MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	**Allogeneic Hematopoietic (STEM) Cell Transplantation (HSCT)**
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Product Disclaimer	• *Services are contract dependent; If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.* • *If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit.* • *If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.* • *If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.* • *If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.*

POLICY STATEMENT

I. Based upon our criteria and review of the peer-reviewed literature, high-dose chemotherapy (HDC) with allogeneic (stem) hematopoietic cell (HSCT) transplant has been medically proven to be effective and, therefore, is considered **medically appropriate** for carefully selected candidates when **ALL** of the following criteria are met:

A. Candidates have met their transplanting institution's selection criteria;

B. Documentation from the multidisciplinary team that includes individual's eligibility and risk for transplantation; (refer to Policy Guidelines I.-VII.) **and**

C. The individual has **ANY** of the following indications when related criteria are met:

1. Leukemias
   a. Adult Acute lymphoblastic Leukemia (ALL)
      i. for first complete remission for any risk level;
      ii. primary refractory; **or**
      iii. relapsed disease in second or greater remission.
   b. Pediatric ALL with **ANY** of the following:
      i. when initially diagnosed as high risk; **or**
      ii. relapsed disease in second or greater remission.
   c. Adult and Pediatric Acute Myeloid Leukemia (AML) with **ANY** of the following:
      i. first remission in patients with cytogenetic intermediate or poor-risk disease or other factors that predict poor outcome;

ii. for primary refractory;
iii. relapsed disease;
iv. second or greater remission; **or**
v. patients who have relapsed following a prior allogeneic HSCT and are medically able to tolerate the procedure.

d. Chronic myeloid leukemia (CML) with **ANY** of the following:
i. for patients not responding to first and second generation of tyrosine kinase inhibitors (TKIs) therapy;
ii. for patients with disease progression to accelerated phase or blast crisis; **or**
iii. molecular signs of leukemia progression, therapy resistant BCR - ABL1 mutations, or high-risk additional cytogenetic abnormalities.

e. Chronic lymphocytic leukemia (CLL) for patients who are at high risk with poor response to novel agents (e.g., ibrutinib, or idelalisib).

f. Small B cell lymphocytic lymphoma for patients who are at high risk with poor response to novel agents (e.g., ibrutinib, or idelalisib). (Refer to policy statement II for investigational indications).

2. Non-Hodgkin lymphomas including but not limited to aggressive lymphomas, mantle cell lymphoma, peripheral T-cell lymphoma, or hepatosplenic T-cell lymphoma; (refer to policy statement II B for investigational indications).
3. Myelodysplastic Diseases (MDS) when patients are considered intermediate or high risk.
4. Multiple Myeloma when treatment consists of tandem transplantation (e.g., an initial round of autologous stem cell transplant, followed by allogeneic HSCT) to treat newly diagnosed disease, preferably in a clinical trial (refer to policy statement II C for investigational indications).
5. <u>Non-Oncological Applications</u>
a. Sickle Cell Anemia
i. Matched related donor: Children or young adults at risk for complication of sickle cell disease who have **ONE** of the following indications:
a.) experienced an overt stroke, or have an abnormal transcranial doppler ultrasound;
b.) patients with frequent pain, who do not respond or have an inadequate response to standard of care treatments (e.g., hydroxyurea, new targeted therapies, or chronic transfusion therapies); **or**
c.) for patients with recurrent episodes of acute chest syndrome (ACS) despite standard of care treatment.

OR

ii. Unrelated Donor: patients with an indication for HSCT in the context of a clinical trial.

b. Homozygous beta-thalassemia (thalassemia major);
c. Bone Marrow Failure Syndromes including but not limited to:
i. Hereditary (e.g., Fanconi anemia, dyskeratosis congenita, Schwachman-Diamond Syndrome, and Diamond Blackfan syndrome); **or**
ii. Acquired severe aplastic anemia.

d. Primary Immunodeficiencies including but not limited to:
i. Wiskott-Aldrich syndrome;
ii. severe combined immunodeficiency;
iii. hemophagocytic lymphohistiocytosis;

iv. X-linked lymphoproliferative syndrome;
v. Chédiak-Higashi syndrome;
vi. Kostmann syndrome;
vii. Chronic granulomatous disease; or
viii. Leukocyte adhesion deficiencies.

e. Inherited Metabolic diseases including but not limited to lysosomal and peroxisomal storage disorders other than Hunter, Sanfilippo, and Morquio syndromes (e.g., Hurler, Maroteaux Lamy variants, Gaucher disease, metachromatic leukodystrophy, globoid cell leukodystrophy, adrenoleukodystrophy;

f. Genetic Disorders Affecting Skeletal Tissue: Infantile malignant osteopetrosis (Albers-Schöberg disease or marble bone disease).

