

MEDICAL POLICY

Medical Policy Title	Allogeneic Hematopoietic Stem Cell Transplantation (Allo-HSCT)
Policy Number	7.02.02
Current Effective Date	February 19, 2026
Next Review Date	February 2027

Our medical policies are guides to evaluate technologies or services for medical necessity. Criteria are established through the assessment of evidence based, peer-reviewed scientific literature, and national professional guidelines. Federal and state law(s), regulatory mandates and the member's subscriber contract language are considered first in the determination of a covered service.

(Link to [Product Disclaimer](#))

POLICY STATEMENT(S)

- I. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is considered **medically appropriate** when **ALL** of the following are met:
 - A. Candidates have met the transplanting institution's selection criteria;
 - B. The multidisciplinary team has evaluated the individual and recommends treatment (see Policy Guidelines for required documentation);

AND

- C. The individual is being treated for **ONE (1)** of the following indication-specific criteria, if applicable:
 1. Acute Lymphoblastic Leukemia (ALL);
 2. Acute Myeloid Leukemia (AML);
 3. Chronic Myeloid Leukemia (CML);
 4. Chronic Lymphocytic Leukemia (CLL)
 5. Non-Hodgkin Lymphoma (B and T-cell Lymphomas);
 6. Myelodysplastic Diseases when the following criteria are met:
 - a. Disease status is considered intermediate or high risk;
 7. Multiple Myeloma;
 8. Sickle Cell Anemia, when the following criteria are met:
 - a. Children or young adults who have a matched related donor* who are at risk for complications of sickle cell disease who meet **ONE (1)** of the following criteria:
 - i. Has experienced an overt stroke, or has an abnormal transcranial doppler ultrasound;
 - ii. Has frequent pain, and does not respond or have an inadequate response to

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standard of care treatments (e.g., hydroxyurea, new targeted therapies, chronic transfusion therapies); **or**

- iii. Has had recurrent episodes of acute chest syndrome despite standard of care treatment;

*Children or young adults who do not have a matched related donor may be eligible for an unrelated donor transplant in the context of a clinical trial, if there is an indication for HSCT as above.

- 9. Transfusion-dependent Thalassemia;
- 10. Bone Marrow Failure Syndromes; including but not limited to:
 - a. Acquired Severe Aplastic Anemia;
 - b. Fanconi Anemia;
 - c. Dyskeratosis Congenita;
 - d. Shwachman-Diamond Syndrome;
 - e. Diamond-Blackfan Syndrome;
 - f. Congenital Amegakaryocytic Thrombocytopenia;
- 11. Severe/Combined Immunodeficiency and Immune Dysregulation, including but not limited to:
 - a. T Cell Immunodeficiency;
 - b. Wiskott-Aldrich Syndrome;
 - c. Immune dysregulation, Polyendocrinopathy, Enteropathy, X-linked syndrome (IPEX) Syndrome;
- 12. Hemophagocytic Disorders (e.g., Hemophagocytic Lymphohistiocytosis [HLH]);
- 13. Phagocytic/Innate Immune Cell Disorders, including but not limited to:
 - a. Severe Congenital Neutropenia (including Kostmann Syndrome);
 - b. Chronic Granulomatous Disease;
 - c. Chediak-Higashi Syndrome;
 - d. Leukocyte Adhesion Deficiencies;
- 14. Common Variable Immunodeficiency;
- 15. Lysosomal/Peroxisomal Storage and Leukodystrophy Disorders, including but not limited to:
 - a. Mucopolysaccharoidosis I (MPS I, Hurler);
 - b. Maroteaux-Lamy Syndrome (MPS VI);
 - c. Gaucher Disease;

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- d. Globoid Cell Leukodystrophy (Krabbe Disease);
 - e. Metachromatic Leukodystrophy;
 - f. Cerebral X-Linked Adrenoleukodystrophy; **or**
16. Skeletal/Metabolic Bone Disorders, including but not limited to:
- a. Osteopetrosis;
 - b. Infantile Malignant Osteopetrosis (Albers-Schöberg disease or marble bone disease).

