Medica

Medica Central Utilization Management Policy

Policy Name:	**Bone Marrow or Stem Cell (Peripheral or Umbilical Cord) Transplantation MP9611**
Effective Date:	**April 01, 2025**

This policy was developed with input from specialists in nephrology, transplants, and oncology, and endorsed by the Medical Policy Committee.

IMPORTANT INFORMATION – PLEASE READ BEFORE USING THIS POLICY

These services may or may not be covered by Medica Central. Coverage is subject to requirements in applicable federal or state laws. Please refer to the member's plan document for other specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare, Medicaid, and other government programs, this policy will apply unless these programs require different coverage. Members may contact Medica Central Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions may call the Provider Service Center. Please use the Quick Reference Guide on the Provider Communications page for the appropriate phone number. https://mo-central.medica.com/Providers/SSM-employee-health-plan-for-IL-MO-OK-providers

Medica Central medical policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care, and treatment.

PURPOSE

To promote consistency between utilization management reviewers by providing the criteria that determines the medical necessity.

BACKGROUND

I. Definitions
   A. **Allogeneic** graft is one in which the donor and recipient are of different genetic origins.
   B. **Autologous** bone marrow transplant (ABMT) refers to the removal and storage of some of the patient's own stem cells for restoring bone marrow function after high dose chemotherapy or radiotherapy.
   C. **Bone marrow transplant** (BMT) is the reconstitution of the full hematopoietic system by transfer of the pluripotent cells present in the bone marrow (stem cells). A BMT involves a transplant not only of the donor myeloid, erythroid, and megakaryocytic systems, but also of lymphoid and macrophage-monocyte systems. There are four types of disease for which BMT has been widely utilized:
      1. **Genetic disease**
         For immunologic deficiency diseases, the objective is to replace the recipient's genetically defective lymphoid system with the normal lymphoid tissue of the donor. For genetic diseases such as thalassemia major or various inborn errors of

metabolism (inherited metabolic disorders), the abnormal marrow must be destroyed and replaced by normal stem cells.

2. **Aplastic anemia**
   Aplastic anemia, which may result from several causes, is a condition that occurs when the body stops producing enough new blood cells and results in loss of the marrow. A stem cell transplant to rebuild the bone marrow with stem cells from a donor may offer the only successful treatment.
3. **Hematologic malignancy**
   For leukemia and other hematologic malignancies, the objective is the complete destruction of the malignant cell population and unavoidably, normal stem cells, by intensive chemo-radiotherapy followed by restoration of normal marrow function by the transplanted stem cells.
4. **Non-hematologic malignancy** (Chemotherapy or high-dose chemotherapy with autologous peripheral stem cell/bone marrow rescue [HDC/ABMT]). For patients with poor-prognosis cancer necessitating treatment with high dose therapy, autologous stem cell transplantation rescue may be used in selected conditions to reconstitute the devastated marrow population.

D. **Chemosensitive** disease is malignant disease that demonstrates at least a partial response to a course of chemotherapy.

E. **Donor Lymphocyte Infusion (DLI),** also known as a donor leukocyte infusion or buffy coat infusion, may be performed following allogeneic transplant. Individuals may be infused with lymphocytes obtained via leukapheresis from the original donor. The DLI attempts to induce a beneficial graft-versus-tumor response or improve the level of engraftment with or without the need for additional stem cell harvest from the donor. This is not a second stem cell transplant.

F. **Stem cell boost** is a Hematopoietic Stem Cell Infusion (HSCI) provided to a transplant recipient to assist with hematopoietic recovery or declining donor chimerism. It is generally not preceded by a preparative regimen and is not considered a new transplant event. In this procedure, the patient receives a boost of hematopoietic stem cells from the original donor's blood or sometimes, the bone marrow. The stem cell boost term is used interchangeably with other terms such as reinfusion, support and rescue.

G. **Stem cells** are blood cells at the earliest stage of development in the bone marrow. They can be taken from the bone marrow, peripheral bloodstream, or from umbilical cord blood.

