis must be confirmed by serum assays of enzyme deficiency of N-acetylgalactosamine-6-sulfatase AND urinary GAG keratin sulfate
 - vi. MPS VI (*Naglazyme*)
 - 1. Diagnosis of MPS VI
 - 2. Diagnosis must be confirmed by serum assays of enzyme deficiency of N-acetylgalactosamine-6-sulfatase AND urinary GAG dermatan sulfate
 - vii. MPS VII (*Mepsevii*)
 - 1. Diagnosis of MPS VII (Sly syndrome)
 - 2. Diagnosis must be confirmed by serum assays showing enzyme deficiency of beta-glucuronidase AND urinary glycosaminoglycan (GAG), dermatan sulfate, heparan sulfate, or chondroitin sulfate
- c. Fabry Disease (*Fabrazyme, Galafold*)
 - i. Diagnosis must be made by or in consultation with a geneticist or metabolic specialist
 - ii. Diagnosis of Fabry Disease
 - 1. All other conditions (such as cardioembolic stroke, or dissection syndromes) have been ruled out
 - 2. Diagnosis of males must show deficient activity of the enzyme α -galactosidase in plasma and/or leukocytes AND molecular genetic testing of GLA mutation
 - 3. Diagnosis of females must include molecular genetic testing of GLA mutation
 - 4. Galafold only – Must have amenable mutation per package insert
 - iii. Must show clinical manifestations of disease (kidney dysfunction, severe pain in the extremities, etc.) and provide baseline kidney, nervous system, and heart function as well overview of patient's quality of life
 - iv. Must provide goals of therapy
 - v. In patients with amenable mutation for Galafold, treatment failure or intolerance to the preferred product
 - vi. Patient will not be on concomitant treatment with Galafold and Fabrazyme
- d. Pompe Disease
 - i. Diagnosis must be made by or in consultation with a geneticist or metabolic specialist
 - ii. Diagnosis of infantile-onset Pompe disease. (*Myozyme or Lumizyme*)
 - 1. All other conditions (such as hypothyroidism or myocarditis) have been ruled out
 - 2. Diagnosis has been confirmed by the absence of GAA (acid alpha glucosidase) activity (via GAA mutation testing or GAA activity testing in fibroblasts or muscle) AND
 - 3. Diagnosis is supported by a series of screening tests including chest x-ray,

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

- electrocardiogram (ECG), electromyogram (EMG), and/or creatine kinase (CK) among other laboratory tests
- iii. Diagnosis of late-onset (non-infantile) Pompe disease and do not have evidence of cardiac hypertrophy. (*Lumizyme*)
 1. A diagnosis must be made by or in consultation with a geneticist or metabolic specialist
 - a) All other conditions (such as Polymyositis or Rheumatoid Arthritis) have been ruled out
 - b) Diagnosis has been confirmed by the reduced activity of GAA (acid alpha glucosidase) activity (via GAA mutation testing or GAA activity testing in fibroblasts or muscle)
AND
 - c) Diagnosis is supported by a series of screening tests including chest x-ray, electrocardiogram (ECG), electromyogram (EMG), and/or creatine kinase (CK) among other laboratory tests.
 - e. Adenosine Deaminase Deficiency (Severe Combined Immunodeficiency) (*Adagen, Revcovi*)
 - i. Diagnosis must be made by or in consultation with an immune specialist
 - ii. Diagnosis of adenosine deaminase (ADA) deficiency in patients with severe combined immunodeficiency disease (SCID)
 - iii. Diagnosis confirmed by evidence of combined immunodeficiency (very low T, B, and NK lymphocyte counts)
AND
 - iv. An absence of thymus and other lymphoid tissues
 - v. Have tried and failed or found to not be a suitable candidate (for example, unable to find donor) for bone marrow transplantation.
AND
 - vi. Does not have severe thrombocytopenia
 - f. Lysosomal acid lipase deficiency (LAL-d) (*Kanuma*)
 - i. Diagnosis must be made by or in consultation with a geneticist or metabolic specialist
 - ii. Diagnosis of LAL-d confirmed by blood test measuring LAL activity
OR genetic testing
 - iii. Symptomatic manifestations of the disease are present such as, elevated liver enzymes, microvesicular steatosis, elevated low-density lipoprotein, low high-density lipoprotein, or coronary artery disease
 - g. Pediatric-onset hypophosphatasia (HPP) (*Strensiq*)
 - i. Patient must be under the age of 18 at onset of symptoms
 - ii. Diagnosis must be made by or in consultation with a geneticist, metabolic specialist, endocrinologist, or bone and mineral specialist
 - iii. Diagnosis must be confirmed by all of the following:
 1. Medical history/physical exam
 2. X-ray skeletal alterations
 3. Low serum alkaline phosphatase (ALP) activity confirmed by high substrate levels (PPI, PEA, and PLP)
 4. Deficiency in TNSALP (tissue non-specific alkaline phosphatase) enzyme activity confirmed by either one or two pathogenic variants in the ALPL gene
 - iv. Must have documentation of active disease manifestations (examples: skeletal malformations/fractures, respiratory difficulties, dental manifestations, kidney damage, and seizures)
 - h. Late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) (*Brineura*)
 - i. Patient must be 3 years of age or older
 - ii. Diagnosis made by or in consultation with a neurologist, geneticist, or metabolic specialist
 - iii. Diagnosis must be confirmed by deficiency in tripeptidyl peptidase 1 enzyme OR genetic mutation in CLN2 gene