II. Based upon our criteria and assessment of the peer-reviewed literature, treatment with HDC and allogeneic HSCT has not been medically proven to be effective and therefore is considered **investigational** for the following malignant conditions including but not limited to:

A. Non-Hodgkin's Lymphomas (NHL)
1. as an initial therapy (e.g., without a full course of standard-dose induction chemotherapy) for any NHL;
2. to consolidate a first complete remission (CR) for individuals with diffuse large B-cell lymphoma and an International Prognostic Index score that predicts a low- or low-intermediate risk of relapse;

B. Multiple Myeloma as upfront therapy of newly diagnosed multiple myeloma or as salvage therapy;

C. Amyloidosis.

D. Autoimmune disease including but not limited to:
1. Rheumatoid arthritis
2. Systemic sclerosis (e.g., scleroderma)
3. Systemic lupus erythematosus (SLE)
4. Type 1 Diabetes Mellitus
5. Multiple sclerosis
6. Chronic inflammatory demyelinating polyneuropathy.

E. Other malignant conditions including but not limited to:
1. Germ cell tumors;
2. Solid tumors of childhood (e.g., neuroblastoma Ewing's sarcoma, Wilms' tumor, rhabdomyosarcoma, osteosarcoma, retinoblastoma or germ cell tumor);
3. Lung cancer, any histology;
4. Rectal cancer;
5. Pancreas cancer;
6. Stomach cancer;
7. Thyroid tumors;
8. Primitive Neuroectodermal Tumor (PNET) (e.g., ependymoma, and other PNETs);
9. Esophageal cancer;
10. Gall bladder cancer;
11. Cancer of the fallopian tubes;
12. Paranasal sinus cancer;

13. Tumors of the thymus;
14. Medulloblastoma;
15. Epithelial ovarian cancer;
16. Cancer or the bile duct;
17. Cervical cancer;
18. Prostate cancer;
19. Neuroendocrine tumors;
20. Tumors of unknown primary origin;
21. Breast Cancer;
22. Colon cancer;
23. Renal cell cancer;
24. Uterine cancer
25. Nasopharyngeal cancer;
26. Soft tissue sarcomas;
27. Malignant melanoma

Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services

POLICY GUIDELINES

Recipient Selection Guidelines: Each individual considered for allogeneic HCT must be evaluated by the transplant center for potential difficulties that would complicate and diminish the success of transplantation. Consideration will be given to the patient's risk of death without transplantation, along with the presence and severity of potential contraindications.

Documentation from the multidisciplinary team must include the following pretransplant evaluations:

I. Clinical Evaluation:
   A. Confirmation of diagnosis;
   B. Identification of comorbidities;
   C. Treatment of co-morbidities;
   D. Current assessment of co-morbidities;
   E. Consult notes (if applicable).

II. Psycho-Social Evaluation and Performance Status:
   A. Karnofsky performance score, Eastern Cooperative Oncology Group (ECOG) performance status, or Palliative Performance Scale (PPS) score;
   B. Identification of stressors (family support, noncompliance issues, motivational issues, alcohol or substance abuse).

III. Oral Health Exam

IV. Lab Tests:
   A. CBC, metabolic profile;
   B. Serologies: CMV, Hepatitis B and C;
   C. HIV testing.

V. Cardiac Assessment:
   A. 12 lead EKG;
   B. Stress (exercise, nuclear, or dobutamine), and
   C. Echo or MUGA Scan

VI. Pulmonary Assessment:
   A. Chest x-ray;
   B. Pulmonary function tests (PFTs).
   C. Low-dose screening CT for individuals considered high-risk for lung cancer (e.g., 20- to 30-pack history of smoking).

VII. Age-Appropriate Screening Tests:

Please refer to the U.S Preventive Services Task Force (USPSTF) website for list of age-appropriate screening guidelines. https://uspreventiveservicestaskforce.org/uspstf/

DESCRIPTION

The FDA regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation (CFR) title 21, parts 1270 and 1271. Hematopoietic stem cells are included in these regulations.

