

# MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	Allogeneic Hematopoietic (STEM) Cell Transplantation
Policy Number	7.02.02
Category	Technology Assessment
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Current Effective Date	11/16/23
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Archived Review Date	N/A
Product Disclaimer	<ul style="list-style-type: none"> <li>• If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.</li> <li>• If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit.</li> <li>• 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.</li> <li>• 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.</li> <li>• If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.</li> </ul>

## POLICY STATEMENT

Based upon our criteria and review of the peer-reviewed literature, high-dose chemotherapy with allogeneic (stem) hematopoietic cell support has been medically proven to be effective and, therefore, is considered **medically appropriate** for carefully selected candidates.

Reduced-intensity conditioning (RIC) regimens are like allogeneic transplant. The stem cell is from a healthy person (the donor), but the chemotherapy given is less intensive. RIC have been proposed as an alternative to traditional myeloablative conditioning regimens. RIC regimens are being commonly used in older patients as well as in disorders in which traditional myeloablative conditioning regimens are associated with high rates of non-relapse mortality. Hodgkin disease, myeloma, and low-grade lymphoid malignancies have been the diseases most impacted by RIC regimens.

The following is a listing of coverage criteria for different medical conditions.

I. <u>Leukemias:</u>	
Medically appropriate indications:	Investigational indications:

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<p><b><u>Adult and Pediatric Acute Myeloid Leukemia (AML):</u></b></p> <ul style="list-style-type: none"><li>• First remission in patients with cytogenetic intermediate or poor-risk disease or other factors that predict poor outcome (please refer to description section of this policy); or</li><li>• Primary refractory or relapsed disease or disease in second or greater remission; or</li><li>• Patients who have relapsed following a prior allogeneic HSCT and are medically able to tolerate the procedure</li></ul> <p><b><u>Adult Acute Lymphoblastic Leukemia (ALL):</u></b></p> <ul style="list-style-type: none"><li>• First complete remission for any risk level; or</li><li>• Primary refractory or relapsed disease or disease in second or greater remission; or</li><li>• Relapsed after prior autologous HCT</li></ul> <p><b><u>Pediatric ALL:</u></b></p> <ul style="list-style-type: none"><li>• First complete remission but at high risk of relapse (e.g., including but not limited to age less than one year or greater than nine years at presentation, WBC greater than or equal to 30,000/ul, hypodiploidy (less than 44 chromosomes) t(9:22) or Pro-B, T lineage; or</li><li>• Second or greater remission or refractory disease; or</li><li>• Relapsed after prior autologous HCT</li></ul> <p><b><u>Chronic myelogenous leukemia (CML):</u></b></p> <ul style="list-style-type: none"><li>• Patients with no hematologic remission after three months of TKI therapy; or</li><li>• Patients with no cytogenetic response or cytogenetic relapse at six, 12, or greater than 15 months after achieving initial hematologic response after three months of TKI therapy; or</li><li>• Patients on TKI therapy who progress to accelerated or blast phase CML; or</li><li>• Patients in the first chronic phase with T315I mutations not sensitive to any tyrosine kinase inhibitors (TKIs)</li></ul> <p><b><u>Chronic lymphocytic leukemia (CLL)/ Small cell B-cell lymphoma</u></b> in previously treated patients with non-response or relapse within 12-24 months:</p> <ul style="list-style-type: none"><li>• After purine analogues; or</li><li>• After having achieved a response with intensive therapy; or</li><li>• With high risk cytogenetic abnormalities (e.g., del (17p) and del(11q))</li></ul>	<p><b><u>Chronic lymphocytic leukemia (CLL)/ Small cell B-cell lymphoma</u></b> with the exception of the small subset of patients with progressive disease refractory to conventional treatments described in the list of medically appropriate indications</p>
<b><u>II. Lymphomas:</u></b>	
<b><u>Hodgkin Lymphomas:</u></b>	
<b>Medically appropriate indications:</b>	<b>Investigational indications:</b>

