Medical Policy Manual

Topic: Hematopoietic Stem-Cell Transplantation for Breast Cancer

Date of Origin: May 2010

Section: Transplant

Last Reviewed Date: January 2014

Policy No: 45.29

Effective Date: April 1, 2014

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

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 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 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 (conventional) 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.

MEDICAL POLICY CRITERIA

I. Single Autologous HSCT

Single autologous HSCT is considered **not medically necessary** to treat any stage of breast cancer.

II. Tandem Autologous HSCT

Tandem autologous HSCT is considered **not medically necessary** to treat any stage of breast cancer.

III. Allogeneic HSCT

Allogeneic HSCT is considered **investigational** to treat any stage of breast cancer.

SCIENTIFIC EVIDENCE[1]

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.[2] 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.[2] 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.[2] 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.[2] 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.[2]

Autologous Stem-Cell Transplant

The PBT-1 trial randomized patients with a complete or partial response to induction therapy for previously untreated metastatic breast cancer to autologous HSCT (n=101) or to conventional-dose maintenance chemotherapy (n=83) for up to 2 years.[3] Of 553 patients enrolled and given initial induction therapy, only 310 achieved a partial (n=252) or complete (n=58) response, and only 199 were randomized. Of 72 partial responders assigned to the HSCT arm after initial induction therapy, only 5 (7%) were converted to complete responses. Median survival (24 vs. 26 months) and overall survival at 3 years (32% vs. 38%) did not differ between arms. There also were no statistically significant differences between arms in time to progression or progression-free survival at 3 years. While treatment

duration was substantially shorter for those randomized to HSCT, acute morbidity was markedly more severe than after conventional-dose maintenance.

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. An editorial that accompanied one of the trials briefly reviewed and commented on factors contributing to the diffusion of autologous HSCT into routine practice of the treatment of certain breast cancer patients, without adequate testing in randomized clinical trials.[4]

A Cochrane systematic review and meta-analysis published in July 2005 pooled data from six randomized controlled trials (RCTs) on metastatic breast cancer reported through November 2004 (N=438 randomized to autologous HSCT, 412 to conventional dose therapy).[5] The relative risk (RR) for treatment-related mortality was significantly higher in the arm randomized to HSCT (15 vs. 2 deaths; RR=4.07; 95% confidence interval [CI]: 1.39–11.88). Treatment-related morbidity also was more severe among those randomized to HSCT. Overall survival did not differ significantly between groups at 1, 3, or 5 years after treatment. Statistically significant differences in event-free survival at 1 year (RR=1.76; 95% CI: 1.40–2.21) and 5 years (RR=2.84; 95% CI: 1.07–7.50) favored the HSCT arms. Only 1 of the 6 included trials that had followed up all patients for at least 5 years. Reviewers recommended further follow-up for patients randomized in the other 5 trials. They also concluded that, in the interim, patients with metastatic breast cancer should not receive HSCT outside of a clinical trial, since available data showed greater treatment-related mortality and toxicity without improved overall survival.

A second Cochrane systematic review and meta-analysis, also published in July 2005, included data from 13 RCTs on patients with high-risk (poor prognosis) early breast cancer (N=2,535 randomized to HSCT, 2,529 to conventional dose therapy).[6] Treatment-related mortality was significantly greater among those randomized to HDC/AuSCT (65 vs. 4 deaths; RR=8.58; 95% CI: 4.13, 17.80). Treatment-related morbidity also was more common and more severe in the high-dose arms. There were no significant differences between arms in overall survival rates at any time after treatment. Event-free survival was significantly greater in the HSCT group at 3 years (RR=1.12; 95% CI: 1.06, 1.19) and 4 years (RR=1.30; 95% CI: 1.16, 1.45) after treatment. However, the two groups did not differ significantly with respect to event-free survival at 5 and 6 years after treatment. Quality of life scores were significantly worse in the HSCT arms than in controls soon after treatment, but differences were no longer statistically significant by 1 year. Reviewers concluded that available data were insufficient to support routine use of HSCT for patients with poor-prognosis early breast cancer.

