Blue Cross Blue Shield Blue Care Network of Michigan

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Effective Date: 10/12/2023

Enzyme Replacement Therapy for Mucopolysaccharidosis (MPS)

Aldurazyme® (laronidase)
Elaprase® (idursulfase)
Mepsevii™ (vestronidase alfa-vjbk)
Naglazyme® (galsulfase)
Vimizim™ (elosulfase alfa)

HCPCS: Aldurazyme: J1931, Elaprase: J1743, Mepsevii: J3397, Naglazyme: J1458, Vimizim: J1322

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. Aldurazyme
      i. FDA approved indications
      ii. FDA approved age
      iii. Confirmation of diagnosis by serum assay showing a decrease of α-L-iduronidase activity followed by genetic testing showing a mutation in the IDUA gene
   b. Elaprase
      i. FDA approved indication
      ii. FDA approved age
      iii. Confirmation of diagnosis by serum assay showing a decrease of iduronate sulfatase activity followed by genetic testing showing a mutation in the I2S gene
   c. Vimizim
      i. FDA approved indication
      ii. FDA approved age
      iii. Confirmation of diagnosis by serum assay showing a decrease in N-acetly-galactosamine-6-sulfatase followed by genetic testing showing a mutation in the GALNS gene
   d. Naglazyme
      i. FDA approved indication
      ii. FDA approved age
      iii. Confirmation of diagnosisby serum assay of enzyme deficiency of N-acetylgalactosamine-4-sulfatase activity followed by genetic testing showing a mutation in the ARSB gene
   e. Mepsevii
      i. FDA approved indication
      ii. FDA approved age

iii. Confirmation of diagnosis by serum assay showing a decrease in β-glucoronidase activity followed by genetic testing showing a mutation in the GUSB gene

f. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list and/or BCBSM/BCN's prior authorization and step therapy documents.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: 1 year at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration 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.

Background Information

- The mucopolysaccharidoses (MPS) are lysosomal storage disorders caused by the deficiency of enzymes required for the stepwise breakdown of glycosaminoglycans (GAGs). All of the MPS subtypes are autosomal recessive disorders, with the exception of MPS II, which is X linked. The phenotype of these disorders covers a broad spectrum, from mild to severe. In general, the severity depends upon the quantity of residual enzyme, which is related to the genotype of the affected patient. The MPS disorders are differentiated clinically by their clinical features and age of presentation and biochemically by their associated enzyme deficiency.

- MPS type I (Hurler syndrome, Hurler-Scheie syndrome, or Scheie syndrome)

    - MPS type I is autosomal recessive lysosomal storage disorder caused by a mutation on the gene IDUA. It is characterized by lysosomal accumulation of undegraded heparan and dermatan sulfate due to a deficiency or insufficient activity of the enzyme α-L-iduronidase. There are three main disease variants: Hurler, the most severe with early onset and neurocognitive regression, Hurler-Scheie, the form with intermediate onset and severity, and Scheie, the most mild of the subtypes. Signs, symptoms, and severity vary greatly among MPS type I patients. The most common symptoms include hepatosplenomegaly, hernias, neurocognitive and developmental issues in the more severe forms, cervical spinal cord compression, corneal clouding, open-angle glaucoma, valvular dysplasia and insufficiency, carpal tunnel, short stature, and osteopenia/osteoporosis.

    - The American College of Medical Genetics 2011 guidelines state MPS type I is confirmed through serum assay showing a decrease of α-L-iduronidase activity. Once shown the patient has a decrease in enzyme activity, a genetic test should be performed which should show a mutation in the IDUA gene. Both tests must be demonstrative of disease for the diagnosis to be confirmed.

    - Enzyme replacement (ERT) and stem cell transplant (SCT) are the only treatment options for MPS type I. Aldurazyme is the only FDA approved enzyme replacement therapy for MPS type I. It is approved for adult and pediatric patients with Hurler and Hurler-Scheie forms of MPS type I and for patients with the Scheie form who have moderate to severe symptoms. ERT should be initiated on the judgement of the treating physician and can be held in milder disease until a more significant clinical picture presents. If patients are found to have severe disease or be at risk for neurocognitive decline, they should be assessed for SCT.