II. Allo-HSCT is considered **investigational** for **ALL** other indications.

RELATED POLICIES

Corporate Medical Policy

7.02.03 Autologous Hematopoietic Stem Cell Transplantation (Auto-HSCT)

7.02.11 Chimeric Antigen Receptor T-cell (CAR-T) Therapy

11.01.03 Experimental or Investigational Services

POLICY GUIDELINE(S)

Recipient Selection Guidelines: Each individual considered for allo- 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.

- I. Required documentation from the multidisciplinary team that includes the individual's eligibility and risk for autologous stem cell transplant should include:
 - A. Clinical Evaluation:
 - 1. Confirmation of diagnosis;
 - 2. Identification of comorbidities;
 - 3. Current assessment of co-morbidities;
 - 4. Management of co-morbidities;
 - 5. Consult notes (if applicable);
 - B. Psycho-Social Evaluation:
 - 1. Identification of stressors (e.g., family support, noncompliance issues, motivational issues, alcohol, or smoking/substance abuse);
 - C. Performance Status:
 - 1. Karnofsky performance score;
 - 2. Eastern Cooperative Oncology Group (ECOG) performance status,

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3. Palliative Performance Scale (PPS) score; or
 4. Lansky Play-Performance Scale (for age 1 to 16 years);
- D. Oral Health Evaluation;
- E. Lab Tests:
1. Complete blood count (CBC), metabolic profile;
 2. Serologies: Cytomegalovirus (CMV), Hepatitis B and C;
 3. Human Immunodeficiency Virus (HIV) testing;
- F. Cardiac Assessment:
1. 12 lead electrocardiogram (EKG);
 2. Echochardiogram or multigated acquisition (MUGA) Scan;
- G. Pulmonary Assessment:
1. Chest x-ray;
 2. Pulmonary function tests (PFTs) for high-risk of respiratory failure (e.g., chronic obstructive pulmonary disease (COPD), emphysema, a-1-antitrypsin deficiency, hepatopulmonary syndrome, or significant smoking history);
- H. Age-Appropriate Screening Tests:

Please refer to the U.S Preventive Services Task Force (USPSTF) website for list of age-appropriate screening guidelines: <https://www.uspreventiveservicestaskforce.org/uspstf/> [accessed 2026 Jan 19.]

DESCRIPTION

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 (allo-HSCT) 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. Allo-HSCT entails the transfer of an entire hematopoietic system, including a foreign adaptive immune system to a new host. Allo-HSCT is 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

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lead to death. A potential benefit, the graft-vs-tumor effect, arises when the donor cells attack the recipient's tumor 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-tumor effect of allo-HSCT. These regimens do not eradicate the patient's hematopoietic ability, and allow for relatively prompt hematopoietic recovery (e.g., 28 days or less) even without a transplant. Patients who undergo RIC with allo-HSCT 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.

Myeloablative conditioning (MAC) is the most intense form of conditioning for allo-HSCT 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 hematopoietic 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 HSCT.

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 HSCT.

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

Chronic Myeloid Leukemia (CML) is a hematopoietic stem cell disorder characterized by the presence of a chromosomal abnormality called the Philadelphia chromosome and predominantly affects 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,

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and spleen; in SLL they are generally confined to lymph nodes. 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. The Revised European-American/World Health Organization Classification of Lymphoid Neoplasms considers B-cell CLL and SLL a single disease entity.

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 follicular lymphoma (FL) and 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 Burkitt's lymphoma) and unique risk factors (Epstein-Barr Virus (EBV) for Burkitt's lymphoma, human T-cell lymphoma virus (HTLV-1) for T-cell lymphoma).

NHLs 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. 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 two 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

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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 of age and can 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 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. Allo-HSCT 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).

Disability Scores

- I. The Karnofsky performance status score describes a patient's functional status as a comprehensive 11-point scale correlating to percentage values ranging from 100% (no evidence of disease, no symptoms) to 0% (death). Adapted from Peus et al 2013:

A: Able to carry on normal activity and to work. No special care is needed.	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.
B: Unable to work. Able to live at home, care for most personal needs. A varying degree of assistance is needed.	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.

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C: Unable to care for self. Requires equivalent of institutional or hospital care. Disease may be progressing rapidly.	40	Disabled, requires special care and assistance. [In bed more than 50% of the time]
	30	Severely disabled, hospitalization is indicated although death not imminent. [Almost completely bedfast]
	20	Very ill, hospitalization and active supportive treatment necessary. [Totally bedfast and requiring extensive nursing care by professionals and/or family]
	10	Moribund, fatal processes progressing rapidly. [Comatose or barely arousable]
	0	Dead.

