



# CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

**Subject Stem-Cell Transplantation for Breast Cancer**

**Effective Date ..... 6/15/2011**  
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**Coverage Policy Number ..... 0100**

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### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2011 CIGNA

## Coverage Policy

**CIGNA does not cover hematopoietic stem-cell transplantation for the treatment of breast cancer because it is considered experimental, investigational or unproven.**

## General Background

Breast cancer is a malignant tumor that starts from cells of the breast, usually the ducts or lobules, and may be invasive, or noninvasive. Although breast cancer is more common in females, it does occur rarely in males. Pathology and overall survival in males is similar to that of women with breast cancer (NCI, 2011). Most invasive breast cancers are adenocarcinomas, which can be classified into several different subtypes with varying prognostic implications. The American Joint Committee on Cancer staging system provides a strategy for grouping patients with respect to prognosis. Therapeutic decisions are formulated in part according to staging categories but primarily according to tumor size, lymph node status, estrogen-receptor and progesterone-

receptor levels in the tumor tissue, menopausal status, and the general health of the patient (National Cancer Institute [NCI], 2011). Breast cancer is commonly treated with various combinations of surgery, radiation therapy, chemotherapy, and hormone therapy. Hematopoietic stem-cell transplantation (HSCT) has been proposed as a treatment option for individuals with breast cancer.

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

Hematopoietic stem-cell transplantation (HSCT) refers to the transplantation of hematopoietic stem cells (HSC) from a donor into a recipient. HSCT can be either autologous (i.e., using the patient's own stem cells) or allogeneic (i.e., using stem cells from a donor).

### **Autologous Hematopoietic Stem-Cell Transplantation (HSCT)**

A correlation between dose-intensity of chemotherapy, response rate and outcomes in high-risk primary and metastatic breast cancer has been suggested by research studies. The use of high-dose chemotherapy with autologous HSCT is based on the hypothesis that major dose escalations within the myeloablative range are needed to overcome tumor cell resistance and produce a meaningful clinical improvement. HSCT allows for an increase in the dose well beyond normal bone-marrow tolerance (Nieto, 2000). Myeloablative chemotherapy followed by autologous HSCT has resulted in improved response rates for some individuals; however, an overall survival (OS) benefit has not been demonstrated.

Biron et al. (2008) reported the results of Pegase 03, a multi-center, prospective randomized phase III trial evaluating the impact of first-line high dose chemotherapy with autologous HSCT on OS, disease-free survival (DFS) and response rate in patients with metastatic breast cancer that responded to induction therapy. Although the response rate was improved in the intensification arm, the OS was not improved at three years (27% and 33.6% for the observation versus intensification arms, respectively,  $p=0.8$ ). Median OS rates were 23.9 months and 22.9 months for the observation versus intensification arms, respectively.

Tokuda et al. (2008) conducted a multi-center, phase III randomized controlled trial (RCT) to study the effectiveness of high-dose chemotherapy as consolidation of the treatment of high-risk postoperative breast cancer in patients with stage I to IIIB breast cancer involving 10 or more axillary lymph nodes. The five-year relapse-free survival rates of 47 eligible patients in the standard-dose and 48 eligible patients in the high-dose chemotherapy arm were 37% and 52%, respectively, on an intent-to-treat basis, ( $p=0.17$ ). Five-year OS of all randomized patients were 62% and 63% for the standard-dose and high-dose arms, respectively ( $p=0.78$ ).

Zander et al. (2008) reported the six-year outcomes of patients who participated in a multi-center RCT of high-dose adjuvant chemotherapy with autologous HSCT ( $n=150$ ) versus standard-dose chemotherapy ( $n=152$ ). Estimated five-year event-free survival rates were 42% and 49% in the standard-dose and high-dose treatment arms, respectively. Estimated five-year OS rates were 62% and 64% in the standard-dose and high-dose arms, respectively.