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<ul style="list-style-type: none"><li>• Biopsy proven refractory disease if responsive to secondary therapy</li></ul>	<ul style="list-style-type: none"><li>• Initial therapy for all HL to consolidate a first complete remission</li></ul>
<b><u>Non Hodgkin Lymphoma:</u></b>	
Non Hodgkin Lymphoma (NHL) can be classified as either indolent (low grade) or aggressive (intermediate or high grade).	
<b>Medically appropriate indications:</b>	<b>Investigational indications:</b>
<p><b><u>Aggressive:</u></b></p> <ul style="list-style-type: none"><li>• To consolidate a first complete response in patients with diffuse large B-cell lymphoma but at high or high-intermediate risk of relapse as predicted by the age-adjusted international prognostic index (IPI); or</li><li>• To achieve or consolidate a complete response in a chemo sensitive first or second relapse; or</li><li>• As salvage therapy for patients who do not achieve a complete response after full first-line induction chemotherapy; or</li><li>• Salvage therapy when a complete response after full first-line induction chemotherapy is not achieved for <i>low</i> or <i>high</i> risk Burkitt lymphoma</li></ul> <p><b><u>Indolent:</u></b></p> <ul style="list-style-type: none"><li>• As salvage therapy for patients who do not achieve complete response after a full dose of first-line induction chemotherapy; or</li><li>• To achieve or consolidate complete response for those in a first or subsequent chemo sensitive relapse, whether or not their lymphoma has undergone transformation to a higher grade</li></ul> <p><b><u>Mantle Cell Lymphoma:</u></b></p> <ul style="list-style-type: none"><li>• As salvage therapy</li></ul> <p><b><u>Peripheral T-cell Lymphoma:</u></b></p> <ul style="list-style-type: none"><li>• As salvage therapy</li></ul>	<ul style="list-style-type: none"><li>• Initial therapy for all NHL; or</li><li>• To consolidate a first complete response for patients with Diffuse Large B-cell lymphoma with a low or low-intermediate risk of relapse as predicted by the IPI; or</li><li>• To consolidate a first complete response for indolent NHL subtypes; or</li><li>• Tandem transplants; or</li><li>• To consolidate a first remission in Mantle Cell lymphoma; or</li><li>• To consolidate a first remission in Peripheral T- Cell lymphoma</li></ul>

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Examples of lymphomas as described by the World Health Organization (WHO) and the Revised European-American Classification of Lymphoid Neoplasms (REAL). This list is not all-inclusive.

(\* denotes indolent types of lymphoma while + denotes aggressive type)