II. Palliative Performance Scale (PPS) score; adapted from Fast Facts and Concepts (Wilner and Arnold 2006):

Percentage	Ambulation	Activity Level/Evidence of Disease	Self-Care	Intake	III. Level of Consciousness
100	Full	Normal No Disease	Full	Normal	Full
90	Full	Normal Some Disease	Full	Normal	Full
80	Full	Normal with Effort Some Disease	Full	Normal or reduced	Full
70	Reduced	Can't do normal job or work. Some Disease	Full	As above	Full
60	Reduced	Can't do hobbies or housework. Significant Disease	Occasional Assistance Needed	As above	Full or confusion

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50	Mainly sit/lie	Can't do any work. Extensive Disease	Considerable Assistance Needed	As above	Full or Confusion
40	Mainly in bed	As above	Mainly Assistance	As above	Full or Drowsy or Confusion
30	Bed Bound	As above	Total Care	Reduced	As above
20	Bed Bound	As above	As above	Minimal	As above
10	Bed Bound	As above	As above	Mouth care only	Drowsy or coma
0	Death	-	-	-	-

III. Eastern Cooperative Oncology Group (ECOG) performance status; adapted from ECOG-ACRIN Cancer Research group:

Grade	ECOG PERFORMANCE STATUS
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 all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
5	Dead

IV. Lansky Play-Performance Scale (for age 1 to 16 years)

The Lansky play-performance scale is used for children aged 1-16 with any type of malignancy. It is typically rated by parents based on their child's activity over the past week. Adapted from: [Performance status | HemOnc.org - A Hematology Oncology Wiki](#) [accessed 2025 Nov 24]:

Rating	Description
100	Fully active, normal

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90	Minor restrictions with strenuous physical activity
80	Active, but gets tired 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 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 or get out of bed
0	Unresponsive

SUPPORTIVE LITERATURE

Masetti et al (2022) conducted a meta-analysis of allo-HSCT for pediatric patients with AML in first complete response. Both prospective and retrospective studies comparing allo-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 overall survival (OS) was improved with allo-HSCT compared with chemotherapy. Similarly, disease-free survival (DFS) was improved compared to chemotherapy. Risk of relapse was higher among patients who received chemotherapy.

Huang and colleagues (2025) performed a cross-study analysis of two-phase III Children's Oncology Group clinical trials to evaluate whether hematopoietic stem cell transplantation (HSCT) improves outcomes for pediatric patients with high-risk acute myeloid leukemia (AML). They compared patients who received HSCT in first complete remission (CR1) with those treated with chemotherapy alone in CR1. The analysis included 463 patients with high-risk cytogenetic or molecular features and 72 patients with standard-risk features who had positive measurable residual disease (MRD) after the first induction cycle. Among these groups, 33.9% of high-risk patients and 45.8% of standard-risk patients underwent HSCT in CR1. Across both risk groups, HSCT was associated with lower relapse rates and improved disease-free survival (DFS). In the high-risk cohort, 5-year DFS was 26% for patients treated with chemotherapy alone, compared with 49.8% for those who received both chemotherapy and HSCT. Similarly, in the standard-risk cohort, 5-year DFS was 16.9% with chemotherapy alone versus 50.9% for those who underwent HSCT. Overall, the authors concluded that HSCT in CR1 is associated with significantly improved outcomes for pediatric patients with high-risk AML.

