Stem Cell Transplantation

MEDICAL POLICY NUMBER: 282

Effective Date: 3/1/2025

Last Review Date: 2/2025

Next Annual Review: 2/2026

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 Company reserves the right to determine the application of medical policies and make revisions to medical policies at any time. 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. 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.

SCOPE: Providence Health Plan, Providence Health Assurance, and Providence Plan Partners as applicable (referred to individually as “Company” and collectively as “Companies”).

PLAN PRODUCT AND BENEFIT APPLICATION

☒ **Commercial** ☐ **Medicaid/OHP*** ☐ **Medicare****

*Medicaid/OHP 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.

Notice to Medicaid Policy Readers: For comprehensive rules and guidelines pertaining to this policy, readers are advised to consult the Oregon Health Authority. It is essential to ensure full understanding and compliance with the state's regulations and directives. Please refer to OHA's prioritized list for the following coverage guidelines:

Stem Cell Transplant: Guideline Notes 7, 11

**Medicare Members

This *Company* policy may be applied to Medicare Plan members only when directed by a separate *Medicare* policy. Note that investigational services are considered **"not medically necessary"** for Medicare members.

COVERAGE CRITERIA

Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

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

   A. Leukemia or leukemia in remission;
   B. Inherited and acquired marrow disorders, including but not limited to the following:
      1. Aplastic anemia
      2. Diamond-Blackfan anemia
      3. Fanconi's anemia
      4. Sickle cell anemia
      5. Beta thalassemia major
      6. Myelodysplastic syndromes (MDS)
      7. Paroxysmal nocturnal hemoglobinuria
      8. Pure red cell aplasia
      9. Amegakaryocytosis
      10. Congenital thrombocytopenia;

C. Autoimmune diseases and inborn errors in metabolism and congenital immune deficiencies including the following:
    1. Severe combined immunodeficiency disease (SCID)
    2. X-linked adrenoleukodystrophy and adrenomyeloneuropathy
    3. Mucopolysaccharidoses
    4. Chronic granulomatous disease
    5. Krabbe disease
    6. NK cell deficiency syndromes
    7. DiGeorge (22q11.2 deletion) syndrome
    8. Wiskott-Aldrich syndrome;
D. Myelofibrosis for intermediate and high-risk individuals;
E. Relapsed or refractory 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 **not medically necessary** when criterion I. above is not met, including but not limited to the treatment of multiple myeloma.

III. Donor lymphocyte infusions may be considered **medically necessary** for the treatment of either of the following (A.-B.):

A. Relapsed or refractory acute myeloid leukemia; **or**
B. Patients with relapsed acute lymphoblastic leukemia or multiple myeloma after receiving allogeneic HCST.

IV. Donor lymphocyte infusions are considered **not medically necessary** when criterion III. above is not met.

Autologous Stem Cell Transplantation (AuSCT)

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

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.
E. High-risk or relapsed neuroblastomas.

VI. Autologous stem cell transplantation (AuSCT) may be considered **medically necessary** for the treatment of multiple myeloma following induction therapy.

VII. High dose melphalan (HDM) together with autologous stem cell transplantation (AuSCT) may be considered **medically necessary** 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%.

VIII. Tandem transplant may be considered **medically necessary** when **both** of the following criteria are met (A.-B.)

A. Patient is a candidate for autologous stem cell transplantation (AuSCT); **and**
B. Treatment is for one of the following conditions (1.-5.):
    1. Testicular tumors, either as salvage therapy or for those with platinum-refractory disease
    2. High-risk neuroblastomas (see Policy Guidelines)
    3. Multiple myeloma if **either** of the following are true (a.-b.):
        a. Patient did not achieve at least a Very Good Partial Rate (VGPR) (see Policy Guidelines) after a previous autologous stem cell transplantation; **or**
        b. Patient has high-risk features (e.g. plasma cell leukemia, extramedullary disease).

IX. Autologous stem cell transplantation (AuSCT) is considered **not medically necessary** when criteria V.-VIII. are not met, or for the treatment of any of the following indications:

A. Acute leukemia not in remission
B. Chronic granulocytic leukemia
C. Solid tumors (other than neuroblastoma)
D. Non primary AL amyloidosis
E. Sickle cell disease.

POLICY CROSS REFERENCES

- Stem Cell Therapy for Orthopedic Applications, MP36

The full Company portfolio of current Medical Policies is available online and can be accessed here.

POLICY GUIDELINES

This policy may be partly based on the following Center for Medicare and Medicaid Services (CMS) guidance resources:

- Centers for Medicare & Medicaid Services National Coverage Determination (NCD) for Stem Cell Transplantation (Formerly 110.8.1) (110.23).[1]

Very Good Partial Response (VGPR)

The NCCN defines VGPR as no measurable monoclonal protein on serum or urine electrophoresis, but positive immunofixation electrophoresis (IFE).[2]

High Risk Neuroblastoma

Patients most commonly at the highest risk for disease progression and mortality are generally those who are older than 18 months of age and have either disseminated disease or localized disease with unfavorable markers such as *MYCN* amplification regardless of age.[3]

BACKGROUND

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.

Donor Lymphocyte Infusion (DLI)

DLI refers the infusion of a bone marrow transplant donor's lymphocytes into a recipient's body. This procedure may be done after the original transplant if the recipient of the transplant suffers a return of their cancer.

