Molina Clinical Policy
Hematopoietic Stem Cell Transplantation for Mucopolysaccharidoses Lysosomal Storage Disorders: Policy No. 256

Last Approval: 4/10/2024
Next Review Due By: June 2024

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

(Deeg & Sandmaier 2022; Hahn 2021; AMR 2019; DynaMed 2018; NINDS & NIH 2023; [1-4]NMDP date unknown)

The mucopolysaccharidoses (MPS) are lysosomal storage disorders caused by the deficiency of enzymes required for the stepwise breakdown of glycosaminoglycans (GAGs), also previously known as mucopolysaccharides. Fragments of partially degraded GAGs accumulate in the lysosomes, resulting in cellular dysfunction and clinical abnormalities. These are rare conditions, with an estimated total incidence of all types of MPS of approximately 1 in 20,000 live births. The MPS disorders are classified as types I (Hurlers Syndrome with three subtypes), II (Hunter), III (Sanfilippo), IV (Morquio), VI (Maroteaux-Lamy), VII (Sly), and IX (Natowicz syndrome). MPS V (formerly Scheie syndrome) and MPS VIII are no longer recognized. The MPS disorders are differentiated clinically by their clinical features and age of presentation and biochemically by their associated enzyme deficiency. These features may not be apparent at birth but progress as storage of GAGs affect bone, skeletal structure, connective tissues, and organs. Neurological complications may include damage to neurons as well as pain and impaired motor function. This results from compression of nerves or nerve roots in the spinal cord or in the peripheral nervous system, the part of the nervous system that connects the brain and spinal cord to sensory organs such as the eyes and to other organs, muscles, and tissues throughout the body. Depending on the MPS subtype, affected individuals may have normal intellect or may be profoundly impaired, may experience developmental delay, or may have severe behavioral problems. Many individuals have hearing loss; hydrocephalus is also common. The cornea often becomes cloudy, and degeneration of the retina and glaucoma may affect vision.

Currently there is no cure for these disorders. Medical care is directed at treating systemic conditions and improving quality of life. Enzyme replacement therapies are currently used for MPS I, MPS II, and MPS VI; testing is being conducted for use for other MPS disorders. Enzyme replacement therapy has proven useful in reducing non-neurological symptoms and pain. Changes to diet will not prevent disease progression, but limiting milk, sugar, and dairy products has helped some experiencing excessive mucus. A MPS disorder should be suspected in a child with coarse facial features, hepatosplenomegaly, and bone disease, with or without central nervous system (CNS) abnormalities. The initial presentation may be subtle, and signs may be variable, depending upon the MPS type and severity, resulting in frequent delays in diagnosis. According to the National Institutes of Health (NIH) *Mucopolysaccharidoses Fact Sheet*, bone marrow transplantation (BMT) and umbilical cord blood transplantation (UCBT) have had limited treatment success. Abnormal physical characteristics, except for those affecting the skeleton and eyes, may be improved, but neurologic outcomes have varied. BMT and UCBT are high-risk procedures and are usually performed only after family members receive extensive evaluation and counseling.

Stem-cell transplantation refers to transplantation of hematopoietic stem cells (HSCs) from a donor into a patient. HSCs are immature cells that can develop into any of the three types of blood cells (red cells, white cells or platelets). HSCs are created in the bone marrow and are found in the bone marrow and peripheral blood. There is also a high concentration of HSCs in umbilical-cord blood. Hematopoietic stem-cell transplantation (HSCT) can be either autologous (using the person's own stem cells) or allogeneic (using stem cells from a donor). In allogeneic HSCT, it is preferable for donors to have a human leukocyte antigen (HLA) type that is identical to the recipient. Matching is performed based on variability at three of more loci of the HLA gene (e.g., HLA-A, HLA-B, HLA-DRB1). As HLA

variability increases, transplant-related morbidity and mortality, including graft rejection and graft-versus-host disease (GVHD), also increase.

