MEDICAL POLICY	Stem Cell Transplantation (All Lines of Business Except Medicare)
Effective Date: 5/1/2022  5/1/2022 Medical Officer Date	Medical Policy Number: 282 Medical Policy Committee Approved Date: 1/2021; 1/2022; 4/2022

See Policy CPT/HCPCS CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:

All lines of business except Medicare

BENEFIT APPLICATION

Medicaid Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

POLICY CRITERIA

Note: This policy is based in part on the Centers for Medicare & Medicaid Services National Coverage Determination (NCD) for Stem Cell Transplantation (Formerly 110.8.1) (110.23).[1]

Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

I. Allogeneic hematopoietic stem cell transplantation (HSCT) may be considered **medically necessary and covered** as a treatment for all of the following indications (A.-G.):

   A. Leukemia, leukemia in remission, or aplastic anemia
   B. Severe combined immunodeficiency disease (SCID)
   C. Wiskott-Aldrich syndrome
   D. Myelodysplastic syndrome
   E. Myelofibrosis for intermediate and high-risk individuals
   F. Sickle cell disease

G. Relapsed or refractory peripheral T-cell lymphomas (e.g. angioimmunoblastic T-cell lymphoma, anaplastic large cell lymphoma) in patients who are not candidates for autologous stem cell transplantation.

II. Allogeneic hematopoietic stem cell transplantation (HSCT) is considered **investigational and not covered** when criterion I is not met, including but not limited to the treatment of multiple myeloma.

Autologous Stem Cell Transplantation (AuSCT)

III. Autologous stem cell transplantation (AuSCT) may be considered **medically necessary and covered** as a treatment for any of the following indications (A-D):

A. Acute leukemia in remission who have a high probability of relapse and who have no human leucocyte antigens (HLA)-matched;
B. Resistant non-Hodgkin's lymphomas or those presenting with poor prognostic features following an initial response;
C. Recurrent or refractory neuroblastoma;
D. Advanced Hodgkin's disease who have failed conventional therapy and have no HLA-matched donor.

IV. Autologous stem cell transplantation (AuSCT) may be considered **medically necessary and covered** as a treatment for Durie-Salmon Stage II or III patients (see Policy Guidelines) that meet all of the following requirements (A-B):
A. Newly diagnosed or responsive multiple myeloma, including:
1. Patients with previously untreated disease,
2. Patients with at least a partial response to prior chemotherapy (defined as a 50% decrease either in measurable paraprotein [serum and/or urine] or in bone marrow infiltration, sustained for at least 1 month), **or**
3. Those in responsive relapse; **and**
B. Adequate cardiac, renal, pulmonary, and hepatic function.

V. High dose melphalan (HDM) together with autologous stem cell transplantation (AuSCT) may be considered **medically necessary and covered** for any age group with primary amyloid light chain (AL) amyloidosis who meet the following criteria (A-B):

A. Amyloid deposition in 2 or fewer organs; **and**
B. Cardiac left ventricular ejection fraction (EF) greater than 45%.

VI. Autologous stem cell transplantation (AuSCT) is considered **not medically necessary and not covered** when criteria I.-IV. are not met or for any of the following indications (A-F):

A. Acute leukemia not in remission
B. Chronic granulocytic leukemia
C. Solid tumors (other than neuroblastoma)

D. Tandem transplantation (multiple rounds of AuSCT) for patients with multiple myeloma
E. Non primary AL amyloidosis
F. Sickle cell disease