CLINICAL EVIDENCE AND LITERATURE REVIEW

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".[4] Furthermore, aplastic anemia and Thalassemia were rated S or "standard of care". The following conditions were also rated R for the allogenic HCT, "standard of care, rare indication": Fanconi's anemia, Dyskeratosis congenita, Blackfan-Diamond anemia, congenital amegakaryocytic thrombocytopenia, severe combined immunodeficiency, T cell immunodeficiency, SCID variants, Wiskott-Aldrich syndrome, Hemophagocytic disorders, Lymphoproliferative disorders, severe congenital neutropenia, chronic granulomatous disease, and other autoimmune and immune dysregulation disorders. These indications include "rare diseases for which clinical trials and observational studies with sufficient number of patients are not currently feasible because of their very low incidence. However, single or multi-center or registry studies in relatively small cohorts of patients have show HCT to be effective treatment with acceptable risks of morbidity and mortality." HCT can be considered as a treatment options for these patients after careful evaluation of risks and benefits. [4]

Autologous HCT for high risk or relapsed neuroblastoma was also rated as S, "standard of care". [4]

The guidelines recommend against autologous HCT for sickle cell disease, aplastic anemia, or Thalassemia, 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."[4]

National Comprehensive Cancer Network (NCCN)

- The NCCN guidelines on T-Cell Lymphomas (Version 2.2024) 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.[5]

- The NCCN guidelines on Myeloproliferative Neoplasms (Version 1.2024) 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."[6]

- The NCCN Guidelines on Myelodysplastic Syndromes (Version 2.2025) recommend the following:

> "Evaluation for allogeneic HCT is recommended for patients with low platelet counts or complex cytogenetics. Identification of higher-risk mutations may be helpful in the decision-making regarding allogeneic HCT for patients with myelofibrosis."[7]

- The NCCN Guidelines on Acute Lymphoblastic Leukemia (Version 3.2024) recommend allogeneic HCT as a consolidative therapy following blinatumomab monotherapy. Authors also noted that optimal timing of HCT was not clear, but that proceeding to allogeneic HCT in patients with minimal residual disease detected is not optimal. In patients where MRD is unavailable, allogeneic HCT is recommended, especially in patients with high-risk features.[8]

- The NCCN Guidelines on Multiple Myeloma (Version 1.2025) 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."[2]

> "According to the NCCN Multiple Myeloma Panel, a tandem transplant with or without maintenance therapy can be considered for all patients who are candidates for HCT and is an option for patients who do not achieve at least a VGPR after the first autologous HCT and those with high-risk features."[2]

HEALTH EQUITY CONSIDERATIONS

The Centers for Disease Control and Prevention (CDC) defines health equity as the state in which everyone has a fair and just opportunity to attain their highest level of health. Achieving health equity requires addressing health disparities and social determinants of health. A health disparity is the occurrence of diseases at greater levels among certain population groups more than among others. Health disparities are linked to social determinants of health which are non-medical factors that

influence health outcomes such as the conditions in which people are born, grow, work, live, age, and the wider set of forces and systems shaping the conditions of daily life. Social determinants of health include unequal access to health care, lack of education, poverty, stigma, and racism.

The U.S. Department of Health and Human Services Office of Minority Health calls out unique areas where health disparities are noted based on race and ethnicity. Providence Health Plan (PHP) regularly reviews these areas of opportunity to see if any changes can be made to our medical or pharmacy policies to support our members obtaining their highest level of health. Upon review, PHP creates a Coverage Recommendation (CORE) form detailing which groups are impacted by the disparity, the research surrounding the disparity, and recommendations from professional organizations. PHP Health Equity COREs are updated regularly and can be found online here.

BILLING GUIDELINES AND CODING

CODES*		
CPT	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
	38204	Management of Recipient Hematopoietic Progenitor Cell Donor Search and Cell Acquisition
	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
HCPCS	None	

***Coding Notes:**

- The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- **See the non-covered and prior authorization lists on the Company Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website for additional information.**
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as "medically unlikely edits" (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCES

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2. National Comprehensive Cancer Network. Multiple Myeloma. Version 1.2025. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Published 2024. Accessed 1/24/2025.
3. UpToDate I. Treatment and prognosis of neuroblastoma. https://www.uptodate.com/contents/treatment-and-prognosis-of-neuroblastoma?sectionName=High-risk%20disease&search=stem%20cell%20transplant%20indications&topicRef=16870&anchor=H21&source=see_link#H2455888061. Published 2024. Accessed 1/24/2025.
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5. National Comprehensive Cancer Network. Peripheral T-Cell Lymphomas. Version 2.2024. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Published 2024. Accessed 1/24/2025.
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7. National Comprehensive Cancer Network. Myelodysplastic syndromes. Version 2.2025. https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Published 2025. Accessed 1/24/2025.
8. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia. Version 3.2024. https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Published 2024. Accessed 1/24/2025.

POLICY REVISION HISTORY

DATE	REVISION SUMMARY
2/2023	Converted to new policy template.
4/2023	Annual review. Expanded criteria on noncancer indications, tandem transplant.
5/2024	Annual review. Changes to criteria. Code added.
3/2025	Annual review. No changes.