Hanrahan et al., with a median follow-up of 12 years, demonstrated no recurrence-free or overall survival advantage for patients with high-risk primary breast cancer treated with autologous HSCT after standard dose chemotherapy (n=39) versus standard chemotherapy alone (n=39).[7] Coombes and colleagues reported on autologous HSCT as adjuvant therapy for primary breast cancer in women free of metastatic disease, with a median follow-up of 68 months.[8] A total of 281 patients were randomized to receive standard chemotherapy or high-dose chemotherapy with HSCT. They found no significant difference in relapse-free survival or overall survival (overall survival hazard ratio 1.18, 95% CI: 0.80-1.75, p=0.40).

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.[9] Major conclusions were that, at 5 years, event-free survival 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.

Crump and colleagues reported the results of a randomized trial of women who had not previously been treated with chemotherapy, and had metastatic breast cancer or locoregional recurrence after mastectomy.[10] After initial response to induction therapy, 112 women were allocated to standard chemotherapy and 112 to autologous HSCT. After a median follow-up of 48 months, 79 deaths were observed in the high-dose group and 77 in the standard. No difference in overall survival was observed between the two groups after a median follow-up of 48 months, with median overall survival being 24 months in the HSCT group (95% CI: 21–35 months) and 28 months for the standard chemotherapy group (95% CI: 22–33 months; hazard ratio: 0.9; 95% CI: 0.6–1.2; p=0.43).

Biron et al. reported the results of a phase III, open, multicenter, prospective trial of women with metastatic breast cancer (and/or local or regional relapse beyond curative treatment by surgery or radiation).[11] After a complete or at least 50% partial response to induction therapy, 88 women were randomized to HSCT, and 91 to no further treatment. No overall survival difference was seen between the two groups, with 3-year survival 33.6% in the high-dose group and 27.3% in the observation group (p=0.8).

Zander et al. reported survival data after 6 years of follow-up[12] on a trial that had previously been reported after 3.8 years of follow-up.[5] Women with surgically resected breast cancer and axillary lymph node dissection with 10 or more positive axillary lymph nodes but no evidence of metastatic disease were randomized to standard chemotherapy (n=152) or HSCT (n=150). No difference in overall survival was observed; the estimated 5-year overall survival rate in the standard arm was 62% (95% CI: 54-70%) and 64% (95% CI: 56-72%) in the high-dose transplant group.

Nieto and colleagues performed a meta-analysis of all randomized trials published or updated since 2006 focusing on those that compared high-dose chemotherapy with standard-dose chemotherapy for high-risk primary breast cancer.[13] The meta-analysis of 15 randomized trials involving patients with high-risk primary breast cancer or metastatic disease (n=6,102) detected an absolute 13% event-free survival benefit in favor of high-dose chemotherapy and autologous HSCT (p=0.0001) at a median follow-up of 6 years. The absolute differences in disease-specific and overall survival did not reach statistical significance (7 % and 5%, respectively). Subset analyses suggested that high-dose chemotherapy could be particularly effective in patients with triple negative tumors (hormone receptor and HER2-negative). The authors concluded that high-dose chemotherapy remains a valid research strategy in certain subpopulations with high-risk primary breast cancer, for example those with triple negative tumors.