Link to Policy Summary

POLICY GUIDELINESS

Durie-Salmon Staging Criteria for Multiple Myeloma

Stage	Criteria	Measured Myeloma Cell Mass (myeloma cells in billions/m^2)*
Stage 1 (low cell mass)	*All of the following:* • Hemoglobin value > 10 g/dl • Serum calcium value normal or <10.5 mg/dL • Bone X-ray, normal bone structure (scale 0), or solitary bone plasmactyoma only • Low M-component production rates IgG value < 5g/dL; IgA value < 3 g/dL • Urine light chain M-component on electrophoresis < 4 g/24h	600 billion*
Stage II (intermediate cell mass)	*Fitting neither Stage I nor Stage III*	600 to 1,200 billion*
Stage III (high cell mass)	*One or more of the following:* • Hemoglobin value < 8.5 g/dL • Serum calcium value > 12 mg/dL • Advanced lytic bone lesions (scale 3) • High M-component production rates IgG value > 7 g/dL; IgA value > 5 g/dL • Urine light chain M-component > 12 g/24h	>1,200 billion*
Subclassification (either A or B)	• ***A***: relatively normal renal function (serum creatinine value) < 2.0 mg/dL • ***B***: abnormal renal function (serum creatinine value) > 2.0 mg/dL *Examples:* • *Stage 1A (low cell mass with normal renal function);*	

	• *Stage IIB (high cell mass with abnormal renal function*	

CPT/HCPCS CODES

All Line of Business Except Medicare	
Prior Authorization Required	
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing, per donor
38210	Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-cell depletion
38211	Transplant preparation of hematopoietic progenitor cells; tumor cell depletion
38212	Transplant preparation of hematopoietic progenitor cells; red blood cell removal
38213	Transplant preparation of hematopoietic progenitor cells; platelet depletion
38214	Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion
38215	Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear, or buffy coat layer
38230	Bone marrow harvesting for transplantation; allogeneic
38232	Bone marrow harvesting for transplantation; autologous
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
38241	Hematopoietic progenitor cell (HPC); autologous transplantation
38242	Allogeneic lymphocyte infusions
No Prior Authorization Required	
0263T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, one leg, including ultrasound guidance, if performed; complete procedure including unilateral or bilateral bone marrow harvest
0264T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, one leg, including ultrasound guidance, if performed; complete procedure excluding bone marrow harvest
0265T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, one leg, including ultrasound guidance, if performed; unilateral or bilateral bone marrow harvest only for intramuscular autologous bone marrow cell therapy

DESCRIPTION

Myelodysplastic Syndromes (MDS)

Myelodysplastic Syndromes (MDS) refers to a group of diverse blood disorders in which the bone marrow does not produce enough healthy, functioning blood cells. These disorders are varied with regard to clinical characteristics, cytologic and pathologic features, and cytogenetics. The abnormal production of blood cells in the bone marrow leads to low blood cell counts, referred to as cytopenias, which are a hallmark feature of MDS along with a dysplastic and hypercellular-appearing bone marrow

Hematopoietic stem cells

Hematopoietic stem cells are multi-potent stem cells that give rise to all the blood cell types; these stem cells form blood and immune cells. A hematopoietic stem cell is a cell isolated from blood or bone marrow that can renew itself, differentiate to a variety of specialized cells, can mobilize out of the bone marrow into circulating blood, and can undergo programmed cell death, called apoptosis – a process by which cells that are unneeded or detrimental will self-destruct.

Stem cell transplantation

Stem cell transplantation is a process in which stem cells are harvested from either a patient's (autologous) or donor's (allogeneic) bone marrow or peripheral blood for intravenous infusion.

Autologous stem cell transplantation (AuSCT)

Autologous stem cell transplantation (AuSCT) is a technique for restoring stem cells using the patient's own previously stored cells. AuSCT must be used to effect hematopoietic reconstitution following severely myelotoxic doses of chemotherapy (HDCT) and/or radiotherapy used to treat various malignancies.

Allogeneic hematopoietic stem cell transplantation (HSCT)

Allogeneic hematopoietic stem cell transplantation (HSCT) is a procedure in which a portion of a healthy donor's stem cell or bone marrow is obtained and prepared for intravenous infusion. Allogeneic HSCT may be used to restore function in recipients having an inherited or acquired deficiency or defect.