<p><b><u>B-cell Neoplasms</u></b></p> <p><u>Precursor B-cell Neoplasms</u></p> <ul style="list-style-type: none"> <li>• Precursor B-lymphoblastic leukemia/lymphoma<sup>+</sup></li> </ul> <p><u>Mature (Peripheral) B-cell Neoplasms-Predominately Disseminated</u></p> <ul style="list-style-type: none"> <li>• CLL/SLL<sup>*</sup></li> <li>• B-Prolymphocyte lymphoma<sup>+</sup></li> <li>• Lymphoplasmacytic lymphoma<sup>*</sup></li> <li>• Splenic Marginal Zone lymphoma<sup>*</sup></li> <li>• Hairy cell lymphoma<sup>*</sup></li> <li>• Plasma cell myeloma/plasmacytoma</li> </ul> <p>Mature (Peripheral) B-cell Neoplasms-Primary Extranodal Mucosa-associated lymphoid tissue<sup>*</sup></p> <p><u>Mature (Peripheral) B-cell Neoplasms-Predominantly Nodal</u></p> <ul style="list-style-type: none"> <li>• Marginal Zone lymphoma<sup>*</sup></li> <li>• Follicular lymphoma<sup>*</sup></li> <li>• Mantle cell lymphoma<sup>+</sup></li> <li>• Diffuse Large B-cell lymphoma (LBCL)<sup>+</sup></li> <li>• Mediastinal LBCL<sup>+</sup></li> <li>• Intravascular LBCL<sup>+</sup></li> <li>• Primary effusion lymphoma<sup>+</sup></li> <li>• Burkitt's lymphoma<sup>+</sup></li> <li>• Lymphomatoid granulomatosis</li> </ul>		<p><b><u>T- and NK-cell Neoplasms</u></b></p> <p><u>Precursor T- and NK-cell Neoplasms</u></p> <ul style="list-style-type: none"> <li>• Precursor T-lymphoblastic leukemia/lymphoma<sup>+</sup></li> <li>• Blastoid NK lymphoma<sup>+</sup></li> </ul> <p><u>Mature (Peripheral) T-cell Neoplasms- Predominately Disseminated</u></p> <ul style="list-style-type: none"> <li>• T-cell Prolymphocytic leukemia<sup>+</sup></li> <li>• T-cell Large Granular Lymphocytic leukemia<sup>*</sup></li> <li>• Aggressive NK-cell leukemia<sup>+</sup></li> <li>• Adult T-cell lymphoma/leukemia-HTLV-1<sup>+</sup></li> </ul> <p><u>Mature (Peripheral) T-cell Neoplasms- Primary Extranodal</u></p> <ul style="list-style-type: none"> <li>• Extranodal NK/T-cell lymphoma, nasal type<sup>+</sup></li> <li>• Enteropathy-type T-cell lymphoma<sup>+</sup></li> <li>• Hepatosplenic T-cell lymphoma<sup>+</sup></li> <li>• Subcutaneous panniculitis-like T-cell lymphoma<sup>+</sup></li> <li>• Mycosis fungoides/Szary syndrome<sup>*</sup></li> <li>• Primary cutaneous anaplastic large-cell lymphoma<sup>+</sup></li> </ul> <p><u>Mature (Peripheral) T-cell Neoplasms-Predominantly Nodal</u></p> <ul style="list-style-type: none"> <li>• Peripheral T-cell lymphoma- NOS<sup>+</sup></li> <li>• Angioimmunoblastic T-cell lymphoma<sup>+</sup></li> <li>• Primary systemic anaplastic Large-cell lymphoma<sup>+</sup></li> </ul>	
<p>**International Prognostic Index: Low Risk = 0-1 points, Low Intermediate = 2, High Intermediate = 3, High Risk = 4-5 points</p>			
<p><b>0 points</b></p> <ul style="list-style-type: none"> <li>• Age less than 60 years</li> <li>• Tumor stage I or II</li> <li>• Extranodal Involvement (ENI) 0-1</li> <li>• Performance status (PS) Eastern Cooperative Oncology Group (ECOG) 0-1</li> <li>• Lactate dehydrogenase (LDH) normal</li> </ul>		<p><b>1 point for presence of each</b></p> <ul style="list-style-type: none"> <li>• Age greater than 60 years,</li> <li>• Tumor stage III or IV,</li> <li>• ENI greater than 1,</li> <li>• PS (ECOG) 2-4,</li> <li>• LDH greater than normal.</li> </ul>	
<p>• **International Follicular Lymphoma Prognostic Index: Low Risk = 0-1 points, Intermediate Risk = 2, High Risk= greater than 5 points</p>			
		<p><b>1 point for presence of each</b></p> <ul style="list-style-type: none"> <li>• Age greater than or equal to 60 years;</li> <li>• Ann Arbor stage III-IV;</li> <li>• Hemoglobin level less than 12 g/dL;</li> <li>• Serum LDH level greater than the upper limit of normal;</li> <li>• Number of nodal sites greater than or equal to 5</li> </ul>	