H. **Stem Cell Transplant**

1. **Allogeneic stem cell transplant** employs chemotherapy, immunosuppressive agents and/or radiation to provide adequate immunosuppression to permit engraftment of stem cells from a human donor other than the patient him/herself. The intensity of the agents used for immunosuppression may be either myeloablative or non-myeloablative depending on the disease being treated and specific patient and donor characteristics. Stem cells may be obtained from the bone marrow, peripheral blood, or umbilical cord blood. The stem cell donor may be related or unrelated to the potential recipient.
2. **Autologous stem cell transplant** utilizes the patient’s own stem cells to re-establish hematopoietic cell function following intensive doses of chemotherapy, with or without radiation. Stem cells may be obtained from repeated aspirations of bone marrow, peripheral blood or umbilical cord blood. Modifications of the autologous graft may at times be performed to enhance the graft function or change gene expression (in hemoglobin or other disorders).
3. **Non-myeloablative stem cell transplant (NST)/Reduced–intensity conditioning stem cell transplant (RICST)** is a stem cell transplant in which full marrow ablation

does not occur. This transplant provides sufficient immunosuppression to achieve donor engraftment, with less toxicity. It is also called a “mini” transplant.

4. **Tandem transplant** involves two sequential courses of high dose chemotherapy, each followed by stem cell transplant, within a six-month period. This is generally an autologous procedure but at times can be an autologous graft, followed later by an allogeneic graft.
5. **Umbilical cord blood stem cell transplant** employs the infusion of stem cells obtained from the umbilical cord or placenta of a newborn child. A two antigen (Ag) mismatch is acceptable. Cord blood transplantation in patients weighing more than 40kg sometimes utilizes cord blood from at least two donors (“double cord”).

I. **Syngeneic** graft describes a graft in which the donor and recipient are genetically identical twins.

J. **Transplant or graft** is a portion of the body or a complete organ removed from its natural site and transferred to a separate site in the same or different individual.

K. Transplant **evaluation** is a physical and psychosocial exam to determine if an individual is an acceptable candidate for transplantation. The specific exams and tests depend on the individual’s diagnosis and health history and vary from hospital to hospital. Tests may include the following: cardiac evaluation; lung function tests; lab tests, including blood typing, chemistry panels, and serology testing for hepatitis, HIV and other common viruses; appropriate cancer surveillance, as indicated (e.g., colonoscopy, pap smear, mammogram, prostate cancer screening); dental evaluation with treatment of existing problems; and psychosocial evaluation. Additional testing or clearance may be required to address other significant coexisting medical conditions.

L. **Treatment response**, in medicine, is an improvement related to treatment. A number of disease specific systems exist for measuring response.

1. A **complete response**, in general, is the disappearance of all signs of cancer in response to treatment. This does not always mean the cancer has been cured. Also called complete remission.
2. A **partial response**, in general, is defined as a decrease in the size of a tumor, or in the extent of cancer in the body, in response to treatment. Also called partial remission.

II. Comments

A. Refer to Appendices for additional terms, definitions and classification tables.

B. Stem cell source and preparative regimens are at the discretion of the treating physician.

C. Donor lymphocyte infusion following allogeneic stem cell transplant is appropriate for incomplete chimerism or sometimes disease relapse. This is not a second stem cell transplant.

D. Chimeric Antigen Receptor Therapy and/or the use of T-cells/natural killer cell protocols provide cellular immune treatment of the underlying disease and are not considered to be a transplant procedure.

BENEFIT CONSIDERATIONS

1. Prior authorization **is required** for:
   - Bone Marrow and Stem Cell Transplant **Evaluation**
   - Bone Marrow and Stem Cell **Transplantation**
   - Bone Marrow or Stem Cell Transplantation related to CAR-T therapy and/or Clinical trial participation

Note: For clinical trial participation related to CAR-T see Utilization Management Policy ***Clinical Trial Utilizing Car-T Therapy, Bone Marrow or Stem Cell Transplantation*, No-III-MED.10**). For clinical trials related to cancer and life-threatening conditions other than CAR-T therapy, bone marrow or stem cell transplantation see coverage policy: ***Clinical Trial Participation***.

- Please see the prior authorization list for product specific prior authorization requirements.