Patients should be reassessed every 3 months and if the physician starts to see developmental delays, skeletal manifestations, or severe organomegaly SCT should be considered at that time.

- MPS type II (Hunter syndrome)

    - MPS type II is a X-linked recessive lysosomal storage disorder caused by a mutation on the I2S gene. It is characterized by lysosomal accumulation of undegraded heparan and dermatan sulfate due to a deficiency of the enzyme iduronate-2-sulfatase. Signs, symptoms, and severity can vary greatly among MPS type II patients due to the multisystem nature of the disease. The most common symptoms include coarsened facial features, an enlarged head, an enlarged tongue, hypertrophic tonsils and adenoids, irregularly shaped teeth, recurrent otitis media, hepatosplenomegaly, abdominal and/or inguinal hernias, thickened pebbled skin, and short stature.

    - The American College of Medical Genetics 2011 guidelines state MPS type II should be confirmed through serum assay showing a decrease of iduronate-2-sulfatase activity. Once shown the patient has a decrease in enzyme activity, a genetic test should be performed which should show a mutation in the I2S gene. Both tests must be demonstrative of disease for the diagnosis to be confirmed.

    - Enzyme replacement is the standard of care in MPS type II. Elaprase the only FDA approved ERT for patients with MPS type II. Safety and efficacy have not been established in patients younger than 16 months of age. Initiation of ERT should be done based on the judgement of the treating physician and parents should be counselled on the inability to reverse the cognitive deficits of the disease.

- MPS type IVA (Morquio A syndrome)

    - MPS type IVA is a autosomal recessive lysosomal storage disorder caused by a mutation on the GALNS gene. It is characterized by lysosomal accumulation of keratan sulfate and chondroitin-6-sulfate due to a deficiency of the enzyme N-acetyl-galactosamine-6-sulfatase. Symptoms include growth delays, a prominent lower face, kyphoscoliosis or concern for a spine abnormality, an abnormally short neck, knees that are abnormally close together, flat feet, abnormal development of the growing ends of the long bones, hip dislocation, arthritis, and/or a prominent breast bone.

    - MPS type IVA diagnosis is suggested by the findings of medical history, physical examinations, skeletal X-rays, and urine GAG analysis. Excessive amounts of keratan sulfate will usually be present in the urine. Diagnosis is confirmed by low N-acetyl-galactosamine-6-sulfatase activity in cultured blood or skin cells and/or molecular genetic testing to identify *GALNS* gene mutations.

    - Vimizim is the only FDA approved ERT for patients with MPS type IVA. Safety and efficacy have not been established in patients younger than 5 years of age. Initiation of ERT should be done based on the judgement of the treating physician. All other therapies are symptomatic and supportive.

- MPS type VI (Maroteaux-Lamy syndrome)

    - MPS type VI is a autosomal recessive lysosomal storage disorder caused by a mutation on the ARSB gene. It is characterized by lysosomal accumulation of undegraded dermatan sulfate due to a deficiency of the enzyme N-acetylgalactosamine-4-sulfatase. Age of presentation and velocity of disease progression are variable, but affected patients typically come to medical attention at 6 – 24 months of age. The most common symptoms include deceleration of growth velocity, macrocephaly, macroglossia, facial coarsening, hepatosplenomegaly, progressive corneal clouding, open-angle glaucoma, skeletal abnormalities, painful hip dysplasia, restriction in joint mobility, cardiac valvular dysfunction, recurrent otitis media, conductive hearing loss, and upper airway obstruction.

- The American College of Medical Genetics 2011 guidelines state MPS type VI should be confirmed through serum assay showing a decrease of N-acetylgalactosamine-4-sulfatase activity. Once shown the patient has a decrease in enzyme activity, a genetic test should be performed which should show a mutation in the ARSB gene. Both tests must be demonstrative of disease for the diagnosis to be confirmed.

