Medical Policy

Hematopoietic Stem Cell Transplantation for Non-Hodgkin Lymphomas

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Policy Number: 143
BCBSA Reference Number: 8.01.20
NCD/LCD: N/A

Related Policies

- Hematopoietic Stem-Cell Transplantation for Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma, #074
- Hematopoietic Stem-Cell Transplantation for Hodgkin Lymphoma, #207
- Hematopoietic Stem-Cell Transplantation for Primary Amyloidosis, #181
- Hematopoietic Stem-Cell Transplantation for Waldenstrom’s Macroglobulinemia, #322

Policy

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

For patients with non-Hodgkin’s lymphoma (NHL), B-cell subtypes considered aggressive (except mantle cell lymphoma), either allogeneic hematopoietic stem cell transplantation (HSCT) using a myeloablative conditioning regimen or autologous HSCT 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 HSCT to consolidate a first remission may be MEDICALLY NECESSARY, or
- Allogeneic HSCT, myeloablative or reduced-intensity conditioning, as salvage therapy may be MEDICALLY NECESSARY.
For patients with NHL B-cell subtypes considered indolent, either allogeneic HSCT using a myeloablative conditioning regimen or autologous HSCT 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 HSCT 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 HSCT.

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

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

The following procedures are **INVESTIGATIONAL**.

- Autologous HSCT for patients with mantle cell lymphoma as salvage therapy, or
- Allogeneic HSCT for patients with mantle cell lymphoma to consolidate a first remission, or
- Autologous or allogeneic HSCT 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 HSCT for patients with peripheral T-cell lymphoma to consolidate a first remission.

**Clinical Trials for Cancer Mandate: BCBSMA Coverage**

- BCBSMA covers services and supplies received as part of a qualified clinical trial (for treatment of cancer) when the member is enrolled in that trial as required by the Massachusetts clinical trial cancer mandate.

The following services are **NOT MEDICALLY NECESSARY**:

- Investigational drugs and devices that have not been approved for use in the trial,
- Investigational drugs and devices that are paid for by the manufacturer, distributor or provider of the drug or device, whether or not the drug or device has been approved for use in the trial,
- Non-covered services under the member’s contract,
- Costs associated with managing the research for the trial,
- Items, services or costs that are reimbursed or otherwise furnished by the sponsor of the trial,
- Costs of services that are inconsistent with widely accepted and established national and regional standards of care, and
- Costs of clinical trials that are not “qualified trials.

**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

Prior Authorization Information
Pre-service approval is required for all inpatient services for all products. See below for situations where prior authorization may be required or may not be required for outpatient services.
Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

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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**

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<td>38205</td>
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<td>38230</td>
<td>Bone marrow harvesting for transplantation; allogeneic</td>
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<td>38232</td>
<td>Bone marrow harvesting for transplantation; autologous</td>
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<td>38240</td>
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Hematopoietic progenitor cell (HPC); autologous transplantation

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Description
Hematopoietic stem-cell transplantation (HSCT) refers to a procedure in 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 radiation therapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HSCT) or from a donor (allogeneic HSCT). They 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.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HSCT. However, immunologic compatibility between donor and patient is a critical factor for achieving a good outcome of allogeneic HSCT.

The success of autologous HSCT is predicated on the ability of cytotoxic chemotherapy with or without radiation to eradicate cancerous cells from the blood and bone marrow.

A heterogeneous group of lymphoproliferative malignancies, Non-Hodgkin Lymphoma (NHL) usually originates in lymphoid tissue. In general, the NHL can be divided into two prognostic groups, indolent and aggressive. Indolent NHL has a relatively good prognosis, with a median survival of 10 years; however, it is not curable in advanced clinical stages. Early stage indolent NHL (stage 1 or 2) may be effectively treated with radiation alone. Although indolent NHL is responsive to radiation and chemotherapy, a continuous rate of relapse is seen in advanced stages. These patients can often be re-treated if their disease remains of the indolent type. Indolent NHL may transform into a more aggressive form, which is generally treated with regimens that are used for aggressive, recurrent NHL. Mantle cell lymphoma comprises approximately 6–8% of NHL and has been recognized within the past 15 years as a unique lymphoma subtype with a particularly aggressive course.

Summary
Randomized trials have shown no survival advantage to HSCT as first-line therapy for indolent B-cell lymphomas; however, randomized studies have shown a survival benefit for relapsed disease. Data from randomized trials have shown conflicting results, but some have shown an overall survival benefit with HSCT to consolidate a first CR in patients with aggressive B-cell lymphomas at high or high-intermediate risk of relapse.

HSCT for relapsed aggressive B-cell lymphomas is the treatment of choice, as randomized studies have shown an overall survival benefit with this approach.
No randomized studies have been conducted on the use of tandem HSCT for the treatment of non-Hodgkin lymphomas, and the published data consist of small numbers of patients. Therefore, the data on tandem transplants is insufficient to determine outcomes with this type of treatment due in part to the relative rarity of the disease, randomized studies on the use of HSCT in mast cell lymphoma have not been conducted. Case series have shown long-term disease control of this aggressive lymphoma with the use of autologous HSCT (with rituximab) to consolidate a first remission; however, the use of autologous HSCT in the relapsed setting has not shown improved outcomes. Allogeneic HSCT has shown prolonged disease control in the relapsed/refractory setting.

The role of HSCT in peripheral T-cell lymphoma (PTCL) is not well-defined. Few studies have been conducted, many of these retrospectively, with small numbers of patients and heterogeneous patient populations including good- and poor-risk patients in the same study. This is partly due to the rarity and heterogeneity of this group of lymphomas. In particular, studies often mix patients with PTCL-NOS (which has a poorer prognosis) with patients with ALK + ALCL which has a better prognosis (even with conventional chemotherapy regimens), and ALK- ALCL patients who have a worse prognosis than ALK+ ALCL but better than PTCL-NOS patients.

There have been no randomized studies comparing chemotherapy regimens solely in patients with peripheral T-cell lymphoma (i.e., some randomized studies have included peripheral T-cell lymphoma with aggressive B-cell lymphomas).

Reviews summarize the most recent and largest studies on the use of HSCT as frontline and salvage therapy for PTCL. For frontline therapy, results from recent Phase II studies with autologous HSCT as consolidation offers the best survival outcomes for patients with high-risk features; randomized trials to confirm this have not been performed. No relevant data for the use of allogeneic HSCT in the front-line setting are available.

Approximately 30–60% of these patients do not reach transplantation due to early disease progression or toxicity, and 20–30% relapse after transplantation. Patients with relapsed or refractory disease are generally considered incurable with chemotherapy alone. In the salvage setting, the data show that the use of HSCT may improve survival outcomes similar to the results seen in corresponding aggressive B-cell lymphomas in the same treatment setting.

**Policy History**

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<td>3/2015</td>
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References
15. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Salvage high-dose chemotherapy with allogeneic stem-cell support for relapse or incomplete remission following high-dose chemotherapy with autologous stem-cell transplantation for hematologic malignancies. TEC Assessments 2000; Volume 15, Tab 9.


Endnotes
1. Based on MGL - Chapter 118G, Section 1