

## Corporate Medical Policy

### Hematopoietic Stem-Cell Transplant for Non-Hodgkin Lymphomas

<b>File Name:</b>	hematopoietic_stem-cell_transplant_for_non_hodgkin_lymphomas
<b>Origination:</b>	2/2001
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#### Description of Procedure or Service

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##### **Hematopoietic Stem-Cell Transplantation**

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 (GVHD). Cord blood is discussed in greater detail in the Cord Blood as a Source of Stem Cells medical policy.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous SCT. However, immunologic compatibility between donor and patient is a critical factor for achieving a good outcome of allogeneic HSCT. Compatibility is established by typing 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 leg of chromosome 6. Depending on the disease being treated, an acceptable donor will match the patient at all or most of the HLA loci (with the exception of umbilical cord blood).

##### **Conventional Preparative Conditioning for Hematopoietic SCT**

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. This permits subsequent engraftment and repopulation of bone marrow space with presumably normal hematopoietic stem cells obtained from the patient prior to undergoing bone marrow ablation. As a consequence, autologous HSCT is typically performed as consolidation therapy when the patient’s disease is in complete remission. Patients who undergo autologous HSCT are susceptible to chemotherapy-related toxicities and opportunistic infections prior to engraftment, but not GVHD.

The conventional (“classical”) practice of allogeneic HSCT involves administration of cytotoxic agents (e.g., 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 (GVM) effect mediated by nonself immunologic effector cells that develop after engraftment of allogeneic stem cells within the patient’s bone marrow space. While the slower GVM effect is considered to be the potentially curative component, 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 effects that include pre-engraftment opportunistic infections secondary to loss

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of endogenous bone marrow function and organ damage and failure caused by the cytotoxic drugs. Furthermore, in any allogeneic HSCT, immune suppressant drugs are required to minimize graft rejection and GVHD, which also increases susceptibility of the patient to opportunistic infections.

## **Reduced-Intensity Conditioning for Allogeneic HSCT**

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 traditional 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 (NRM) in the period during which the beneficial GVM effect of allogeneic transplantation develops. Although the definition of RIC remains arbitrary, with numerous versions employed, all seek to balance the competing effects of NRM and relapse due to residual disease. RIC regimens can be viewed as a continuum in effects, from nearly totally myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allogeneic HSCT 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 the purposes of this Policy, the term “reduced-intensity conditioning” will refer to all conditioning regimens intended to be nonmyeloablative, as opposed to fully myeloablative (traditional) regimens.

## **Non-Hodgkin Lymphoma (NHL)**

A heterogeneous group of lymphoproliferative malignancies, NHL usually originates in lymphoid tissue. Historically, uniform treatment of patients with NHL was hampered by the lack of a uniform classification system. In 1982, the Working Formulation (WF) was developed to unify different classification systems into one. The WF divided NHL into low-, intermediate-, and high-grade, with subgroups based on histologic cell type. Since our understanding of NHL has improved, the diagnosis has become more sophisticated and includes the incorporation of new immunophenotyping and genetic techniques. As a result, the WF has become outdated.

European and American pathologists proposed a new classification, the Revised European American Lymphoma (REAL) Classification, and an updated version of the REAL system, the new, 2008, World Health Organization (WHO) classification. The WHO/REAL classification recognizes 3 major categories of lymphoid malignancies based on morphology and cell lineage: B-cell neoplasms, T-cell/natural killer (NK)-cell neoplasms, and Hodgkin lymphoma.

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. Histologic transformation to higher grade lymphoma occurs in up to 70% of patients with low-grade lymphoma, and median survival with conventional chemotherapy is 1 year or less.

Follicular lymphoma (FL) is the most common indolent NHL (70%–80% of cases), and often the terms indolent lymphoma and FL are used synonymously. Also included in the indolent NHL are SLL/CLL, lymphoplasmatic lymphoma, marginal zone lymphomas, and cutaneous T-cell lymphoma.