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<b>III. Solid Tumors of Childhood</b>		
Defined as not arising from myeloid or lymphoid cells. The most common are neuroblastoma, Ewing’s sarcoma, Wilms’ tumor, rhabdomyosarcoma, osteosarcoma, retinoblastoma or germ cell tumor		
Neuroblastoma can be categorized according to the stage and number of copies of the N myc oncogene		
<u>Low Risk</u>	<u>Intermediate Risk</u>	<u>High Risk: Stage II and greater than 10 N-myc</u>
Stage I	Stage III and N-myc = 1 and ferritin less than 143 and favorable histology	Stage III; greater than 10 N-myc or ferritin greater than 143 or unfavorable histology
Stage II; N-myc = 1	Stage IV; N-myc =1 and less than 1 year at diagnosis	Stage IV and greater than 1 year at diagnosis
Stage IVS	Stage III and less than 1 year at diagnosis	Stage IV at less than 1 year at diagnosis and greater than 10 N-myc
<b>Medically appropriate indications:</b>		<b>Investigational indications:</b>
None		<ul style="list-style-type: none"> <li>Salvage allogeneic transplant for relapsing neuroblastoma or other solid tumors <i>after autologous</i> transplant or fail to respond; or</li> <li>Pediatric solid tumors</li> </ul>
<b>IV. Genetic Diseases and Acquired Anemias</b>		
Based upon our criteria and assessment of the peer-reviewed literature, treatment with HDC and allogeneic hematopoietic (stem) cell transplant for the following conditions has been medically proven to be effective and, therefore, is considered <b>medically appropriate</b> for the following conditions:		
<u>Hemoglobinopathies:</u>		
<ul style="list-style-type: none"> <li>Sickle cell anemia for children or young adults with either a history of prior stroke or at increased risk of stroke or end-organ damage; or</li> <li>Homozygous beta-thalassemia (thalassemia major)</li> </ul>		
<u>Bone Marrow Failure Syndromes – Aplastic Anemia:</u>		
<ul style="list-style-type: none"> <li>Hereditary: Fanconi anemia, dyskeratosis congenita, Schwachman-Diamond Syndrome, and Diamond Blackfan syndrome; or</li> <li>Acquired: secondary to drug or toxin exposure</li> </ul>		
<u>Primary Immunodeficiencies</u>		
<ul style="list-style-type: none"> <li>Absent or defective T-cell function: Wiskott-Aldrich syndrome, severe combined immunodeficiency, hemophagocytic lymphohistiocytosis, and X-linked lymphoproliferative syndrome; or</li> <li>Absent or defective natural killer function: Chédiak-Higashi syndrome; or</li> <li>Absent or defective neutrophil function: Kostmann syndrome, chronic granulomatous disease, leukocyte adhesion deficiencies</li> </ul>		
<u>Genetic Disorders Affecting Skeletal Tissue:</u>		
<ul style="list-style-type: none"> <li>Infantile malignant osteopetrosis (Albers-Schöberg disease or marble bone disease)</li> </ul>		
<u>Inherited Metabolic Diseases:</u>		
<ul style="list-style-type: none"> <li>Lysosomal and peroxisomal storage disorders (e.g., Hurler, Maroteaux Lamy variants, and Gaucher disease, metachromatic leukodystrophy, globoid cell leukodystrophy, adrenoleukodystrophy) <i>except</i> Hunter, Sanfilippo, and Morquio syndromes</li> </ul>		