COVERAGE POLICY

All transplants require prior authorization from the Corporate Transplant Department. Solid organ transplant requests will be reviewed by the Corporate Senior Medical Director or qualified clinical designee. All other transplants will be reviewed by the Corporate Senior Medical Director or covering Medical Director. If the criteria are met using appropriate NCD and/or LCD guidelines, State regulations, and/or MCP policies the Corporate Senior Medical Director's designee can approve the requested transplant.

Office visits with participating Providers do NOT require prior authorization. Providers should see the Member in office visits as soon as possible and without delay. Failure to see the Member in office visits may be considered a serious quality of care concern.

Transplant Evaluation

(Hahn 2021; NINDS & NIH 2023; AMR 2019; [1-4] NMDP date unknown)

Please see *MCP-323 Pre-Transplant Evaluation* for additional criteria and information.

Criteria for transplant evaluation include:

1. History and physical examination; **AND**

2. Psychosocial evaluation and clearance:
   a. No behavioral health disorder by history or psychosocial issues:
      - If history of behavioral health disorder, no severe psychosis or personality disorder;
      - Mood/anxiety disorder must be excluded or treated;
      - Member has understanding of surgical risk and post procedure compliance and follow-up required.

   AND
   b. Adequate family and social support.

AND

3. EKG; **AND**

4. Chest x-ray; **AND**

5. Cardiac clearance in the presence of any of the following:
   a. Chronic smokers; **OR**
   b. Members > 50 years age; **OR**
   c. Those with a clinical or family history of heart disease or diabetes.

AND

6. Pulmonary clearance if evidence of pulmonary artery hypertension or chronic pulmonary disease; **AND**

AND

7. A Performance Status that includes **ONE** of the following:
   a. Karnofsky score 70-100%; **OR**
   b. Eastern Cooperative Oncology Group (ECOG) Grade 0-2.

AND

8. Lab studies that include:

a. Complete blood count; kidney profile (blood urea nitrogen, creatinine); electrolytes; calcium; phosphorous; albumin; liver function tests; and coagulation profile (prothrombin time, and partial thromboplastin time);*
b. Serologic screening for: Human Immunodeficiency Virus (HIV); Epstein Barr virus (EBV); Hepatitis B virus (HBV); Hepatitis C virus (HCV); cytomegalovirus (CMV); rapid plasma reagin (RPR) and/or fluorescent treponemal antibody (FTA):*
   - If HIV positive **ALL** of the following must be met:
     i. CD4 count >200 cells/mm-3 for >6 months; **AND**
     ii. Human Immunodeficiency Virus 1 (HIV-1) ribonucleic acid undetectable; **AND**
     iii. On stable anti-retroviral therapy >3 months; **AND**
     iv. No other complications from Acquired Immunodeficiency Syndrome (AIDS) (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioides mycosis, resistant fungal infections, Kaposi's sarcoma, or other neoplasm).
c. Urine drug screen if Member is current or gives a history of past drug abuse.

AND

9. Colonoscopy (if indicated or if Member is age ≥ 45) with complete workup and treatment of abnormal results as indicated; an initial screening colonoscopy after initial negative screening requires a follow-up colonoscopy every 10 years).*

AND

10. Gynecological examination with Pap smear for women ages ≥ 21 to ≤ 65 years of age or if indicated (not indicated in women who have had a total abdominal hysterectomy or a total vaginal hysterectomy) within the last three years with complete workup and treatment of abnormal results as indicated.*

Within the last 12 months:

1. Dental examination or oral exam showing good dentition and oral care or no abnormality on panorex or plan for treatment of problems pre- or post-transplant; **AND**
2. Mammogram (if indicated or > age 40) with complete workup and treatment of abnormal results as indicated;* **AND**
3. Prostate Specific Antigen (PSA) if history of prostate cancer or previously elevated PSA with complete workup and treatment of abnormal results as indicated.*

* Participating Centers of Excellence may waive these criteria.

