



## MASSACHUSETTS

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### Medical Policy

## Hematopoietic Cell Transplantation for Non-Hodgkin Lymphomas

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### Policy Number: 143

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NCD/LCD: N/A

### Related Policies

- Hematopoietic Cell Transplantation for Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma, [#074](#)
- Hematopoietic Cell Transplantation for Hodgkin Lymphoma, [#207](#)
- Hematopoietic Cell Transplantation for Primary Amyloidosis, [#181](#)
- Hematopoietic Cell Transplantation for Waldenstrom's Macroglobulinemia, [#322](#)
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### Policy

#### Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue<sup>SM</sup> and Medicare PPO Blue<sup>SM</sup> Members

For patients with non-Hodgkin's lymphoma (NHL), B-cell subtypes considered aggressive (except mantle cell lymphoma), either allogeneic hematopoietic stem cell transplantation (HCT) using a myeloablative conditioning regimen or autologous HCT for the following indications may be considered **MEDICALLY NECESSARY**:

- As salvage therapy for patients who do not achieve a complete remission (CR) after first-line treatment (induction) with a full course of standard-dose chemotherapy,
- To achieve or consolidate a CR for those in a chemosensitive first or subsequent relapse, or
- To consolidate a first CR in patients with diffuse large B-cell lymphoma, with an adjusted International Prognostic Index score that predicts a high- or high-intermediate risk of relapse.

For patients with mantle cell lymphoma:

- Autologous HCT to consolidate a first remission may be **MEDICALLY NECESSARY**, or
- Allogeneic HCT, myeloablative or reduced-intensity conditioning, as salvage therapy may be **MEDICALLY NECESSARY**.

For patients with NHL B-cell subtypes considered indolent, either allogeneic HCT using a myeloablative conditioning regimen or autologous HCT for the following indications may be **MEDICALLY NECESSARY**:

- As salvage therapy for patients who do not achieve CR after first-line treatment (induction) with a full course of standard-dose chemotherapy, or
- To achieve or consolidate CR for those in a first or subsequent chemosensitive relapse, whether or not their lymphoma has undergone transformation to a higher grade.

Reduced-intensity conditioning allogeneic HCT as a treatment of NHL may be **MEDICALLY NECESSARY** in patients who meet criteria for an allogeneic HSCT but who do not qualify for a myeloablative allogeneic HCT.

For patients with mature T-cell or NK-cell (peripheral T-cell) lymphoma for the specified indications:

- Autologous HCT may be **MEDICALLY NECESSARY** to consolidate a first complete remission in high-risk peripheral T-cell lymphoma, or
- Autologous or allogeneic HCT (myeloablative or reduced-intensity conditioning) may be **MEDICALLY NECESSARY** as salvage therapy.

The following procedures are **INVESTIGATIONAL**.

- Autologous HCT for patients with mantle cell lymphoma as salvage therapy, or
- Allogeneic HCT for patients with mantle cell lymphoma to consolidate a first remission, or
- Autologous or allogeneic HCT for the following conditions:
  - As initial therapy (i.e., without a full course of standard-dose induction chemotherapy) for any NHL, or
  - To consolidate a first CR for patients with diffuse large B-cell lymphoma and an International Prognostic Index score that predicts a low- or low-intermediate risk of relapse, or
  - To consolidate a first CR for those with indolent NHL B-cell types.
- Tandem transplants to treat patients with any stage, grade, or subtype of NHL, or
- Allogeneic HCT for patients with peripheral T-cell lymphoma to consolidate a first remission.

#### Guidelines for use of bone marrow

Stem cells when harvested from the patient's bone marrow prior to marrow ablative therapy or from a donor's marrow after verifying the donor and recipient are well matched with respect to human leukocyte antigens (HLA) may be considered **MEDICALLY NECESSARY**. Verification of well-matched HLA donor and recipient is based on the attending or treating physician's clinical judgment.

Umbilical cord stem cell support as an acceptable cell source for transplants that are otherwise covered for either high-dose chemo with stem cell support, or for bone marrow transplant may be considered **MEDICALLY NECESSARY** when ALL the following are met:

1. Recipient is a child or adult, AND
2. There is no other available stem-cell donor with the same or better matching characteristics, AND
3. Donors may be related or unrelated.

Collection and storage of cord blood from neonate when an allogeneic transplant is "imminent" in an identified recipient with a diagnosis that is consistent with the possible need for allogeneic transplant may be considered **MEDICALLY NECESSARY**.

#### Exclusions:

1. Facility providing umbilical cord blood that is not in compliance with any existing FDA regulations governing umbilical cord transplants. FDA regulations are currently under development.
2. There is a suitable stem cell donor of equal or superior HLA match, and
3. Storage for future use, in case of a future need for transplant (prophylactic collection and storage).