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Aggressive NHL has a shorter natural history; however, 30%–60% of these patients can be cured with intensive combination chemotherapy regimens. Aggressive lymphomas include DLBCL, MCL, PTCL, anaplastic large cell lymphoma, and Burkitt's lymphoma.

Oncologists developed a clinical tool to aid in predicting the prognosis of patients with aggressive NHL (specifically DLBCL), referred to as the International Prognostic Index (IPI). Prior to the development of IPI in 1993, prognosis was predominantly based on disease stage.

## Mantle Cell Lymphoma (MCL)

Mantle cell lymphoma (MCL) 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. MCL is characterized by a chromosomal translocation t(11;14), and the term mantle cell lymphoma was proposed in 1992 by Banks et al. The number of therapeutic trials are not as numerous for MCL as for other NHL as it was not widely recognized until the REAL classification. MCL shows a strong predilection for elderly men, and the majority of cases (70%) present with disseminated (stage 4) disease and extranodal involvement is common. Localized MCL is quite rare. MCL has a median survival of approximately 2–4 years, and although most patients achieve remission with first-line therapy, relapse inevitably occurs, often within 12–18 months. MCL is rarely, if ever, cured with conventional therapy, and no standardized therapeutic approach to MCL is used.

There had been no generally established prognostic index for patients with MCL. Application of the IPI or FLIPI system to patients with MCL showed serious limitations, which included no separation of some important risk groups. In addition, some of the individual IPI and FLIPI risk factors, including number of extranodal sites and number of involved nodal areas showed no prognostic relevance, and hemoglobin showed no independent prognostic relevance in patients with MCL. Therefore, a new prognostic index for patients with MCL was developed, and should prove useful in comparing clinical trial results for MCL.

## Peripheral T-Cell Lymphoma (PTCL)

The majority of peripheral T-cell lymphomas are aggressive and fall into the category of PTCL, unspecified (PTCL-u) or not otherwise specified (PTCL-NOS), angioimmunoblastic or anaplastic large cell which, combined make up approximately 60–70% of T-cell lymphomas. PTCLs are less responsive to standard chemotherapy than DLBCLs and carry a worse prognosis than aggressive B-cell counterparts. Survival rates at 5 years with standard chemotherapy regimens range from 20–35%. The poor results with conventional chemotherapy have prompted exploration of the role of HSCT as therapy.

## **Staging**

The Ann Arbor staging classification is commonly used for the staging of lymphomas and is the scheme defined in the American Joint Committee on Cancer (AJCC) Manual for Staging Cancer. Originally developed for Hodgkin's disease, this staging scheme was later expanded to include non-Hodgkin's lymphoma.

### *Staging of Lymphoma: Ann Arbor Classification*

#### Stage I

Involvement of a single lymph node region (I) or of a single extralymphatic organ or site (IE)

#### Stage II

Involvement of 2 or more lymph node regions on the same side of the diaphragm (II) or localized involvement of extralymphatic organ or site and of one or more lymph node regions on the same side of the diaphragm (IIE).

#### Stage III

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Involvement of lymph node regions on both sides of the diaphragm (III) which may also be accompanied by localized involvement of extralymphatic organ or site (IIIE) or by involvement of the spleen (IIIS) or both (IIISE)

## Stage IV

Diffuse or disseminated involvement of one or more extralymphatic organs or tissues with or without associated lymph node enlargement.

### **Related Policies:**

Hematopoietic Stem-Cell Transplantation for CLL and SLL

Hematopoietic Stem-Cell Transplantation for Primary Amyloidosis

Hematopoietic Stem-Cell Transplantation for Waldenstrom Macroglobulinemia

Hematopoietic Stem-Cell Transplantation for Hodgkin Lymphoma

***\*\*\*Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

## **Policy**

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**BCBSNC will provide coverage for hematopoietic stem-cell transplantation for Non Hodgkin Lymphomas when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.**

**Some patients may be eligible for coverage under Clinical Trials. Refer to the policy on Clinical Trial Services.**

## **Benefits Application**

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This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