Berry and colleagues performed a meta-analysis with individual patient data from 15 randomized trials comparing autologous HSCT with HDC (n=3,118) to standard chemotherapy (n= 3,092) for patients with high-risk primary breast cancer.[14] A survival analysis was adjusted for trial, age, number of positive lymph nodes, and hormone receptor status. HSCT was associated with a non-significant 6% reduction in risk of death (HR: 0.94; 95% CI: 0.87-1.02; p=0.13) and a significant reduction in the risk of recurrence (HR: 0.87; 95% CI: 0.81-0.93; p<0.001). Toxic death was higher in the HSCT group with 72 (6%) of 1,207 deaths in these trial arms compared to 17 (1.4%) of 1,261 deaths in the standard therapy arms. In a subgroup analysis, the authors investigated whether age, number of positive lymph nodes, tumor size, histology, hormone receptor status, or HER2 status impacted survival when comparing HSCT versus standard treatment. The authors found that HER2-negative patients receiving HSCT had a 21% reduction in the risk of death and HER2-negative and hormone receptor negative patients receiving HSCT had a 33% reduction in the risk of death. In their discussion, the authors state

that this relationship could be spurious due to the amount of missing data on HER2 status and suggest that HSCT is unlikely to show much benefit in these subgroups of patients.

A meta-analysis by Wang et al. included aggregate data from 14 trials (n=5,747) published since March 2010.[15] Clinical trials of patients receiving HSCT as a first-line treatment for primary breast cancer were eligible for inclusion. A higher treatment-related mortality was found among the patients who received HSCT compared to standard chemotherapy (RR=3.42, 95% CI: 1.32-8.86). Overall survival did not differ significantly between groups with a hazard ratio of 0.91 (95% CI: 0.82-1.00) for the HSCT compared to standard treatment. Risk of secondary, non-breast cancer was higher in the HSCT group (RR=1.28, 95% CI: 0.82-1.98). Disease free survival was better in the HSCT group compared to chemotherapy alone (RR=0.89, 95% CI: 0.79-0.99). Patients receiving HSCT had a greater risk of dying during remission than patients treated with nonmyeloablative chemotherapy due to the toxicity of the regimen. This increase in treatment-related mortality may help explain why there was no observed overall survival benefit for patients receiving HSCT when disease-free survival was observed to be superior to standard chemotherapy.

Tandem Autologous Stem-Cell Transplant

Kroger et al. reported on the comparison of single versus tandem autologous HSCT in 187 patients with chemotherapy-sensitive metastatic breast cancer.[16] Only 52 of 85 patients completed the second high-dose chemotherapy cycle in the tandem arm, mostly due to withdrawal of consent (most common reason), adverse effects, progressive disease, or death. The rate of complete remission was 33% in the single-dose arm versus 37% in the tandem arm (p=.48). Although there was a trend toward improved progression-free survival after tandem HSCT, median overall survival tended to be greater after single versus tandem high-dose chemotherapy (29 vs. 23.5 months, respectively; p=0.4). The authors concluded that tandem HSCT cannot be recommended for patients with chemotherapy-sensitive metastatic breast cancer because of a trend for shorter overall survival and higher toxicity compared with single HSCT.

Schmid et al. published results of 93 patients without prior chemotherapy for metastatic breast cancer who were randomized to standard-dose chemotherapy or double high-dose chemotherapy with autologous HSCT.[17] The primary study objective was to compare complete response (CR) rates. Objective response rates for the patients in the high-dose group were 66.7% versus 64.4% for the standard group (p=0.82). There were no significant differences between the two treatments in median time to disease progression, duration of response, or overall survival (overall survival 26.9 months vs. 23.4 months for the double high-dose arm versus the standard arm, respectively [p=0.60]).

Allogeneic Stem-Cell Transplant

To date, allogeneic HSCT for breast cancer has mostly been used in patients who have failed multiple lines of conventional chemotherapy.[18]

Ueno et al. reported the results of allogeneic HSCT in 66 women with poor-risk metastatic breast cancer from 15 centers who underwent transplantation between 1992 and 2000.[19] Thirty-nine (59%) received myeloablative and 27 (41%) reduced-intensity conditioning (RIC) regimens. A total of 17 (26%) patients had received a prior autologous HSCT. Median follow-up time for survivors was 40 months (range 3–64 months). Treatment-related mortality was lower in the RIC group (7% vs. 29% at 100 days; p=0.03). Progression-free survival at 1 year was 23% in the myeloablative group versus 8% in the RIC group (p=0.09). Overall survival rates after myeloablative conditioning versus the RIC group were 51%

(95% CI: 36–67%) versus 26% (95% CI: 11–45%) [p=0.04] at 1 year, 25% (95% CI: 13–40%) versus 15% (95% CI: 3–34%; p=0.33) at 2 years, and 19% (95% CI: 8–33%) versus 7% (95% CI: <1–25%; p=0.21) at 3 years, respectively.

