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Corporate Medical Policy

Hematopoietic Cell Transplantation for CLL and SLL

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Description of Procedure or Service

Hematopoietic Cell Transplantation

Hematopoietic cell transplantation (HCT) 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 HCT) or from a donor (allogeneic HCT). 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 HCT. However, immunologic compatibility between donor and patient is a critical factor for achieving a good outcome of allogeneic HCT. 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 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.

Conventional Preparative Conditioning for HCT

The conventional ("classical") practice of allogeneic HCT 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 that develops 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 of endogenous bone marrow function and organ damage and failure caused by the cytotoxic drugs. Furthermore, in any allogeneic HCT, immune suppressant drugs are required to minimize graft rejection and GVHD, which also increases 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 prior to 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 prior to engraftment, but not GVHD.

Reduced-Intensity Conditioning for Allogeneic HCT

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 non-relapse 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 total 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 (conventional) regimens.

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 blood, bone marrow, lymph nodes, and spleen, while in SLL they are generally confined to lymph nodes. The Revised European-American/WHO Classification of Lymphoid Neoplasms considers B-cell CLL and SLL a single disease entity.

CLL 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 in nature, but can undergo transformation to a more aggressive form of disease (e.g., Richter's transformation). The median age at diagnosis of CLL is approximately 72 years, but it may present in younger individuals, often as poor-risk disease with significantly reduced life expectancy.

Treatment regimens used for CLL are generally the same as those used for SLL, and outcomes of treatment are comparable for the two diseases. Both low- and intermediate-risk CLL and SLL demonstrate relatively good prognoses with median survivals of 6 to 10 years, while the median survival of high-risk CLL or SLL may be only 2 years (see Policy Guidelines). 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 history prompted investigation of hematopoietic stem-cell transplantation as a possible curative regimen.

******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

BCBSNC will provide coverage for Hematopoietic Cell Transplantation for Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL) 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, Clinical Trial Services.

Benefits Application

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 Cell Transplantation for CLL and SLL is covered

Allogeneic hematopoietic cell transplantation may be considered medically necessary to treat chronic lymphocytic leukemia or small lymphocytic lymphoma in patients with markers of poor-risk disease (see Policy Guidelines).

Use of a myeloablative or reduced-intensity pretransplant conditioning regimen should be individualized based on factors that include patient age, the presence of comorbidities, and disease burden.

When Hematopoietic Cell Transplantation for CLL and SLL is not covered

Allogeneic hematopoietic cell transplantation is considered investigational to treat chronic lymphocytic leukemia or small lymphocytic lymphoma except as noted above.

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

Policy Guidelines

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

For individuals who have CLL/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 and a TEC Assessment. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related mortality and morbidity. Data suggests 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.

For individuals who have CLL/SLL who receive autologous hematopoietic cell transplantation, the evidence includes randomized controlled trials (RCTs), systematic reviews, and a TEC Assessment. 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 suggests 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.

Billing/Coding/Physician Documentation Information

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.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable 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

Bone Marrow Transplant for CLL and SLL

TEC Assessment, February, 2000; Volume 14, No. 20

BCBSA Medical Policy Reference Manual, 4/30/2000

BCBSA Medical Policy Reference Manual, 5/15/2002; 8.01.15

TEC Assessment, June, 2002; Volume 17, No. 4

Specialty Matched Consultant Advisory Panel - 11/2002

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.15, 7/15/2004

Specialty Matched Consultant Advisory Panel - 11/2004

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.15, 7/20/2006

Specialty Matched Consultant Advisory Panel - 11/2006

National Comprehensive Cancer Network. Non-Hodgkin's Lymphoma. Clinical Practice Guidelines in Oncology. V.3.2008. Retrieved 9/17/2008 from http://www.nccn.org/professionals/physician_gls/PDF/nhl.pdf

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.15, 9/11/2008

Specialty Matched Consultant Advisory Panel - 11/2008

Hematopoietic Stem-Cell Transplantation for CLL and SLL

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.15, 1/14/2010

Senior Medical Director Review - 5/3/2010

Specialty Matched Consultant Advisory Panel – 11/2010

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.15, 1/13/2011

Specialty Matched Consultant Advisory Panel – 11/2011

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.15, 1/12/2012

Specialty Matched Consultant Advisory Panel – 12/2012

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.15, 1/10/2013

Specialty Matched Consultant Advisory Panel – 11/2013

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.15, 1/9/2014

Specialty Matched Consultant Advisory Panel – 11/2014

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BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.15, 4/14/2016