### **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**.

	<b>Outpatient</b>
<b>Commercial Managed Care (HMO and POS)</b>	Prior authorization is <b>required</b> .
<b>Commercial PPO and Indemnity</b>	Prior authorization is <b>required</b> .
<b>Medicare HMO Blue<sup>SM</sup></b>	Prior authorization is <b>required</b> .
<b>Medicare PPO Blue<sup>SM</sup></b>	Prior authorization is <b>required</b> .

### 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, Indemnity, Medicare HMO Blue and Medicare PPO Blue:**

#### CPT Codes

<b>CPT codes:</b>	<b>Code Description</b>
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
38241	Hematopoietic progenitor cell (HPC); autologous transplantation

#### HCPCS Codes

<b>HCPCS codes:</b>	<b>Code Description</b>
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

<b>ICD-10-PCS procedure codes:</b>	<b>Code Description</b>
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
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
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach

3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach

## Description

### Treatment for Non-Hodgkin Lymphoma

#### Hematopoietic Cell Transplantation

HCT is a procedure in which hematopoietic stem cells are intravenously infused to restore bone marrow and immune function in cancer patients who receive bone marrow-toxic doses of cytotoxic 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 the umbilical cord blood shortly after delivery of neonates. Cord blood transplantation is discussed in detail in policy #285.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. In allogeneic stem cell transplantation, immunologic compatibility between donor and patient is a critical factor for achieving a successful outcome. Compatibility is established by typing of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. HLA refers to the gene complex expressed at the HLA-A, -B, and -DR (antigen-D related) loci on each arm of chromosome 6. An acceptable donor will match the patient at all or most of the HLA loci.

#### Conditioning for Hematopoietic Cell Transplantation

##### Conventional Conditioning

The conventional ("classical") practice of allo-HCT involves administration of cytotoxic agents (e.g., cyclophosphamide, busulfan) with or without total body irradiation at doses sufficient to cause bone marrow ablation in the recipient. The beneficial treatment effect of this procedure is due to a combination of the initial eradication of malignant cells and subsequent graft-versus-malignancy effect mediated by non-self-immunologic effector cells. While the slower graft-versus-malignancy effect is considered the potentially curative component, it may be overwhelmed by existing disease in the absence of pretransplant conditioning. Intense conditioning regimens are limited to patients who are sufficiently medically fit to tolerate substantial adverse effects. These include opportunistic infections secondary to loss of endogenous bone marrow function and organ damage or failure caused by cytotoxic drugs. Subsequent to graft infusion in allo-HCT, immunosuppressant drugs are required to minimize graft rejection and graft-versus-host disease (GVHD), which increases susceptibility to opportunistic infections. The success of autologous HCT is predicated on the potential of cytotoxic chemotherapy, with or without radiotherapy, to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of the bone marrow with presumably normal hematopoietic stem cells obtained from the patient before undergoing bone marrow ablation. Therefore, autologous HCT is typically performed as consolidation therapy when the patient's disease is in complete remission. Patients who undergo autologous HCT are also susceptible to chemotherapy-related toxicities and opportunistic infections before engraftment, but not GVHD.

##### Reduced-Intensity Conditioning Allogeneic Hematopoietic Cell Transplantation

Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses of cytotoxic drugs or less intense regimens of radiotherapy than are used in traditional full-dose myeloablative conditioning treatments. Although the definition of RIC is variable, with numerous versions employed, all regimens seek to balance the competing effects of relapse due to residual disease and non-relapse mortality. The goal of RIC is to reduce disease burden and to minimize associated treatment-related morbidity and non-relapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. RIC regimens range from nearly total 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. In this review, the term reduced-intensity conditioning will refer to all conditioning regimens intended to be nonmyeloablative.

## Summary

Hematopoietic cell transplantation (HCT) refers to a procedure by which hematopoietic stem cells are infused to restore bone marrow function in cancer patients who receive bone-marrow-toxic doses of cytotoxic 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]). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates. Although umbilical cord blood is an allogeneic source, the stem cells in it are antigenically “naive” and thus are associated with a lower incidence of rejection or graft-versus-host disease. Umbilical cord blood is discussed in greater detail in policy [#285](#).

