

## Corporate Medical Policy

# Hematopoietic Stem-Cell Transplantation for Breast Cancer

**File Name:** hematopoietic\_stem\_cell\_transplantation\_for\_breast\_cancer  
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**Last CAP Review:** 4/2012  
**Next CAP Review:** 4/2013  
**Last Review:** 4/2012

### 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 policy entitled “Cord Blood as a Source of Stem Cells”.

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 Class I and Class II loci on 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 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. 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 non-self 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 of endogenous bone marrow function and organ damage and failure caused

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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 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 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 non-myeloablative, as opposed to fully myeloablative (traditional) regimens.

## **HSCT in Solid Tumors in Adults**

HSCT is an established treatment for certain hematologic malignancies; however, its use in solid tumors in adults continues to be largely experimental. Initial enthusiasm for the use of autologous transplant with the use of high-dose chemotherapy and stem cells for solid tumors has waned with the realization that dose intensification often fails to improve survival, even in tumors with a linear-dose response to chemotherapy. With the advent of reduced-intensity allogeneic transplant, interest has shifted to exploring the generation of alloreactivity to metastatic solid tumors via a graft-versus-tumor effect of donor-derived T cells.

### **Related Policies:**

Cord Blood as a Source of Stem Cells

**\*\*\*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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**Single or tandem autologous hematopoietic stem-cell transplantation is considered not medically necessary to treat any stage of breast cancer.**

**Allogeneic hematopoietic stem-cell transplantation is considered investigational to treat any stage of breast cancer. BCBS NC does not cover investigational services or procedures.**

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

## **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.**

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## **When Hematopoietic Stem-Cell Transplantation for Breast Cancer is covered**

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Hematopoietic stem-cell transplantation may be covered for members participating in a clinical trial, (see Corporate Medical Policy “Clinical Trial Services for Life-Threatening Conditions”).

## **When Hematopoietic Stem-Cell Transplantation for Breast Cancer is not covered**

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- Single or tandem autologous hematopoietic stem-cell transplantation is considered not medically necessary to treat any stage of breast cancer.
- Allogeneic hematopoietic stem-cell transplantation is investigational to treat any stage of breast cancer.

## **Policy Guidelines**

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

### **History of Hematopoietic Stem-Cell Transplant for Breast Cancer**

In the late 1980s/early 1990s, initial results of phase II trials for breast cancer and autologous hematopoietic stem-cell transplant (HSCT) were promising, showing high response rates in patients with metastatic disease who underwent high-dose consolidation, with a subset of up to 30% remaining disease-free for prolonged periods. In the early 1990s, larger prospective comparisons of conventional-dose chemotherapy to high-dose therapy with SCT were initiated but accrued slowly, with up to a decade from initiation to the reporting of results. The first results from randomized trials at a single institution in early stage and metastatic disease showed survival benefits, but were ultimately shown to be based on fraudulent data. In the interim, though, the treatment became almost standard of care, while many patients received high-dose therapy off protocol, further reducing accrual to ongoing randomized trials. The results of the randomized trials were presented beginning in 1999, and showed little survival benefit; subsequently, the number of HSCT procedures performed for breast cancer has fallen from thousands every year to only a few.

The 2011 National Comprehensive Cancer Network guidelines do not address the use of HSCT in the treatment of breast cancer.

### **Autologous SCT**

During 2003 and 2004, 4 trials reported final outcomes analyses from randomized comparisons of autologous HSCT versus conventional dose chemotherapy for adjuvant therapy of high-risk non-metastatic breast cancer. Two of the studies involved women with at least 4 positive axillary lymph nodes, and the other 2 at least 10 positive lymph nodes. The 4 studies pooled included 2,337 patients. Evidence from these trials did not support the conclusion that autologous HSCT improved outcomes when compared with conventional-dose adjuvant therapy, as no overall survival difference was seen in any of the studies.