Fleskens and colleagues reported the results of a Phase II study of 15 patients with metastatic breast cancer treated with HLA-matched reduced-intensity allogeneic HSCT.[20] Median patient age was 49.5 years (range: 39.7-60.8 years) and all patients had been extensively pretreated and had undergone at least one palliative chemotherapy regimen for metastatic disease. Treatment-related mortality was 2/15 (13%). One-year progression-free survival (PFS) was 20% and 1- and 2-year overall survival (OS) was 40% and 20%, respectively. The authors noted no objective tumor responses, but concluded that the relatively long PFS suggests a graft-versus-tumor effect.

Clinical Practice Guidelines

The 2014 National Comprehensive Cancer Network guidelines do not address the use of HSCT in the treatment of breast cancer.[21]

Summary

Randomized trials of autologous hematopoietic stem cell transplantation (HSCT) versus standard dose chemotherapy for patients with high risk non-metastatic or metastatic breast cancer have shown greater treatment-related mortality and toxicity and have not shown a survival advantage with HSCT. Therefore, autologous HSCT is considered not medically necessary for this indication. Non-randomized studies using reduced-intensity or myeloablative allogeneic HSCT for metastatic breast cancer have suggested a possible graft-versus-tumor effect, however, the data are insufficient to determine whether there is a survival benefit. Therefore allogeneic HSCT remains investigational for the treatment of high risk non-metastatic or metastatic breast cancer.

REFERENCES

1. BlueCross BlueShield Association Medical Policy Reference Manual "Hematopoietic Stem-Cell Transplantation for Breast Cancer." Policy No. 8.01.27
2. Vogl, DT, Stadtmauer, EA. High-dose chemotherapy and autologous hematopoietic stem cell transplantation for metastatic breast cancer: a therapy whose time has passed. *Bone Marrow Transplant*. 2006 Jun;37(11):985-7. PMID: 16708060
3. Stadtmauer, EA, O'Neill, A, Goldstein, LJ, et al. Conventional-dose chemotherapy compared with high-dose chemotherapy plus autologous hematopoietic stem-cell transplantation for metastatic breast cancer. Philadelphia Bone Marrow Transplant Group. *N Engl J Med*. 2000 Apr 13;342(15):1069-76. PMID: 10760307
4. Hortobagyi, GN. What is the role of high-dose chemotherapy in the era of targeted therapies? *J Clin Oncol*. 2004 Jun 15;22(12):2263-6. PMID: 15111620
5. Farquhar, C, Marjoribanks, J, Basser, R, Hetrick, S, Lethaby, A. High dose chemotherapy and autologous bone marrow or stem cell transplantation versus conventional chemotherapy for women with metastatic breast cancer. *Cochrane Database Syst Rev*. 2005(3):CD003142. PMID: 16034887
6. Farquhar, C, Marjoribanks, J, Basser, R, Lethaby, A. High dose chemotherapy and autologous bone marrow or stem cell transplantation versus conventional chemotherapy for women with

