BENEFIT COVERAGE POLICY

Title: BCP-67 Hematopoietic Stem Cell Transplantation

Effective Date: 07/01/2023

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:

The 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.

The 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 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 incidence 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:

See InterQual for the following criteria:

1. InterQual Transplantation, Allogeneic Stem Cell.
2. InterQual Transplantation, Allogeneic Stem Cell (Pediatric).
3. InterQual Transplantation, Autologous Stem Cell.
4. InterQual Transplantation, Autologous Stem Cell (Pediatric).

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; 8 = ASO group L0002184; 9 = ASO group L0002237, 10 = ASO L0002193.

COVERED CODES			
Code	**Description**	**Prior Approval**	**Benefit Plan Reference**
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic	Y	Transplantation Services
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous	Y	Transplantation Services
38230	Bone marrow harvesting for transplantation; allogeneic	Y	Transplantation Services
38232	Bone marrow harvesting for transplantation; autologous	Y	Transplantation Services
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor	Y	Transplantation Services
38241	Hematopoietic progenitor cell (HPC); autologous transplantation	Y	Transplantation Services
38242	Allogeneic lymphocyte infusions	Y	Transplantation Services

	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	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	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	Experimental/Investigational

5.0 Unique Configuration/Prior Approval/Coverage

ASO groups L0001631 and L0002237 plans have a Travel and Lodging Benefit included in the Transplant Benefit (see 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 multiply 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 – a rarest type 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 at 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 cancer has been cured.

Cytotoxic – Destructive to cells.

Eastern Cooperative Oncology Group (ECOG) Performance Status – Scale is 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 housework, 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.

	Confined to bed or chair
5	Deceased

Failure to engraft – When the HSCs infused during a stem cell transplant do not grow 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 the disease.
80	Normal activity with effort. Some signs or symptoms of the 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 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 is necessary. Very sick, active supportive treatment is 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 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, 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
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 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 grow 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 the 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. The 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. InterQual Transplantation, Allogeneic Stem Cell.
2. InterQual Transplantation, Allogeneic Stem Cell (Pediatric).
3. InterQual Transplantation, Autologous Stem Cell.
4. InterQual Transplantation, Autologous Stem Cell (Pediatric).
5. HemOnc.Org, 04/22/22 @ http://hemonc.org/Performance_status.
6. Leukemia & Lymphoma Society. @ https://www.lls.org/treatment/types-of-treatment/stem-cell-transplantation/allogeneic-stem-cell-transplantation.
7. Medicare National Coverage Determination (NCD) for Stem Cell Transplantation (ID#110.23); effective date 01/27/2016 available at http://www.cms.gov.
8. National Comprehensive Cancer Network. @ https://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
9. National Marrow Donor Program. @ https://bethematch.org/.
10. CBI. 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]:

Benefit Coverage Policies - BCP-33 Pre-Transplant Services.

Policies and Procedures (P&Ps) - MMP-09 Benefit Determinations MMP-02 Transition and Continuity of Care ; UMPP-02 Peer to Peer Conversations

Standard Operating Procedures (SOPs) – MMS-03 Algorithm for Use of Criteria for Benefit Determinations; MMS-05 Completing a High-Cost Notification Form; MMS- 10 Pre-Transplant Process, MMS-11 Transplant Event, and Listing, MMS-12 Post-Transplant Process, MMS-48 CCA Outpatient Services for Transplant, MMS-49 CCA Transplant Event, and Listing.

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, and Emerging Therapy Solutions (ETS).

9.0 Revision History

Original Effective Date: 06/12/2013

Next Review Date: 07/01/2024

Revision Date	Reason for Revision
5/15	Revised entire policy; standardized Product Application language, rewrote General Background information, and clinical criteria defined under Clinical Determination Guidelines and added several new terms associated with the procedure.
5/16	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.
5/17	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.
3/18	Initial review by BCC, annual renewal by QI/MRM June 2018. No changes to criteria. References/Resources updated.
8/19	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

Revision Date	Reason for Revision
4/21	Annual review; removed criteria and referenced InterQual criteria; aligned codes with InterQual criteria; updated associated documents.
4/22	Annual review, removed Interlink, updated InterQual references, removed non-covered codes section.
4/23	Annual review, Updated LOB: added L0002193, updated LifeTracs name to Emerging Transplant Solution, updated policies and SOP's in section 8.0, updated language in section 5.0: ASO group L0001631 and L0002237 plans have a Travel and Lodging Benefit included in the Transplant Benefit (see SPDs for details). Removed language from 5.0 re: Fully Insured SPD plan, plan discontinued. Moved 0263T, 0264T, and 0265T from covered to non-covered section.