**Some health benefit plans may exclude benefits for transplantation.**

## **When Hematopoietic Stem-Cell Transplantation for Non-Hodgkin Lymphoma is covered**

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1. For patients with non-Hodgkin 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 may be considered medically necessary:
  - a. 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;
  - b. to achieve or consolidate a CR for those in a chemosensitive first or subsequent relapse; or
  - c. to consolidate a first CR in patients with diffuse large B-cell lymphoma, with an age-adjusted International Prognostic Index score that predicts a high- or high-intermediate risk of relapse.
2. For patients with mantle cell lymphoma:
  - a. autologous HSCT may be considered medically necessary to consolidate a first remission.

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- b. allogeneic HSCT, myeloablative or reduced-intensity conditioning, may be considered medically necessary as salvage therapy.
3. For patients with NHL B-cell subtypes considered indolent, either allogeneic HSCT using a myeloablative conditioning regimen or autologous HSCT may be considered medically necessary:
  - a. as salvage therapy for patients who do not achieve CR after first-line treatment (induction) with a full course of standard-dose chemotherapy; or
  - b. 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.
4. Reduced-intensity conditioning allogeneic HSCT may be considered medically necessary as a treatment of NHL in patients who meet criteria for an allogeneic HSCT but who do not qualify for a myeloablative allogeneic HSCT (see Policy Guidelines).
5. For patients with mature T-cell or NK-cell (peripheral T-cell) neoplasms:
  - a. autologous HSCT may be considered medically necessary to consolidate a first complete remission in high-risk subtypes. (see Policy Guidelines)
  - b. autologous or allogeneic HSCT (myeloablative or reduced-intensity conditioning) may be considered medically necessary as salvage therapy.

## When Hematopoietic Stem-Cell Transplantation for Non-Hodgkin Lymphoma is not covered

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1. For patients with mantle cell lymphoma:
  - a. autologous HSCT is considered investigational as salvage therapy.
  - b. allogeneic HSCT is considered investigational to consolidate a first remission.
2. Either autologous HSCT or allogeneic HSCT is considered investigational:
  - a. as initial therapy (i.e., without a full course of standard-dose induction chemotherapy) for any NHL;
  - b. to consolidate a first complete remission (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;
  - c. to consolidate a first complete remission (CR) for those with indolent NHL B-cell subtypes.
3. Tandem transplants are considered investigational to treat patients with any stage, grade, or subtype of NHL.
4. For Patients with mature T-cell or NK-cell (peripheral T-cell) neoplasms, allogeneic HSCT is considered investigational to consolidate a first remission.

**Note:** Small lymphocytic lymphoma (SLL) may be considered a node-based variant of chronic lymphocytic leukemia (CLL) and is considered in policy, Hematopoietic Stem-Cell Transplantation for CLL and SLL.

**Note:** Lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia is considered in policy, Hematopoietic Stem-Cell Transplantation for Waldenstrom Macroglobulinemia.

## Policy Guidelines

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# Hematopoietic Stem-Cell Transplant for Non-Hodgkin Lymphomas

Refer to the individual member's benefit booklet for prior review requirements.

Reduced-intensity conditioning (RIC) would be considered an option in patients who meet criteria for an allogeneic hematopoietic stem-cell transplant (HSCT) but whose age (typically older than 55 years) or comorbidities (e.g., liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy) preclude use of a standard conditioning regimen.

In patients who qualify for a myeloablative allogeneic HSCT on the basis of overall health and disease status, allogeneic HSCT using either myeloablative or RIC may be considered. However, a myeloablative conditioning regimen with allogeneic HSCT may benefit younger patients with good performance status and minimal comorbidities more than allogeneic HSCT with RIC.

The term salvage therapy describes therapy given to patients who have either: 1) failed to achieve complete remission after initial treatment for newly diagnosed lymphoma; or 2) relapsed after an initial complete remission.

A chemosensitive relapse is defined as relapsed non-Hodgkin Lymphoma (NHL) that does not progress during or immediately after standard-dose induction chemotherapy (i.e., achieves stable disease or a partial response).