Stem cells differ from other blood cells in that they are capable of both unlimited self-renewal and differentiation to form white blood cells, red blood cells or platelets. Stem cells can be collected from two sources: direct aspiration of bone marrow *or* through a pheresis procedure to harvest peripheral blood stem cells (PBSC). Prior to harvesting the stems cells, pretreatment with drugs called "growth factors" or "colony stimulating factors" are given to the donor to enhance stem cell production. The harvested stem cells are then cryopreserved until transplanted.

Hematopoietic stem cell transplantation refers to a procedure that infuses hematopoietic stem cells to restore bone marrow function in cancer patients who receive bone marrow-toxic doses of drugs with or without whole-body radiotherapy.

In allogeneic hematopoietic (stem) cell transplantation cells are obtained from a matched related or unrelated donor. The more closely matched the donor to the recipient's tissue type, the more favorable the outcome for the transplant. Allogeneic HSCT entails the transfer of an entire hematopoietic system, including a foreign adaptive immune system to a new host. Allogeneic HSCT are associated with potential complications and benefits. One complication that may develop is graft-vs-host disease (GVHD). In GVHD, the donor cells may attack the recipient tissue which could eventually lead to death. A potential benefit, the graft-vs-tumor effect, arises when the donor cells attack the recipient tissue. This effect may account for lower relapse rates.

Reduced-intensity conditioning (RIC) refers to chemotherapy regimens that seek to reduce adverse effects secondary to bone marrow toxicity while retaining the beneficial graft-versus-malignancy effect of allogeneic transplantation. These regimens do not eradicate the patient's hematopoietic ability, thereby allowing for relatively prompt hematopoietic recovery (e.g., 28 days or less) even without a transplant. Patients who undergo RIC with allogeneic HCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full donor chimerism, which may be supplemented with donor lymphocyte infusions to eradicate residual malignant cells. A number of different cytotoxic regimens, with or without radiotherapy, may be used for RIC allotransplantation. They represent a continuum in their effects, from nearly totally myeloablative to minimally myeloablative with lymphoablation.

In this review, the term reduced-intensity conditioning will refer to all conditioning regimens intended to be nonmyeloablative.

Myeloablative conditioning (MAC) is the most intense form of conditioning for HCT and has the greatest risk for regimen-related toxicity. The classic MAC regimen combines myeloablative doses of busulfan with cyclophosphamide and ATG. Commonly referred to as Bu-Cy-ATG, this regimen has been used successfully to treat a broad range of immunodeficiency disorders. MAC agents are expected to produce profound pancytopenia and myeloablation within 1–3 weeks from administration. Pancytopenia is long lasting, usually irreversible and in most instances fatal, unless hematopoiesis is restored by hemopoietic stem cell infusion.

Acute lymphoblastic leukemia (ALL) is a heterogeneous disease with different genetic variations resulting in distinct biologic subtypes. Patients are stratified to risk-adapted therapy according to certain clinical and genetic risk factors that predict an outcome. Therapy may include hematopoietic cell transplantation.

Acute myeloid leukemia (AML) refers to leukemias that arise from a myeloid precursor in the bone marrow. AML has a high incidence of relapse, which has prompted research into various post-remission strategies using either allogeneic or autologous HCT.

Primary refractory acute myeloid leukemia (AML) is defined as leukemia that does not achieve a complete remission after conventionally dosed (non-marrow ablative) chemotherapy.

Tyrosine kinase inhibitors (TKIs) are a group of pharmacologic agents that disrupt the signal transduction pathways of protein kinases by several modes of inhibition. Tyrosine kinase enzymes can be categorized into receptor tyrosine kinases (RTKs), non-receptor tyrosine kinases (NRTKs), and a small group of dual-specificity kinases (DSK). There are over 50 FDA approved TKIs. Molecular therapy with TKIs has significantly reduced the indication for allogeneic hematopoietic stem cell trans plantation (allo - HSCT) in chronic myeloid leukemia (CML).