Crump et al. (2008) conducted a multi-center RCT comparing progression-free survival, OS, and quality of life in 112 women with metastatic breast cancer. Treated-related mortality in the high-dose arm was 6%. At 24 months the median OS was 28 and 24 months for the standard-dose and high-dose therapy arms, respectively ( $p=0.43$ ). Actual OS rates at three years were 38% and 37% for the standard-dose and high-dose therapy arms, respectively. Median progression-free survival was nine months and 11 months for the standard-dose and high-dose therapy arms, respectively.

Additional RCTs and meta-analyses have examined outcomes related to the effectiveness of autologous HSCT for the treatment of breast cancer. Although response rates and disease-free and/or relapse-free survival rates were noted to be improved in some individuals, no statistically significant survival benefit was noted in the majority of patients (Farquhar, 2007; Moore, 2007; Kroger, 2006; Vredenburgh, 2006; Coombes, 2005; Isaacs, 2005; Nitz, 2006; Peters, 2005; Farquhar, 2004; Leonard, 2004; Tallman, 2003).

### **Allogeneic Hematopoietic Stem-Cell Transplant (HSCT)**

Data are lacking in the published peer-reviewed scientific literature regarding the safety and effectiveness of allogeneic HSCT for the treatment of breast cancer. To date clinical studies have been limited by small patient populations utilizing allogeneic HSCT. The role of this therapy has not yet been established for this indication.

### **Professional Societies/Organizations**

**National Cancer Institute (NCI):** The NCI (2011) notes “The information to date does not support the use of high-dose chemotherapy outside the context of a randomized clinical trial.”

**American Cancer Society (ACS):** The ACS (2011) notes “At this time most experts recommend that women with breast cancer not receive high-dose chemotherapy, except as part of a clinical trial.”

### Summary

There is insufficient evidence in the published, peer-reviewed scientific literature to support the safety and effectiveness of hematopoietic stem-cell transplantation (HSCT) for the treatment of breast cancer. Although a subject of ongoing research, at this time the role of HSCT has not been established for this indication.

## Coding/Billing Information

**Note:** This list of codes may not be all-inclusive.

### Experimental/Investigational/Unproven/Not Covered:

CPT* Codes	Description
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing
38210	Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-cell depletion
38211	Transplant preparation of hematopoietic progenitor cells; tumor cell depletion
38212	Transplantation preparation of hematopoietic progenitor cells; red blood cell removal
38213	Transplant preparation of hematopoietic progenitor cells; platelet depletion
38214	Transplantation preparation of hematopoietic progenitor cells; plasma (volume) depletion
38215	Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear, or buffy coat layer
38230	Bone marrow harvesting for transplantation
38240	Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic
38241	Bone marrow or blood-derived peripheral stem cell transplantation; autologous
38242	Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic donor lymphocyte infusions

HCPCS Codes	Description
S2140	Cord blood harvesting for transplantation, allogeneic
S2142	Cord blood-derived stem-cell transplantation, allogeneic
S2150	Bone marrow or blood-derived stem cells (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications; including pheresis and cell preparation/storage; marrow ablative therapy; drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days or pre-and post-transplant care in the global definition

ICD-9-CM Diagnosis Codes	Description
174.0-174.9	Malignant neoplasm of female breast
175.0-175.9	Malignant neoplasm of male breast
198.81	Secondary malignant neoplasm of breast
233.0	Carcinoma in situ of breast

**\*Current Procedural Terminology (CPT®) ©2010 American Medical Association: Chicago, IL.**

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## Policy History

<b>Pre-Merger Organizations</b>	<b>Last Review Date</b>	<b>Policy Number</b>	<b>Title</b>
CIGNA HealthCare	6/15/2008	0100	Stem-Cell Transplant for Breast Cancer
Great-West Healthcare	10/07/2005	05.327.02	Bone Marrow Transplantation (BMT) for Breast Cancer

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