BENEFIT COVERAGE POLICY

Title: BCP-67 Hematopoietic Stem Cell Transplantation

Effective Date: 10/01/2020

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following coverage policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Coverage determinations for individual requests require consideration of:

- The terms of the applicable benefit document in effect on the date of service.
- Any applicable laws and regulations.
- Any relevant collateral source materials including coverage policies.
- The specific facts of the situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

Health Plan covers allogeneic or autologous, bone marrow, peripheral stem cell or hematopoietic stem cell transplant (HSCT) as medically necessary for patients with specific conditions and when clinical criteria below are met.

Health Plan considers compatibility (HLA) testing of prospective donors who are members of the immediate family (first-degree relatives, i.e., parents, siblings and children) and harvesting with short-term storage [up to 48 hours] of peripheral stem cells or bone marrow from the identified donor as medically necessary when an allogeneic bone marrow or peripheral stem cell transplant is authorized by Health Plan.

All transplant related services require prior approval for coverage of Covered Health Services provided at a Health Plan designated transplant facility. Contact the Transplant Case Manager to verify if a provider is contracted as a designated transplant facility.

Non-network services are not covered.

Refer to member's benefit coverage document for specific benefit description, guidelines, coverage and exclusions.

2.0 Background:

Stem cell transplantation is a procedure that is most often recommended as a treatment option for people with leukemia, multiple myeloma, and some types of lymphoma. It may also be used to treat some genetic diseases that involve the blood.

During a stem cell transplant, diseased bone marrow (the spongy, fatty tissue found inside larger bones) is destroyed with chemotherapy and/or radiation therapy and then replaced with highly specialized stem cells that develop into healthy bone marrow. Although this procedure used to be referred to as a bone marrow transplant, today it is more commonly called a stem cell transplant because it is stem cells in the blood that are typically being transplanted, not the actual bone marrow tissue.

Bone marrow produces more than 20 billion new blood cells every day throughout a person's life. The driving force behind this process is the hematopoietic stem cell. Hematopoietic stem cells are immature cells found in both the bloodstream and bone marrow. These specialized cells can create more blood-forming cells or to mature into one of the three different cell types that make up our blood. These include red blood cells (cells that carry oxygen to all parts of the body), white blood cells (cells that help the body fight infections and diseases), and platelets (cells that help blood clot and control bleeding). Signals passing from the body to the bone marrow tell the stem cells which cell types are needed the most.

For people with bone marrow diseases and certain types of cancer, the essential functions of red blood cells, white blood cells, and platelets are disrupted because the hematopoietic stem cells don't mature properly. To help restore the bone marrow's ability to produce healthy blood cells, doctors may recommend stem cell transplantation.

Stem cells for transplant come from the following sources:

- Autologous transplant: cells are taken from the patient's own bone marrow or more commonly, peripheral blood. Peripheral stem cells are harvested via one or more pheresis procedures. A course of chemotherapy (typically cyclophosphamide) or growth factors or both can increase the number of circulating stem cells.

- Allogeneic transplant: stem cells come from a donor whose tissue most closely matches the patient.

- Umbilical cord blood: blood harvested from the umbilical cord and placenta shortly after delivery of neonates. Although cord blood is an allogeneic source, these stem cells are antigenically "naïve" and thus are associated with a lower incident of rejection or graft vs. host disease.

Human leukocyte antigen, or HLA, typing is the method by which stem cell transplant patients are matched with eligible donors. HLA are proteins that exist on the surface of most cells in the body. HLA markers help the body distinguish normal cells from foreign cells, such as cancer cells.

The closest possible match between the HLA markers of the donor and the patient reduces the risk of graft versus host disease (GVHD). This condition occurs after transplant when your immune cells attack the donor cells, or when the donor cells attack your cells.

The best match is usually a first degree relative (children, siblings or parents). However, about 75% of patients do not have a suitable donor in their family and require cells from matched unrelated donors (MUD). These donors are found through registries such as the National Marrow Donor Program.

HLA typing is done with a blood sample taken from the patient, which is then compared with samples from a family member or a donor registry.

3.0 Clinical Determination Guidelines:

A. Allogeneic or Autologous bone marrow or peripheral stem cell transplants are considered medically necessary and appropriate when all the following are met:

   1. One evaluation per transplant approval; and

      Note: A second opinion consult only would be approved to determine candidacy at a Health Plan designated transplant facility if a second transplant evaluation is requested and the member has been previously turned down for transplant.

