Page: 1 of 13

MEDICAL POLICY



An independent licensee of the Blue Cross Blue Shield Association

MEDICAL POLICY DETAILS		
Medical Policy Title	Allogeneic Hematopoietic (STEM) Cell Transplantation	
Policy Number	7.02.02	
Category	Technology Assessment	
Original Effective Date	11/19/99	
Committee Approval Date	01/18/01, 03/21/02, 06/19/03, 06/17/04, 05/18/05, 03/16/06, 05/17/07, 07/17/08,	
	10/29/09, 10/28/10, 12/15/11, 10/18/12, 10/17/13, 10/16/14, 10/15/15, 10/20/16,	
	11/16/17, 11/15/18, 02/20/20, 02/18/21, 12/22/22, 11/16/23	
Current Effective Date	11/16/23	
Archived Date	N/A	
Archived Review Date	N/A	
Product Disclaimer	• 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

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 allogenic 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:

Medical Policy: ALLOGENEIC HEMATOPOIETIC (STEM) CELL TRANSPLANTATION Policy Number: 7.02.02 Page: 2 of 13 Adult and Pediatric Acute Myeloid Leukemia (AML): 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 Primary refractory or relapsed disease or disease in second or greater remission; or Patients who have relapsed following a prior allogeneic HSCT and are medically able to tolerate the procedure Adult Acute Lymphoblastic Leukemia (ALL): First complete remission for any risk level; or Primary refractory or relapsed disease or disease in second or greater remission; or Relapsed after prior autologous HCT **Pediatric ALL:** 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 Second or greater remission or refractory disease; or

Relapsed after prior autologous HCT

Chronic myelogenous leukemia (CML):

- Patients with no hematologic remission after three months of TKI therapy; or
- 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
- Patients on TKI therapy who progress to accelerated or blast phase CML; or
- Patients in the first chronic phase with T315I mutations not sensitive to any tyrosine kinase inhibitors (TKIs)

Chronic lymphocytic leukemia (CLL)/ Small cell B-cell lymphoma in previously treated patients with non-

response or relapse within 12-24 months:

- After purine analogues; or
- After having achieved a response with intensive therapy; or
- With high risk cytogenetic abnormalities (e.g., del

Chronic lymphocytic leukemia (CLL)/ Small cell Bcell lymphoma with the exception of the small subset of patients with progressive disease refractory to conventional treatments described in the list of medically appropriate indications

(17p) and del(11q))	
II. <u>Ly</u>	mphomas:
<u>Hodgkin</u>	Lymphomas:
Medically appropriate indications:	Investigational indications:

Policy Number: 7.02.02

As salvage therapy
Peripheral T-cell Lymphoma:
As salvage therapy

Page: 3 of 13

Biopsy proven refractory disease if responsive to Initial therapy for all HL to consolidate a first secondary therapy complete remission Non Hodgkin Lymphoma: Non Hodgkin Lymphoma (NHL) can be classified as either indolent (low grade) or aggressive (intermediate or high grade). **Medically appropriate indications: Investigational indications: Aggressive:** Initial therapy for all NHL; or To consolidate a first complete response for patients To consolidate a first complete response in patients with Diffuse Large B-cell lymphoma with a low or with diffuse large B-cell lymphoma but at high or highlow-intermediate risk of relapse as predicted by the intermediate risk of relapse as predicted by the ageadjusted international prognostic index (IPI); or IPI: or To consolidate a first complete response for indolent To achieve or consolidate a complete response in a chemo sensitive first or second relapse; or NHL subtypes; or Tandem transplants; or As salvage therapy for patients who do not achieve a complete response after full first-line induction To consolidate a first remission in Mantle Cell lymphoma; or chemotherapy; or Salvage therapy when a complete response after full To consolidate a first remission in Peripheral T- Cell first-line induction chemotherapy is not achieved for lymphoma low or high risk Burkitt lymphoma **Indolent:** As salvage therapy for patients who do not achieve complete response after a full dose of first-line induction chemotherapy; or 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 Mantle Cell Lymphoma:

Policy Number: 7.02.02

Page: 4 of 13

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)

B-cell Neoplasms

Precursor B-cell Neoplasms

• Precursor B-lymphoblastic leukemia/lymphoma⁺ Mature (Peripheral) B-cell Neoplasms-Predominately Disseminated

- CLL/SLL*
- B-Prolymphocyte lymphoma⁺
- Lymphoplasmacytic lymphoma*
- Splenic Marginal Zone lymphoma*
- Hairy cell lymphoma*
- Plasma cell myeloma/plasmacytoma

Mature (Peripheral) B-cell Neoplasms-Primary Extranodal

Mucosa-associated lymphoid tissue*

Mature (Peripheral) B-cell Neoplasms-Predominantly

Nodal

- Marginal Zone lymphoma*
- Follicular lymphoma*
- Mantle cell lymphoma⁺
- Diffuse Large B-cell lymphoma (LBCL)⁺
- Mediastinal LBCL⁺
- Intravascular LBCL⁺
- Primary effusion lymphoma⁺
- Burkitt's lymphoma⁺
- Lymphomatoid granulomatosis