A systematic review and meta-analysis published in 2007 included RCTs comparing autologous HSCT to standard dose chemotherapy in women with early, poor prognosis breast cancer, which included 13 trials to September 2006 with 5,064 patients. Major conclusions were that, at 5 years, event-free survival

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approached statistical significance for the high-dose group, but no overall survival differences were seen. There were more transplant-related deaths in the high-dose group. The end conclusion was that there was insufficient evidence to support routine use of autologous HSCT for treating early, poor prognosis breast cancer.

## **Allogeneic SCT**

Nonrandomized studies using reduced-intensity or myeloablative allogeneic HSCT for metastatic breast cancer have suggested a possible graft-versus-tumor effect, but remains unproven for this indication.

## **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.bcbsnc.com](http://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, 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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### **For Policy titled: Bone Marrow Transplant for Breast Cancer**

BCBSA TEC Evaluation, February 1999; Tab 24

BCBSA Medical Policy Reference Manual, 12/1/1999; 8.01.27

Specialty Matched Consultant Advisory Panel - 11/2002

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.27, 12/18/2002

Specialty Matched Consultant Advisory Panel - 11/2004

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.27, 12/14/05

Specialty Matched Consultant Advisory Panel - 3/2006

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.27, 12/13/07

Specialty Matched Consultant Advisory Panel - 3/2008

### **For Policy renamed Hematopoietic Stem-Cell Transplantation for Breast Cancer**

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.27, 12/10/2009

Specialty Matched Consultant Advisory Panel – 5/2010

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.27, 1/13/2011

Specialty Matched Consultant Advisory Panel – 4/2011

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.27, 1/12/12

Specialty Matched Consultant Advisory Panel – 4/2012

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## Policy Implementation/Update Information

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### **For Policy titled: Bone Marrow Transplant for Breast Cancer**

- 1/01 Specialty Matched Consultant Advisory Group.
- 4/01 Original policy issued.
- 2/03 Specialty Matched Consultant Advisory Panel meeting 11/2002 and 12/2002. Revised policy under "when it is covered" to clarify that services may be covered for members participating in a clinical trial. Removed specific criteria from "when it is covered" and "when it is not covered" sections. Term "refractory" removed from the Medical Term Definitions. 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 section. "Hematopoietic" and "Opportunistic" added to Definitions. References added.
- 4/10/06 Specialty Matched Consultant Advisory Panel meeting 3/15/2006. No changes to policy. References added.
- 6/2/08 Specialty Matched Consultant Advisory Panel meeting 3/17/2008. No changes to policy. Format changes for consistency. Policy status changed to "Active policy, no longer scheduled for routine review." References added. (btw)
- 6/22/10 Policy Number(s) removed. (amw)

### **For Policy renamed Hematopoietic Stem-Cell Transplantation for Breast Cancer**

- 7/6/10 Policy name changed from Bone Marrow Transplant for Breast Cancer. Policy status changed from "Active policy, no longer scheduled for literature review" to "Active" status. Description section extensively revised. "When Hematopoietic Stem-Cell Transplantation Is Not Covered" changed to read "Single or tandem autologous hematopoietic stem-cell transplantation is considered not medically necessary to treat any stage of breast cancer. Allogeneic hematopoietic stem-cell transplantation is investigational to treat any stage of breast cancer." Policy Guidelines section updated with new research information. Reference added. (btw)
- 5/24/11 Specialty Matched Consultant Advisory Panel review 4/27/2011. The following statement was removed from the "Policy" section; "BCBSNC will provide coverage for Hematopoietic Stem-Cell Transplantation for Breast Cancer when it is determined to be medically necessary because the medical criteria and guidelines shown below are met." The policy continues to have the statement in the "When Covered" section indicating; "Hematopoietic stem-cell transplantation may be covered for members participating in a clinical trial, (see Clinical Trial Services for Life-Threatening Conditions policy)." No change to policy intent. References added. (btw)
- 2/21/12 Added new 2012 CPT code, 38232, to Billing/Coding section. (btw)
- 5/15/12 Specialty Matched Consultant Advisory Panel review 4/18/2012. No change to policy intent. Reference added. Single or tandem autologous hematopoietic stem-cell transplantation changed from investigational to not medically necessary.(btw)

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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.