CML is a hematopoietic stem cell disorder characterized by the presence of a chromosomal abnormality called the Philadelphia chromosome, and predominantly affect older adult males over the age 60. The natural history of the disease consists of an initial (indolent) chronic phase, lasting a median of 3 years, and typically transforms into an accelerated phase, followed by a blast crisis which is usually the terminal event. Most patients present in chronic phase, often with nonspecific symptoms secondary to anemia and splenomegaly. A diagnosis is based on the presence of the Philadelphia chromosome abnormality by routine cytogenetics, or by detection of abnormal BCR-ABL products by fluorescence in situ hybridization or molecular studies, in the setting of persistent unexplained leukocytosis. Conventional dose chemotherapy regimens used for chronic phase disease can induce multiple remissions and delay the onset of blast crisis to a median of 4 to 6 years. However, successive remissions are invariably shorter and more difficult to achieve than their predecessors. HSCT has shown to be the only curative option.

Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are neoplasms of hematopoietic origin characterized by the accumulation of lymphocytes with a mature, generally well-differentiated morphology. In CLL, these cells accumulate in the blood, bone marrow, lymph nodes, and spleen; in SLL they are generally confined to lymph nodes. The Revised European-American/World Health Organization Classification of Lymphoid Neoplasms considers B-cell CLL and SLL a single disease entity.

Chronic lymphocytic leukemia and SLL share many common features and are often referred to as blood and tissue counterparts of each other, respectively. Both tend to present as asymptomatic enlargement of the lymph nodes, tend to be indolent, but can undergo transformation to a more aggressive form of the disease (e.g., Richter transformation). The median age at diagnosis of CLL is approximately 72 years, but it may present in younger individuals, often as a poor-risk disease with significantly reduced life expectancy.

Non-Hodgkin's Lymphoma (NHL) is the most common hematological malignancy worldwide (Thandra et al., 2021). NHL refers to a diverse class of B-cell and T-cell proliferations. NHL differs from Hodgkin's lymphoma by the clinical characteristics, the absence of Reed-Sternberg cells, and Cd15 and Cd30 staining on histology (Thandra et al., 2021). There are over 40 major subtypes, the most common types include indolent follicular lymphoma (FL) and aggressive diffuse large B-cell lymphoma (DLBCL). Each type is associated with unique driver genetic mutations (e.g., 14:18 translocation in FL, 11:14 translocation in Mantle Cell, 8:14 in Burkitts lymphoma) and unique risk factors (Epstein–Barr Virus (EBV) for Burkitt's lymphoma, human T-cell lymphoma virus (HTLV-1) for T-cell lymphoma).

NHL are often divided into two groups, indolent and aggressive depending on the types of affected cells and the rate of growth of the cells. Indolent Non-Hodgkin Lymphomas (NHLs) tend to grow and spread slowly with few symptoms. They are low-grade cancers which are often very responsive to treatments like chemotherapy, radiation, and immunotherapy. However, treatment is often deferred until the patient becomes symptomatic. The goal of treatment is often management as indolent lymphomas are rarely cured unless it is diagnosed when still localized. Thus, treatment options are more varied with no standardization. Aggressive Non-Hodgkin Lymphomas (NHLs) are fast growing and are

described as intermediate or high grade. They can be treated with chemotherapy, radiotherapy, monoclonal antibody therapy or a combination. The decision on the exact course of treatment is usually dependent on a number of factors such as, the stage of the disease, the number of nodes involved, the presence of lymphoma in other organs, and age.

Tandem transplants usually are defined as the planned administration of 2 successive cycles of high dose myeloablative chemotherapy, each followed by infusion of autologous hematopoietic stem cells, whether or not there is evidence of persistent disease following the first treatment cycle. Sometimes, the second cycle may use nonmyeloablative immunosuppressive conditioning followed by infusion of allogeneic stem cells.

The term salvage therapy describes therapy given to patients with refractory or relapsed disease. For patients with peripheral T-cell lymphoma, salvage therapy includes patients who do not achieve a complete response (e.g., achieve only a partial response, have no response, or have progressive disease) with first-line induction chemotherapy (refractory disease) or who relapse after achieving a complete response with first-line induction chemotherapy.

Sickle cell disease (SCD) is the most common inherited hemoglobinopathy in the United States. In SCD, the shape of the red blood cells is affected and have a sickle or crescent moon appearance. This abnormal shape can cause blood flow disruption or a total blockage. SCD is characterized by continuous intravascular hemolysis and microvascular occlusion resulting in recurrent vaso-occlusive painful events and severe organ complications (Aydin et al., 2021). SCD symptoms can begin to show when a child is about 5 to 6 months. Some people may have mild to more serious symptoms that lead to complications. Pain is the most common symptom of SCD. These pain crises may be mild or severe and can start suddenly and last for any length of time. Pain crises can affect your chest, back, legs and arms. Individuals with SCD are affected by multiple disease-related complications that result in significant morbidities and early mortality.

