

Corporate Medical Policy

Hematopoietic Stem-Cell Transplantation for Chronic Myelogenous Leukemia

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Origination:	2/2001
Last CAP Review:	11/2011
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Description of Procedure or Service

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).

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. 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.

Conventional Preparative Conditioning for HSCT

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 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 HSCT, 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 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

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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.

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 conventional full-dose myeloablative conditioning treatments. The goal of RIC is not only 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 (conventional) regimens.

Chronic Myelogenous Leukemia

Chronic myelogenous leukemia (CML) is a hematopoietic stem-cell disorder that is characterized by the presence of a chromosomal abnormality called the Philadelphia chromosome, which results from reciprocal translocation between the long arms of chromosomes 9 and 22. This cytogenetic change results in constitutive activation of BCR-ABL, a tyrosine kinase (TK) that stimulates unregulated cell proliferation, inhibition of apoptosis, genetic instability, and perturbation of the interactions between CML cells and the bone marrow stroma only in malignant cells.

The natural history of the disease consists of an initial (indolent) chronic phase, lasting a median of 3 years that typically transforms into an accelerated phase, followed by a "blast crisis," which is usually the terminal event. Conventional-dose regimens used for chronic-phase disease can induce multiple remissions and delay the onset of blast crisis to a median of 4–6 years. However, successive remissions are invariably shorter and more difficult to achieve than their predecessors.

Imatinib mesylate (Gleevec®), a selective inhibitor of the abnormal BCR-ABL TK protein, is considered the treatment of choice for newly diagnosed CML. While imatinib can be highly effective in suppressing CML in most patients, it is not curative and is ineffective in 20% to 30%, initially or due to development of BCR-ABL mutations that cause resistance to the drug. Two other TK inhibitors (TKIs, dasatinib, nilotinib) have received marketing approval from the U.S. Food and Drug Administration (FDA) to treat CML following failure or patient intolerance of imatinib. In any case, allogeneic SCT remains the only treatment capable of inducing durable remissions or cure in CML patients.

******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 Stem-Cell Transplantation for Chronic Myelogenous Leukemia when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

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If the medical criteria and guidelines are not met, some patients may be eligible for coverage under clinical trials. Refer to the policy, Clinical Trial Services for Life-Threatening Conditions.

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 Stem-Cell Transplant for Chronic Myelogenous Leukemia is covered

Allogeneic stem-cell transplantation using a myeloablative conditioning regimen may be considered medically necessary as a treatment of chronic myelogenous leukemia (see Policy Guidelines).

Allogeneic SCT using a reduced-intensity conditioning (RIC) regimen may be considered medically necessary as a treatment of chronic myelogenous leukemia in patients who meet clinical criteria for an allogeneic SCT but who are not considered candidates for a myeloablative conditioning allogeneic SCT.

When Hematopoietic Stem-Cell Transplant for Chronic Myelogenous Leukemia is not covered

Autologous stem-cell transplantation is considered investigational as a treatment of chronic myelogenous leukemia. BCBSNC does not provide coverage for investigational services or procedures.

Policy Guidelines

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

Some patients for whom a conventional myeloablative allotransplant could be curative may be considered candidates for reduced-intensity conditioning (RIC) allogeneic SCT. These include patients whose age (typically older than 60 years) or comorbidities (e.g., liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy, low Karnofsky Performance Status) preclude use of a standard myeloablative conditioning regimen.

For patients who qualify for a myeloablative allogeneic SCT on the basis of clinical status, either a myeloablative or RIC regimen may be considered medically necessary.

The NCCN recommends allogeneic bone marrow transplant as an alternative treatment option only for high-risk settings:

- patients who do not achieve hematologic remission after 3 months of imatinib therapy
- patients with no cytogenetic response or those in cytogenetic relapse at 6, 12, or 18 months, after achieving initial hematologic remission after 3 months of imatinib therapy
- patients progressing on a TKI to accelerated phase or blast crisis.

Autologous bone marrow transplant for CML is not addressed in the NCCN guidelines.

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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 service codes: 38205, 38206, 38230, 38232, 38240, 38241, 38242, 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 Chronic Myelogenous Leukemia

BCBSA Medical Policy Reference Manual, 12/1/1999

The Merck Manual of Diagnosis and Therapy, Seventeenth Edition, Centennial Edition, Section 11, Hematology and Oncology, Chapter 138, Leukemias. www.merck.com

BCBSA Medical Policy Reference Manual, 10/8/2002; 8.01.30

Specialty Matched Consultant Advisory Panel - 11/2002

National Comprehensive Cancer Network. (2003). NCCN practice guidelines in oncology, chronic myelogenous leukemia. Retrieved 9/7/2004 from http://www.nccn.org/physician_gls/PDF/cml.pdf.

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.30, 7/15/2004

Specialty Matched Consultant Advisory Panel - 11/2004

National Comprehensive Cancer Network. (2006). NCCN practice guidelines in oncology, chronic myelogenous leukemia. Retrieved 8/7/2006 from http://www.nccn.org/physician_gls/PDF/cml.pdf.

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.30, 9/27/2005

Specialty Matched Consultant Advisory Panel - 11/2006

National Comprehensive Cancer Network. (2008). NCCN practice guidelines in oncology, chronic myelogenous leukemia. Retrieved 9/17/2008 from http://www.nccn.org/professionals/physician_gls/PDF/cml.pdf

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.30, 6/12/2008

Specialty Matched Consultant Advisory Panel - 11/2008

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BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.30, 12/10/2009

Medical Director – 8/2010

Specialty Matched Consultant Advisory Panel - 11/2010

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.30, 6/9/2011

Specialty Matched Consultant Advisory Panel - 11/2011

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.30, 12/8/11

Policy Implementation/Update Information

Bone Marrow Transplant for Chronic Myelogenous Leukemia

- 1/01 Specialty Matched Consultant Advisory Group.
- 2/01 Original policy issued.
- 2/03 Specialty Matched Consultant Advisory Panel review 11/2002. No change in criteria. 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. Revised wording in When Bone Marrow Transplant for Chronic Myelogenous Leukemia is covered 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. Added the following statement to the "Policy" section; "If the medical criteria and guidelines are not met, some patients may be eligible for coverage under clinical trials. Refer to the policy, Clinical Trial Services for Life-Threatening Conditions." References added.
- 12/22/08 Specialty Matched Consultant Advisory Panel review 11/13/2008. No change to policy statement. References added. (btw)
- 6/22/10 Policy Number(s) removed. (amw)

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- 9/14/10 Policy name changed from Bone Marrow Transplant for Chronic Myelogenous Leukemia. "Description" section completely revised. Removed statement under "Benefit Application" indicating that "Services for or related to the search for a donor are not covered." Changed wording in the "When Covered" section to indicate; "Allogeneic stem-cell transplantation using a myeloablative conditioning regimen may

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be considered medically necessary as a treatment of chronic myelogenous leukemia (see Policy Guidelines). Allogeneic SCT using a reduced-intensity conditioning (RIC) regimen may be considered medically necessary as a treatment of chronic myelogenous leukemia in patients who meet clinical criteria for an allogeneic SCT but who are not considered candidates for a myeloablative conditioning allogeneic SCT.” Updated “Policy Guidelines” section. References updated. (btw)

- 1/4/11 Specialty Matched Consultant Advisory Panel review 11/29/2010. No change to policy statement. (btw)
- 1/10/12 Specialty Matched Consultant Advisory Panel review 11/30/2011. No change to policy statement. References added. (btw)
- 2/21/12 New 2012 CPT code, 38232, added to Billing/Coding section. (btw)
- 4/17/12 Reference added. (btw).

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.