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Barge et al (2025) aimed to examine the use of Allo-HSCT in the modern era of chronic lymphocytic leukemia (CLL) treatment by collecting data from the Australian and New Zealand Transplant and Cellular Therapy Registry for all patients who underwent HSCT for CLL between January 2009 and December 2018. Outcomes were compared between two periods of time, 2009-2013 (n=94) vs. 2014-2018 (n=50) and included patients who were treated with pathway inhibitors prior to transplant, which was more likely for those patients treated in the later cohort. Authors reviewed median time to engraftment, incidence of graft vs host disease, cytomegalovirus reactivation, survival, and cause of death. The median time to neutrophil engraftment for the 2009-2013 cohort was 16 days, and 17 days for the 2014-2018, while median platelet engraftment occurred at 19 and 16 days for the 2009-2013 and 2014-2018 cohorts, respectively. The cumulative incidence of graft versus host disease at 100 days was less for the later cohort at 33% vs. 52% for 2009-2013 with similar differences seen at 5 years. At the follow up time frame of 7.6 years for 2009-2013 cohort and 5.0 years for the 2014-2018 cohorts, there were no differences in OS, progression free survival (PFS), reported cause of death or relapse, but there was a significant improvement in non-relapse mortality from 42% to 23% in the later cohort. Authors concluded that allo-HSCT remains a viable treatment option for select patients with CLL.

Allo-HSCT is an established curative treatment option for patients with sickle cell disease (SCD). The pediatric population has primarily been the focus of published data. 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 of 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 review and meta-analysis on the efficacy of allo-HSCT for the treatment of sickle cell disease. There were 33 studies representing 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) had an OS rate of 96%, DFS 90%, acute graft versus host disease (aGVHD) of 20%, chronic graft versus host disease (cGVHD) of 10%, nonrelapse mortality of 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 allo-HSCT and autologous HSCT for R/R-PTCL. Individuals in the two 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. Individuals with R/R-PTCL with lower-risk stratification might prefer autologous HSCT, although allo-HSCT can still serve as a salvage therapy in those with a higher-risk disease stage.

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PROFESSIONAL GUIDELINE(S)

In 2020, the American Society of Transplantation and Cellular Therapy (ASTCT) convened a guideline committee to make recommendations for the use of hematopoietic cell transplantation and immune effector cell therapy. Indications were categorized as (1) Standard of care, where indication is well defined and supported by evidence; (2) Standard of care, clinical evidence available, where large clinical trials and observational studies are not available but have shown to be effective therapy; (3) Standard of care, rare indication, for rare diseases where demonstrated effectiveness exists but large clinical trials and observational studies are not feasible; (4) Developmental, for diseases where preclinical or early-phase clinical studies show promising results, and (5) not generally recommended, where available evidence does not support the routine use of hematopoietic stem cell transplantation. For updated guidelines, visit: <https://www.guidelinecentral.com/guideline/26026/#section-336178> [accessed 2026 Jan 19].

Following the ASTCT guideline recommendations, several indication specific guidelines have been published, including:

- Newly Diagnosed Adult Acute AML (Dholaria et al 2021);
- Pediatric Acute AML and Myelodysplastic Syndromes (Tarlock et al 2022);
- Follicular Lymphoma (a collaborative effort on behalf of ASTCT and the European Society for Blood and Marrow Transplantation (Iqbal et al 2024);
- Severe Aplastic Anemia (Iftikhar et al 2024);
- Mycosis Fungoides and Sézary Syndrome (a joint recommendation with the United States Cutaneous Lymphoma Consortium [USCLC]) (Goyal et al 2024);
- Diffuse Large B Cell Lymphoma (Epperla et al 2023);
- Classical Hodgkin Lymphoma (Pre-proof, Ahmed et al 2025);
- Evaluation of Children with Malignancies for Blood and Marrow Transplantation (Fraint et al 2023);

In 2020, the European Society for Medical Oncology (ESMO) published clinical practice guidelines for the diagnosis, treatment, and follow up of chronic lymphocytic leukemia (CLL) (Eichhorst et al) that are endorsed by the European Hematology Association (EHA) through the Scientific Working Group on CLL/European research initiative on CLL (ERIC). The panel recommended that patients who are refractory to chemoimmunotherapy with TP53 mutation or del(17p), but fully responsive to novel inhibitor therapy; patients refractory to chemoimmunotherapy and to novel inhibitor therapy, even those with a higher risk of non-relapse mortality (evidence level III,B), as well as patients with Richter's transformation in remission after therapy and clonally related to CLL.