   2. Documentation of compliance with medical management; and

   3. Member should have received prior approval for pre-transplant services (evaluation, outpatient diagnostics and labs) at a Health Plan-designated transplant facility linked to one of the transplant networks: Interlink, LifeTrac or Cigna LifeSource. If a member is not receiving services at a Health Plan-designated facility, the member is redirected to a designated facility; and

4. Social work evaluation indicating member does not have any unresolvable psychosocial problems which may interfere with compliance with transplant management; and
5. Member has completed an evaluation and has been accepted by the transplant committee at a designated transplant facility. Documentation must include a summary letter from the transplant center indicating acceptance and outlining the preoperative tests and their results; and
6. Member meets transplant institution's protocol eligibility criteria regarding age; and
7. Attending physician has determined there are no prohibitive risk factors or absolute contraindications for transplant recipients, which include but not limited to ANY of the following:
    a. Poor cardiac function (ejection fraction <45%); or
    b. Poor liver function (bilirubin >2.0 mg/dl, INR >1.6 unless on oral anticoagulants); or
    c. Poor renal function (creatinine clearance < 50 ml/min.); or
    d. Poor pulmonary function (diffusion capacity [DLCO] or forced expiratory volume in one second [FEV1] < 50% of predicted); or
    e. Ongoing alcohol or drug abuse (members with a history of using alcohol, tobacco or other substances of abuse must be abstinent for a minimum of three consecutive months before being considered an eligible transplant candidate as determined by random urine drug screens with negative results). Use of marijuana for medical purposes requires written approval from the referring specialist (cardiologist, oncologist, etc.) and transplant eligibility is subject to the transplanting institution's criteria.
    f. No malignancy (except for non-melanomatous skin cancers). For patients, having been treated for a malignancy, they must meet defined facility eligibility protocol of being cancer free prior to being scheduled for a transplant evaluation. This cancer free period may range from three to five years; or
    g. Ongoing or recurring infections that are not effectively treated; or
    h. Presence of human immunodeficiency virus OR an active form of any ONE of the following:
        i. Hepatitis B virus (HBV).
        ii. Hepatitis C virus (HCV).
        iii. Human T-cell lymphotropic virus (HTLV)-1.
        i. Demonstrated patient noncompliance, which places the transplanted organ at risk by not adhering to medical recommendations; or
    j. Potential complications from immunosuppressive medications are unacceptable to the patient.
8. Member has received dental clearance for transplantation; and
9. For autologous bone marrow or stem cell transplantation, pediatric patients should have a Lansky score > 50%; adult patients should have a Karnofsky or Lansky score > 70% or EOCG score of 2 or less.

B. Hematopoietic stem cell transplantation (HSCT) coverage by diagnosis when criteria above are met:
    1. Non-Malignant Conditions – Allogeneic HSCT may be considered medically necessary for selected patients with the following:

a. Aplastic anemia – severe or very severe, including congenital (e.g., Fanconi's anemia or Diamond-Blackfan syndrome) or acquired (e.g., secondary to drug or toxin exposure). Appropriate patients include those with:
    i. Platelets less than 20 x 10^9/L; and
    ii. Granulocytes less than 0.5 x 10^9/L; and
    iii. Reticulocytes less than 1% (corrected for hematocrit) and who have failed antithymocyte globulin therapy.
b. Homozygous beta-thalassemia (i.e., thalassemia major) in children or young adults (up to age 45 years) with an HLA-matched donor.
c. Infantile malignant osteopetrosis (Albers-Schonberg disease or marble bone disease).
d. Mucolipidoses (e.g., Gaucher's disease, metachromatic leukodystrophy, globoid cell leukodystrophy, adrenoleukodystrophy) for patients who have failed conventional therapy (e.g., diet, enzyme replacement) and who are neurologically intact.
e. Mucopolysaccharidosis (e.g., Hunter's, Hurler's Sanfilippo, Maroteaux-Lamy variants) in patients who are neurologically intact).
f. Primary immunodeficiency disorders (PID) (not an all-inclusive list):
    i. Chediak-Higashi syndrome.
    ii. DiGeorge syndrome.
    iii. Griscelli syndrome type 2.
    iv. Immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (IPEX).
    v. Kostmann syndrome (severe congenital neutropenia, autosomal recessive type 3/SCN3).
    vi. Leukocyte adhesion deficiency type 1.
    vii. Severe combined immunodeficiency (SCID).
    viii. Severe congenital neutropenia.
    ix. Wiskott-Aldrich syndrome (WAS).
    x. X-linked lymphoproliferative syndrome.
g. Sickle cell anemia for children or young adults with:
    i. A history of a prior stroke or at increased risk of stroke or end-organ damage (associated factors include: recurrent chest pain syndrome, recurrent vaso-occlusive crises, red blood cell alloimmunization or chronic transfusion therapy); and
    ii. An HLA-identical donor identified.
h. Autologous HSCT for treatment of severe aplastic anemia, Diamond-Blackfan anemia, Fanconi's anemia, paroxysmal nocturnal hemoglobinuria and pure red cell aplasia is considered experimental and investigational