Acute chest syndrome (ACS) is a complication of SCD, and it can cause chest pain, cough, fever, low oxygen levels and cause injury to the lungs. ACS syndrome is the leading cause of hospitalization and death in people with sickle cell disease. Hematopoietic stem cell transplantation (HSCT) is currently the only established curative intervention for SCD that can restore normal hematopoiesis.

High-risk (aggressive) T-cell and natural killer cell neoplasms are a clinically heterogeneous group of rare disorders, most of which have an aggressive clinical course and poor prognosis. The exception includes the following subtypes, which typically have a relatively indolent and protracted course (T-cell large granulocyte leukemia, chronic lymphoproliferative disorder of natural killer cells, early-stage mycosis fungoides, primary cutaneous anaplastic large-cell lymphoma, and anaplastic lymphoma kinase-anaplastic large-cell lymphomas).

Myelodysplastic syndromes (MDS) and myeloproliferative neoplasms refer to a heterogeneous group of clonal hematopoietic disorders with the potential to transform into acute myelocytic leukemia. Allogeneic HCT has been proposed as a curative treatment option for patients with these disorders (Saber and Horowitz 2016).

Myeloid neoplasms are categorized according to criteria developed by the World Health Organization (WHO). Neoplasms are risk-stratified using the International Prognostic Scoring System (IPSS).

RATIONALE

Published studies demonstrate that allogeneic hematopoietic (stem) cell and bone marrow transplantation improve health outcomes for patients with certain diagnoses who meet specific criteria. Improved outcomes have been achieved outside the investigational setting for those patients. Available evidence does not demonstrate improved outcomes in other diagnoses and/or where listed criteria are not met.

This policy incorporates the National Comprehensive Cancer Network (NCCN) guidelines for various types of treatments, procedures and specific drug regimens for cancers outline in this document. NCCN guidelines were developed to help guide quality patient care and to give guidance on expected workup and treatment options based on patient presentation, cancer type and stage of disease. NCCN guidelines are regularly updated based on current standards of care and evidenced based research. The criteria are a comprehensive set of guidelines detailing the sequential management decisions and interventions that currently apply to 97 percent of cancers affecting patients in the United States.

AML is the second most common leukemia in children, accounting for approximately 20% of pediatric leukemias (Masetti et al., 2022). Allogenic HSCT improves relapse free survival and OS for those who are an immediate and poor risk and in CR1 compared to chemotherapy alone for adults. In children, the benefit of allogenic HSCT as a consolidation strategy for patients with newly diagnosed AML remains controversial. Risk factors to be considered include the risk of relapse, the non-relapse mortality risk, and the wide plethora of late effects related to the procedure. Currently, a consensus of which children would benefit from allogenic HSCT in CR1 remain controversial. Masetti et al. (2022) conducted a meta-analysis of allogenic HSCT for pediatric patients with AML in CR1. Both prospective and retrospective studies comparing allogenic HSCT to chemotherapy in higher-risk patients were considered. A total of 9 studies (5 prospective, 4 retrospective) were included. None of the prospective studies were randomized. The meta-analysis showed that OS was improved with allogeneic HSCT compared with chemotherapy. Similarly, disease-free survival (DFS) was improved with allogeneic HSCT compared to chemotherapy. Risk of relapse was higher among patients who received chemotherapy.

Recent developments in the treatment of CML requires continued assessment of indicators for when a curative HSCT would be needed. Patients with chronic CML should be started with first generation or second generation TKIs and monitored according to European LeukemiaNet (ELN) or US National Comprehensive Cancer Network (NCCN) guidelines. Patients with resistant disease should be regarded as candidates for HSCT to a matched related donor or a fully matched unrelated donor and the intensity of the conditioning regime should be adjusted according to the age and core morbidities (Niederwieser and Kröger 2022).