Transformation describes a lymphoma whose histologic pattern has evolved to a higher grade lymphoma. Transformed lymphomas typically evolve from a nodular pattern to a diffuse pattern.

Tandem transplants usually are defined as the planned administration of 2 successive cycles of high-dose myeloablative chemotherapy, each followed by infusion of autologous hematopoietic stem cells, whether or not there is evidence of persistent disease following the first treatment cycle. Sometimes, the second cycle may use non-myeloablative immunosuppressive conditioning followed by infusion of allogeneic stem cells.

## High-risk (aggressive) T-cell and NK-cell neoplasms

The T-cell and NK-cell neoplasms are a clinically heterogeneous group of rare disorders, most of which have an aggressive clinical course and poor prognosis. The exception would include the following subtypes which typically have a relatively indolent and protracted course:

T-cell large granulocyte leukemia (T-LGL), chronic lymphoproliferative disorder of NK cells, early stage mycosis fungoides, primary cutaneous ALCL, and ALK+ ALCL.

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 complete remission in patients with aggressive B-cell lymphomas at high or high-intermediate risk of relapse.

No randomized studies have been conducted on the use of tandem HSCT for the treatment of non-Hodgkin lymphoma (NHL) and the published evidence comprises small numbers of patients.

Due in part to the relative rarity of the disease, randomized studies on the use of HSCT in mantle cell lymphoma (MCL) have not been conducted.

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

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patient populations including good- and poor- risk patients in the same study. This is due to the rarity and heterogeneity of this group of lymphomas. .

## **Billing/Coding/Physician Documentation Information**

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This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcsnc.com](http://www.bcsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable service codes: 38205, 38206, 38230, 38232, 38240, 38241, 38242, 38243, S2150*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

## **Scientific Background and Reference Sources**

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### **Bone Marrow Transplant for Non-Hodgkin Lymphoma**

BCBSA Medical Policy Reference Manual, 12/1/1999; 8.01.20

The Merck Manual of Diagnosis and Therapy, Seventeenth Edition, Centennial Edition, Section 11, Hematology and Oncology, Chapter 139, Leukemias. [www.merck.com](http://www.merck.com)

TEC Assessment, August, 2000; Volume 15, No. 9

BCBSA Medical Policy Reference Manual, 8/18/2000; 8.01.20

Specialty Matched Consultant Advisory Panel - 11/2002

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.20, 4/29/2003

Specialty Matched Consultant Advisory Panel - 11/2004

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.20, 12/14/05

Specialty Matched Consultant Advisory Panel - 11/2006

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.20, 6/12/08

Specialty Matched Consultant Advisory Panel - 11/2008

### **Hematopoietic Stem-Cell Transplantation for Non-Hodgkin Lymphomas**

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.20, 3/12/09

Senior Medical Director Review - 8/2009

Medical Director - 9/2010

Specialty Matched Consultant Advisory Panel – 11/2010

# Hematopoietic Stem-Cell Transplant for Non-Hodgkin Lymphomas

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.20, 2/10/2011

Medical Director – 5/2011

National Cancer Institute. Cellular classification of adult non-hodgkin lymphoma. Retrieved 11/2011 from <http://www.cancer.gov/cancertopics/pdq/treatment/adult-non-hodgkins/HealthProfessional/page2>

Specialty Matched Consultant Advisory Panel – 11/2011

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.20, 2/9/2012

Specialty Matched Consultant Advisory Panel – 12/2012

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.20, 2/14/2013

Specialty Matched Consultant Advisory Panel – 11/2013

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.20, 2/13/2014

Specialty Matched Consultant Advisory Panel- 11/2014

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.20, 2/12/2015

Specialty Matched Consultant Advisory Panel- 11/2015

Specialty Matched Consultant Advisory Panel- 11/2016

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.20, 9/14/2017

Specialty Matched Consultant Advisory Panel- 11/2017

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.20, 1/11/2018

Specialty Matched Consultant Advisory Panel- 11/2018

## **Policy Implementation/Update Information**

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### **Bone Marrow Transplant for Non-Hodgkin Lymphoma**