2. Autoimmune Diseases and Miscellaneous conditions – HSCT (autologous or allogeneic) is considered experimental, investigational or unproven for any of the following (not an all-inclusive list):
    a. Age-related macular degeneration.
    b. Amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease).
    c. Autoimmune cytopenia (e.g., autoimmune hemolytic anemia, Evans syndrome, and idiopathic thrombocytopenia purpura).

d. Autoimmune hepatitis.
e. Celiac disease.
f. Chronic inflammatory demyelinating polyradiculopathy.
g. Crohn's disease.
h. Cryptogenic cirrhosis.
i. Dermatomyositis.
j. Essential thrombocythemia.
k. Juvenile rheumatoid arthritis.
l. Multiple sclerosis.
m. Neuromyelitis optica.
n. Polycythemia vera.
o. Polymyositis.
p. Recessive dystrophic epidermolysis bullosa.
q. Retinitis pigmentosa.
r. Rheumatoid arthritis.
s. Systemic lupus erythematosus.
t. Systemic sclerosis (scleroderma).
u. Systemic vasculitis.
v. Thrombotic thrombocytopenic purpura.
w. Type I diabetes mellitus.
x. Ulcerative colitis.

3. Solid Tumors in Adults – autologous or allogeneic HSCT (ablative and non-myeloablative) is considered experimental and investigational because its effectiveness has not been established for treatment of any of the following:
   a. Bile duct (cholangiocarcinoma).
   b. Breast.
   c. Central nervous system tumors (e.g., astrocytoma, choroid plexus tumors, ependymoma, gliomas, oligodendroglioma; not an all-inclusive list) *
   d. Cervix.
   e. Colon.
   f. Epithelial ovarian.
   g. Esophagus.
   h. Gallbladder.
   i. Kidney.
   j. Liver.
   k. Lung.
   l. Melanoma.
   m. Nasopharynx.
   n. Neuroendocrine tumors.

o. Pancreas.

p. Paranasal sinus.

q. Prostate.

r. Rectum.

s. Renal cell carcinoma.

t. Soft tissue sarcomas *

u. Stomach.

v. Thymus.

w. Thyroid.

x. Uterus.

* Autologous HSCT may be medically necessary in young adults with primitive neuroectodermal tumors, medulloblastoma, and Ewing sarcoma family of tumors when criteria are met.

4. Childhood Solid Tumors – high-dose chemotherapy followed by autologous HSCT is covered for the following:

   a. Relapsed Wilms' tumor.

   b. Metastatic non-central nervous system (non-CNS) retinoblastoma.

   c. Relapsed or progressive Ewing family of tumors.

5. Neuroblastoma is covered for the following:

   a. Autologous HSCT is considered medically necessary for treatment of high-risk* neuroblastoma. A maximum of three tandem autologous HSCT are covered as medically necessary for the treatment of high-risk neuroblastoma.

   b. Allogeneic SCT from an appropriately-matched HLA donor following high-dose chemotherapy is considered medically necessary treatment of high risk neuroblastoma when the individual is not a candidate for autologous HSCT.

   * Link to Children's Oncology Group risk stratification for children with neuroblastoma: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3261589/ ; Table 3.

6. Primitive Neuroectodermal Tumors (PNET) – autologous SCT is covered for the treatment of PNET, including medulloblastoma and pineoblastoma.

7. Ependymoma – autologous stem cell transplantation is a covered treatment, if the patient is ineligible for radiotherapy.

8. Ovarian or Testicular Germ Cell Tumors:

   a. Single or tandem autologous HCT is considered as medically necessary for relapsed or refractory germ cell tumors (history of remission or responsive to standard chemotherapy).

   b. Autologous HCT when used as initial treatment is considered experimental and investigational as its effectiveness for this indication has not been established.

   c. Allogeneic HCT is considered experimental and investigational as its effectiveness for this indication has not been established.

   d. HSCT (autologous or allogeneic) for the treatment in persons with epithelial ovarian cancers is considered experimental and investigational because its effectiveness for this indication has not been established.

