Stem-Cell Transplantation for Breast Cancer

Table of Contents

Coverage Policy .......................................................... 1
Overview ..................................................................... 1
General Background .................................................. 1
Coding/Billing Information ....................................... 3
References .................................................................. 4

Related Coverage Resources

Cryoablation of Breast Lesions
Mammary Ductoscopy, Aspiration and Lavage
Screening Mammography
Microwave Thermotherapy for Breast Cancer
Prophylactic Mastectomy

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, 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 supersedes 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. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Coverage Policy

Hematopoietic stem-cell transplantation for the treatment of breast cancer is considered experimental, investigational or unproven.

Overview

This Coverage Policy addresses hematopoietic stem-cell transplantation (HSCT) for the treatment of breast cancer.

HSCT is a method of replacing immature blood-forming cells in the bone marrow that have been destroyed by drugs, radiation, or disease. It may be autologous (i.e., using a person’s own stem cells) or allogeneic (i.e., using stem-cells donated by someone else).

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, 2016b). 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], 2016a). 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 (HDC) 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. 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.

A systematic review of 14 randomized controlled trials including 5600 women was reported by Farquhar et al. (2016). Women with evidence of multiple axillary lymph node involvement and no evidence of distant metastasis were randomized to receive high-dose chemotherapy and autograft (bone marrow transplantation or HSCT) versus chemotherapy without autograft. Data suggest that high-dose chemotherapy does not increase the likelihood of overall survival at any stage of follow-up (i.e., three, five, six, eight and 12-years: p=0.51, p=0.88, p=0.36, p=0.13, p=0.07, respectively). There was an increased risk of treatment-related deaths with high-dose chemotherapy. There was high-quality evidence that high-dose chemotherapy improves the likelihood of event-free survival at three years but this effect was no longer apparent at five, six, eight and 12-years of follow-up (p=0.003 and p=0.13, p=0.69, p=0.06, p=0.13, respectively).

Wang et al. (2012) reported a meta-analysis of fourteen prospective randomized clinical trials (RCT) involving 5747 women (HDC with autologous transplantation [HDCT], n=2987; control, n=2850) with primary breast cancer. The primary outcome was disease-free survival (DFS) and OS. Secondary endpoints included treatment-related mortality (TRM) and second (non-breast) cancers. Patients randomly assigned to HDCT and autologous transplantation (HDCT) had a statistically significantly greater risk of death than those assigned to chemotherapy only (relative risk [RR] = 3.42) as reported in 10 studies. The risk of second (non-breast) cancers was not significantly different in the HDCT group compared with chemotherapy only (RR = 1.28) as reported in 11 studies. A DFS benefit was noted with HDCT (hazard ratio [HR] = 0.89); however, the difference in OS was not statistically significant (RR =0.91, p= 0.062). Data do not suggest a benefit regarding the use of HDCT and autologous transplantation for the treatment of primary breast cancer.

Berry et al. (2011a) reported results of an analysis of six RCT involving 866 women with metastatic breast cancer (MBC). Women were randomized to the HDCT (n=447) or a control regimen without transplant (n=419). Results were presented as the HR for OS based on the indicated comparison with 95% confidence intervals. The adjusted HR of OS comparing HDCT with control was 0.89 (p=0.13). After adjusting for trial, age, and hormone receptor status, the HR per unit increase of maximum dose intensity (MDI) was 0.94 (p=0.046). As regards progression-free survival (PFS), after adjusting for trial, age, and hormone receptor status, the HR of HDC compared with control per unit increase in MDI was 0.88 (p<.001). Although data suggest a small non-significant OS difference between HDCT and control (p=0.08), the authors concluded that the associations are weak, and interactions are not sufficiently robust to withstand adjustments for multiple comparisons.

Berry et al. (2011b) also merged data from 15 RCTs involving 6210 total patients (HDCT, n=3118; control, n=3092) with high-risk primary breast cancer. Prospectively defined primary end points were relapse-free survival (RFS) and OS. After analysis was adjusted for trial, age, number of positive lymph nodes, and hormone receptor status, HDCT was associated with a non-significant 6% reduction in the risk of death (HR, 0.94; p=.13) and a significant 13% reduction in the risk of recurrence (HR, 0.87; p<.001). After analysis was adjusted for trial, age, number of positive lymph nodes, and hormone receptor status patients in the HDCT arm had a highly
significant 16% increase in the risk of death after disease recurrence compared with patients in the control arm (HR, 1.16; p<.001). The authors concluded that HDCT does not have a statistically significant benefit in OS. The authors also note that data from both studies leave open the possibility of a modest reduction in the hazards of OS in the range of 5% to 10%, but neither was able to identify subsets of patients who may benefit from HDC.

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 (Biron, 2008; Takuda, 2008; Zander, 2008; Crump, 2008; 2007, Moore, 2007; Kroger, 2006; Vredenburgh, 2006; Coombes, 2005; Isaacs, 2005; Nitz, 2006; Peters, 2005; Leonard, 2004; Tallman, 2003).

**Allogeneic Hematopoietic Stem-Cell Transplantation (HSCT)**

High quality, randomized control trial 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], 2017):** Regarding metastatic disease, treatment guidelines note that no overall survival or relapse-free survival benefit was noted for patients receiving high-dose chemotherapy with stem cell support compared with conventional chemotherapy. Because of the absence of data suggesting a benefit from high-dose chemotherapy with stem cell support, this should be considered only as part of a clinical trial.

**The American Board of Internal Medicine’s (ABIM) Foundation Choosing Wisely® Initiative (2014):** No relevant statements.

**Use Outside of the US**

No relevant information.

**Coding/Billing Information**

**Note:** 1) This list of codes may not be all-inclusive.  
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

**Considered Experimental/Investigational/Unproven when used to report hematopoietic stem-cell transplantation for the treatment of breast cancer:**

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>38205</td>
<td>Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic</td>
</tr>
<tr>
<td>38206</td>
<td>Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous</td>
</tr>
<tr>
<td>38207</td>
<td>Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage</td>
</tr>
<tr>
<td>38208</td>
<td>Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor</td>
</tr>
<tr>
<td>38209</td>
<td>Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing, per donor</td>
</tr>
<tr>
<td>38210</td>
<td>Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-cell depletion</td>
</tr>
<tr>
<td>38211</td>
<td>Transplant preparation of hematopoietic progenitor cells; tumor cell depletion</td>
</tr>
<tr>
<td>38212</td>
<td>Transplant preparation of hematopoietic progenitor cells; red blood cell removal</td>
</tr>
<tr>
<td>38213</td>
<td>Transplant preparation of hematopoietic progenitor cells; platelet depletion</td>
</tr>
</tbody>
</table>
38214 Transplant 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; allogeneic

38232 Bone marrow harvesting for transplantation; autologous

38240 Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor

38241 Hematopoietic progenitor cell (HPC); autologous transplantation

38242 Allogeneic lymphocyte infusions

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S2140</td>
<td>Cord blood harvesting for transplantation, allogeneic</td>
</tr>
<tr>
<td>S2142</td>
<td>Cord blood-derived stem cell transplantation, allogeneic</td>
</tr>
<tr>
<td>S2150</td>
<td>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 of pre-and post-transplant care in the global definition</td>
</tr>
</tbody>
</table>


References