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<b><u>V. Myelodysplastic Diseases</u></b>	
<p><u>Myelodysplastic syndrome (MDS)</u> refers to a heterogeneous group of hematopoietic disorders characterized by impaired maturation of hematopoietic cells and a tendency to transform into acute myelocytic leukemia. The 2008 WHO classification of MDS includes but is not limited to: refractory anemia (RA), refractory anemia with ring sideroblasts (RARS), refractory cytopenia with multilineage dysplasia (RCMD), refractory cytopenia with ring sideroblasts, refractory anemia with excess blasts 1 and 2 (RAEB 1 and 2), del 5q syndrome, and unclassified myelodysplastic syndrome.</p> <p><u>Myeloproliferative disorders</u> are characterized by the slow but relentless expansion of a clone of cells with the potential evolution into a blast crisis similar to acute myelocytic leukemia. Examples of myeloproliferative disorders include polycythemia vera, primary myelofibrosis, essential thrombocythemia, and chronic myelogenous leukemia (<i>please refer to leukemia section I.</i>) Other less common types of myeloproliferative disorders include chronic neutrophilic leukemia, chronic eosinophilic leukemia, hypereosinophilic leukemia, and mast cell disease.</p>	
<p><b>Conditions eligible for coverage: <u>Progression; No response to standard therapy</u></b></p>	
<ul style="list-style-type: none"> <li>• Myelodysplastic syndrome</li> </ul>	<ul style="list-style-type: none"> <li>• Myeloproliferative disorders</li> </ul>
<b><u>VI. Multiple Myeloma</u></b>	
<p><b>Medically appropriate indications:</b></p> <ul style="list-style-type: none"> <li>• Tandem transplantation with an initial round of autologous stem cell transplant followed by allogeneic hematopoietic (stem) cell transplant to treat newly diagnosed multiple myeloma preferably in a clinical trial</li> </ul>	<p><b>Investigational indications (except in the context of a clinical trial):</b></p> <ul style="list-style-type: none"> <li>• As upfront therapy of newly diagnosed multiple myeloma or as salvage therapy</li> </ul>
<b><u>VII. Amyloidosis:</u></b>	
<p>Based upon our criteria and assessment of the peer-reviewed literature, treatment with HDC and allogeneic hematopoietic (stem) cell transplant for Primary Systemic Amyloidosis has not been medically proven to be effective and therefore is considered <b>investigational</b>.</p>	
<b><u>VIII. Other Malignant Conditions:</u></b>	
<p>Based upon our criteria and assessment of the peer-reviewed literature, treatment with HDC and allogeneic hematopoietic (stem) cell transplant for the following malignant conditions has not been medically proven to be effective and therefore is considered <b>investigational</b> for the following indication but not limited to:</p>	
<ul style="list-style-type: none"> <li>• Germ Cell Tumors</li> </ul>	
<ul style="list-style-type: none"> <li>• Primitive Neuroectodermal Tumor (PNET) (e.g., ependymoma, and other PNETs)</li> </ul>	
<ul style="list-style-type: none"> <li>• Medulloblastoma</li> </ul>	
<ul style="list-style-type: none"> <li>• Breast Cancer</li> </ul>	
<ul style="list-style-type: none"> <li>• Other malignant conditions and diseases</li> </ul>	
<ul style="list-style-type: none"> <li>• Epithelial ovarian cancer</li> </ul>	<ul style="list-style-type: none"> <li>• Colon cancer</li> </ul>
<ul style="list-style-type: none"> <li>• Lung cancer, any histology</li> </ul>	<ul style="list-style-type: none"> <li>• Rectal cancer</li> </ul>
<ul style="list-style-type: none"> <li>• Pancreas cancer</li> </ul>	<ul style="list-style-type: none"> <li>• Stomach cancer</li> </ul>
<ul style="list-style-type: none"> <li>• Esophageal cancer</li> </ul>	<ul style="list-style-type: none"> <li>• Gall bladder cancer</li> </ul>
<ul style="list-style-type: none"> <li>• Cancer of the bile duct</li> </ul>	<ul style="list-style-type: none"> <li>• Renal cell cancer</li> </ul>
<ul style="list-style-type: none"> <li>• Cervical cancer</li> </ul>	<ul style="list-style-type: none"> <li>• Uterine cancer</li> </ul>
<ul style="list-style-type: none"> <li>• Cancer of the fallopian tubes</li> </ul>	<ul style="list-style-type: none"> <li>• Prostate cancer</li> </ul>
<ul style="list-style-type: none"> <li>• Nasopharyngeal cancer</li> </ul>	<ul style="list-style-type: none"> <li>• Paranasal sinus cancer</li> </ul>
<ul style="list-style-type: none"> <li>• Neuroendocrine tumors</li> </ul>	<ul style="list-style-type: none"> <li>• Soft tissue sarcomas</li> </ul>