- iv. Patient must be ambulatory at the time of treatment initiation
- v. Documentation patient will be on standard of care regimen for CLN2 (e.g. seizure management, nutritional support, physical therapy)
- i. Trial and failure of the preferred products as listed in the BCBSM/BCN prior authorization and step therapy documents or the BCBSM/BCN utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria

a. Quantity Limit:

- i. *Cerezyme, Elelyso, Vpriv*:
 - 1. Lowest risk patients: 30 U/kg every 2 weeks
 - 2. Increased risk patients: 60U/kg every 2 weeks (please see Appendices 2 and 3)
- ii. *Aldurazyme*: 0.58 mg/kg intravenous (IV) infusion once weekly
- iii. *Elaprase*: 0.5 mg/kg as an IV infusion once a week
- iv. *Vimizim*: 2 mg/kg/week with no more than one dose per week.
- v. *Naglazyme*: 1 mg/kg once weekly
- vi. *Fabrazyme*: 1 mg/kg body weight infused every 2 weeks
- vii. *Mepsevii*: 4mg/kg every 2 weeks
- viii. *Myozyme/Lumizyme*: 20 mg/kg body weight administered every 2 weeks
- ix. *Adagen*: 30 units/kg intramuscularly once weekly
- x. *Kanuma*:
 - 1. Pediatric and adult patients with LAL-d: 1 mg/kg every 2 weeks
 - 2. Patients < 6 months with rapidly progressive LAL-d: 3 mg/kg once weekly
- xi. *Strensiq*: 2 mg/kg subcutaneously three times a week or 1 mg/kg subcutaneously six times a week.
- xii. *Brineura*: 300 mg every other week by intraventricular injection followed by infusion of intraventricular electrolytes over 4.5 hours
- xiii. *Galafold*: 14 capsules per 28 days
- xiv. *Revcovi*: 0.2 mg/kg – 0.4 mg/kg weekly based on initial therapy or transitioning from Adagen