9. Hodgkin's Disease:

a. High dose chemotherapy with either autologous or allogeneic stem cell support may be covered in patients with refractory, primary progressive or recurrent Hodgkin's disease.

b. Non-myeloablative allogeneic SCT is considered medically necessary for relapsed or refractory Hodgkin's disease following a previous SCT.

c. Tandem transplants for treatment of Hodgkin's Disease are considered investigational as there is insufficient evidence of its effectiveness and safety for this indication.

d. Autologous or allogeneic SCT as initial treatment is considered experimental and investigational as its effectiveness for this indication has not been established.

10. Non-Hodgkin's Lymphoma:

a. Autologous or allogeneic stem cell is a covered benefit for relapsed or primary refractory non-Hodgkin's lymphoma (NHL).

b. Autologous HCT may be considered medically necessary for persons in first clinical remission with lymphoblastic NHL, Burkitt's lymphoma, mediastinal B-cell lymphoma, mantle cell lymphoma, high-risk diffuse large B-cell lymphoma and other NHLs associated with a poor prognosis.

c. Non-myeloablative allogeneic HCT may be covered for relapsed or primary refractory NHL when a reduced intensity regimen is preferred by the transplant center.

d. High dose chemotherapy with autologous or allogeneic SCT is considered experimental and investigational as initial treatment as its effectiveness for this indication has not been established.

e. Tandem autologous hematopoietic cell transplantation (auto-auto) or tandem autologous hematopoietic cell transplantation followed by allogenic hematopoietic cell transplantation (auto-allo) is considered experimental and investigational for NHL due to a lack of adequate evidence in the peer-reviewed published medical literature of their safety and effectiveness.

11. Myelofibrosis (MF):

a. Allogeneic (ablative and non-myeloablative) SCT is considered medically necessary for persons with myelofibrosis when any of the following criteria are met:

i. The individual is transfusion dependent (red blood cells or platelets); or

ii. The individual is resistant to conservative therapy; or

iii. The individual has intermediate or high-risk MF.

b. A repeat allogeneic (ablative or non-myeloablative) HSCT is considered medically necessary for individuals with myelofibrosis and primary graft failure or who have relapsed.

c. A repeat allogeneic (ablative or non-myeloablative) HSCT due to persistent, progressive or relapsed disease is considered experimental and investigational.

d. Autologous HSCT for MF is considered experimental and investigational due to insufficient evidence in peer-reviewed literature.

12. Myelodysplastic Syndrome (MDS):

a. Allogeneic (ablative and non-myeloablative) HSCT is considered medically necessary for individuals with intermediate-risk or high-risk MDS, and have not responded to prior therapy and have an available HLA-matched donor.

b. A repeat allogeneic (ablative or non-myeloablative) hematopoietic cell transplantation is considered medically necessary for individuals with intermediate-risk or high-risk MDS due to primary graft failure, failure to engraft, or late relapse (greater than 18 months after HSCT) (salvage therapy).

c. A repeat allogeneic (ablative or non-myeloablative) HSCT for individuals with MDS who have an early relapse is considered experimental.

d. Autologous SCT for individuals with MDS is considered experimental and investigational as the effectiveness has not been established.

13. Chronic Myelogenous Leukemia (CML):

a. High dose chemotherapy with allogeneic HSCT is considered medically necessary for the treatment of CML in patients who have failed to respond to, have developed a resistance to, or are intolerant of tyrosine kinase inhibitors (TKI), (e.g., imatinib/Gleevec, dasatinib/Sprycel, nilotinib/Tasigna).

b. A repeat allogeneic HSCT due to primary graft failure or failure to engraft is considered medically necessary.

c. Autologous HSCT for the treatment of CML under all circumstances is considered experimental and investigational because its effectiveness has not been established.

14. Acute Myelogenous Leukemia (AML):

a. Autologous HSCT is considered medically necessary for the treatment of AML for individuals who:

i. Are in first or second remission; or

ii. Relapsed AML if responsive to intensified induction chemotherapy; and

iii. Do not have a suitable donor for an allogeneic transplant.

b. Allogeneic HSCT (ablative or non-myeloablative) is considered medically necessary for any of the following:

i. Relapsed following a prior autologous HSCT are medically able to tolerate the procedure; or

ii. Poor-risk to intermediate-risk AML in remission; or

iii. Primary refractory AML (i.e., has not achieved complete remission after conventional dose chemotherapy).

c. A repeat allogeneic HSCT (ablative or non-myeloablative) for treatment of AML is considered medically necessary when the first allogeneic HSCT was unsuccessful due to primary graft failure or failure to engraft or for persons who have relapsed after a previous HSCT.

d. A repeat autologous or allogeneic HSCT for members with persistent or progressive AML who have not been in remission is considered experimental and investigational.

e. Tandem stem cell transplants to treat AML is considered experimental and investigational as their effectiveness has not been established.