Criteria for Allogeneic HSCT

(Deeg & Sandmaier 2022; Hahn 2021; AMR 2019; [3] NMDP date unknown)

Allogeneic HSCT *ablative or non-myeloablative* from an HLA-matched donor (i.e., at least six out of eight match of the HLA-A, HLA-B, HLA-C and HLA-DRB1 markers) or from cord blood when there are no matched sibling or unrelated donors (i.e. at least four out of six match of the HLA-A, HLA-B and HLA-DRB-1 markers) **is considered medically necessary** and may be authorized for the treatment of MPS lysosomal storage disorders when **ALL** of the following criteria are met:

1. All transplant criteria are met; **AND**
2. Age ≤ 2 years; **AND**
3. Neurologically intact or with moderate cognitive impairment:
   a. Developmental Quotient (DQ) > 70); **AND**
4. Failed conventional therapy if applicable (e.g., diet modification and/or enzyme replacement therapy); **AND**
5. Diagnosis of one of the following MPS lysosomal storage disorders:
   a. Hurler Syndrome (MPS I); **OR**
   b. Hunter Syndrome (MPS II); **OR**
   c. Maroteaux-Lamy Syndrome (MPS VI); **OR**
   d. SanFilippo's (MPS III).

AND

6. The requesting transplant recipient should not have any of the following absolute contraindications:
   a. Cardiac, pulmonary, and nervous system disease that cannot be corrected and is a prohibitive risk for surgery; **OR**
   b. Malignant neoplasm with a high risk for reoccurrence, non-curable malignancy (excluding localized skin cancer); **OR**
   c. Systemic and/or uncontrolled infection; **OR**
   d. AIDS (CD4 count < 200cells/mm3); **OR**
   e. Unwilling or unable to follow post-transplant regimen:
      - Documented history of non-compliance
      - Inability to follow through with medication adherence or office follow-up

   OR
   f. Chronic illness with one year or less life expectancy; **OR**
   g. Limited, irreversible rehabilitation potential; **OR**
   h. Active untreated substance abuse issues, requires documentation supporting free from addiction for minimally 6 months if previous addiction was present; **OR**
   i. No adequate social/family support.

AND

7. The requesting transplant recipient should be evaluated carefully and potentially treated if any of the relative contraindications below are present. (Irreversible lung disease patients require consultation and clearance by a Pulmonologist prior to consideration of transplantation).
   a. Smoking, documentation supporting free from smoking for 6 months; **OR**
   b. Active peptic ulcer disease; **OR**
   c. Active gastroesophageal reflux disease; **OR**
   d. Cerebrovascular accident (CVA) with long term impairment that is not amendable to rehabilitation or a patient with CVA/transient ischemic attack within past 6 months; **OR**
   e. Obesity with body mass index of >30 kg/m^2 may increase surgical risk; **OR**
   f. Chronic liver disease such as Hepatitis B/C/D, or cirrhosis which increases the risk of death from sepsis and hepatic failure requires consultation by a gastroenterologist or hepatologist; **OR**
   g. Gall bladder disease requires ultrasound of the gall bladder with treatment prior to transplantation.

Criteria for Subsequent HSCT

Allogeneic HSCT (ablative or non-myeloablative) **may be authorized** after the first prior allogeneic HSCT has occurred only one time for Members with MPS lysosomal storage disorders who meet **ALL** of the *above* criteria for transplant and have **ANY** of the following:

1. Primary graft failure indicated by no signs of engraftment* by 42 days after the transplant; **OR**
2. Failure to engraft*; **AND**
3. A suitable allogeneic donor has been identified.

* Engraftment is defined as the first 3 consecutive days on which the absolute neutrophil count (ANC) exceeds 0.5 x 10^9/L or > ANC500 at any time after transplantation ([5] NMDP date unknown).

Continuation of Therapy

When extension of a previously approved transplant authorization is requested, review using updated clinical information is appropriate.

1. If Molina Healthcare has authorized prior requests for transplantation **ALL** of the following information is required for medical review:
   a. Presence of no absolute contraindication as listed above; **AND**
   b. History and physical within the last 12 months; **AND**
   c. Kidney profile within the last 12 months; **AND**
   d. Cardiac update if history of cardiac disease within two years (≥ 50 years of age); **AND**
   e. Psychosocial evaluation or update within the last 12 months; **AND**
   f. Per initial and updated history and physical, any other clinically indicated tests and/or scans as determined by transplant center physician or Molina Medical Director.