2. Coverage may vary according to the terms of the member's plan document.
3. The Health Plan has entered into separate contracts with designated facilities to provide transplant-related health services, as described in the member's plan document.
4. Complex cases require medical director or external review, and as necessary, discussion with the patient's physician.
5. Underlying co-morbidity that significantly alters the risk/benefit of transplant may preclude transplant eligibility.
6. Coverage of costs related to chemotherapy, drugs, other related supplies and services is limited to individuals who have one of the indications listed and are transplant candidates.
7. Coverage of costs related to collection and storage of umbilical cord blood stem cells is addressed in the member's plan document.
8. Medical director or external review is required for any of the following procedures if not performed in a clinical trial:
   - Any tandem stem cell transplant or third stem cell transplants, except for the indications noted in the Medical Necessity Criteria
9. Use of progenitor/stem cells from bone marrow, peripheral blood or umbilical cord blood for non-conventional indications (such as direct injection into the heart muscle, bone or other body tissue) requires medical director or external review. Please refer to the following related Coverage Policies: *Stem Cell and Cellular Bone Matrix Products for Orthopedic Applications; Stem Cell Therapy for Peripheral Artery Disease; and Cell Therapy for the Treatment of Cardiac Disease.*
10. If the Medical Necessity Criteria and Benefit Considerations are met, The Health Plan will authorize benefits within the limits in the member's plan document.
11. If it appears that the Medical Necessity Criteria and Benefit Considerations are not met, the individual's case will be reviewed by the medical director or an external reviewer. Practitioners are advised of the appeal process in their Provider Administrative Manual.

MEDICAL NECESSITY CRITERIA

I. Indications for Bone Marrow or Stem Cell Transplant **Evaluation**

Documentation from the medical record indicates that **one of the following** criteria are met:

A. For **allogeneic** transplant, documentation from the medical record indicates that the individual has **one of the following** diagnoses**:**

1. Leukemia
   a. Acute Lymphocytic/Lymphoblastic Leukemia (ALL)
   b. Acute Myeloid Leukemia (AML)
   c. Chronic Lymphocytic Leukemia (CLL)
   d. Chronic Myeloid Leukemia (CML)
   e. Prolymphocytic Leukemia

2. Lymphoma (*See Appendix 1)*
    a. Hodgkin's Lymphoma
    b. Non-Hodgkin's Lymphoma
        i. Small B-Cell Lymphocytic Lymphoma
        ii. Follicle Center Lymphoma
        iii. Lymphoplasmacytoid Lymphoma/Immunocytoma
        iv. Marginal Zone Lymphoma
        v. Burkitt Lymphoma
        vi. Diffuse Large Cell Lymphoma (mediastinal large cell, primary effusion)
        vii. Mantle Cell Lymphoma
        viii. Precursor B-Cell Leukemia/Lymphoma
        ix. T-Cell Lymphoma
3. Myelodysplastic Syndromes and Mixed Myelodysplastic/Myeloproliferative Disorders and Neoplasms
    a. Myelodysplastic syndrome (MDS)
    b. Primary Myelofibrosis and related conditions (e.g., Polycythemia Rubra Vera)
    c. Secondary Myelofibrosis (Polycythemia Vera or Essential Thrombocythemia)
    d. Chronic Myelomonocytic Leukemia (CMML), including Juvenile Myelomonocytic Leukemia (JMML/JCML)
4. Multiple Myeloma/Plasma Cell Disorders
    a. Waldenstrom's Macroglobulinemia
5. Hematological Disorders
    a. Aplastic Anemia
    b. Blackfan-Diamond Syndrome
    c. Chronic Granulomatous Disease
    d. Congenital Agranulocytosis (Kostmann Syndrome)
    e. Congenital Amegakaryocytic Thrombocytopenia
    f. Dyskeratosis Congenita
    g. Fanconi Anemia (FA)
    h. Paroxysmal Nocturnal Hemoglobinuria (PNH)
    i. Schwachman-Diamond Syndrome (SDS)
    j. Sickle Cell Disease
    k. Thalassemia Major
6. Plasma Cell Disorders
    a. Waldenstrom macroglobulinemia
7. Immunodeficiency Syndromes

a. CD40 Ligand Deficiency
b. Chediak-Higashi Syndrome
c. Gaucher disease type I
d. Hemophagocytic Lymphohistiocytosis (HLH) (same as familial erythrophagocytic lymphohistiocytosis [FEL])
e. Immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome
f. Leukocyte Adhesion Deficiency
g. Lysosomal storage disease
h. Niemann-Pick type B
i. Omenn Syndrome
j. Severe combined immunodeficiency disease (SCID)
k. Wiskott-Aldrich Syndrome
l. X-linked Lymphoproliferative Syndrome
m. Fucosidosis