- 1/01 Specialty Matched Consultant Advisory Group.
- 2/01 Original policy issued.
- 2/03 Specialty Matched Consultant Advisory Panel meeting 11/2002. Revised the Policy statement to include the statement that, "Some patients may be eligible for coverage under Clinical Trials. Refer to the policy on Clinical Trial Services for Life-Threatening Conditions." Codes 86812-86822 removed; codes 38231 and 86915 deleted and codes 38242, 38205 and 38206 added to the Billing/Coding section. System coding changes.
- 1/04 Benefits Application and Billing/Coding sections updated for consistency.

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- 2/04 Individual CPT codes listed for CPT code ranges 38240-38242 under Billing/Coding section.
- 7/29/04 HCPCS code S2150 added to Billing/Coding section.
- 12/23/04 Specialty Matched Consultant Advisory Panel review 11/29/2004. Revised Description of Procedure or Service section. Added additional indications under "When covered" section which indicates; "1. High-dose chemotherapy with either autologous or allogeneic stem-cell support may be medically necessary in patients with either intermediate or high grade Non-Hodgkin lymphoma in any of the following circumstances: a. As salvage therapy for patients who do not achieve a complete remission after first-line treatment (induction) with a full course of standard-dose chemotherapy; b. To consolidate a first complete remission for patients with an age-adjusted IPI (International Prognostic Indicator) that predicts a high or high-intermediate risk of relapse; c. To achieve or consolidate complete remission in a chemosensitive first or subsequent relapse. 2. High-dose chemotherapy with either autologous or allogeneic stem-cell support may be considered medically necessary in patients with Non-Hodgkin lymphoma who are classified as indolent and for new subtypes defined by the WHO/REAL scheme in any of the following circumstances: a. As salvage therapy for patients who do not achieve a complete remission after first-line treatment (induction) with a full course of standard-dose chemotherapy; b. To achieve or consolidate complete remission for those in first or subsequent chemosensitive relapse, whether or not their lymphoma has undergone transformation to a higher grade." Added additional information under the "When not covered" section which indicates; "High-dose chemotherapy with either autologous or allogeneic stem-cell support is considered investigational in the following: 1. High-dose chemotherapy with either autologous or allogeneic stem-cell support is considered investigational in the following: a. As initial therapy without full course of standard-dose induction chemotherapy for all types of Non-Hodgkin Lymphoma; b. To consolidate a first complete remission for patients with Non-Hodgkin Lymphoma subtypes classified as intermediate or high grade with IPI scores that predict a low or low-intermediate risk of relapse; and c. To consolidate a first complete remission for those with Non-Hodgkin Lymphoma classified as indolent or new subtypes defined by the WHO/REAL scheme. 2. Tandem transplants with any stage, grade, or sub-type of Non-Hodgkin Lymphoma is considered investigational. 3. High-dose chemotherapy with allogeneic stem-cell support is considered investigational when Non-Hodgkin Lymphoma progresses or relapses soon after a prior course of high-dose chemotherapy with autologous stem-cell support." Additional information added to Policy Guidelines section related to "chemosensitive relapse". Policy number added to Key Words. "Hematopoietic" and "Opportunistic" added to definitions. Notice given 12/23/2004. Effective date of policy 3/3/2005.
- 12/11/06 Specialty Matched Consultant Advisory Panel review 11/6/2006. Clarified mantle cell lymphoma, marginal lymph node lymphoma and lymphoplasmacytoid lymphoma in "When Covered" section. References added.
- 12/22/08 Specialty Matched Consultant Advisory Panel review 11/13/08. Removed reference to "intermediate" lymphoma in #1. Under the "When covered" section. Added wording to "1.b. To consolidate a first complete remission (for patients with diffuse large B-cell lymphoma, only those with an age-adjusted International Prognostic Index ( IPI) score that predicts a high- or high-intermediate risk of relapse)". Removed the statement in #2, "and for marginal zone lymphoma with indolent behavior or lymphoma or lymphoplasmacytoid lymphoma". Under the "When not covered" section removed wording in 1.b "intermediate or high grade" and replaced it with "aggressive". Added

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"1.d. For peripheral T-cell lymphoma (PTCL) at any stage of disease." References added. Notice given 12/22/08. Effective date 3/30/09.