2. If authorized prior requests for transplantation were obtained from another insurer, **ALL** of the following information is required for medical review:
   a. Authorization letter/documentation from previous insurer; **AND**
   b. Presence of no absolute contraindication as listed above; **AND**
   c. History and physical within the last 12 months; **AND**
   d. Cardiac update if history of cardiac disease within two years (≥ 50 years of age); **AND**
   e. Psychosocial evaluation or update within the last 12 months; **AND**
   f. Per initial and updated history and physical, any other clinically indicated tests and/or scans as determined by transplant center physician or Molina Medical Director.

For Members with Significant or Daily Cannabis Use

1. Documentation of compliance with a physician prescribed and managed program of abstinence, and a reasonable expectation that the Member will be abstinent from cannabis use during the transplant and immediate post-transplant time period. Daily cannabis use is an absolute contraindication for both transplant and pre-transplant evaluation unless there is a state mandate applicable for medical cannabis use and transplants, and there is documentation of Member compliance with a physician prescribed plan of care for prescribed cannabis use.
2. If the Member's cannabis use follows a formal, State-based program for managed medical cannabis, the request should include:
   - Documentation of the Plan of Care for medical cannabis (including the medical decision making that supports the use of medical cannabis); **AND**
   - Transplant Provider agreement with the Plan of Care (including agreement to be accountable for managing the Member's use of medical cannabis).

Limitations and Exclusions

1. Allogeneic (ablative or non-myeloablative) HSCT when the above criteria are not met.
2. A second or repeat allogeneic (ablative or non-myeloablative) HSCT due to persistent, progressive, or relapsed disease.
3. Autologous HSCT.
4. A planned tandem allogeneic HSCT.
5. HSC collection, storage, and freezing for a future unplanned transplant.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

The published medical evidence and outcomes for HSCT for MPS lysosomal storage disorders in the United States consists of registry data obtained from transplant centers that perform adult and pediatric transplantation and is available

from the United Network for Organ Sharing (UNOS) database. Registry data demonstrates graft survival rates and outcomes for stem cell transplantation based on demographic and clinical information. ([2] NMDP date unknown).

Qu et al. (2022) completed a single-center study of 42 children with MPS who received HSCT and had follow-up ≥ 1 year following transplant. Children included in the study had MPS type I (n=9), type II (n=14), type IV (n=15), or type VI (n=4) and received either peripheral blood stem cells (n=24) or umbilical cord stem cells (n=18). Those that received umbilical cord stem cells received the blood from a matched family fresh cord blood donor (n=1), a mismatched unrelated cord blood donor (7/10 to 9/10 HLA-matched [n=15]), or from a double-mismatched unrelated cord blood donor (1 from a 6/10 to 8/10 HLA-matched donor and 1 from a 6/10 to 7/10 HLA-matched donor). Those that received peripheral blood stem cells received the blood from a matched family donor (n=4), a matched unrelated donor (n=10), a mismatched unrelated donor (7/10 to 9/10 HLA-matched [n=4]), or from a haploid donor (n=6). Children receiving peripheral blood stem cell transplants were condition with intravenous busulfan every 6 hours for 16 doses, intravenous cyclophosphamide, and antihuman thymocyte globulin. Specific lysosomal enzyme levels returned to normal in all recipients and 95.2% achieved full chimerism. The estimated overall survival (OS) at 1-year was 92.9% with no significant difference between peripheral or umbilical cord blood transplants. There was also no significant difference in acute or chronic GVHD between either group. High rates of pneumonia were noted in both groups (45.8% for peripheral blood and 33.3% for umbilical blood). A total of 3 deaths were reported following peripheral blood HSCT, 1 each due to grade III and IV GVHD, thrombotic microangiopathy, and combined grade III and IV GVHD and thrombotic microangiopathy. No patients with MPS type IV or VI died following transplantation. Researchers noted improvement in respiratory and CNS functions following HSCT. Valvular heart disease improved in some patients but progressed in others.