15. Acute Lymphocytic Leukemia (ALL)

a. Allogeneic HSCT is considered medically necessary for the treatment of ALL, including primary refractory ALL (i.e., leukemia that does not achieve a complete remission after conventional dose chemotherapy), except for refractory relapse (i.e., persons in relapse and are unresponsive to three or more months of adequate chemotherapy).

b. Non-myeloablative allogeneic HSCT is considered medically necessary for the treatment of ALL without persistent disease. Persons with persistent disease should not be candidates for a “mini-allograft.”

c. A second myeloablative allogeneic HSCT from an appropriately-matched HLA donor may be a covered benefit for the treatment of ALL when the relapsed disease occurs more than six months after the first allogeneic HSCT.

d. Autologous HSCT for treatment of ALL is considered experimental and investigational because its effectiveness has not been established.

e. Tandem stem cell transplants for ALL is considered experimental.

16. Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL):

a. Allogeneic HSCT is considered medically necessary for the treatment of CLL that is not responsive to standard therapy.

b. Autologous HSCT is considered medically necessary for the treatment of CLL in persons who are in complete or good partial remission.

c. A repeat allogeneic (ablative or non-myeloablative HSCT due to primary graft failure or failure to engraft is considered medically necessary.

17. Multiple Myeloma:

a. Autologous HSCT is considered medically necessary for the treatment of persons with active, symptomatic multiple myeloma for either of the following indications:

i. Responsive to primary therapy.

ii. Refractory to primary therapy with a relapse or progressive disease.

b. A repeat autologous HSCT may be considered medically necessary for treatment of responsive multiple myeloma that has relapsed after a complete or partial remission.

c. Tandem autologous transplants or autologous transplant followed by an allogeneic transplant from haploidentical to fully matched related donor or well-matched unrelated donor are medically necessary if planned first and second transplantations are within a six-month period.

d. Three or more autologous HSCT within a 12-month period are considered experimental and investigational.

e. Allogeneic (ablative or non-myeloablative) HSCT after a previous autologous HSCT for treatment of active, symptomatic multiple myeloma is considered medically necessary.

f. A repeat allogeneic (ablative or non-myeloablative) HSCT due to primary graft failure, failure to engraft or rejection is considered medically necessary.

g. A repeat allogeneic (ablative or non-myeloablative) HSCT due to persistent, progressive or relapsed disease is considered experimental and investigational.

18. Amyloidosis:

a. Autologous HSCT for treatment of amyloidosis (AL) is considered medically necessary who meet the following criteria:

i. If the heart is involved with AL, the individual is symptomatic or has compensated congestive heart failure; and

ii. Left ventricular ejection fraction (LVEF) greater than or equal to 45%; and

iii. Must have documented disease on biopsy without a preceding diagnosis of multiple myeloma.

b. A repeat autologous HSCT due to primary graft failure or failure to engraft is considered medically necessary.

c. Allogeneic (ablative or non-myeloablative) HSCT for the treatment of amyloidosis is considered experimental and investigational.

d. A tandem autologous HSCT for treatment of POEMS Syndrome is considered experimental and investigational.

e. A repeat autologous HSCT due to persistent, progressive or relapsed POEMS is considered experimental and investigational.

19. Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Gammopathy and skin changes (POEMS):
    a. Autologous HSCT is considered medically necessary for the treatment of POEMS Syndrome when diagnostic criteria for that syndrome are met.
    b. A repeat autologous HSCT due to primary graft failure or failure to engraft is considered medically necessary.
    c. A repeat autologous HSCT due to persistent, progressive or relapsed POEMS is considered experimental and investigational.
    d. A tandem autologous HSCT for treatment of POEMS Syndrome is considered experimental and investigational.
    e. Allogeneic (ablative or non-myeloablative) HSCT for treatment of POEMS Syndrome is considered experimental and investigational.
20. Other Non-Covered Indications – the following are considered experimental and unproven as its effectiveness has not been established and excluded from coverage:
    a. Autologous stem cell transplantation for treatment of:
        i. Thalassemia major.
        ii. Sickle cell anemia.
        iii. Primary immunodeficiency disorder.
        iv. Erectile dysfunction.
        v. Hypergammaglobulinemia.
        vi. Autologous bone marrow cells for coronary artery disease, left ventricular dysfunction, heart failure or angina, including trans-endocardial delivery.
    b. Allogeneic stem cell transplantation for treatment of:
        i. Primitive neuroectodermal tumors (PNET), including medulloblastoma and pineoblastoma.
        ii. Ependymoma.
        iii. Retinoblastoma.
        iv. Waldenstrom macroglobulinemia.
    c. Stem cell implants for spinal cord injury are considered experimental and investigational.
21. Umbilical Cord Blood Stem Cell Transplant (UCBSCT):
    a. Covered for patients who meet all eligibility requirements for an allogeneic HSCT.
    b. Not a covered benefit for patients who do not meet selection criteria for an allogeneic HSCT. There is a lack of evidence regarding safety and efficacy of HSCT in patients whose primary disease or overall physical condition does not warrant this procedure.