b. Initial Authorization Period: 6 months

c. Renewal Criteria: Must meet initial criteria above AND

- i. Gaucher Disease (*Cerezyme, Elelyso, Vpriv*)
 - 1. Documentation showing maintenance or improvement in disease must be provided including assessments of hemoglobin, platelet count, and liver and/or spleen volumes by MRI, if the MRI is clinically indicated
- ii. Mucopolysaccharidosis (*Aldurazyme, Elaprase, Vimizim, Naglazyme, Mepsevii*)
 - 1. Patient must have improved or stabilized from baseline disease status
 - 2. Examples of improvement vary by disease; however, they could include improved quality of life, decreased hepatosplenomegaly, or decreased urinary GAG levels
- iii. Fabry Disease (*Fabrazyme, Galafold*)
 - 1. Documentation that goals of therapy have been met. These goals may include decreases in pain, fatigue or overall improvement in kidney or cardiovascular function
- iv. Pompe Disease (*Myozyme, Lumizyme*)
 - 1. Documentation of patient's progress of disease status from notes by physician
- v. Adenosine Deaminase Deficiency (Severe Combined Immunodeficiency) (*Adagen, Revcovi*)
 - 1. Documentation of patient's progress of disease status from notes by physician
- vi. Lysosomal Acid Lipase Deficiency (*Kanuma*)
 - 1. Documentation showing maintenance or improvement in disease must be provided
 - 2. Examples of improvement may include (but are not limited to) normal liver enzymes and improved lipid levels
- vii. Hypophosphatasia (*Strensiq*)
 - 1. Documentation of response to therapy
 - 2. Examples of response to therapy may include (but are not limited to) improvement in respiratory status and skeletal structure

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

- viii. Late infantile neuronal ceroid lipofuscinosis type 2 (*Brineura*)
 - 1. Documentation of response to therapy
 - 2. Currently ambulatory while on therapy
- d. Renewal Authorization Period: 1 year

C. Enzyme Replacement Therapy is considered investigational when used for all other conditions, including but not limited to:

- a. Types 2 or 3 Gaucher Disease
- b. Enzyme deficiency other than the N-acetylgalactosamine-6-sulfase (GALNS) enzyme deficiency
- c. Non-ambulatory patients with ventilator dependence
- d. Use in combination with Zavesca for Type 1 Gaucher
- e. Adult-onset HPP for hypophosphatasia
- f. Other forms of Batten Disease
- g. Use for anything other than FDA approved indication

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Therapeutic considerations:

A. FDA approved indication/Diagnosis

Table 1

Drug/ Manufacturer/ Approval Date	J Codes	Pharmacy /Medical	FDA Indications
Adagen® March 21, 1990 <i>P&T History:</i> <i>Unknown</i>	J2504	Medical	Injection is indicated for enzyme replacement therapy (ERT) for adenosine deaminase (ADA) deficiency in patients with severe combined immunodeficiency disease (SCID) who are not suitable candidates for – or who have failed – bone marrow transplantation.
Aldurazyme® April 30, 2003 <i>P&T History:</i> <i>Unknown</i>	J1931	Medical	Indicated for patients with Hurler and Hurler-Scheie forms of Mucopolysaccharidosis (MPS) I and for patients with the Scheie form who have moderate to severe symptoms.
Brineura® April 27, 2017 <i>P&T History:</i> 11/9/2017	J0567	Medical	Indicated to slow 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.
Cerezyme® May 23, 1994 <i>P&T History: Unknown</i> <i>Drug Review/Type 1 Gaucher</i> <i>– 8/9/12</i>	J1786	Medical	Indicated for long-term ERT for 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.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

