



Medical Policy

Hematopoietic Cell Transplantation for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

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Policy Number: 074

BCBSA Reference Number: 8.01.15 (For Plan internal use only)

Related Policies

Hematopoietic Cell Transplantation for Non- Hodgkin Lymphomas, #[143](#)

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Allogeneic hematopoietic cell transplantation is considered **MEDICALLY NECESSARY** to treat chronic lymphocytic leukemia or small lymphocytic lymphoma in individuals with markers of poor-risk disease.

Poor risk disease for transplant purposes is classified according to the EBMT CLL Transplant Consensus Criteria as having one of the following:

- Non-response or early relapse (within 12 months) after purine analogue containing therapy,
- Relapse (within 24 months) after purine analogue combination therapy or treatment of similar, efficacy (i.e., autologous stem cell transplantation), or
- p53 deletion/mutation (del 17p) requiring treatment.

Autologous hematopoietic cell transplantation is considered **INVESTIGATIONAL** to treat chronic lymphocytic leukemia or small lymphocytic lymphoma.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is required .
Commercial PPO and Indemnity	Prior authorization is required .

Requesting Prior Authorization Using Authorization Manager

Providers will need to use [Authorization Manager](#) to submit initial authorization requests for services. Authorization Manager, available 24/7, is the quickest way to review authorization requirements, request authorizations, submit clinical documentation, check existing case status, and view/print the decision letter. For commercial members, the requests must meet medical policy guidelines.

To ensure the service request is processed accurately and quickly:

- Enter the facility's NPI or provider ID for where services are being performed.
- Enter the appropriate surgeon's NPI or provider ID as the servicing provider, *not* the billing group.

Authorization Manager Resources

Refer to our [Authorization Manager](#) page for tips, guides, and video demonstrations.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO and Indemnity:

CPT Codes

CPT codes:	Code Description
38240	Bone marrow or blood-derived peripheral stem-cell transplantation; allogeneic

HCPCS Codes

HCPCS codes:	Code Description
S2142	Cord blood derived stem-cell transplantation, allogeneic
S2150	Bone marrow or blood-derived peripheral stem-cell harvesting and transplantation, allogeneic or autologous, including pheresis, high-dose chemotherapy, and the number of days of post-transplant care in the global definition (including drugs; hospitalization; medical surgical, diagnostic and emergency services)

ICD-10 Procedure Codes

ICD-10-PCS procedure codes:	Code Description
30230AZ	Transfusion of Embryonic Stem Cells into Peripheral Vein, Open Approach
30230G1	Transfusion of Nonautologous Bone Marrow into Peripheral Vein, Open Approach
30230X1	Transfusion of Nonautologous Cord Blood Stem Cells into Peripheral Vein, Open Approach
30230Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Peripheral Vein, Open Approach

30233AZ	Transfusion of Embryonic Stem Cells into Peripheral Vein, Percutaneous Approach
30233G1	Transfusion of Nonautologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30233X1	Transfusion of Nonautologous Cord Blood Stem Cells into Peripheral Vein, Percutaneous Approach
30233Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach
30240AZ	Transfusion of Embryonic Stem Cells into Central Vein, Open Approach
30240G1	Transfusion of Nonautologous Bone Marrow into Central Vein, Open Approach
30240X1	Transfusion of Nonautologous Cord Blood Stem Cells into Central Vein, Open Approach
30240Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Vein, Open Approach
30243AZ	Transfusion of Embryonic Stem Cells into Central Vein, Percutaneous Approach
30243G1	Transfusion of Nonautologous Bone Marrow into Central Vein, Percutaneous Approach
30243X1	Transfusion of Nonautologous Cord Blood Stem Cells into Central Vein, Percutaneous Approach
30243Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach
30250G1	Transfusion of Nonautologous Bone Marrow into Peripheral Artery, Open Approach
30250X1	Transfusion of Nonautologous Cord Blood Stem Cells into Peripheral Artery, Open Approach
30250Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Peripheral Artery, Open Approach
30253G1	Transfusion of Nonautologous Bone Marrow into Peripheral Artery, Percutaneous Approach
30253X1	Transfusion of Nonautologous Cord Blood Stem Cells into Peripheral Artery, Percutaneous Approach
30253Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Peripheral Artery, Percutaneous Approach
30260G1	Transfusion of Nonautologous Bone Marrow into Central Artery, Open Approach
30260X1	Transfusion of Nonautologous Cord Blood Stem Cells into Central Artery, Open Approach
30260Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Artery, Open Approach
30263G1	Transfusion of Nonautologous Bone Marrow into Central Artery, Percutaneous Approach
30263X1	Transfusion of Nonautologous Cord Blood Stem Cells into Central Artery, Percutaneous Approach
30263Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Artery, Percutaneous Approach
3E03005	Introduction of Other Antineoplastic into Peripheral Vein, Open Approach
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E04005	Introduction of Other Antineoplastic into Central Vein, Open Approach
3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
3E05005	Introduction of Other Antineoplastic into Peripheral Artery, Open Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E06005	Introduction of Other Antineoplastic into Central Artery, Open Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach

The following CPT and ICD Procedure codes are considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:

CPT Codes

CPT codes:	Code Description
38241	Bone marrow or blood-derived peripheral stem-cell transplantation; autologous

ICD-10 Procedure Codes

ICD-10-PCS procedure codes:	Code Description
30230G0	Transfusion of Autologous Bone Marrow into Peripheral Vein, Open Approach
30230X0	Transfusion of Autologous Cord Blood Stem Cells into Peripheral Vein, Open Approach
30230Y0	Transfusion of Autologous Hematopoietic Stem Cells into Peripheral Vein, Open Approach
30233G0	Transfusion of Autologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30233X0	Transfusion of Autologous Cord Blood Stem Cells into Peripheral Vein, Percutaneous Approach
30233Y0	Transfusion of Autologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach
30240G0	Transfusion of Autologous Bone Marrow into Central Vein, Open Approach
30240X0	Transfusion of Autologous Cord Blood Stem Cells into Central Vein, Open Approach
30240Y0	Transfusion of Autologous Hematopoietic Stem Cells into Central Vein, Open Approach
30243G0	Transfusion of Autologous Bone Marrow into Central Vein, Percutaneous Approach
30243X0	Transfusion of Autologous Cord Blood Stem Cells into Central Vein, Percutaneous Approach
30243Y0	Transfusion of Autologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach
30250G0	Transfusion of Autologous Bone Marrow into Peripheral Artery, Open Approach
30250X0	Transfusion of Autologous Cord Blood Stem Cells into Peripheral Artery, Open Approach
30250Y0	Transfusion of Autologous Hematopoietic Stem Cells into Peripheral Artery, Open Approach
30253G0	Transfusion of Autologous Bone Marrow into Peripheral Artery, Percutaneous Approach
30253X0	Transfusion of Autologous Cord Blood Stem Cells into Peripheral Artery, Percutaneous Approach
30253Y0	Transfusion of Autologous Hematopoietic Stem Cells into Peripheral Artery, Percutaneous Approach
30260G0	Transfusion of Autologous Bone Marrow into Central Artery, Open Approach
30260X0	Transfusion of Autologous Cord Blood Stem Cells into Central Artery, Open Approach
30260Y0	Transfusion of Autologous Hematopoietic Stem Cells into Central Artery, Open Approach
30263G0	Transfusion of Autologous Bone Marrow into Central Artery, Percutaneous Approach
30263X0	Transfusion of Autologous Cord Blood Stem Cells into Central Artery, Percutaneous Approach

30263Y0	Transfusion of Autologous Hematopoietic Stem Cells into Central Artery, Percutaneous Approach
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Description

Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma

Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are neoplasms of hematopoietic origin characterized by the accumulation of lymphocytes with a mature, generally well-differentiated morphology. In CLL, these cells accumulate in the blood, bone marrow, lymph nodes, and spleen; in SLL they are generally confined to lymph nodes. The Revised European-American/World Health Organization Classification of Lymphoid Neoplasms considers B-cell CLL and SLL a single disease entity. Chronic lymphocytic leukemia and SLL share many common features and are often referred to as blood and tissue counterparts of each other, respectively. Both tend to present as asymptomatic enlargement of the lymph nodes, tend to be indolent, but can undergo transformation to a more aggressive form of the disease (eg, Richter transformation). The median age at diagnosis of CLL is approximately 72 years, but it may present in younger individuals, often as a poor-risk disease with significantly reduced life expectancy.

Treatment regimens used for CLL are generally the same as those used for SLL, and treatment outcomes are comparable for both diseases. Both low- and intermediate-risk CLL and SLL demonstrate relatively good prognoses, with median survivals of 6 to 10 years; however, the median survival of high-risk CLL or SLL may only be 2 years. Although typically responsive to initial therapy, CLL and SLL are rarely cured by conventional therapy, and nearly all patients ultimately die of their disease. This natural disease history prompted an investigation of HCT as a possible curative regimen.

Hematopoietic Cell Transplantation

Hematopoietic cell transplantation (HCT) is a procedure in which hematopoietic stem cells are infused to restore bone marrow function in cancer patients who receive bone marrow-toxic doses of drugs with or without whole-body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or a donor (allogeneic HCT [allo-HCT]). These cells can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates. Although cord blood is an allogeneic source, the stem cells in it are antigenically "naïve" and thus are associated with a lower incidence of rejection or graft-versus-host disease (GVHD). Cord blood is addressed in evidence review 7.01.50.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. However, immunologic compatibility between donor and patient is critical for achieving a good outcome of allo-HCT. Compatibility is established by typing of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. HLA refers to the tissue type expressed at the HLA-A, -B, and -DR loci on each arm of chromosome 6. Depending on the disease being treated, an acceptable donor will match the patient at all or most of the HLA loci.