4.0 Coding:

Prior Approval Legend: Y = All lines of business; N = None required; 1 = HMO/POS; 2 = PPO; 3 = ASO group L0000264; 4 = ASO group L0001269 Non-Union & Union; 5 = ASO group L0001631; 6 = ASO group L0002011; 7 = ASO group L0001269 Union Only.

COVERED CODES			
Code	**Description**	**Prior Approval**	**Benefit Plan Reference**
38204	Management of recipient hematopoietic progenitor cell donor search and cell acquisition	Y	Benefits and Coverage, Transplantation Services
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic	Y	Benefits and Coverage, Transplantation Services
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous	Y	Benefits and Coverage, Transplantation Services
38207–38215	Transplant preparation of hematopoietic progenitor cells; (describes various steps used to preserve, prepare and purify bone marrow/stem cells prior to transplantation or reinfusion.)	Y	Benefits and Coverage, Transplantation Services
38230	Bone marrow harvesting for transplantation; allogeneic	Y	Benefits and Coverage, Transplantation Services
38232	Bone marrow harvesting for transplantation; autologous	Y	Benefits and Coverage, Transplantation Services
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor	Y	Benefits and Coverage, Transplantation Services
38241	Hematopoietic progenitor cell (HPC); autologous transplantation	Y	Benefits and Coverage, Transplantation Services
38242	Allogeneic lymphocyte infusions	Y	Benefits and Coverage, Transplantation Services
86812–86821	HLA (tissue) typing	N	Benefits and Coverage, Transplantation Services
86920–86923	Compatibility testing	N	Benefits and Coverage, Transplantation Services
96401-96450	Chemotherapy administration	N	Benefits and Coverage; Chemotherapy
S2140	Cord blood harvesting for transplantation, allogeneic	Y	Benefits and Coverage, Transplantation Services
S2142	Cord blood-derived stem cell transplantation; allogeneic	Y	Benefits and Coverage, Transplantation Services
S2150	Bone marrow or blood-derived peripheral 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,	Y	Benefits and Coverage, Transplantation Services

COVERED CODES			
Code	**Description**	**Prior Approval**	**Benefit Plan Reference**
	emergency, and rehabilitative services, and the number of days of pre- and post-transplant care in the global definition (when specified as autologous)		

NON-COVERED CODES		
Code	**Description**	**Benefit Plan Reference/Reason**
0263T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, 1 leg, including ultrasound guidance, if performed; complete procedure including unilateral or bilateral bone marrow harvest	General Exclusions and Limitations; Experimental/investigational
0264T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, 1 leg, including ultrasound guidance, if performed; complete procedure excluding bone marrow harvest	General Exclusions and Limitations; Experimental/investigational
0265T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, 1 leg, including ultrasound guidance, if performed; unilateral or bilateral bone marrow harvest only for intramuscular autologous bone marrow cell	General Exclusions and Limitations; Experimental/investigational

5.0 Unique Configuration/Prior Approval/Coverage

Fully-insured SPD Product ID plans have unique language: hematopoietic stem cell transplants do not have to be done at designated facilities and are also covered at non-network facilities.

Fully-insured SPD Product ID plans and ASO group L0001631 plans have a Travel and Lodging Benefit included in the Transplant Benefit (see COCs/SPDs for details).

6.0 Terms & Definitions:

Ablative – A very high dose of a treatment, calculated to kill a tumor or malignant cells.

Allogeneic hematopoietic stem cell transplantation (HSCT) – Infusion of HSCs obtained from a genetically different donor. Allogeneic stem cells can be harvested from either the bone marrow or peripheral blood.

Autologous HSCT – Infusion of previously harvested HSCs to the same individual from whom they were harvested. Allogeneic stem cells can be harvested from either the bone marrow or more commonly, peripheral blood. Peripheral stem cells are harvested via one or more pheresis procedures. A prior course of chemotherapy (typically cyclophosphamide) or growth factors or both can increase the number of circulating stem cells.