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<ul style="list-style-type: none"><li>• Thyroid tumors</li></ul>	<ul style="list-style-type: none"><li>• Tumors of the thymus</li></ul>
<ul style="list-style-type: none"><li>• Tumors of unknown primary origin</li></ul>	<ul style="list-style-type: none"><li>• Malignant Melanoma</li></ul>
<b>VI. <u>Non-malignant Diseases</u></b>	
<b><u>Autoimmune Diseases</u></b>	
Based upon our criteria and assessment of the peer-reviewed literature, treatment with HDC and allogeneic hematopoietic (stem) cell transplant for autoimmune conditions has not been medically proven to be effective and, therefore, is considered <b>investigational</b> for all autoimmune diseases, including but not limited to:	
<ul style="list-style-type: none"><li>• Rheumatoid arthritis</li><li>• Systemic sclerosis (e.g., scleroderma)</li><li>• Systemic lupus erythematosus (SLE)</li><li>• Type 1 Diabetes Mellitus</li></ul>	<ul style="list-style-type: none"><li>• Multiple sclerosis</li><li>• Chronic inflammatory demyelinating polyneuropathy</li></ul>

*Refer to Corporate Medical Policy #11.01.03 Experimental and Investigational Services*

**POLICY GUIDELINES**

**Pre-Transplant Evaluation Guidelines:**

**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:**

- A. Karnofsky performance score; and/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/>

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### Recipient Selection Guidelines:

Each individual considered for allogeneic (stem) cell transplant will 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 to transplantation.

### 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.

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 (stem) cell transplants 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.

Classification of the risk of disease for acute myeloid leukemia is has been identified in the National Comprehensive Cancer Network treatment guidelines (2013). Risk is based on cytogenetic stratification of good, intermediate and poor-risk AML. Treatment depends on the risk category of the disease.

<u>Risk Status</u>	<u>Cytogenetics</u>	<u>Molecular Abnormalities</u>
Better-risk	<ul style="list-style-type: none"><li>• inv(16)</li><li>• t(8;21)</li><li>• t(16;16)</li><li>• t(15;17)</li></ul>	<ul style="list-style-type: none"><li>• Normal cytogenetics with NPM1 mutation in the absence of FLT3-ITD or isolated biallelic CEBPA mutation</li></ul>
Intermediate risk	<ul style="list-style-type: none"><li>• Normal cytogenetics</li><li>• +8 alone</li><li>• t(9;11)</li><li>• Other non-defined</li></ul>	<ul style="list-style-type: none"><li>• t(8;21)</li><li>• inv(16)</li><li>• t(16;16): with</li><li>• c-KIT mutation *</li></ul>
Poor-risk	<ul style="list-style-type: none"><li>• Complex (greater than or equal to 3 clonal chromosomal abnormalities)</li><li>• -5</li><li>• -7</li><li>• 5q-</li><li>• 7q-</li><li>• 11q23 – non t(9;11),</li><li>• Inv(3)</li><li>• t(3;3)</li><li>• t(6;9)</li><li>• t(9;22)</li></ul>	<ul style="list-style-type: none"><li>• Normal cytogenetics with FLT3 ITD mutation**</li></ul>

\*Emerging data indicates that the presence of c-KIT mutations in patients with t (8; 21) and to a lesser extent inv (16) confers a higher risk of relapse. These patients should be considered for clinical trials, if available.

\*\*FLT3-ITD mutations are considered to confer a significantly poorer outcome in patients with normal karyotype, and these patients should be considered for clinical trials where available. There is controversy as to whether FLT3-TKD mutations carry an equally poor prognosis.



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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.

Non-Hodgkin Lymphomas (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. 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.

### 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.

### 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

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<b>Code</b>	<b>Description</b>
86812-86821, 81370-81383	HLA typing (code range)

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<b>Code</b>	<b>Description</b>
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**

<b>Code</b>	<b>Description</b>
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
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)

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Code	Description
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)

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**KEY WORDS**

Allogeneic, Hematopoietic, cell transplantation, Leukemias, Lymphomas, Anemias, Multiple Myeloma,

**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=AgAAgAAAAAAAAAA%3d%3d&>. accessed 10/16/23.