Allo HSCT is an established curative treatment option for patients with SCD. The pediatric population has primarily been the focus of published data on allo HSCT in the SCD population. Studies have shown that allo HSCT, if performed before the age of 10 are associated with reduced mortality and lower health care costs (Iqbal et al., 2021). There are few studies that evaluate the efficacy allo HSCT for adults. Recently an international effort on behalf of the pediatric diseases working party of European Society for blood and bone marrow transplantation and sickle cell disease transplantation international consortium, conducted a systematic and meta-analysis on the efficacy of allogeneic hematopoietic cell transplantation and sickle cell disease. There were 33 studies and a total of 2853 patients who met inclusion criteria. Data was collected on patients undergoing allo-HSCT between 1986 and 2017 who had recurrent vaso-occlusive crisis, acute chest syndrome and stroke. The majority of patients had multiple indications, but the most common indication was for vaso occlusive crisis. A matched related sibling was the most common donor source, and bone marrow was the most common hematopoietic cell source. All groups both adults and pediatric has an overall survival (OS) rate of 96%, disease free survival (DFS) 90%, acute graft versus host disease (aGVHD)20%, chronic graft versus host disease (cGVHD) 10%, nonrelapse mortality 4% and graft failure of 5% (Iqbal et al., 2021).

Du et al. (2023) performed a systematic review and meta-analysis on transplant for refractory or relapsed peripheral T cell-lymphoma (R/R-PTCL) and reported outcomes of allogeneic HSCT and autologous HSCT for R/R-PTCL. Individuals in the 2 groups had similar survival rates, as opposed to individuals with R/R-PTCL who underwent autologous HSCT had fewer adverse events than those who underwent allogeneic HSCT. Per researchers this could possibly be due to GVHD counterbalances the accompanying graft versus lymphoma effect after allogeneic HSCT. In considering the pretransplant status, most patients in the allogeneic HSCT group were insensitive to chemotherapy, and allogeneic HSCT served as a salvage therapy, which provided an additional survival advantage for patients with R/R-PTCL. The findings of this study suggest that, overall, HSCT is an effective therapy for R/R-PTCL. Individual's with R/R-PTCL with lower-risk stratification might prefer autologous HSCT, although allogeneic HSCT can still serve as a salvage therapy in those with a higher-risk disease stage.

CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- *CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.*

- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*
- *Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).*

CPT Codes

Code	Description
38205	Blood derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38210	Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-cell depletion
38212	Transplant preparation of hematopoietic progenitor cells; red blood cell removal
38213	Transplant preparation of hematopoietic progenitor cells; platelet depletion
38230	Bone marrow harvesting for transplantation, allogeneic
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
38242	Allogeneic lymphocyte infusions
38243	Hematopoietic progenitor cell (HPC); HPC boost

HCPCS Codes

Code	Description
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 posttransplant care in the global definition

ICD10 Codes

Code	Description
C26.0-C26.9	Malignant neoplasm of other and ill-defined digestive organs (code range)
C33	Malignant neoplasm of trachea
C34.00-C34.92	Malignant neoplasm of bronchus and lung (code range)
C38.1-C38.8	Malignant neoplasm of mediastinum and pleura (code range)
C47.0-C47.9	Malignant neoplasm of peripheral nerves and autonomic nervous system (code range)
C48.0	Malignant neoplasm of retroperitoneum
C49.0-C49.9	Malignant neoplasm of other connective and soft tissue (code range)
C50.011-C50.919	Malignant neoplasm of breast (code range)
C62.00-C62.92	Malignant neoplasm of testis (code range)

Code	Description
C71.0-C71.9	Malignant neoplasm of brain (code range)
C81.00-C81.99	Hodgkin lymphoma (code range)
C82.00-C82.59	Follicular lymphoma (code range)
C82.60-C82.99	Cutaneous follicle center lymphoma
C83.00-C83.99	Non-follicular lymphoma (code range)
C84.60-C84.79	Anaplastic large cell lymphoma, ALK-positive or ALK-negative (code range)
C86.5	Angioimmunoblastic T-cell lymphoma
C86.6	Primary cutaneous CD30-positive T-cell proliferations
C88.2-C88.9	Malignant immunoproliferative diseases and certain other B-cell lymphomas (code range)
C90.00-C90.32	Multiple myeloma and malignant plasma cell neoplasms (code range)
C91.10-C91.12	Chronic lymphocytic leukemia of B-cell type (code range)
C94.40-C94.42	Acute panmyelosis with myelofibrosis (code range)
C94.6	Myelodysplastic disease, not classified
D46.0-D46.9	Myelodysplastic syndromes (code range)
D46.A-D46.Z	Refractory cytopenia with multilineage dysplasia (code range)
D47.1	Chronic myeloproliferative disease
D47.3	Essential (hemorrhagic) thrombocythemia
D47.9	Neoplasm of uncertain behavior of lymphoid, hematopoietic and related tissue, unspecified
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)
D47.Z9	Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic and related tissue
D56.0-D56.9	Thalassemia (code range)
D57.00-D57.819	Sickle-cell disorders (code range)
D60.0-D61.9	Acquired pure red cell aplasia [erythroblastopenia] (code range)
D81.0-D82.0	Combined immunodeficiencies (code range)
E75.21-E75.3	Other sphingolipidosis (code range)
E76.01-E76.03	Disorders of glycosaminoglycan metabolism (code range)
E77.0-E77.9	Disorders of glycoprotein metabolism (code range)
G35	Multiple sclerosis
M32.0-M32.9	Systemic lupus erythematosus (SLE) (code range)
M34.0-M34.9	Systemic sclerosis [scleroderma] (code range)