8. Inherited Metabolic Disorders
   a. Adrenoleukodystrophy
   b. Epidermolysis Bullosa
   c. Globoid Cell Leukodystrophy (Krabbe Disease)
   d. Hurler Syndrome (MPS-1)
   e. Hunter Syndrome (MPS II)
   f. Mannosidosis and other liposomal storage diseases
   g. Maroteaux-Lamy Syndrome (MPS-VI)
   h. Metachromatic Leukodystrophy
   i. Mitochondrial Neurogastrointestinal Encephalopathy (MNGIE)
   j. Osteopetrosis (also called marble-bone disease, malignant osteopetrosis, or autosomal recessive osteopetrosis)
   k. Rett Syndrome
8. Other Malignancies
   a. Blastic Plasmacytoid Dendritic Cell Neoplasm
9. Additional Conditions
   Allogeneic stem cell transplantation may be considered medically necessary in rare and unusual conditions. **See APPENDIX 2**.

B. For **autologous** transplant, documentation from the medical record indicates that the individual has **one of the following** diagnoses**:**

1. Leukemia
   a. Acute Lymphoblastic Leukemia (ALL)

b. Acute Myelogenous Leukemia (AML) (also known as Acute Non-Lymphocytic Leukemia [ANLL])

c. Prolymphocytic Leukemia

2. Lymphoma *(See Appendix 1)*

a. Hodgkin's Lymphoma

b. Non-Hodgkin's Lymphoma

i. Follicle center lymphoma

ii. Lymphoplasmacytoid lymphoma/Immunocytoma

iii. Marginal zone lymphoma (mucosa-associated lymphoid tissue, splenic, nodal)

iv. Burkitt lymphoma

v. Diffuse large cell lymphoma (mediastinal large cell, primary effusion)

vi. Mantle cell lymphoma

vii. Precursor B-cell leukemia/lymphoma

viii. T-cell lymphoma

Note: Autologous hematopoietic stem cell transplantation is not considered standard of care or medically necessary for small lymphocytic lymphoma and should be treated in the same manner as chronic lymphocytic leukemia (CLL).

3. Multiple Myeloma/Plasma Cell Disorders

a. Multiple myeloma (*Single or Tandem auto is appropriate*)

b. AL Amyloidosis

c. Waldenstrom's Macroglobulinemia

d. POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monocloncal Gammopathy Skin defects Syndrome)

4. Germ Cell Tumors (*Single or Tandem auto is appropriate for all of the germ cell tumors below*)

a. Testicular Germ Cell Tumor

b. Ovarian Germ Cell Tumor

c. Extragonadal Germ Cell Tumor

d. Seminoma

e. Choriocarcinoma

f. Embryonal carcinoma

g. Mixed germ cell tumors

h. Teratoma

i. Yolk sac tumor

5. Brain Tumors

a. Medulloblastoma

b. Embryonal Tumors with Multi-layered Rosettes (ETMR). Formerly known as Primitive Peripheral Neuro-ectodermal Tumor (PNET)

c. Oligodendroglioma

d. Pineoblastoma

Note:

- *Tandem may be appropriate for the pediatric brain tumors listed above*)
- Glioblastoma multiforme (GBM) may be considered in infants (refer to Medical Director)

6. Other Malignancies
   a. Atypical teratoid rhabdoid tumors
   b. Neuroblastoma (*Single or Tandem auto is appropriate*)
   c. Retinoblastoma
   d. Ewing Sarcoma
   e. Supratentorial ependymoma
   f. Wilms Tumor.
7. Autoimmune Diseases
   a. Multiple Sclerosis
   b. Systemic Sclerosis (Scleroderma)
8. Monoclonal Gammopathy of Renal Significance (MGRS)
   Note: Targeting the underlying B-cell clone with high-dose chemotherapy/autologous hematopoietic stem cell transplantation, although it is not a malignant clone per se, is the only available therapeutic option in some patients with MGRS.

II. Indications For Bone Marrow Or Stem Cell **Transplantation**
Autologous/allogeneic bone marrow or stem cell transplantation is considered medically necessary when documentation in the medical record indicates that **all of the following** criteria are met:

A. Individual meets the institution's eligibility criteria for transplant

B. Individual meets the criteria in Section I.

III. Indications For Bone Marrow/Stem Cell **Retransplantation**
Documentation in the medical records indicates that **all of the following** criteria are met:

A. The individual has **one of the following**:
   1. Relapse of original disease
   2. Failure to engraft.

B. All of the criteria in section II are met.

C. No history of behaviors since the previous transplant that would jeopardize a subsequent transplant.

CENTERS FOR MEDICARE & MEDICAID SERVICES (CMS)