Gentner et al. (2021) reported interim results on an ongoing phase 1-2, non-randomized, single-center study involving 8 children diagnosed with MPS type I who lacked a suitable allogeneic donor for HSCT. The participants received autologous HSCT and progenitor cells transduced ex vivo with an alpha-L-iduronidase (IDUA) encoding lentiviral vector after myeloablative conditioning. Median age at time of autologous HSCT was 1.9±0.5 years. Primary safety end points of the study include overall survival, hematologic engraftment by day 45, short- and long-term safety of drug-product infusion, and adverse event monitoring. The primary efficacy end point is blood IDUA activity at 1-year post-treatment. Secondary efficacy end points include anti-IDUA antibody immune response and engraftment of transduced cells at levels of 30% or more, normalization of GAGs, and growth velocity at 1- and 3-years post-treatment. The study has an expected 5-year duration and is currently at a median follow-up period of 2.1 years. Patients will continue to be followed for at least 15 years. Interim results reported showed hematologic engraftment that was rapid and consistent in all patients. Neutrophil recovery occurred at a median of 20 days and early spontaneous platelet recovery occurred at a median of 14 days. There were no reports of graft-versus-host disease due to the autologous nature of transplantation. A total of 19 serious adverse events were reported with only 1 of those (an acute allergic reaction) potentially related to the treatment. Previously undetectable levels of IDUA in the cerebrospinal fluid at baseline were detectable starting at 3-months post-treatment and persisting through each subsequent follow-up. GAG levels in the cerebrospinal fluid were also noted to decline. The IDUA and GAG results suggest a rapid and profound metabolic correction of the central nervous system. All patients also progressively acquired motor skills with 6 patients having a total motor performance within normal range or in the low average of normal. Other typical clinical manifestations, such as coarse facial features, upper airway obstruction, hearing loss, and corneal opacity, which were evident at the time of treatment showed improvement or stabilization at 1- and 2-year follow-ups.

Rodgers et al. (2017) completed a review to determine how HSCT has affected the mortality of patients with MPS type I over the previous 30 years at the University of Minnesota. Researchers used chart review and the National Death Index to determine the survival of 134 patients that were transplanted at the institution. Specific statistics observed were OS at specific times following HSCT. OS rates from 2004 and onward were noted to be higher than OS rates before 2004. OS before 2004 was 65% at 1-year and 57% at 8-years compared to 84% at 1-year and 81% at 8-years for 2004 and onward. The all-inclusive OS was 70% at 1-year and 37% at 25-years. Males were noted to have a higher rate of survival than females. This review determined that long-term survival has improved since 2004.

Aldenhoven et al. ([1] 2015) identified predictors of the long-term outcome of patients with MPS-IH after successful HCT. Two hundred seventeen patients with MPS-IH successfully engrafted with a median follow-up age of 9.2 years were included in this retrospective analysis. Primary endpoints were neurodevelopmental outcomes and growth. Secondary endpoints included neurologic, orthopedic, cardiac, respiratory, ophthalmologic, audiologic, and endocrinologic outcomes. Considerable residual disease burden was observed in the majority of the transplanted patients with MPS-

IH, with high variability between patients. Preservation of cognitive function at HCT and a younger age at transplantation were major predictors for superior cognitive development post-transplant. A normalα-l-iduronidase enzyme level obtained post-HCT was another highly significant predictor for superior long-term outcome in most organ systems. The long-term prognosis of patients with MPS-IH receiving HCT can be improved by reducing the age at HCT through earlier diagnosis, as well as using exclusively non-carrier donors and achieving complete donor chimerism.