CLINICAL PRACTICE GUIDELINES

American Society for Blood and Marrow Transplantation

In 2015, the American Society for Blood and Marrow Transplantation published guidelines on 'Indications for Autologous and Allogeneic Hematopoietic Cell Transplantation'. In the guidelines, they recommend allogeneic HCT for treating sickle cell anemia, categorizing the indication as a C for "standard of care, clinical evidence available. This category includes "indications for which large clinical trials and observational studies are not available. However, HCT has been shown to be an effective therapy with acceptable risk of morbidity and mortality in sufficiently large single- or multi-center cohort studies. HCT can be considered as a treatment option for individual patients after careful evaluation of

risks and benefits. As more evidence becomes available, some indications may be reclassified as "Standard of Care".[2]

The guidelines recommend against autologous HCT for sickle cell disease, because the current evidence and current practice do not support the routine use of HCT. The guidelines state, "However, this recommendation does not preclude investigation of HCT as a potential treatment and transplantation may be pursued for these indications within the context of a clinical trial."[2]

National Comprehensive Cancer Network (NCCN)

- The 2022 NCCN guidelines on T-Cell Lymphomas (Version 2.2022) recommend allogenic hematopoietic cell transplant as an option for "consolidation/additional therapy" in patients with relapsed/refractory peripheral T-cell lymphomas who experienced complete or partial response to clinical therapy or second-line therapy regiments.[3]

- The 2021 NCCN guidelines on Myeloproliferative Neoplasms (Version 2.2022) recommend the following:

  > "Allogeneic HCT is included as an option for patients with INT-1-risk MF [intermediate risk 1 myelofibrosis]. Although the outcomes following allogeneic HCT are better for patients with low-risk or INT-1-risk MF, due to high transplanted-related morbidity and mortality, treatment decisions regarding allogeneic HCT should be individualized for patients with INT-1-risk MF. Allogeneic HCT should be considered for low-risk or INT-1-risk MF inpatients with either refractory, transfusion-dependent anemia; circulating blast cells >2% in peripheral blood; or adverse cytogenetics…. Evaluation for allogeneic HCT is recommended for all patients with INT-2risk and high-risk MF."[4]

- The 2021 NCCN Guidelines on Myelodysplastic Syndromes (Version 2.2022) recommend the following:

  > "Therapeutic options for MDS [myelodysplastic syndrome] include supportive care, low-intensity therapy, high-intensity therapy including allogeneic HCT, and participation in a clinical trial."[5]

- The 2021 NCCN Guidelines on Multiple Myeloma (Version 4.2022) recommend the following:

  > "Patients presenting with active (symptomatic) myeloma are initially treated with primary therapy and primary therapy is followed by high-dose chemotherapy with autologous hematopoietic cell transplant (HCT) in transfer-eligible patients... Allogeneic stem cell transplant should preferentially be done in the context of a trial when possible."[6]

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days' notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

MEDICAL POLICY CROSS REFERENCES

- Stem Cell Therapy for Orthopedic Applications

REFERENCES

1. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for Stem Cell Transplantation (Formerly 110.8.1) (110.23). Effective 1/27/2016. https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?ncdid=366. Accessed 11/13/2020.
2. Majhail NS, Farnia SH, Carpenter PA, et al. Indications for Autologous and Allogeneic Hematopoietic Cell Transplantation: Guidelines from the American Society for Blood and Marrow Transplantation. *Biol Blood Marrow Transplant.* 2015;21(11):1863-1869.https://pubmed.ncbi.nlm.nih.gov/26256941.
3. NCCN. NCCN clinical practice guidelines in Oncology. Peripheral T-Cell Lymphomas Version 2.2022 https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed 3/8/2022.
4. NCCN. NCCN clinical practice guidelines in Oncology. Myeloproliferative Neoplasms. Version 2.2022 Published 8/18/2021. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed 12/22/2021.
5. NCCN. NCCN clinical practice guidelines in Oncology. Myelodysplastic syndromes. Version 2.2022. Published 11/15/2021. https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed 12/22/2021.

6. NCCN. NCCN clinical practice guidelines in Oncology. Multiple Myeloma. Version 4.2022. Published 12/14/2021. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed 12/22/2021.