- For Medicare members, refer to the following, as applicable at: https://www.cms.gov/medicare-coverage-database/new-search/search.aspx

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APPENDIX 1

WHO Classification of Haematolymphoid Tumours, 5th edition: B-cell lymphoid proliferations and lymphomas (2022)

WHO Classification, 5th edition	WHO Classification, revised 4th edition
Tumour-like lesions with B-cell predominance	
Reactive B-cell-rich lymphoid proliferations that can mimic lymphoma	*Not previously included*
IgG4-related disease	*Not previously included*
Unicentric Castleman disease	*Not previously included*
Idiopathic multicentric Castleman disease	*Not previously included*
KSHV/HHV8-associated multicentric Castleman disease	Multicentric Castleman disease
Precursor B-cell neoplasms	
B-cell lymphoblastic leukaemias/lymphomas	
B-lymphoblastic leukaemia/lymphoma, NOS	(Same)
B-lymphoblastic leukaemia/lymphoma with high hyperdiploidy	B-lymphoblastic leukaemia/lymphoma with hyperdiploidy
B-lymphoblastic leukaemia/lymphoma with hypodiploidy	(Same)
B-lymphoblastic leukaemia/lymphoma with iAMP21	(Same)
B-lymphoblastic leukaemia/lymphoma with *BCR*::*ABL1* fusion	B-lymphoblastic leukaemia/lymphoma with t(9;22)(q34;q11.2); *BCR-ABL1*
B-lymphoblastic leukaemia/lymphoma with *BCR*::*ABL1*-like features	B-lymphoblastic leukaemia/lymphoma, *BCR-ABL1*-like
B-lymphoblastic leukaemia/lymphoma with *KMT2A* rearrangement	B-lymphoblastic leukaemia/lymphoma with t(v;11q23.3); *KMT2A*-rearranged
B-lymphoblastic leukaemia/lymphoma with *ETV6*::*RUNX1* fusion	B-lymphoblastic leukaemia/lymphoma with t(12;21)(p13.2;q22.1); *ETV6-RUNX1*
B-lymphoblastic leukaemia/lymphoma with *ETV6*::*RUNX1*-like features	*Not previously included*
B-lymphoblastic leukaemia/lymphoma with *TCF3*::*PBX1* fusion	B-lymphoblastic leukaemia/lymphoma with t(1;19)(q23;p13.3); *TCF3-PBX1*
B-lymphoblastic leukaemia/lymphoma with *IGH*::*IL3 fusion*	B-lymphoblastic leukaemia/lymphoma with t(5;14)(q31.1;q32.1); *IGH/IL3*
B-lymphoblastic leukaemia/lymphoma with *TCF3*::*HLF* fusion	*Not previously included*
B-lymphoblastic leukaemia/lymphoma with other defined genetic abnormalities	(Same)
Mature B-cell neoplasms	
Pre-neoplastic and neoplastic small lymphocytic proliferations	
Monoclonal B-cell lymphocytosis	(Same)

WHO Classification, 5th edition	WHO Classification, revised 4th edition
Chronic lymphocytic leukaemia/small lymphocytic lymphoma	(Same)
Entity deleted)	B-cell prolymphocytic leukaemia
Splenic B-cell lymphomas and leukaemias	
Hairy cell leukaemia	(Same)
Splenic marginal zone lymphoma	(Same)
Splenic diffuse red pulp small B-cell lymphoma	(Same)
Splenic B-cell lymphoma/leukaemia with prominent nucleoli	*Not previously included* (encompassing hairy cell leukaemia variant and some cases of B-cell prolymphocytic leukaemia)
Lymphoplasmacytic lymphoma	
Lymphoplasmacytic lymphoma	(Same)
Marginal zone lymphoma	
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue	(Same)
Primary cutaneous marginal zone lymphoma	*Not previously included (*originally included under "extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue")
Nodal marginal zone lymphoma	(Same)
Paediatric marginal zone lymphoma	(Same)
Follicular lymphoma	
In situ follicular B-cell neoplasm	In situ follicular neoplasia
Follicular lymphoma	(Same)
Paediatric-type follicular lymphoma	(Same)
Duodenal-type follicular lymphoma	(Same)
WHO Classification, 5th edition	WHO Classification, revised 4th edition
Cutaneous follicle centre lymphoma	
Primary cutaneous follicle centre lymphoma	(Same)
Mantle cell lymphoma	
In situ mantle cell neoplasm	In situ mantle cell neoplasia
Mantle cell lymphoma	(Same)
Leukaemic non-nodal mantle cell lymphoma	(Same)
Transformations of indolent B-cell lymphomas	
Transformations of indolent B-cell lymphomas	*Not previously included*
Large B-cell lymphomas	
Diffuse large B-cell lymphoma, NOS	(Same)
T-cell/histiocyte-rich large B-cell lymphoma	(Same)