In 2021, Kanter and colleagues published clinical guidelines for sickle cell disease (SCD): stem cell transplantation on behalf of the American Society of Hematology (ASH). The review of the evidence conducted by the panel yielded no randomized controlled trials, with all recommendations being made based upon very low certainty in the evidence and resulting in a recommendation for the

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development of a robust SCD registry to serve as a comparator for future HSCT studies. The conditional recommendations were as follows:

- “The ASH guideline panel suggests HLA-matched related HSCT rather than standard of care (hydroxyurea (H/U)/transfusion) in patients with SCD who have experienced an overt stroke or have an abnormal transcranial Doppler ultrasound;
- For patients with frequent pain, the ASH guideline panel suggests using related matched allogeneic transplantation rather than standard of care;
- For patients with recurrent episodes of acute chest syndrome (ACS), the ASH guideline panel suggests using related allogeneic transplantation over standard of care;
- For patients with SCD with an indication for HSCT who lack an MSD, the ASH guideline panel suggests using transplants from alternative donors in the context of a clinical trial;
- For allogeneic HSCT, the ASH guideline panel suggests using either total-body irradiation (TBI) #400 cGy or chemotherapy-based conditioning regimens.
- For children with SCD who have an indication for allogeneic HSCT and an MSD, the ASH guideline panel suggests using myeloablative conditioning over RIC that contains melphalan/fludarabine regimens;
- For adults with SCD who have an indication for allogeneic HSCT and an MSD, the ASH guideline panel suggests nonmyeloablative conditioning over RIC that contains melphalan/fludarabine regimens;
- In patients with an indication eligible for HSCT, the ASH guideline panel suggests using allogeneic transplantation at an earlier age rather than an older age;
- The ASH guideline panel suggests the use of HLA-identical sibling cord blood when available (and associated with an adequate cord blood cell dose and good viability) over bone marrow (BM)”

In 2023, Frait and colleagues published a report from the ASTCT Committee on practice guidelines for the evaluation of children with malignancies for blood and marrow transplantation. ASTCT states, “Children with malignancy who require HCT for cure have a unique set of psychosocial needs, physical comorbidities, and disease risk features that differentiate them from adults. Given the inability for some of the important pre-HCT risk indices developed for adults to be applied to children, a specialized approach is needed, ideally with harmonization among centers.” Although rigorous data on physiologic differences and randomized trials on management are lacking for children, the recommendations provided are meant to serve as a guide for pre-HCT preparations.

In 2025, Damaj et al published recommendations from the European Society for Blood and Marrow Transplantation (EBMT) Practice Harmonisation and Guidelines Committee for allogeneic hematopoietic cell transplantation in peripheral T-cell lymphoma. Recommendations included:

- “Allogeneic HCT is the treatment of choice in patients with insufficient response or refractory to first-line therapy; and with relapsed disease after first complete response regardless of prior treatment, including autologous HCT;

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- Eligibility for allogeneic HCT should be established early, donor search should be initiated as soon as no response to first-line treatment becomes obvious; proceed to allogeneic HCT, regardless of result of salvage therapy, as long as transplant eligibility is retained;
- There is no strict age limit for allogeneic HCT; age should be evaluated in context of other risk factors, candidates with a HCT comorbidity Index (HCT-CI) score of 2 or less with good performance status are most suitable for allogeneic HCT; however these factors must be considered together with age, comorbidities, and disease status to determine the overall risks of allogeneic HCT;
- Although patients in complete remission have the best outcomes after allogeneic HCT, patients in partial remission should also proceed directly to allogeneic HCT; Patients with stable or progressive disease can expect a probability of long-term survival and thus should be considered for allogeneic HCT, if eligible, on an individual basis;
- The preferred donor hierarchy is in the order: matched sibling donor, matched unrelated donor, haploidentical donor, mismatched unrelated donor; both peripheral blood stem cells and bone marrow are acceptable graft sources.

The National Comprehensive Cancer Network (NCCN) V.1.2026 Guidelines for B-Cell Lymphomas recommend consolidation with allo-HCT in patients with relapsed/refractory mantle cell lymphoma that is in remission following second-line therapy with fixed-duration regimens, additionally for those patients with MCL that is refractory to or progressing on second-line subsequent therapy and for disease relapse or progressive disease following CAR T-cell therapy.

NCCN V.5.2026 Guidelines for Multiple Myeloma identifies the potential use of allo-HCT given the lack of significant cure rate for single or tandem autologous HCT, for those individuals with multiple myeloma as initial therapy or as therapy for relapsed or refractory disease.