Elaprase® July 24, 2006 <i>P&T History: 10/26/06</i>	J1743	Medical	Indicated for patients with Hunter syndrome (MPSII).
Drug/ Manufacturer/ Approval Date	J Codes	Pharmacy /Medical	FDA Indications
ElELYso® May 1, 2012 <i>P&T History: 8/9/12/ Type 1 Gaucher – 8/9/12</i>	J3060	Medical	A hydrolytic lysosomal glucocerebroside-specific enzyme indicated for long-term ERT for adults and children with a confirmed diagnosis of Type 1 Gaucher disease.
Fabrazyme® April 24, 2003 <i>P&T History: Unknown</i>	J0180	Medical	Indicated for use in patients with Fabry disease.
Galafold™ August 10, 2018 <i>P&T History: 11/1/18</i>		Pharmacy	Indicated for use in patients with Fabry disease and an amenable galactosidase alpha gene (GLA) variant
Kanuma® December 8, 2015 <i>P&T History: 5/5/2015</i>	J2840	Medical	Indicated for lysosomal acid lipase deficiency
Lumizyme® May 24, 2010 <i>P&T History: 7/15/10</i>	J0221	Medical	Patients with Pompe Disease (acid α-glucosidase deficiency)
Mepsevii™ November 15, 2017 <i>P&T History: 3/15/18</i>	J3397	Medical	Indicated for the treatment of Mucopolysaccharidosis VII (MPS VII, Sly syndrome) in pediatric and adult patients.
Myozyme® April 28, 2006 <i>P&T History: 10/26/06</i>	J0220	Medical	Indicated for use in patients with Pompe disease.
Naglazyme® May 31, 2005 <i>P&T History: 10/20/05</i>	J1458	Medical	Indicated for patients with MPS VI
Revcovi™ October 5, 2018 <i>P&T History: 11/1/2018</i>	J3490	Pharmacy	Indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients
Strensiq® October 23, 2015 <i>P&T History: 11/05/2015</i>	J3490/ J3590	Pharmacy	Indicated for the treatment of patients with hypophosphatasia (HPP) whose first signs and symptoms occurred prior to 18 years of age, including perinatal, infantile, and juvenile-onset forms of the disease.
Vimizim® February 14, 2014 <i>P&T History: 4/22/2010</i>	J1322	Medical	Indicated for patients with MPS IVA
Vpriv® February 26, 2010 <i>P&T History: 4/22/2010/ Type 1 Gaucher – 8/9/12</i>	J3385	Medical	Indicated for long-term ERT for patients with type 1 Gaucher disease.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

**Please refer to most recent prescribing information.*

B. Background Information

- a. ERT is a lifelong therapy that falls under multiple disease state categories. The most common is the lysosomal storage diseases (LSDs) which covers Gaucher disease, Fabry disease, Pompe Disease, LAL-d, and the mucopolysaccharidoses among many others
- b. LSDs are genetic diseases defined by the lack of sufficient enzymatic activity (via enzyme deficiency or dysfunction) to prevent the accumulation of specific macromolecules
 - i. *Gaucher Disease*
 1. Type 1 Gaucher Disease is the most common of the LSDs (and much more common than Type 2 or 3 Gaucher disease). Onset of symptoms vary from early childhood to late adulthood with early childhood cases typically being the most severe
 2. Signs and symptoms include anemia, hepatosplenomegaly, skeletal disease and sometimes lung or liver impairment
 3. International Collaborative Gaucher Group (ICGG) International and US Regional Coordinators have made multiple recommendations (these descriptions will not be used in determinations when patients are new members to BCBSM/BCN, and stable on therapy):
 - a) Decisions regarding dose management should be made by physicians who are experienced in caring for patients with Gaucher disease
 - b) Patients with severe manifestations are not recommended to have dose reductions after initial improvement
 - c) The deciding factor for dosing is achieving the therapeutic goals. It is recommended that dose reductions may not be appropriate until significant improvements are achieved and maintained for at least a year
 - d) Failure to achieve goals may indicate a need for an increase in enzyme dose or frequency of administration
 - e) Adult increased risk patients who have achieved all therapeutic goals can have the dose decreased in small increments (approx. 15-20%) until next scheduled evaluation in 3 - 6 months. Similar decreases may be considered if patient continues to meet therapeutic goals
 - f) Increased risk adults with severe disease and all children, it is not recommended for long term maintenance dose <30 U/kg every 2 weeks
 - g) Lower-risk adult patients may tolerate larger dose reductions of 25-50% per dose. Minimum long-term dose is recommended to be no < 20 U/kg every 2 weeks
 - h) The time required from start of ERT to achieve therapeutic goals is approximately 12 - 36 months
 4. Enzyme Replacement treatments used to treat Type 1 Gaucher Disease include Cerezyme, VPRIV, and Elelyso
 - ii. *Fabry Disease*
 1. Incidence of this condition is estimated at 1 in 50,000 individuals and affects primarily males. Without treatment males typically live to 41-55 years and females about 15 years less than the average life-span of females
 2. Major organ dysfunction can occur in this disease, including the kidney, cardiovascular system and GI tract. Therapy is recommended to start initial prior to obvious organ dysfunction
 3. Drugs used to treat Fabry disease include Fabrazyme and Galafold
 - iii. *Pompe Disease (Glycogen Storage Disease Type 2)*
 1. Caused by deficiency of alpha-glucosidase resulting in lysosomal glycogen accumulation
 2. Divided into early and late onset forms
 3. Life expectancy in early forms is less than 1 year