## **Bone Marrow Transplant for Non-Hodgkin Lymphoma**

9/14/09 Policy name changed from "Bone Marrow Transplant for Non Hodgkin Lymphomas" to Hematopoietic Stem-Cell Transplant for Non Hodgkin Lymphomas". Revised the "Description" section. Reworded the "Policy" statement to indicate; "BCBSNC will provide coverage for hematopoietic stem-cell transplantation for Non Hodgkin Lymphomas when it is determined to be medically necessary because the medical criteria and guidelines shown below are met." Removed reference to "high dose chemotherapy and stem cell support". Replaced the word "support" with "transplant" throughout the document as appropriate. Changed wording in the "When Covered" section from "1. High-dose chemotherapy with either autologous or allogeneic stem-cell support may be considered medically necessary in patients that are classed as aggressive or a mantle cell lymphoma with aggressive clinical behavior in any of the following circumstances:" to "Allogeneic stem-cell transplant (SCT) using myeloablative conditioning regimen or autologous stem-cell transplant may be considered medically necessary in patients with non-Hodgkin lymphoma (NHL) subtypes that are classed as aggressive any of the following circumstances:" In number 2. removed "High-dose chemotherapy with either autologous or allogeneic stem-cell support" and replaced with same wording as indicated in number 1. Added "3. Autologous stem-cell may be considered medically necessary in patients with mantle cell lymphoma to consolidate a first remission." and "4. Reduced-intensity conditioning allogeneic stem-cell transplantation may be considered medically necessary as a treatment of non-Hodgkin lymphoma in patients who meet the criteria above for an allogeneic stem-cell transplant but who do not qualify for a myeloablative allogeneic stem-cell transplant." Under the "When Not Covered" section removed reference to "High-dose chemotherapy" in number 1. Replaced the wording "Non-Hodgkin Lymphoma subtypes classified as aggressive" with "diffuse large B-cell lymphoma" in 1.b. Changed the wording from 1.c. "To consolidate a first complete remission for those with Non-Hodgkin Lymphoma classified as indolent or new defined by the WHO(World Health Organization)/REAL (Revised European and American Lymphoma) scheme" to "To consolidate a first complete remission for those with indolent Non-Hodgkin Lymphoma subtypes". Added the following to #3; (Note: This policy statement is based on a strict evidence-based analysis on outcomes of allotransplants after a failed autotransplant. However, see further discussion in the Policy Guidelines section.)". Added the following information to the "Policy Guidelines" section; "Reduced-intensity conditioning (RIC) would be considered an option in patients who meet criteria for an allogeneic stem-cell transplant (SCT) but whose age (typically older than 55 years) or comorbidities (e.g., liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy) preclude use of a standard conditioning regimen." "In patients who qualify for a myeloablative allogeneic hematopoietic SCT on the basis of overall health and disease status, allogeneic SCT using either myeloablative or RIC may be considered. However, a myeloablative conditioning regimen with allogeneic SCT may benefit younger patients with good performance status and minimal comorbidities more than allogeneic SCT with RIC." "Few NHL patients are considered eligible for allo-transplant relatively soon after a failed autotransplant. Thus, it is unlikely that prospective trials will ever be conducted to rigorously compare outcomes of this strategy with alternatives. Nevertheless, retrospective studies report long-term disease-free survival for a minority of patients treated this way. Note that a second transplant (autologous or allogeneic) may be considered to manage relapsed NHL, if the initial autotransplant was followed by a long disease-free interval." Reviewed with Senior Medical Director 8/26/09. References added. (btw)