Specialty Matched Consultant Advisory Panel – 11/2016

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BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.15, 1/12/2017

Medical Director review 1/2017

Specialty Matched Consultant Advisory Panel – 11/2017

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.15, 1/11/2018

Specialty Matched Consultant Advisory Panel – 11/2018

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.15, 1/17/2019

Specialty Matched Consultant Advisory Panel – 11/2019

Policy Implementation/Update Information

Bone Marrow Transplant for CLL and SLL

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.

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. 12/9/04 Specialty Matched Consultant Advisory Panel review 11/29/04. No changes to criteria. Revised Description of Procedure or Service section. Added rationale to Policy Guidelines section. Added policy number to Policy Key Words. "Hematopoietic" and "Opportunistic" added to Definitions. References added.

12/11/06 Specialty Matched Consultant Advisory Panel review 11/6/06. Updated "Policy Guidelines" section. References added.

12/22/08 Specialty Matched Consultant Advisory Panel review 11/13/2008. No change to policy statement. "Policy Guidelines" section updated. References added. (btw)

Hematopoietic Stem-Cell Transplantation for CLL and SLL

8/31/10 Policy name changed from "Bone Marrow Transplant for CLL and SLL" to Hematopoietic Stem-Cell Transplantation for CLL and SLL'. Removed policy number. Policy extensively revised. "Description" section revised. **"**Hematopoietic Stem-Cell Transplantation for Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL) when it is determined to be medically necessary because the medical criteria and guidelines shown below are met." Added two indications under the "When Covered" section to state; "Allogeneic hematopoietic stem-cell transplantation may be considered medically necessary to treat chronic lymphocytic leukemia or small lymphocytic lymphoma in patients with markers of poor-risk disease (see Guidelines). "Use of a myeloablative or reduced-intensity pretransplant conditioning regimen should be individualized based on factors that include patient age, the presence of comorbidities, and disease burden." Added the following statements to the "When Not Covered" section: "Allogeneic hematopoietic stem-cell transplantation is considered investigational to treat chronic lymphocytic leukemia or small lymphocytic lymphoma except as noted above." "Autologous hematopoietic stem-cell transplantation is considered investigational to treat chronic lymphocytic leukemia or small lymphocytic lymphoma." Policy Guidelines written to include staging information, "Table 1 Rai and Binet Classification for CLL/SLL", and "Table 2. Markers of Poor Prognosis in CLL/SLL". Reviewed by Senior Medical Director 5/3/2010. (btw)

1/4/11 Specialty Matched Consultant Advisory Panel review 11/29/2010. No change to policy statement.

3/29/11 References updated. (btw)

1/10/12 Specialty Matched Consultant Advisory Panel review 11/30/2011. "Description" section revised. No change to policy statement. (btw)

2/21/12 New 2012 CPT code, 38232, added to Billing/Coding section. (btw)

4/17/12 Reference added. (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)

2/26/13 Reference added. (btw)

12/10/13 Specialty Matched Consultant Advisory Panel review 11/20/2013. No change to policy intent. (btw)

4/1/14 Reference added. (btw)

12/9/14 Specialty Matched Consultant Advisory Panel review 11/24/2014. No change to policy intent. (lpr)

2/24/15 Reference added. (lpr)12/30/15 Specialty Matched Consultant Advisory Panel review 11/18/2015. No change to policy statement. (lpr)

5/31/16 Updated Policy Guidelines. Reference added. No change to policy statement. (lpr)

12/30/16 Specialty Matched Consultant Advisory Panel review 11/30/2016. No change to policy intent. (lpr)

Hematopoietic Cell Transplantation for CLL and SLL

4/28/17 Policy title changed from "Hematopoietic Stem Cell Transplantation for CLL and SLL" to Hematopoietic Cell Transplantation for CLL and SLL." Description and Policy Guidelines sections revised. Reference added. No change to policy intent. Medical Director review 1/2017. (lpr)

12/15/17 Specialty Matched Consultant Advisory Panel review 11/29/2017. 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)

12/31/19 Specialty Matched Consultant Advisory Panel review 11/20/2019. Reference added. No change to policy statement. (lpr)