REFERENCES

*Anagnostopoulos A, et al. Stem cell transplantation (SCT) for Waldenstrom's macroglobulinemia (wm). Bone Marrow Transplant 2002;29:943-947.

Aydin M, et al. Haploidentical Allogeneic Stem Cell Transplantation in Sickle Cell Disease: A Systematic Review and Meta-Analysis. Transplant Cell Ther 2021 Dec;27(12):1004.e1-1004.e8.

*Bashir Q, et al. Predictors of prolonged survival after allogeneic hematopoietic stem cell transplantation for multiple myeloma. Am J Hematol 2012 Mar;87(3):272-6.

*Bensinger W, et al. Allo-SCT for multiple myeloma: a review of outcomes at a single transplant center. Bone Marrow Transplant 2012; 47(10):1312–1317.

*Bernt KM, et al. Current concepts in pediatric Philadelphia chromosome-positive acute lymphoblastic leukemia. Front Oncol 2014 Mar 25;4:54.

Bishop MR et al. Second-line Tisagenlecleucle to standard care in aggressive B Cell Lymphoma. The England Journal of Medicine 2022 Feb;386 (7):629-639.

Chakraborty R, et al. Impact of autologous transplantation on survival in patients with newly diagnosed multiple myeloma who have high-risk cytogenetics: A meta-analysis of randomized controlled trials. Cancer 2022 Jun;128(12)2288-2297.

*Cortelazzo S, et al. Mantle cell lymphoma. Crit Rev Oncol Hematol 2012 Apr;82(1):78-101.

*Crocchiolo R, et al. Tandem autologous-allo-SCT is feasible in patients with high-risk relapsed non-Hodgkin's lymphoma. Bone Marrow Transplant 2013;48(2):249-52.

*Dietrich SA, et al. Patterns and outcome of relapse after autologous stem cell transplantation for mantle cell lymphoma. Cancer 2011 May 1;117(9):1901-10.

*Dodero A, et al. Allogeneic transplantation following a reduced-intensity conditioning regimen in relapsed/refractory peripheral T-cell lymphomas: long-term remissions and response to donor lymphocyte infusions support the role of a graft-versus-lymphoma effect. Leukemia 2012 Mar;26(3):520-6.

Du J, et al. Comparison of Allogeneic Stem Cell Transplant and Autologous Stem Cell Transplant in Refractory or Relapsed Peripheral T-Cell Lymphoma: A Systematic Review and Meta-analysis. JAMA Netw Open 2021 May 3;4(5):e219807.

*Garnier A, et al. Allogeneic hematopoietic stem cell transplantation allows long-term complete remission and curability in high-risk Waldenström's macroglobinemia. Results of a retrospective analysis of the Société Française de Greffe de Moelle et de Thérapie Cellulaire. Hematologica 2010 Jun;95(6):950-5.

*Gertz MA, et al. Stem cell transplant for Waldenström macroglobulinemia: an underutilized technique. Bone Marrow Transplant 2012 Sep;47(9):1147-53.

*Gupta V, et al. Allogeneic, but not autologous, hematopoietic cell transplantation improves survival only among younger adults with acute lymphoblastic leukemia in the first remission: an individual patient data meta-analysis. Blood 2013;121(2):339-50.

Gribben JG. How and when I do allogeneic transplant in CLL. Blood 2018 Jul 5;132(1):31-39.

*Hamadani M, et al. How we approach patient evaluation for hematopoietic stem cell transplantation. Bone Marrow Transplant 2010;45(8):1259-68.