T- and NK-cell Neoplasms

Precursor T- and NK-cell Neoplasms

- Precursor T-lymphoblastic leukemia/lymphoma⁺
- Blastoid NK lymphoma⁺

<u>Mature (Peripheral) T-cell Neoplasms- Predominately</u> Disseminated

- T-cell Prolymphocytic leukemia⁺
- T-cell Large Granular Lymphocytic leukemia*
- Aggressive NK-cell leukemia⁺
- Adult T-cell lymphoma/leukemia-HTLV-1+

 Mature (Peripheral) T-cell Neoplasms- Primary

 Extranodal
- Extranodal NK/T-cell lymphoma, nasal type⁺
- Enteropathy-type T-cell lymphoma⁺
- Hepatosplenic T-cell lymphoma⁺
- Subcutaneous panniculitis-like T-cell lymphoma⁺
- Mycosis fungoides/Sezary syndrome*
- Primary cutaneous anaplastic large-cell lymphoma⁺ Mature (Peripheral) T-cell Neoplasms-Predominantly

Nodal

- Peripheral T-cell lymphoma- NOS⁺
- Angioimmunoblastic T-cell lymphoma⁺
 Primary systemic anaplastic Large-cell lymphoma⁺

**International Prognostic Index: Low Risk = 0-1 points, Low Intermediate = 2, High Intermediate = 3, High Risk = 4-5 points

O points Age less than 60 years Tumor stage I or II Extranodal Involvement (ENI) 0-1 Performance status (PS) Eastern Cooperative Oncology Group (ECOG) 0-1 Lactate dehydrogenase (LDH) normal Age greater than 60 years, Tumor stage III or IV, ENI greater than 1, PS (ECOG) 2-4, LDH greater than normal.

• **International Follicular Lymphoma Prognostic Index: Low Risk = 0-1 points, Intermediate Risk = 2, High Risk = greater than 5 points

1 point for presence of each Age greater than or equal to 60 years; Ann Arbor stage III-IV; Hemoglobin level less than 12 g/dL; Serum LDH level greater than the upper limit of normal; Number of nodal sites greater than or equal to 5

Policy Number: 7.02.02

Page: 5 of 13

III. Solid Tumors of Childhood

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

willis tullor, maddonly osarcoma, ostcosarcoma, retinoblastoma of gerni cen tullor			
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-</u>			
Stage I	Stage III and N-myc = 1 and ferritin	Stage III; greater than 10 N-myc or ferritin	
	less than 143 and favorable histology	greater than 143 or unfavorable histology	
Stage II; N -myc = 1	Stage IV; N-myc =1 and less than 1	Stage IV and greater than 1 year at diagnosis	
	year at diagnosis	Stage IV at less than 1 year at diagnosis and	
Stage IVS	Stage III and less than 1 year at	greater than 10 N-myc	
Stage IVD	diagnosis		

Medically appropriate indications:	Investigational indications:	
None	• Salvage allogeneic transplant for relapsing neuroblastoma or other solid tumors <i>after autologous</i> transplant or fail to respond; or	
	Pediatric solid tumors	

IV. Genetic Diseases and Acquired Anemias

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 **medically appropriate** for the following conditions:

Hemoglobinopathies:

- 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
- Homozygous beta-thalassemia (thalassemia major)

Bone Marrow Failure Syndromes – Aplastic Anemia:

- Hereditary: Fanconi anemia, dyskeratosis congenita, Schwachman-Diamond Syndrome, and Diamond Blackfan syndrome; or
- Acquired: secondary to drug or toxin exposure

Primary Immunodeficiencies

- Absent or defective T-cell function: Wiskott-Aldrich syndrome, severe combined immunodeficiency, hemophagocytic lymphohistiocytosis, and X-linked lymphoproliferative syndrome; or
- Absent or defective natural killer function: Chédiak-Higashi syndrome; or
- Absent or defective neutrophil function: Kostmann syndrome, chronic granulomatous disease, leukocyte adhesion deficiencies

Genetic Disorders Affecting Skeletal Tissue:

Infantile malignant osteopetrosis (Albers-Schöberg disease or marble bone disease)

Inherited Metabolic Diseases:

 Lysosomal and peroxisomal storage disorders (e.g., Hurler, Maroteaux Lamy variants, and Gaucher disease, metachromatic leukodystrophy, globoid cell leukodystrophy, adrenoleukodystrophy) except Hunter, Sanfilippo, and Morquio syndromes

Policy Number: 7.02.02

Page: 6 of 13

V. Myelodysplastic Diseases

Myelodysplastic syndrome (MDS) 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.

<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 (*please refer to leukemia section I.*) Other less common types of myeloproliferative disorders include chronic neutrophilic leukemia, chronic eosinophilic leukemia, hypereosinophilic leukemia, and mast cell disease.