Aldenhoven et al. ([2] 2015) evaluated the survival and graft outcomes of MPS patients receiving HCT according to these guidelines in 2 European centers of expertise. Two consecutive conditioning regimens were used, busulfan/cyclophosphamide or fludarabine/busulfan-based, both with exposure-targeted intravenous busulfan. A noncarrier matched sibling donor (MSD), matched unrelated cord blood (UCB), or matched unrelated donor (MUD) were considered to be preferred donors. If not available, a mismatched UCB donor was used. Participants were 62 MPS patients (56 MPS type I-Hurler, 2 MPS type II, 2 MPS type III, and 2 MPS type VI) receiving HCT at median age 13.5 months (range, 3 to 44). Forty-one patients received a UCB donor, 17 MSD, and 4 MUD. High overall survival (95.2%) and event-free survival (90.3%) were achieved with only low toxicity: 13.3% acute graft-versus-host disease aGVHD) grades II to IV and 14.8% chronic GVHD (1.9% extensive). A mismatched donor predicted for lower event-free survival (P = .04). A higher age at HCT was a predictor for both aGVHD (P = .001) and chronic GVHD (P = .01). The use of a mismatched donor was a predictor for aGVHD (P = .01). Higher rates of full donor chimerism were achieved in successfully transplanted UCB recipients compared with MSD/MUD (P = .002). If complying with the international HCT guidelines, HCT in MPS patients results in high safety and efficacy. This allows extension of HCT to more attenuated MPS types. Because a younger age at HCT is associated with reduction of HCT-related toxicity, newborn screening may further increase safety.

Boelens et al. (2013) reported transplantation outcomes of 258 children with Hurler syndrome after a myeloablative conditioning regimen from 1995 to 2007. Median age at transplant was 16.7 months and median follow-up was 57 months. The cumulative incidence of neutrophil recovery at day 60 was 91%, acute GVHD (grade II-IV) at day 100 was 25%, and chronic GVHD at 5 years was 16%. OS and event-free survival (EFS) at 5 years were 74% and 63%, respectively. EFS after HLA-matched sibling donor (MSD) and 6/6 matched unrelated cord blood (CB) donor were similar at 81%, 66% after 10/10 HLA-matched unrelated donor (UD), and 68% after 5/6 matched CB donor. EFS was lower after transplantation in 4/6 matched unrelated CB (UCB) (57%; P = .031) and HLA-mismatched UD (41%; P = .007). Full donor chimerism (P = .039) and normal enzyme levels (P = .007) were higher after CB transplantation (92% and 98%, respectively) compared with the other graft sources (69% and 59%, respectively). In conclusion, results of allogeneic transplantation for HS are encouraging, with similar EFS rates after MSD, 6/6 matched UCB, 5/6 UCB, and 10/10 matched UD. The use of mismatched UD and 4/6 matched UCB was associated with lower EFS.

National and Specialty Organizations

The **American Society for Transplantation and Cellular Therapy (ASTCT)** guidelines recommend allogeneic HSCT for MPS type I (Hurlers Syndrome) with a “standard of care, rare indication” recommendation. MPS types II, IV, and VI are currently considered “developmental” based on ASTCT guidelines. ASTCT guidelines do not recommend the use of autologous HSCT for treatment of any type of MPS (Kanate et al. 2020).

The **National Institute of Neurological Disorders and Stroke (NINDS) and National Institutes of Health (NIH)** recommend patients be treated with enzyme replacement therapy. HSCT has had limited success in treating MPS (NINDS & NIH 2023).

The **National Marrow Donor Program (NMDP)** recommends HSCT at time of diagnosis for Hurler Syndrome. (NMDP 2017).

The **International Consensus Panel on the Management and Treatment of Mucopolysaccharidosis I** recommends the following (de Ru et al. 2011):

- All patients with MPS type I should receive a comprehensive baseline evaluation, including neurologic, ophthalmologic, auditory, cardiac, respiratory, gastrointestinal, and musculoskeletal assessments, and should be monitored every 6 to 12 months with individualized specialty assessments, to monitor disease progression and effects of intervention.
- A multidisciplinary team best treats patients.
- Treatments consist of palliative/supportive care, HSCT, and enzyme replacement therapy.