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

4. Late onset form can occur from childhood into the 60s with primary musculoskeletal involvement
5. Drugs used to treat Pompe disease is Myozyme and Lumizyme
- iv. *Mucopolysaccharidoses (MPS)*
 1. Group of LSDs that result in abnormal tissue accumulations of glycosaminoglycans
 2. There are multiple MPS disorders with 4 of the disorders having enzyme replacement therapy available: MPS I (Hurler, Hurler-Scheie, and Scheie syndrome), MPS II (Hunter Syndrome), MPS VI (Maroteaux-Lamy Syndrome), and MPSVII (Sly Syndrome)
 3. Stem cell or bone marrow transplant (BMT) is the standard of care for patients with severe MPS I (Hurler syndrome) if diagnosed and performed under the age of 2 years old
 4. Drugs used to treat MPS diseases include Aldurazyme, Elaprase, Mepsevii, Naglazyme, and Vimizim
 5. Rationale for treatment is to provide the patient with active enzyme to replace the deficient enzyme
- v. *Lysosomal Acid Lipase Deficiency*
 1. LAL-d is a rare autosomal recessive genetic disease caused by a mutation in the LIPA gene
 2. LAL is necessary for cleavage of triglycerides and cholesteryl esters delivered to lysosomes and deficiencies leads to accumulation of esters in vital organs and tissues with subsequent progressive multi-system organ damage with symptoms such as elevated in liver enzymes and changes to the lipid profile that eventually leads to death
 3. Two major phenotypes of this condition are Wolman disease, which manifest in infancy, and cholesteryl ester storage disease (CESD)
 4. Drug used to treat LAL-d is Kanuma
- c. Adenosine deaminase (ADA) deficiency in a patient with severe combined immunodeficiency disease (SCID):
 - i. ADA is a systemic purine metabolic disorder that primarily affects lymphocyte development, viability, and function
 - ii. Deficiency is typically shown by very low T, B, and NK lymphocyte counts in peripheral blood and an absence of thymus and other lymphoid tissues
 - iii. SCID is most often diagnosed between 6 and 12 months of age, but can have a delayed onset into adulthood
 - iv. ERT is not curative and must be given in order to maintain non-toxic metabolic environment
 1. Adagen has been used as a primary therapy in individuals who lack an HLA-identical marrow/stem cell donor when the risks associated with a partially mismatched transplant are deemed too great or when the risk of graft failure is high, as in older individuals with a delayed or late-onset phenotype
 2. Also, been used as a secondary therapy in patients who have failed to engraft following an unconditioned BMT/SC, or in whom an acceptable recovery of immune function has not been achieved following experimental gene therapy
 - v. Drug used to treat this disease is Adagen and Revcovi
- d. Hypophosphatasia (HPP):
 - i. HPP is an inherited metabolic disorder caused by a mutation of the enzyme tissue-nonspecific isoenzyme of alkaline phosphatase (TNSALP)
 - ii. HPP has an incidence rate of 1 in 100,000 live births. Patients who develop symptoms of HPP by 6 months of age have a mortality rate of over 70% by the age of 5
 - iii. Alterations in the TNSALP gene can lead to low alkaline activity levels and ultimately to bone pain and fractures, seizures, respiratory depression, rickets, osteomalacia, or both, which characterize this disorder
- e. Late infantile neuronal ceroid lipofuscinosis type 2 (CLN2)
 - i. CLN2 is one of a group of disorders known as neuronal ceroid lipofuscinoses (NCLs) collectively referred to as Batten disease
 - ii. The estimated incidence of CLN2 is approximately one in 200,000
 - iii. It is a rare inherited disorder caused by a mutation in the CLN2 gene that directs production of the

enzyme TPP1

- iv. CLN2 is a rapidly progressing, fatal disease usually presenting between the ages of 2 to 4 years. Initial symptoms can include language delay and seizures, followed by movement disorders, motor deterioration, dementia and blindness, death often occurs between 8 and 12 years of age