Conditions eligible for coverage: Progression; No response to standard therapy

•	Myelodysplastic syndrome	•	Myeloproliferative disorders
---	--------------------------	---	------------------------------

VI. Multiple Myeloma

<u>vi. Mulupie Myeloma</u>		
Medically appropriate indications:	Investigational indications (except in the context of a	
	clinical trial):	
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	As upfront therapy of newly diagnosed multiple myeloma or as salvage therapy	

VII. Amyloidosis:

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 **investigational**.

VIII. Other Malignant Conditions:

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 **investigational** for the following indication but not limited to:

- Germ Cell Tumors
- Primitive Neuroectodermal Tumor (PNET) (e.g., ependymoma, and other PNETs)
- Medulloblastoma
- Breast Cancer
- Other malignant conditions and diseases

Epithelial ovarian cancer	Colon cancer
 Lung cancer, any histology 	Rectal cancer
 Pancreas cancer 	Stomach cancer
Esophageal cancer	Gall bladder cancer
Cancer or the bile duct	Renal cell cancer
• Cervical cancer • Uterine cancer	
 Cancer of the fallopian tubes 	Prostate cancer
Nasopharyngeal cancer	Paranasal sinus cancer
Neuroendocrine tumors	Soft tissue sarcomas

Policy Number: 7.02.02

Page: 7 of 13

 Thyroid tumors Tumors of the thymus 			
 Tumors of unknown primary origin 	Malignant Melanoma		
VI. Non-malignant Diseases			
Autoimmune Diseases			
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 investigational for all autoimmune diseases, including but not limited to:			
Rheumatoid arthritis Multiple sclerosis			
 Systemic sclerosis (e.g., scleroderma) Chronic inflammatory demyelinating 			
• Systemic lupus erythematosus (SLE) polyneuropathy			
Type 1 Diabetes Mellitus			

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. <u>Psycho-Social Evaluation</u>:

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

Policy Number: 7.02.02

Page: 8 of 13

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 poorrisk AML. Treatment depends on the risk category of the disease.

Risk Status	Cytogenetics	Molecular Abnormalities
Better-risk	 inv(16) t(8;21) t(16;16) t(15;17) 	Normal cytogenetics with NPM1 mutation in the absence of FLT3-ITD or isolated biallelic CEBPA mutation
Intermediate risk	 Normal cytogenetics +8 alone t(9;11) Other non-defined 	 t(8;21) inv(16) t(16;16): with c-KIT mutation *
Poor-risk	 Complex (greater than or equal to 3 clonal chromosomal abnormalities) -5 -7 5q- 7q- 11q23 - non t(9;11), Inv(3) t(3;3) t(6;9) t(9;22) 	Normal cytogenetics with FLT3 ITD mutation**

^{*}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.

Policy Number: 7.02.02

Page: 9 of 13

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

Policy Number: 7.02.02

Page: 10 of 13

Code	Description
86812-86821,	HLA typing (code range)
81370-81383	

Copyright © 2023 American Medical Association, Chicago, IL

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)
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)

Policy Number: 7.02.02

Page: 11 of 13

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)

REFERENCES

Bishop MR et al. Second-line Tisagenlecleucle to standard care in aggressive B Cell Lymphoma. <u>The England Journal of Medicine</u> 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. <u>Cancer</u> 2022 Jun;128(12)2288-2297.

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

^{*}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. <u>Bone Marrow Transplant</u> 2012; 47(10):1312–1317.

^{*}Bernt KM, et al. Current concepts in pediatric Philadelphia chromosome-positive acute lymphoblastic leukemia. <u>Front Oncol</u> 2014 Mar 25;4:54.

Policy Number: 7.02.02

Page: 12 of 13

*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. <u>Bone Marrow Transplant</u> 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. <u>Leukemia</u> 2012 Mar;26(3):520-6.

*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. <u>Bone Marrow Transplant</u> 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. <u>Blood</u> 2013;121(2):339-50.

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

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

*Koehne G, et al. Allogeneic hematopoietic stem cell transplantation for multiple myeloma: curative but not the standard of care. <u>Curr Opin Oncol</u> 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. <u>J Clin Oncol</u> 2010;28(33):4926-34.

National Comprehensive Cancer Network. Practice guidelines in oncology: acute myeloid leukemia. V.5.2023. https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf accessed 10/16/2023.

National Comprehensive Cancer Network. Practice guidelines in oncology: b-cell lymphoma. V.6.2023 [https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf] accessed 10/16/2023.

National Comprehensive Cancer Network. Practice guidelines in oncology: Hodgkin lymphoma. V.1.2024. [http://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf] accessed 10/16/23.

National Comprehensive Cancer Network. Practice guidelines in oncology: multiple myeloma. V.1.2024. [http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf] accessed 10/16/2023.

National Comprehensive Cancer Network. Practice guidelines in oncology: Waldenström's macroglobinemia /lymphoplasmocytic lymphoma. V.1.2024. [http://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf] accessed 10/16/2023.

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

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

Policy Number: 7.02.02

Page: 13 of 13

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=AgAgAAAAAAAAAAA3d%3d&. accessed 10/16/23.