WHO Classification, 5th edition	WHO Classification, revised 4th edition
Diffuse large B-cell lymphoma/ high grade B-cell lymphoma with *MYC* and *BCL2* rearrangements	High-grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* rearrangements
ALK-positive large B-cell lymphoma	(Same)
Large B-cell lymphoma with *IRF4* rearrangement	(Same)
High-grade B-cell lymphoma with 11q aberrations	Burkitt-like lymphoma with 11q aberration
Lymphomatoid granulomatosis	(Same)
EBV-positive diffuse large B-cell lymphoma	EBV-positive diffuse large B-cell lymphoma, NOS
Diffuse large B-cell lymphoma associated with chronic inflammation	(Same)
Fibrin-associated large B-cell lymphoma	*Not previously included* (Previously considered a subtype of diffuse large B-cell lymphoma associated with chronic inflammation)
Fluid overload-associated large B-cell lymphoma	*Not previously included*
Plasmablastic lymphoma	(Same)
Primary large B-cell lymphoma of immune-privileged sites	*Not previously included*, encompassing primary diffuse large B-cell lymphoma of the CNS in revised 4th edition (*plus primary large B-cell lymphoma of the vitreoretina and primary large B-cell lymphoma of the testis)*
Primary cutaneous diffuse large B-cell lymphoma, leg type	(Same)
Intravascular large B-cell lymphoma	(Same)
Primary mediastinal large B-cell lymphoma	(Same)
Mediastinal grey zone lymphoma	B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classic Hodgkin lymphoma
High-grade B-cell lymphoma, NOS	(Same)
***Burkitt** lymphoma*	
Burkitt lymphoma	(Same)
KSHV/HHV8-associated B-cell lymphoid proliferations and lymphomas	
Primary effusion lymphoma	(Same)
KSHV/HHV8-positive diffuse large B-cell lymphoma	HHV8-positive diffuse large B-cell lymphoma, NOS
KSHV/HHV8-positive germinotropic lymphoproliferative disorder	HHV8-positive germinotropic lymphoproliferative disorder
Lymphoid proliferations and lymphomas associated with immune deficiency and dysregulation	
Hyperplasias arising in immune deficiency/dysregulation	*Not previously included*, encompassing non-destructive post-transplant lymphoproliferative disorders, among others
Polymorphic lymphoproliferative disorders arising in immune deficiency/dysregulation	*Not previously included*, encompassing polymorphic posttransplant lymphoproliferative disorders, other iatrogenic immunodeficiency-associated lymphoproliferative disorders, among others
EBV-positive mucocutaneous ulcer	(Same)

WHO Classification, 5th edition	WHO Classification, revised 4th edition
Lymphomas arising in immune deficiency / dysregulation	*Not previously included*, encompassing monomorphic posttransplant lymphoproliferative disorders, classic Hodgkin lymphoma posttransplant lymphoproliferative disorders, lymphomas associated with HIV infection, among others
Inborn error of immunity-associated lymphoid proliferations and lymphomas	Lymphoproliferative diseases associated with primary immune disorders
Hodgkin lymphoma	
Classic Hodgkin lymphoma	(Same)
Nodular lymphocyte predominant Hodgkin lymphoma	(Same)
Plasma cell neoplasms and other diseases with paraproteins	
Monoclonal gammopathies	
Cold agglutinin disease	*Not previously included*
IgM monoclonal gammopathy of undetermined significance	(Same)
Non-IgM monoclonal gammopathy of undetermined significance	(Same)
Monoclonal gammopathy of renal significance	*Not previously included*
Diseases with monoclonal immunoglobulin deposition	
Immunoglobulin-related (AL) amyloidosis	Primary amyloidosis
Monoclonal immunoglobulin deposition disease	Light chain and heavy chain deposition disease
Heavy chain diseases	
Mu heavy chain disease	(Same)
Gamma heavy chain disease	(Same)
Alpha heavy chain disease	(Same)
Plasma cell neoplasms	
Plasmacytoma	(Same)
Plasma cell myeloma	(Same)
Plasma cell neoplasms with associated paraneoplastic syndrome -POEMS syndrome -TEMPI syndrome -AESOP syndrome	(Same) Except AESOP syndrome *not previously included*

APPENDIX 2

Hematopoietic Stem Cell Transplant Reference Sheet

The following is a list of rare and unusual conditions where allogeneic transplant may be indicated. The list was reviewed and accepted by the Optum Hematopoietic Stem Cell Transplant Expert Panel.