Cross References	
Vimizim (elosulfase alfa)	08/14/2014
Ellyso (taliglucerase alfa)	08/09/2012
Enzyme Replacement Therapy for the Treatment of Gaucher Disease	08/09/2012
Strensiq (asfotase alfa)	02/11/2016
Kanuma (sebelipase alfa)	05/05/2016

C. Efficacy

**Please refer to most recent prescribing information.*

D. Medication Safety Considerations

Black Box Warning: Yes

**Please refer to most recent prescribing information.*

E. Dosing and administration

**Please refer to most recent prescribing information.*

F. How supplied

**Please refer to most recent prescribing information.*

References:

1. Adagen Package Insert. Retrieved from the U.S. Food and Drug Administration website: [http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/019818s053lbl.pdf].
2. Aldurazyme Package Insert. Retrieved from the U.S. Food and Drug Administration website: [http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/125058s220lbl.pdf].
3. Cerezyme Package Insert. Retrieved from the U.S. Food and Drug Administration website: [http://www.accessdata.fda.gov/drugsatfda_docs/label/2005/20367s066lbl.pdf].
4. Elaprase Package Insert. Retrieved from the U.S. Food and Drug Administration website: [http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/125151s0184lbl.pdf].
5. Ellyso Package Insert. Retrieved from the U.S. Food and Drug Administration website: [http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/022458s013lbl.pdf].
6. Fabrazyme Package Insert. Retrieved from the U.S. Food and Drug Administration website: [http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/103979s5135lbl.pdf].
7. Lumizyme Package Insert. Retrieved from the U.S. Food and Drug Administration website: [http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125291s133lbl.pdf].
8. Mepsevii [prescribing information]. Novato, CA: Ultragenyx Pharmaceutical Inc.; November 2017.
9. Myozyme Package Insert. Retrieved from the U.S. Food and Drug Administration website: [http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125141s219lbl.pdf].
10. Naglazyme Package Insert. Retrieved from the U.S. Food and Drug Administration website: [http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/125117s111lbl.pdf].
11. Vpriv Package Insert. Retrieved from the U.S. Food and Drug Administration website:

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

- [http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/022575s017lbl.pdf].
12. Vimizim Package Insert. Retrieved from the U.S. Food and Drug Administration website: [http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125460s000lbl.pdf].
 13. Andersson HC et al. Individualization of long-term enzyme replacement therapy for Gaucher disease. *Genetics in Medicine*. 2005; 7(2): 105-110.
 14. Weinreb N et al. A benchmark analysis of the achievement of therapeutic goals for type 1 Gaucher disease patients treated with imiglucerase. *Am J Hematol*. 2008; 83(12):890-95.
 15. Gonzalez DE et al. Enzyme replacement therapy with velaglucerase alfa in Gaucher disease: Results from a randomized, double blind, multinational, Phase 3 study. *Am J Hematol*. 2013; 88(3):166-71.
 16. Lehman TJ et al. Diagnosis of Mucopolysaccharidosis. *Rheumatology*. 2011; 50:v41-v48. Available at: http://rheumatology.oxfordjournals.org/content/50/suppl_5/v41.full.pdf+html. Accessed: August 11, 2014.
 17. Valayannaopoulos V and Wijburg F. Therapy for mucopolysaccharidosis. *Rheumatology*. 2011; 50:v49-459. Available at: http://rheumatology.oxfordjournals.org/content/50/suppl_5/v49.full.pdf+html. Accessed August 11, 2014.
 18. Mehta A and Hughes D. Fabry Disease. Gene Reviews® [Internet]. Seattle (WA): University of Washington, Seattle: 1993-2014. Available at: <http://www.ncbi.nlm.nih.gov/books/NBK1292/>. Accessed: August 8, 2014.
 19. Lidove O, et al. Effects of enzyme replacement therapy in Fabry disease – A comprehensive review of the medical literature. *Genetics in Medicine*. November, 2010;12(11):668-679. Available at: <http://www.nature.com/gim/journal/v12/n11/full/gim2010112a.html>. Accessed: August 8, 2014.
 20. Kishnani P et al. Pompe disease diagnosis and management guideline. ACMG Practice Guideline. May 2006: 8(5):267-288. Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3110959/pdf/16702877.pdf>. Accessed: July 29, 2014.
 21. Hassan A et al. Outcome of hematopoietic stem cell transplantation for adenosine deaminase-deficient severe combined immunodeficiency. *Blood* 2012; 120(17): 3612-3624. Bone Marrow Transplant for ADA-SCID: Available at: <http://www.bloodjournal.org/content/bloodjournal/120/17/3615.full.pdf?sschecked=1>. Accessed August 12, 2014.
 22. Adagen Provides Efficacious ERT. Available at: http://www.adagen.com/adagen_efficacy_data.html. Accessed 8/12/14.
 23. Cimaz R, La Torre F. Mucopolysaccharidoses. *Curr Rheumatol Rep*. 2014; 16(389):1-9.
 24. Burton BK, Balwani M, Feillet F et al. A Phase 3 Trial of Sebelipase Alfa in Lysosomal Acid Lipase Deficiency. *N Engl J Med*. 2015;373:1010-1020.
 25. European Commission Grants Marketing Authorization for Strensiq (asfotase alfa) for the Treatment of Patients with Pediatric-Onset Hypophosphatasia (HPP). Available at <http://www.businesswire.com/news/home/20150831006265/en/European-Commission-Grants-Marketing-Authorization-Strensiq%E2%84%A2-asfotase#.Vq2CHuxViko>. Accessed 9/9/2015.
 26. First Treatment Recommended for Rare Bone Disease. Available at http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/06/news_detail_002355.jsp&mid=WC0b01ac058004d5c1. Accessed 9/9/2015.
 27. Jones SA, Plantaz D, Vara R et al. Effect of sebelipase alfa on survival and liver function in infants with rapidly progressive lysosomal acid lipase deficiency. *Molecular Genetics and Metabolism*. 2015;114(2):S59.
 28. Kanuma Package Insert. Retrieved from the U.S. Food and Drug Administration website: [http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125561s000lbl.pdf].
 29. Brineura Package Insert. Retrieved from the U.S. Food and Drug Administration website: [https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761052lbl.pdf].
 30. de los Reyes E, Schulz A, Specchio N, et al. Intracerebroventricular cerliponase alfa (BMN 190) in children with CLN2 disease: Results from a Phase 1/2, open-label, dose-escalation study [poster 228]. Presented at: the 12th Annual WORLDSymposium; San Diego, CA; February 29 - March 3, 2016.
 31. Williams RE, Adams HR, Blohm M, et al. Management strategies for CLN2 disease. *Pediatr Neurol*. 2017;69:102-112.
 32. Mepsevii [prescribing information]. Novato, CA: Ultragenyx Pharmaceutical Inc.; November 2017.
 33. A Phase 3 Study of UX003 rhGUS Enzyme Replacement Therapy in Patients with MPS 7. *ClinicalTrials.gov*. <https://clinicaltrials.gov/ct2/show/NCT02230566>. 2017.
 34. A Long-term Open-Label Treatment and Extension Study of UX003 rhGUS Enzyme Replacement Therapy in Subject