Iftikhar R, et al. Allogeneic hematopoietic cell transplantation for the treatment of severe aplastic anemia: evidence-based guidelines from the american society for transplantation and cellular therapy. Transplant Cell Ther 2024 Sep 20:S2666-6367(24)00682-1.

Iqbal M, et al. Systematic review/meta-analysis on efficacy of allogeneic hematopoietic cell transplantation in sickle cell disease: An international efffort on behalf of the pediatric diseases working party of european society for blood and marrow transplantation and the sickle cell transplantation international consortium. Transplant Cell Ther 2021 Feb;27(2):167.e1-167.e12.

Kanate AS, et al. Indications for hematopoietic cell transplantation and immune effector cell therapy: guidelines from the american society for transplantation and cellular therapy. Biology of Blood and Marrow Transplantation 2020 Jul;26(7):1247-1256.

Kanter J, et al. American Society of Hematology 2021 guidelines for sickle cell disease: stem cell transplantation. Blood Adv 2021 Sep 28;5(18):3668-3689.

*Koehne G, et al. Allogeneic hematopoietic stem cell transplantation for multiple myeloma: curative but not the standard of care. Curr Opin Oncol 2012 Nov;24(6):720-6.

*Kyriakou C. et al. Allogeneic stem-cell transplantation in patients with Waldenström Macroglobulinemia: report from the Lymphoma Working Party of the European Group for Blood and Marrow Transplantation. J Clin Oncol 2010;28(33):4926-34.

Masetti R, et al. Allogeneic hematopoietic stem cell transplantation for pediatric acute myeloid leukemia in first complete remission: a meta-analysis. Ann Hematol 2022 Nov;101(11):2497-2506.

National Comprehensive Cancer Network. Practice guidelines in oncology: acute myeloid leukemia. V.4.2024. [https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf[accessed 11/10/24.

National Comprehensive Cancer Network. Practice guidelines in oncology: B-cell lymphoma. V.3.2024 [https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf] accessed 11/10/24.

National Comprehensive Cancer Network. Practice guidelines in oncology: Hodgkin lymphoma. V.4.24. October 22, 2024. [http://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf] accessed 11/10/24.

National Comprehensive Cancer Network. Practice guidelines in oncology: multiple myeloma. V.1.2025. September 17, 2024 [http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf] accessed 11/10/24.

National Comprehensive Cancer Network. Practice guidelines in oncology: Waldenström's macroglobinemia /lymphoplasmocytic lymphoma. V.1.2025. [http://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf] accessed 11/10/24.

Niederwieser C, Kröger N. Transplantation in CML in the TKI era: who, when, and how? Hematology Am Soc Hematol Educ Program. 2022 Dec 9;2022(1):114-122.

Rotin LE, et al. A systematic review comparing allogeneic hematopoietic stem cell transplant to gene therapy in sickle cell disease. Hematology 2023 Dec;28(1):2163357.

Saber W, and Horowitz MM. Transplantation for myelodysplastic syndromes: who, when, and which conditioning regimens. American Society of Hematology 2016 Dec 2;2016(1):478-484.

Sung AD, et al. Home-based hematopoietic cell transplantation in the United States. Transplant Cell Ther 2022 Apr;28(4):207.el-207.e8.

Thandra KC, et al. Epidemiology of Non-Hodgkin's Lymphoma. Med Sci (Basel) 2021 Jan 30;9(1):5.

Thomson RJ et al. Tyrosine Kinase Inhibitors. [Updated 2023 Jul 18]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan Available from: [https://www.ncbi.nlm.nih.gov/books/NBK563322/] accessed 11/21/24.

Wilhelmsson M, et al. Long-term outcomes in survivors of childhood AML treated with allogeneic HSCT: a NOPHO-AML study. Bone Marrow Transplant 2019;54:726-736.

*Key Article

KEY WORDS

Allogeneic, Hematopoietic, cell transplantation, Leukemias, Lymphomas, Anemias, Multiple Myeloma, myeloablative conditioning (MAC), nonmyeloablative (NMA), tandem transplants, salvage therapy, reduced-intensity conditioning.

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a National Coverage Determination (NCD)110.23 Stem Cell Transplantation (Formerly 110.8.1). Please refer to the following NCD website for Medicare Members: [https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=366&ncdver=1&bc=AgAAgAAAAAAAAA%3d%3d&] accessed 11/11/24.