1. Lymphocyte Immunodeficiencies (many fall under 'severe combined immunodeficiency' classification)

- Adenosine deaminase deficiency
- Artemis deficiency
- Calcium channel deficiency
- Cernunnos-XLF immunodeficiency
- CHARGE syndrome with immune deficiency Common gamma chain deficiency
- Deficiencies in CD 45, CD3, CD8
- DiGeorge syndrome
- DNA ligase IV
- DOCK8 immunodeficiency syndrome
- GATA2 deficiency
- Interleukin-7 receptor alpha deficiency
- Janus-associated kinase 3 (JAK3) deficiency
- Major histocompatibility class II deficiency
- Purine nucleoside phosphorylase deficiency
- Recombinase-activating gene (RAG) 1/2 deficiency
- Reticular dysgenesis
- Winged helix deficiency
- Zeta-chain-associated protein-70 (ZAP-70) deficiency

2. Phagocytic Deficiencies

- Chediak-Higashi syndrome
- Griscelli syndrome, type 2
- Interferon-gamma receptor deficiencies
- Leukocyte adhesion deficiency
- Shwachman-Diamond syndrome (may be considered as marrow failure syndrome rather than immunodeficiency)

3. Other Immunodeficiencies

- Autoimmune lymphoproliferative syndrome
- Cartilage hair hypoplasia
- CD25 deficiency
- Familial hemophagocytic lymphohistiocytosis
- Hyper IgD and IgE syndromes
- ICF syndrome IPEX syndrome NEMO deficiency
- NF-κB inhibitor, alpha (IκB-alpha)

Appendix 3

Hematopoietic Stem Cell Transplant Quick Reference Guide

Appendix 3 is to be used solely as a quick reference guide to identify standard of care. This guide does not reflect potential exceptions such as enrollment in a clinical trial. It is required that the user read the Medical Necessity Criteria section for important criteria and directions.

Disease/Indication	Autologous	Allogeneic
Leukemias		
Acute Lymphoblastic Leukemia (ALL)	Yes	Yes
Acute myeloid leukemia (AML)	Yes	Yes
Chronic lymphocytic leukemia (CLL)	No	Yes
Chronic myeloid leukemia (CML)	No	Yes
Prolymphocytic leukemia	Yes	Yes
Myelodysplastic Syndromes & Mixed Myelodysplastic/Myeloproliferative Neoplasms		
Myelodysplastic syndromes (MDS)	No	Yes
Juvenile myelomonocytic leukemia (JMML/JCML)	No	Yes
Chronic myelomonocytic leukemia (CMML)	No	Yes
Myeloproliferative Disorders		
Primary myelofibrosis and related conditions	No	Yes
Secondary myelofibrosis	No	Yes
Brain Tumors		
Anaplastic astrocytoma	No	No
Brain stem glioma	No	No
Ependymoma	No	No
Germinoma	No	No
Glioblastoma Multiforme (GBM)	No	No
Medulloblastoma	Yes	No
Oligodendroglioma	Yes	No
Pineoblastoma	Yes	No
Embryonal Tumors with Multi-layered Rosettes (ETMR). Formerly known as Primitive Neuroectodermal Tumor (PNET)	Yes	No
Germ Cell Tumors		
Testicular germ cell tumor	Yes	No
Extragonadal germ cell tumor	Yes	No
Seminoma	Yes	No
Choriocarcinoma	Yes	No
Embryonal carcinoma	Yes	No
Mixed germ cell tumors	Yes	No
Teratoma	Yes	No
Yolk-sac tumor (endodermal sinus tumor)	Yes	No
Germ cell tumor of the ovary	Yes	No
Multiple Myeloma/ Plasma Cell Disorders		
Multiple Myeloma		
Single Auto	Yes	No
Tandem (auto followed by auto)	Yes	No
Tandem (auto followed by allo)	Yes	No
Allogenic	No	Yes
AL-Amyloidosis	Yes	No
Waldenstrom macroglobulinemia	Yes	Yes
Monoclonal gammopathy of renal significance (MGRS)	Yes	No
Monoclonal gammopathy of uncertain significance (MGUS)	No	No