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- 6/22/10 Policy Number(s) removed (amw)
- 1/4/11 Added the following to the “Description” section; “Related Policies: Hematopoietic Stem-Cell Transplantation for CLL and SLL and Hematopoietic Stem-Cell Transplantation for Primary Amyloidosis and Waldenstrom Macroglobulinemia.” Removed the following statement from the “Benefits Application” section; “Services for or related to the search for a donor are not covered.” No change to policy intent. “Added the following to the “When Not Covered” section; “Note: Small lymphocytic lymphoma may be considered a node-based variant of chronic lymphocytic leukemia (CLL) and is considered in policy, Hematopoietic Stem-Cell Transplantation for CLL and SLL. Lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia is considered in policy, Hematopoietic Stem-Cell Transplantation for Primary Amyloidosis and Waldenstrom Macroglobulinemia.” Updated “Policy Guidelines” section. Specialty Matched Consultant Advisory Panel review 11/29/2010. References added. (btw)
- 5/24/11 “Description” section revised. Formatting changes throughout policy for consistency. Added the following statements to the “When Covered” section; “2. For patients with mantle cell lymphoma: a. Autologous HSCT may be considered medically necessary to consolidate a first remission. b. Allogeneic HSCT, myeloablative or reduced-intensity conditioning, may be considered medically necessary as salvage therapy.” and “5. For patients with peripheral T-cell lymphoma: a. Autologous HSCT may be considered medically necessary to consolidate a first complete remission in high-risk peripheral T-cell lymphoma. (see Policy Guidelines) b. Autologous or allogeneic HSCT (myeloablative or reduced-intensity conditioning) may be considered medically necessary as salvage therapy.” Removed statement under the “When Not Covered” section indicating that “autologous or allogeneic HSCT is considered investigational for peripheral T-cell lymphoma (PTCL) at any stage of disease.” Inserted the following statements: “1. For patients with mantle cell lymphoma: a. Autologous HSCT is considered investigational as salvage therapy. b. Allogeneic HSCT is considered investigational to consolidate a first remission.” and “4. For Patients with peripheral T-cell lymphoma: a. allogeneic HSCT is considered investigational to consolidate a first remission.” “Policy Guidelines” section updated. References added. Medical Director review 5/5/2011. (btw)
- 1/10/12 Specialty Matched Consultant Advisory Panel review 11/30/2011. “Description” section revised. No change to policy intent. Reference added. (btw)
- 2/21/12 New 2012 CPT code, 38232, added to Billing/Coding section. (btw)
- 5/1/12 Clarification that peripheral T-cell lymphomas encompass mature T-cell and NK-cell neoplasms in the When and When Not Covered sections. Policy Guidelines updated. Reference added. Medical Director review 4/11/2012. (btw)
- 12/28/12 Specialty Matched Consultant Advisory Panel review 12/4/12. No change to policy intent. Added new 2013 CPT code, 38243 to Billing/Coding section. (btw)
- 4/1/13 Reference added. (btw)
- 12/10/13 Specialty Matched Consultant Advisory Panel review 11/20/2013. No change to policy intent. (btw)
- 4/15/14 Reference added. (btw)
- 12/9/14 Specialty Matched Consultant Advisory Panel review 11/24/2014. No change to policy intent. (lpr)

# Hematopoietic Stem-Cell Transplant for Non-Hodgkin Lymphomas

- 3/31/15 Updated Policy Guidelines. Reference added. No change to policy intent. (lpr)
- 12/30/15 Specialty Matched Consultant Advisory Panel review 11/18/2015. No change to policy statement. (lpr)
- 12/30/16 Specialty Matched Consultant Advisory Panel review 11/30/2016. No change to policy intent. (lpr)
- 12/15/17 Specialty Matched Consultant Advisory Panel review 11/29/2017. Reference added. No change to policy statement. (lpr)
- 1/15/19 Specialty Matched Consultant Advisory Panel review 11/2018. Reference added. No change to policy statement. (lpr)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.