Blood cancer – there are three main types of blood cancers:

- Leukemia – a type of cancer found in blood and bone marrow, caused by the rapid production of abnormal white blood cells. Can be either acute or chronic and include four classifications:
    - Acute lymphoblastic/ lymphocytic leukemia (ALL)
    - Acute myeloid/ myelogenous leukemia (AML)

- Chronic lymphocytic leukemia (CLL)
- Chronic myeloid leukemia (CML)

- Lymphoma – a type of blood cancer that affects the lymphatic system. Abnormal lymphocytes become lymphoma cells, that multiple and collect in the lymph nodes and other tissues. Lymphomas are divided into two categories:
  - Non-Hodgkin lymphoma – the most common lymphoma with about 61 different types. Diagnoses as either B-cell or T-cell lymphoma. B-cell lymphomas are classified as high-grade (grow quickly) or low-grade (grow slowly).
  - Hodgkin lymphoma – rarest types of the disease with six different subtypes.
- Myeloma (multiple myeloma) – a cancer of a type of white blood cell called plasma cells. Because myeloma frequently occurs as many sites in the bone marrow, it is often referred to as "multiple myeloma."

Bone marrow – A spongy tissue within flat bones of the hip, sternum and skull. This tissue contains stem cells, the precursors of platelets, red blood cells and white cells.

Chimerism – Cell populations derived from different individuals, which may be mixed or complete.

Complete response/remission (CR) – The disappearance of all signs of cancer in response to treatment. This does not always mean the cancer has been cured.

Cytotoxic – Destructive to cells.

Eastern Cooperative Oncology Group (ECOG) Performance Status – Scale used to determine the individual's level of functioning. The score is based on the following:

Score	Comments
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of self-care but unable to carry out any work activities, Up and about more than 50% of waking hours.
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours.
4	Completed disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Deceased

Failure to engraft – When the HSCs infused during a stem cell transplant do not grown and function adequately in the bone marrow.

Graft-versus-host disease (GVHD) – A life-threatening complication of allogeneic bone marrow transplants in which the donated marrow causes an immune reaction against the recipient's body.

Hematopoietic stem cells (HSC) – Primitive cells capable of replication and formation into mature blood cells to repopulate the bone marrow.

Hematopoietic stem cell transplantation (HSCT) – the intravenous infusion of autologous or allogeneic stem cells collected from bone marrow, peripheral blood or umbilical cord blood to reestablish hematopoietic function in patients with a variety of acquired or inherited malignant and non-malignant disorders.

Human leukocyte antigen (HLA**)** – A group of protein molecules located on most cells in the body and can provoke an immune response.

Karnofsky Performance Scale – A measure of an individual's overall physical health, judged by his or her level of activity. The score is based on the following:

Performance status %	Comments
100	Normal. No complaints. No evidence of disease.
90	Able to carry on normal activity. Minor signs or symptoms of disease.
80	Normal activity with effort. Some signs or symptoms of disease.
70	Cares for self. Unable to carry on normal activity or to do active work.
60	Requires occasional assistance, but is able to care for most of personal needs.
50	Requires considerable assistance and frequent medical care.
40	Disabled. Requires special care and assistance.
30	Severely disabled. Hospital admission is indicated although death is not imminent.
20	Hospitalization necessary. Very sick, active supportive treatment necessary.
10	Moribund; fatal processes progressing rapidly.
0	Dead.

Comparing Karnofsky performance scale & ECOG performance status:
Karnofsky score of 80-100% = ECOG performance status of 0 or 1
Karnofsky score of 60-70% = ECOG performance status of 2
Karnofsky score of 10-50% = ECOG performance status of 3 or 4
Karnofsky score of 0% = ECOG performance status of 5

Lansky Score – Play -performance scale for pediatric patients. This scale may be used with children age one to16 that have any type of malignancy. It may be used for both inpatients & outpatients, and for patients undergoing active treatment as well as long-term follow-up. It is rated by parents based on their child's activity over the past week. Parents fill out the assessment based on the directions on the form, and the form is re-administered over time to assess for changes in performance status.