Conditioning for Hematopoietic Cell Transplantation

Conventional Conditioning for Hematopoietic Cell Transplantation

The conventional practice of allo-HCT involves administration of cytotoxic agents (eg, cyclophosphamide, busulfan) with or without total body irradiation at doses sufficient to destroy endogenous hematopoietic capability in the recipient. The beneficial treatment effect in this procedure is due to a combination of initial eradication of malignant cells and subsequent graft-versus-malignancy effect that develops after engraftment of allogeneic stem cells within the patient's bone marrow space. The slower graft-versus-malignancy effect is considered the potentially curative component, but it may be overwhelmed by extant disease without the use of pretransplant conditioning. However, intense conditioning regimens are limited to patients who are sufficiently fit medically to tolerate substantial adverse events that include pre-engraftment opportunistic infections secondary to loss of endogenous bone marrow function and organ damage and failure caused by the cytotoxic drugs. Furthermore, in any allo-HCT, immunosuppressant

drugs are required to minimize graft rejection and GVHD, which also increases the susceptibility of the patient to opportunistic infections.

The success of autologous HCT is predicated on the ability of cytotoxic chemotherapy with or without radiation to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of bone marrow space with presumably normal hematopoietic stem cells obtained from the patient before undergoing bone marrow ablation. As a consequence, autologous HCT is typically performed as consolidation therapy when the patient's disease is in complete remission. Patients who undergo autologous HCT are susceptible to chemotherapy-related toxicities and opportunistic infections before engraftment, but not GVHD.

Reduced-Intensity Conditioning for Allogeneic Hematopoietic Cell Transplantation

Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses or less intense regimens of cytotoxic drugs or radiation than are used in conventional full-dose myeloablative conditioning treatments. The goal of RIC is to reduce disease burden but also to minimize as much as possible associated treatment-related morbidity and nonrelapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. Although the definition of RIC remains arbitrary, with numerous versions employed, all seek to balance the competing effects of nonrelapse mortality and relapse due to residual disease. Reduced-intensity conditioning regimens can be viewed as a continuum in effects, from near totally myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allo-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. For this evidence review, the term reduced-intensity conditioning will refer to all conditioning regimens intended to be nonmyeloablative, as opposed to fully myeloablative (conventional) regimens.

Summary

Description

Risk stratification of patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) guides therapy decisions, which may include hematopoietic cell transplantation (HCT) for those with poor risk features.

Summary of Evidence

For individuals who have chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) and markers of poor-risk disease who receive allogeneic hematopoietic cell transplantation (allo-HCT), the evidence includes single-arm prospective and registry-based studies. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related mortality and morbidity. Data have suggested that allo-HCT can provide long-term disease control and overall survival in patients with poor-risk CLL/SLL. High rates of treatment-related morbidity discourage this approach in lower-risk disease, particularly among older patients whose health status typically precludes the use of myeloablative conditioning. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have CLL/SLL who receive autologous HCT, the evidence includes randomized controlled trials (RCTs) and a systematic review. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related mortality and morbidity. Autologous HCT is feasible in younger patients but is not curative, particularly in those with poor-risk CLL. Studies of autologous HCT published to date have not shown improvement in overall survival in patients with CLL/SLL, and results must be considered in the context of improved outcomes with the use of newer chemoimmunotherapy agents. Furthermore, evidence from the European Intergroup RCT has suggested quality of life issues are important in selecting patients for autologous HCT and may dictate the management course for patients who are otherwise candidates for this approach. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Policy History

Date	Action
3/2025	Annual policy review. Policy updated with literature review through November 25, 2024; no references added. Policy statements unchanged.
3/2024	Annual policy review. Description, summary, and references updated. Policy statements unchanged
9/2023	Policy clarified to include prior authorization requests using Authorization Manager.
3/2023	Annual policy review. Minor editorial refinements to policy statements; intent unchanged.
2/2022	Annual policy review. Policy statements unchanged.
3/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
1/2021	Medicare information removed. See MP #132 Medicare Advantage Management for local coverage determination and national coverage determination reference.
4/2020	Bone marrow harvesting codes were removed. Outpatient prior authorization is not required.
3/2020	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
3/2019	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
1/2019	Outpatient prior authorization is required for all commercial products. Effective 1/1/2019.
2/2018	Annual policy review. New references added.
1/2018	Clarified coding information.
2/2017	Annual policy review. New references added.
6/2016	Annual policy review. "Hematopoietic stem cell transplantation (HSCT)" was replaced with "hematopoietic cell transplantation (HCT)" in the policy statements, title, and text; there were no further changes to the policy statements. 6/1/2016
1/2015	Clarified coding information.
5/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
4/2014	Annual policy review. New references added.
2/2013	Annual policy review. New references added.
2/2012	Updated to add new CPT code 38243.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
7/2011	Reviewed - Medical Policy Group Hematology and Oncology. No changes to policy statements.
9/2010	Reviewed - Medical Policy Group Hematology and Oncology. No changes to policy statements.
9/1/10	Medical Policy 074 effective 9/1/10 describing covered and non-covered indications.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

[Medical Policy Terms of Use](#)

[Managed Care Guidelines](#)

[Indemnity/PPO Guidelines](#)

[Clinical Exception Process](#)

[Medical Technology Assessment Guidelines](#)

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