Disease/Indication	Autologous	Allogeneic
Polyneuropathy organomegaly endocrinopathy, monoclonal gammopathy skin defects syndrome (POEMS)	Yes	No
Solitary Plasmacytoma	No	No
Hodgkin Lymphoma		
Hodgkin Lymphoma	Yes	Yes
Non-Hodgkin Lymphoma (NHL)		
Small B-cell lymphocytic lymphoma	No	Yes
Follicular lymphoma	Yes	Yes
Lymphoplasmacytoid lymphoma/immunocytoma	Yes	Yes
Marginal zone lymphoma (mucosa-associated lymphoid tissue, splenic, nodal)	Yes	Yes
Burkitt lymphoma	Yes	Yes
Diffuse, large cell lymphoma (mediastinal large cell, primary effusion)	Yes	Yes
Mantle cell lymphoma	Yes	Yes
Precursor B-cell leukemia/lymphoma	Yes	Yes
T-cell Lymphoma	Yes	Yes
Other Malignancies		
Atypical teratoid rhabdoid tumors	Yes	No
Blastic plasmacytoid dendritic cell neoplasm	No	Yes
Epithelial ovarian cancer	No	No
Ewing tumor (Ewing sarcoma)	Yes	No
Neuroblastoma	Yes	No
Osteogenic sarcoma	No	No
Renal cell carcinoma	No	No
Retinoblastoma	Yes	No
Rhabdomyosarcoma/soft tissue sarcoma	No	No
Supratentorial ependymoma	Yes	No
Wilms tumor	Yes	No

Hematological Disorders	Autologous	Allogeneic
Aplastic Anemia	No	Yes
Blackfan-Diamond Syndrome	No	Yes
Chronic Granulomatous Disease	No	Yes
Congenital Agranulocytosis (Kostmann Syndrome)	No	Yes
Congenital Amegakaryocytic Thrombocytopenia	No	Yes
Dyskeratosis Congenita	No	Yes
Fanconi Anemia	No	Yes
Paroxysmal Nocturnal Hemoglobinuria (PNH)	No	Yes
Shwachman-Diamond Syndrome	No	Yes
Sickle Cell Disease (SCD)	No	Yes
Thalassemia Major	No	Yes
Immunodeficiency Syndromes		
CD40 ligand deficiency	No	Yes
Chediak-Higashi syndrome	No	Yes
Hemophagocytic Lymphohistiocytosis (HLH) (same as familial Erythrophagocytic lymphohistiocytosis - FEL)	No	Yes
Leukocyte adhesion deficiency	No	Yes
Omenn syndrome	No	Yes
Severe Combined Immunodeficiency Disease (SCID)	No	Yes
Wiskott-Aldrich syndrome	No	Yes
X-linked lymphoproliferative syndrome	No	Yes
Gaucher disease type 1	No	Yes

Disease/Indication	Autologous	Allogeneic
Niemann-Pick type B	No	Yes
Fucosidosis	No	Yes
Lysosomal storage diseases	No	Yes
Autoimmune Diseases		
Crohn's disease	No	No
Multiple sclerosis	Yes	No
Rheumatoid arthritis	No	No
Systemic lupus erythematosus (SLE)	No	No
Systemic sclerosis (Scleroderma)	Yes	No
Inherited Metabolic Disorders		
Adrenoleukodystrophy	No	Yes
Epidermolysis bullosa	No	Yes
Globoid cell leukodystrophy (Krabbe Disease)	No	Yes
Hurler syndrome (MPS I)	No	Yes
Hunter syndrome (MPS II)	No	Yes
Mannosidosis	No	Yes
Maroteaux-Lamy Syndrome (MPS VI)	No	Yes
Metachromatic leukodystrophy	No	Yes
Mitochondrial neurogastrointestinal encephalopathy (MNGIE)	No	Yes
Osteopetrosis	No	Yes
Rett syndrome	No	Yes
Cardiac Conditions		
Heart disease	No	No
Additional condition/disease indications		
Refer to Appendix 3: *Hematopoietic Stem Cell Transplant Reference Sheet.*	No	Yes