Rating	Description
100	Fully active, normal
90	Minor restrictions with strenuous physical activity
80	Active, but gets tired more quickly
70	Both greater restriction of, and less time spent in, active play
60	Up and around, but minimal active play; keeps busy with quieter activities
50	Lying around much of the day, but gets dressed; no active play; participates in all quiet play and activities
40	Mostly in bed; participates in quiet activities

Rating	Description
30	Stuck in bed; needs help even for quiet play
20	Often sleeping; play is entirely limited to very passive activities
10	Does not play nor get out of bed
0	Unresponsive

Myeloablative chemotherapy – High-dose chemotherapy that kills cells in the bone marrow, including cancer cells. It lowers the number of normal blood-forming cells in the bone marrow, and can cause severe side effects. Myeloablative chemotherapy is usually followed by a bone marrow or stem cell transplant to rebuild the bone marrow.

Non-myeloablative chemotherapy – Lower and less toxic doses of chemotherapy and radiation are given, followed by the infusion of donor stem cells. Also, called “mini-transplant,” mini-allograft, or reduced intensity conditioning transplant.

Primary graft failure – When the hematopoietic stem cells infused during a stem cell transplant do not grown and function adequately in the bone marrow.

Refractory disease – A failure to attain a complete or partial response. The refractoriness can be primary or secondary.

Relapse – the recurrence of disease after initial therapy and complete remission.

Syngeneic stem cells – Refers to genetically identical bone marrow or peripheral stem cells harvested from an identical twin.

Tandem transplantation – Two or more planned courses of high dose chemotherapy and stem cell support, either autologous or allogeneic. Tandem transplants are typically administered at intervals of two to six months, contingent on recovery from prior toxicity. Multiple cycles of high-dose chemotherapy with stem cell transplantation differs from tandem transplant in that more time is allowed between transplantation to permit hematopoietic recovery. Use of tandem transplants for some conditions is considered experimental and investigational.

Umbilical Cord Blood Stem Cell Transplant (UCBSCT**)** – blood harvested from the umbilical cord and placenta shortly after delivery of neonates that contains stem and progenitor cells. Although cord blood is an allogeneic source, these stem cells are antigenically “naïve” and thus are associated with a lower incidence of rejection or graft vs host disease.

7.0 References, Citations & Resources:

1. HemOnc.Org, 05/07/17 @ http://hemonc.org/Performance_status.

2. Leukemia & Lymphoma Society. @ https://www.lls.org/treatment/types-of-treatment/stem-cell-transplantation/allogeneic-stem-cell-transplantation.

3. Medicare National Coverage Determination (NCD) for Stem Cell Transplantation (ID#110.23); effective date 01/27/2016 available at http://www.cms.gov.

4. National Comprehensive Cancer Network. @ https://www.nccn.org/professionals/physician_gls/f_guidelines.asp.

5. National Marrow Donor Program. @ https://bethematch.org/.

6. NCBI. National Library of Medicine. National Institutes of Health. Neuroblastoma. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3261589/.

8.0 Associated Documents [For internal use only]:

Policies - MM-03 Benefit Determinations; MM-25 Transition/Continuity of Care; MM-55 Peer-to-Peer Conversations.

Standard Operating Procedure (SOP) – SOP 001 Completing a HCN; MMS-03 Algorithm for Use of Criteria for Benefit Determinations; SOP 028 Pre-Transplant Process, SOP 029 Transplant Event and Listing, and SOP 30 Post-Transplant Process.

Sample Letter – TCS Approval Letter; Clinically Reviewed Exclusion Letter; Specific Exclusion Denial Letter.

Form – Out of Network/ Prior Authorization; High Cost Notification Form; Transplant Travel and Lodging Reimbursement Form.

Other – Transplant Network contracts with Cigna LifeSource, Interlink, and LifeTrac.

9.0 Revision History

Original Effective Date: 06/12/2013

Next Review Date: 10/01/2021

Revision Date	Reason for Revision
5/27/15	Revised entire policy; standardized Product Application language, rewrote General Background information, clinical criteria defined under Clinical Determination Guidelines, and added several new terms associated with procedure.
5/20/16	Annual review with revisions: Retitled from MRM Benefit Determination to Medical Policy, Responsible Party changed from Medical Resource Management (MRM) removed and reassigned to Case Management team, removed information related to Medicaid and Department of Health & Human Services, Updated CPT codes, References and Resources, and Definitions.
May 2017	Annual review – changed from MRM Medical Policy MP 027 to benefit Coverage Committee Policy formatting. Added criteria for use of medical marijuana. Removed reference to using MCG criteria. Annual renewal by QI/MRM June 2017.
March 2018	Initial review by BCC, annual renewal by QI/MRM June 2018. No changes to criteria. References/Resources updated.
August 2019	Annual review; new definition added, deleted code removed, approved by QIMRM 6/12/19 and leadership 8/20/19
4/20	Annual review; approved by BCC 7/6/20, formatting updated