- with MPS 7. ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT02230566>. 2017.
35. An Open-Label Phase 1/2 Study to Assess the Safety, Efficacy and Dose of Study Drug UX003 Recombinant Human Beta-glucuronidase (rhGUS) Enzyme Replacement Therapy in Patients with MPS 7. ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT01856218>. 2017.
 36. Montañó AM, Lock-hock N, Steiner RD, et al. Clinical course of sly syndrome (mucopolysaccharidosis type VII). J Med Genet. 2016;53(6):403-18.
 37. FDA Press Release. FDA approves treatment for rare genetic enzyme disorder. Available at: <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm585308.htm>. Accessed November 21, 2017.
 38. Ultragenyx Press Release. Ultragenyx Announces FDA Approval of MEPSEVII™ (vestronidase alfa), the First Therapy for Progressive and Debilitating Rare Genetic Disease Mucopolysaccharidosis VII. Available at <http://ir.ultragenyx.com/releasedetail.cfm?releaseid=1048901>. Accessed November 21, 2017.
 39. National Organization for Rare Disorders. Mucopolysaccharidosis Type VII. Available at: <https://rarediseases.org/rare-diseases/sly-syndrome>. Accessed November 21, 2017.
 40. FiercePharma. Ultragenyx snares FDA nod for ultraorphan med Mepsevii, and a valuable voucher, too. Available from: <https://www.fiercepharma.com/regulatory/ultragenyx-picks-up-fda-nod-for-ultra-orphan-med-mepsevii> Accessed November 21, 2017.
 41. Galafold™ [Prescribing Information]. Cranbury, NJ: Amicus Therapeutics U.S., Inc; 2018.
 42. Amicus Therapeutics. U.S. FDA Files New Drug Application Under Priority Review for Migalastat for Treatment of Fabry Disease. February 12, 2018. Available at: <http://ir.amicusrx.com/news-releases/news-release-details/us-fda-files-new-drug-application-under-priority-review>. Accessed September 12, 2018.
 43. Revcovii™ [prescribing information]. Gaithersburg, MD. Leadiant Biosciences; 2018.

Policy History		
#	Date	Change Description
3.6	Effective Date: 10/08/2020	Policy to be retired and broken down into multiple smaller class policies
3.5	Effective Date: 08/13/2020	Annual Review
3.4	Effective Date: 08/15/2019	Updated criteria for Strensiq
3.3	Effective Date: 06/03/2019	PA added to Mepsevii for BCNA and MAPPO
3.2	Effective Date: 02/14/2019	Updated to add Recovi
3.1	Effective Date: 02/01/2019	PA added to Kanuma for MAPPO
3.0	Effective Date: 06/03/2019	PA added to Mepsevii for BCNA and MAPPO
2.9	Effective Date: 05/20/2019	PA removed from Myozyme for MAPPO and BCNA
2.8	Effective Date: 02/01/2019	PA added to Kanuma for MAPPO
2.7	Effective Date: 05/03/2018	Updated with Mepsevii
2.6	Effective Date: 03/01/2018	PA added to Mepsevii for BCBSM and BCN
2.5	Effective Date: 11/09/2017	Updated with Brineura
2.4	Effective Date: 10/01/2017	PA added to Brinuria for BCN

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

2.3	Effective Date: 09/01/2017	PA added to Brinuria for BCBS
2.2	Effective Date: 07/20/2017	PA added to Myozyme for MAPPO and BCNA
2.1	Effective Date: 07/05/2017	PA added for the following drugs to MAPPO and BCNA: Adagen, Aldurazyme, Cerezyme, Elaprase, Elelyso, Fabrazyme, Lumizyme, Vimizim, and VPriv
2.0	Effective Date: 05/04/2017	Annual Review Update
1.9	Effective Date: 01/01/2017	PA added to Kanuma for BCNA
1.8	Effective Date: 05/05/2016	Updates with newly approved Kanuma
1.7	Effective Date: 02/11/2016	Updates with newly approved drug Strensiq
1.6	Effective Date: 02/01/2016	PA added to Kanuma for BCBS
1.5	Effective Date: 01/01/2016	PA added to Kanuma for BCN
1.4	Effective Date: 11/05/2015	Updated with preliminary UM criteria two new therapies (sebelipase alfa and asfotase alfa)
1.3	Effective Date: 07/01/2015	PA added to the following drugs for BCN: Adagen, Aldurazyme, Lumizyme, and Naglazyme
1.2	Effective Date: 02/01/2015	PA added to the following drugs for BCN: Cerezyme, Elaprase, Elelyso, Fabrazyme, Vimizim, and VPriv
1.1	Effective Date: 01/01/2015	PA added to the following drugs for BCBS: Adagen, Aldurazyme, Cerezyme, Elaprase, Elelyso, Fabrazyme, Lumizyme, Naglazyme, Vimizim, and VPriv
1.0	Effective Date: 10/30/2014	New Class Criteria Document

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.*