NCCN V.1.2026 Guidelines for Pediatric Acute Lymphoblastic Leukemia recommends the use of allo-HCT in those with persistent disease, or disease with high-risk features (KMT2A rearrangements) based on limited data available, stating it is "reasonable to consider HCT in first remission for certain patients."

NCCN V.2.2025 Guidelines for Acute Lymphoblastic Leukemia acknowledge that allo-HCT is more likely to be a utilized treatment in adult patients with evidence of high-risk features (Ph-like disease, or persistent measurable residual disease) and in post consolidative therapy in adolescents and young adults, and therefore recommend that, "HLA typing and bone marrow transplant referral should be considered for all patients with newly diagnosed disease and patients with relapsed disease who have not yet undergone transplant to facilitate timely donor identification, and ultimately allogeneic transplant if warranted.

NCCN V.2.2026 Guidelines for Acute Myeloid Leukemia (AML), allo-HCT can be considered an option for individuals with intermediate-risk and poor-risk AML in those who have already achieved remission and have a donor available.

NCCN V.1.2026 Guidelines for T-Cell Lymphomas recommend that allo-HCT can be a treatment option for patients who achieve a complete or partial response after initial therapy and also

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acknowledge that given the poor prognosis associated with T-cell prolymphocytic leukemia, patients should be enrolled in a clinical trial.

NCCN V.3.2025 Guidelines for Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma recommend that myeloablative or non-myeloablative allo-HSCT be considered only within the context of a clinical trial.

REGULATORY STATUS

The U.S. Food and Drug Administration (FDA) regulates vaccines, blood, and blood products (including hematopoietic stem cells), and biologics via the Center for Biologics Evaluation and Research (CBER) which ensures the safety, efficacy, and quality of these products. Refer to the FDA vaccines/blood/biologics website. Available from: <https://www.fda.gov/vaccines-blood-biologics> [accessed 2026 Jan 21]

The FDA maintains information for consumers and health professionals on vaccine, blood and biologics warnings and other safety information. Available from: <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/recalls-biologics> [accessed 2026 Jan 21]

CODE(S)

- Codes may not be covered under all circumstances.
- Code list may not be all inclusive (AMA and CMS code updates may occur more frequently than policy updates).
- (E/I)=Experimental/Investigational
- (NMN)=Not medically necessary/appropriate

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

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HCPCS Codes

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

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Code	Description
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)

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Code	Description
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)

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SEARCH TERMS

Peripheral blood stem cell transplant, umbilical cord blood transplant, allo transplant, allograft.

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

[Stem Cell Transplantation \(NCD 110.23\)](#) [accessed 2026 Jan 21]

[Allogeneic Hematopoietic Stem Cell Transplant for MDS \(Coverage with Evidence Development\)](#) [accessed 2026 Jan 21]

[Allogeneic Hematopoietic Stem Cell Transplant for Multiple Myeloma \(Coverage with Evidence Development\)](#) [accessed 2026 Jan 21]

[Allogeneic Hematopoietic Stem Cell Transplant for Myelofibrosis \(Coverage with Evidence Development\)](#) [accessed 2026 Jan 21]

[Allogeneic Hematopoietic Stem Cell Transplant for Sickle Cell Disease \(Coverage with Evidence Development\)](#) [accessed 2026 Jan 21]

[Allogeneic Hematopoietic Stem Cell Transplantation \(HSCT\) for Myelodysplastic Syndromes \(MDS\) \(NCA CAG-00415R\)](#) [accessed 2026 Jan 21]

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- Services are contract dependent; if a product does not cover a service, medical policy criteria do not apply.
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POLICY HISTORY/REVISION

Committee Approval Dates

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Date	Summary of Changes
04/22/26	<ul style="list-style-type: none">Policy edit, addition of references, formatting. No change to policy intent.
03/04/26	<ul style="list-style-type: none">Policy edit, policy reference correction. No change to policy intent.
02/19/26	<ul style="list-style-type: none">Annual review, simplification of criteria to the indication level, removal of investigational indications list, added HCPCS code S2142.
01/01/25	<ul style="list-style-type: none">Summary of changes tracking implemented.
10/18/01	<ul style="list-style-type: none">Original effective date