- The patient's age (>2 years or ≤ 2 years), predicted phenotype, and developmental quotient help define the risk/benefit profile for hematopoietic stem cell transplantation (higher risk but can preserve central nervous system function) versus enzyme replacement therapy (low risk but cannot cross the blood-brain barrier).

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology) Codes

Code	Description
	Collection Codes
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38230	Bone marrow harvesting for transplantation; allogeneic
38232	Bone marrow harvesting for transplantation; autologous
	Cell Processing Services
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing, per donor
38210	Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-cell depletion
38211	Transplant preparation of hematopoietic progenitor cells; tumor cell depletion
38212	Transplant preparation of hematopoietic progenitor cells; red blood cell removal
38213	Transplant preparation of hematopoietic progenitor cells; platelet depletion
38214	Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion
38215	Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear, or buffy coat layer
	Cell Infusion Codes
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
38241	Hematopoietic progenitor cell (HPC); autologous transplantation
38242	Allogeneic lymphocyte infusions
38243	Hematopoietic progenitor cell (HPC); HPC boost
	Histocompatibility Codes
86812	HLA typing; A, B, or C (e.g., A10, B7, B27), single antigen
86813	HLA typing; A, B, or C, multiple antigens
86816	HLA typing; DR/DQ, single antigen
86817	HLA typing; DR/DQ, multiple antigens

HCPCS (Healthcare Common Procedure Coding System) Codes

Code	Description
S2140	Cord blood harvesting for transplantation, allogeneic
S2142	Cord blood derived stem-cell transplantation, allogeneic
S2150	Bone marrow or blood-derived stem cells (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications; including pheresis and cell preparation/storage; marrow ablative therapy; drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days of pre-and post-transplant care in the global definition

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices,

Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

04/10/2024	Correction to ANC value in coverage section. Annual review scheduled for June 2024.
06/14/2023	Policy reviewed, changes to criteria include: "Pre-Transplant Evaluation" changed to "Transplant Evaluation," new criteria 7b, removal of abnormal serology criteria from new criteria 8b, new criteria 9 changed to age 45 years, and asterisk added to transplant criteria 11 to denote it may be waived by a Center of Excellence. Grammatical edits to Disclaimer section and Documentation Requirements disclaimer. Updated Overview, Summary of Medical Evidence, and References sections. "Marijuana" changed to "cannabis" throughout policy. Codes 86812, 86813, 86816, 86817 added and code descriptions updated for codes 38208, 38209, 38240, 38241, 38242, and 38243. ICD-10 codes removed. Policy reviewed on May 18, 2023, by a practicing, board-certified physician in the areas of Medical Oncology and Hematology.
06/08/2022	Policy reviewed, no changes to criteria; included section on marijuana use; updated references.
06/09/2021	Policy reviewed, no changes to criteria, updated references and guidelines.
06/17/2020	Policy reviewed, no changes to criteria, updated references and guidelines.
06/19/2019	Policy reviewed, no changes to criteria, updated references and guidelines. IRO Peer Review completed on April 5, 2019, by a practicing, board-certified physician in the area of Surgery Transplant.
06/22/2017	Policy reviewed, criteria have not changed, updated references and guidelines.
03/08/2018	Policy reviewed, criteria have not changed, updated references and guidelines.
02/02/2016	New policy.

REFERENCES

1. [1] Aldenhoven M, Wynn RF, Orchard PJ, O'Meara A, Veys P, Fischer A, et al. Long-term outcome of Hurler syndrome patients after hematopoietic cell transplantation: An international multicenter study. Blood. 2015 Mar 26;125(13):2164-72. doi: 10.1182/blood-2014-11-608075.
2. [2] Aldenhoven M, Jones SA, Bonney D, Borrill RE, et al. Hematopoietic cell transplantation for mucopolysaccharidosis patients is safe and effective: Results after implementation of international guidelines. Biol Blood Marrow Transplant. 2015 Jun;21(6):1106-9. doi: 10.1016/j.bbmt.2015.02.011.
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