- Enzyme replacement (ERT) and stem cell transplant (SCT) are the only treatment options for MPS type VI. Naglazyme is the only FDA approved enzyme replacement therapy for MPS type VI. It has been studied in patients 3 months of age and older. Families should be counselled on both treatment choices. If ERT is the modality of choice, it should be started immediately.

- MPS type VII (Sly syndrome)

    - MPS type VII is a autosomal recessive lysosomal storage disorder caused by a mutation on the GUSB gene. It is characterized by lysosomal accumulation of undegraded dermatan sulfate, chondroitin-4,6-sulfate, and heparan sulfate due to a deficiency of the enzyme β-glucuronidase. Signs, symptoms, and severity can vary among MPS type VII patients. The most severe cases are characterized by hydrops fetalis which can result in stillbirth or death shortly after birth. More mild cases start to present in early childhood with the most common symptoms including short trunk, growth disability, short trunk dwarfism, macrocephalic head, short neck, dysostosis multiplex, coarse facial appearance, cloudy corneas, developmental delays in language and speech, hepatosplenomegaly, hearing loss, hernias, thickening of the soft tissues of the throat, abnormally large tongue, and heart problems.

    - MPS type VII diagnosis is suggested by the findings of medical history and urine GAG analysis. Excessive amounts of dermatan sulfate, chondroitin-4,6-sulfate, and heparan sulfate will usually be present in the urine. Diagnosis is confirmed by low β-glucuronidase activity in cultured blood or skin cells and/or molecular genetic testing to identify GUSB gene mutations.

    - Mepsevii is the only FDA approved ERT for use in pediatric and adult patients for the treatment of MPS type VII. Safety and efficacy have been established in patients younger than 18 months of age. All other therapies are symptomatic and supportive.

References:

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2. Elaprase [prescribing information]. Lexington, MA: Shire Human Genetics Therapies, Inc.; September 2021.
3. Vimizim [prescribing information]. Novato, CA: BioMarin Pharmaceuticals, Inc.; December 2019.
4. Naglazyme [prescribing information]. Novato, CA: BioMarin Pharmaceuticals, Inc.; December 2019.
5. Mepsevii [prescribing information]. Novato, CA: Ultragenyx Pharmaceuticals, Inc.; December 2020.
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15. 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 of Rare Dis. 2011; 6: 72 – 90.
16. National Organization for Rare Disorders. Mucopolysaccharidosis IV. 2019. Available at: https://rarediseases.org/rare-diseases/morquio-syndrome/. Accessed on June 29, 2020.
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Policy History		
#	Date	Change Description
1.9	Effective Date: 10/12/2023	Updated to remove prescriber requirement
1.8	Effective Date: 10/06/2022	Annual review – no changes to the criteria at this time
1.7	Effective Date: 10/07/2021	Annual review – no changes to the criteria at this time
1.6	Effective Date: 10/08/2020	New policy created for this disease state and class of drugs. The Enzyme Replacement Therapy policy will be retired
1.5	Effective Date: 06/03/2019	UM medical management system update for Mepsevii for BCNA and MAPPO
1.4	Effective Date: 03/01/2018	PA added to Mepsevii for BCBSM and BCN
1.3	Effective Date: 07/05/2017	UM medical management system update for the following drugs to MAPPO and BCNA: Aldurazyme, Elaprase, Naglazyme, and Vimizim
1.2	Effective Date: 07/01/2015	UM medical management system update for the following drugs for BCN: Aldurazyme and Naglazyme
1.1	Effective Date: 02/01/2015	UM medical management system update for the following drugs for BCN: Elaprase and Vimizim
1.0	Effective Date: 01/01/2015	UM medical management system update for BCBS: Aldurazyme, Elaprase, Naglazyme, and Vimizim

** 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.*