For individuals who have indolent B-cell non-Hodgkin lymphomas (NHL) who receive autologous HCT as first-line therapy, the evidence includes randomized trials and systematic reviews. Relevant outcomes are overall survival (OS), disease-specific survival (DSS), change in disease status, morbid events, and treatment-related mortality and morbidity. Randomized trials have not shown a survival advantage with HCT as first-line therapy for indolent B-cell lymphomas; however, randomized studies have shown a survival benefit for relapsed disease. Observational studies have shown similar results. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have aggressive B-cell NHL, excluding mantle cell lymphoma (MCL), who receive autologous HCT as consolidation therapy after first complete remission, the evidence includes randomized trials and a systematic review. Relevant outcomes are OS, DSS, change in disease status, morbid events, and treatment-related mortality and morbidity. While the data from the randomized trials offer conflicting results, some data have revealed an OS benefit in patients with aggressive B-cell lymphomas (at high- or high-intermediate risk of relapse) who receive HCT to consolidate a first complete remission. Randomized studies of HCT for relapsed aggressive B-cell lymphomas have also shown an OS benefit with the previously described approach. Results of a retrospective study comparing autologous and allo-HCT for relapsed or refractory B-cell NHL showed more positive outcomes for autologous HCTs. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have NHL, excluding MCL, who receive tandem autologous and allo-HCT, the evidence includes several nonrandomized trials. Relevant outcomes are OS, DSS, change in disease status, morbid events, and treatment-related mortality and morbidity. No randomized studies have been conducted on the use of tandem HCT for the treatment of NHL, and the published evidence comprises a limited number of patients. Presently, conclusions on the use of tandem transplants cannot be made about autologous and allo-HCT. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have MCL who receive autologous, allogeneic, or tandem HCT, the evidence includes case series. Relevant outcomes are OS, DSS, change in disease status, morbid events, and treatment-related mortality and morbidity. Due in part to the rarity of this disease, randomized trials on the use of HCT for MCL have not been conducted. Case series have shown long-term disease control of this aggressive lymphoma with autologous HCT (with rituximab) to consolidate a first remission; however, the use of autologous HCT in the relapsed setting has not shown improved outcomes. Allo-HCT has shown prolonged disease control in the relapsed or refractory setting. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have peripheral T-cell lymphoma (PTCL) who receive autologous or allo-HCT, the evidence mainly includes prospective trials and case reports/series. Relevant outcomes are OS, DSS, change in disease status, morbid events, and treatment-related mortality and morbidity. The role of HCT in PTCL is not well-defined. Few studies have been conducted, and most were performed retrospectively with a limited number of patients; moreover, the patient populations were heterogeneous and included

good- and poor-risk patients in the same study. Patient population and characteristics of the studies can be explained partially by the rarity and heterogeneity of the particular group of lymphomas addressed. Additionally, studies of this nature often mix 3 types of patients: 1 type of patient has PTCL not otherwise specified, which has a poorer prognosis; another type has anaplastic lymphoma kinase-positive anaplastic large-cell lymphomas, which has a better prognosis-even with conventional chemotherapy regimens; and a third type has anaplastic lymphoma kinase-negative anaplastic large-cell lymphomas, which has a worse prognosis than anaplastic lymphoma kinase-positive anaplastic large-cell lymphomas (but better than patients with PTCL not otherwise specified). There have been no randomized studies comparing chemotherapy regimens solely in patients with PTCL (ie, some randomized studies have included PTCL with aggressive B-cell lymphomas). For first-line therapy, results from recent phase 2 studies with autologous HCT as consolidation offers the best survival outcomes for patients with high-risk features; randomized trials to confirm this have not been performed. A single retrospective registry study showed a potential survival benefit among patients treated with allo-HCT in the front-line setting; however, prospective studies are not available. Patients with relapsed or refractory PTCL are generally considered incurable with chemotherapy alone. In the salvage setting, data have shown that the use of HCT may improve survival outcomes similar to the results seen in corresponding aggressive B-cell lymphomas in the same treatment setting. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

## Policy History

Date	Action
2/2022	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
3/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
10/2020	Clarified coding information
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 including Medicare Advantage. Effective 1/1/2019.
8/2018	Clinical trials for cancer information removed. For information on clinical trials for cancer, see subscriber certificate. 8/13/2018
2/2018	Annual policy review. New references added.
2/2018	Clarified coding information.
11/2017	Annual policy review. "Stem" removed from title and policy. HSCT changed to HCT in Policy statements otherwise unchanged. 11/1/2017
3/2016	Annual policy review. New references added
3/2015	Annual policy review. New references added
1/2015	Clarified coding information.
5/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
4/2013	New references from Annual policy review.
2/2013	Annual policy review. No change in medical policy statement. Effective 2/4/2013.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
11/1/2011	Annual policy review. Changes to policy statements.
7/2011	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
7/2009	New policy, effective 7/2009, 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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