early poor prognosis breast cancer. *Cochrane Database Syst Rev*. 2005(3):CD003139. PMID: 16034886
7. Hanrahan, EO, Broglio, K, Frye, D, et al. Randomized trial of high-dose chemotherapy and autologous hematopoietic stem cell support for high-risk primary breast carcinoma: follow-up at 12 years. *Cancer*. 2006 Jun 1;106(11):2327-36. PMID: 16639731
8. Coombes, RC, Howell, A, Emson, M, et al. High dose chemotherapy and autologous stem cell transplantation as adjuvant therapy for primary breast cancer patients with four or more lymph nodes involved: long-term results of an international randomised trial. *Ann Oncol*. 2005 May;16(5):726-34. PMID: 15817602
9. Farquhar, CM, Marjoribanks, J, Lethaby, A, Basser, R. High dose chemotherapy for poor prognosis breast cancer: systematic review and meta-analysis. *Cancer Treat Rev*. 2007 Jun;33(4):325-37. PMID: 17382477
10. Crump, M, Gluck, S, Tu, D, et al. Randomized trial of high-dose chemotherapy with autologous peripheral-blood stem-cell support compared with standard-dose chemotherapy in women with metastatic breast cancer: NCIC MA.16. *J Clin Oncol*. 2008 Jan 1;26(1):37-43. PMID: 18025439
11. Biron, P, Durand, M, Roche, H, et al. Pegase 03: a prospective randomized phase III trial of FEC with or without high-dose thiotepa, cyclophosphamide and autologous stem cell transplantation in first-line treatment of metastatic breast cancer. *Bone Marrow Transplant*. 2008 Mar;41(6):555-62. PMID: 18037940
12. Zander, AR, Schmoor, C, Kroger, N, et al. Randomized trial of high-dose adjuvant chemotherapy with autologous hematopoietic stem-cell support versus standard-dose chemotherapy in breast cancer patients with 10 or more positive lymph nodes: overall survival after 6 years of follow-up. *Ann Oncol*. 2008 Jun;19(6):1082-9. PMID: 18304964
13. Nieto, Y, Shpall, EJ. High-dose chemotherapy for high-risk primary and metastatic breast cancer: is another look warranted? *Curr Opin Oncol*. 2009 Mar;21(2):150-7. PMID: 19532017
14. Berry, DA, Ueno, NT, Johnson, MM, et al. High-dose chemotherapy with autologous stem-cell support as adjuvant therapy in breast cancer: overview of 15 randomized trials. *J Clin Oncol*. 2011;29:3214-23. PMID: 21768471
15. Wang, J, Zhang, Q, Zhou, R, Chen, B, Ouyang, J. High-dose chemotherapy followed by autologous stem cell transplantation as a first-line therapy for high-risk primary breast cancer: a meta-analysis. *PLoS One*. 2012;7:e33388. PMID: 22428041
16. Kroger, N, Frick, M, Gluz, O, et al. Randomized trial of single compared with tandem high-dose chemotherapy followed by autologous stem-cell transplantation in patients with chemotherapy-sensitive metastatic breast cancer. *J Clin Oncol*. 2006 Aug 20;24(24):3919-26. PMID: 16921043
17. Schmid, P, Schippinger, W, Nitsch, T, et al. Up-front tandem high-dose chemotherapy compared with standard chemotherapy with doxorubicin and paclitaxel in metastatic breast cancer: results of a randomized trial. *J Clin Oncol*. 2005 Jan 20;23(3):432-40. PMID: 15659490
18. Carella, AM, Bregni, M. Current role of allogeneic stem cell transplantation in breast cancer. *Ann Oncol*. 2007 Oct;18(10):1591-3. PMID: 17846023
19. Ueno, NT, Rizzo, JD, Demirer, T, et al. Allogeneic hematopoietic cell transplantation for metastatic breast cancer. *Bone Marrow Transplant.* 2008 Mar;41(6):537-45. PMID: 18084340
20. Fleskens, AJ, Lalisang, RI, Bos, GM, van Gelder, M, Jansen, RL, Schouten, HC. HLA-matched allo-SCT after reduced intensity conditioning with fludarabine/CY in patients with metastatic breast cancer. *Bone Marrow Transplant*. 2010 Mar;45(3):464-7. PMID: 19633692
21. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology™. Breast Cancer. v.2.2014. [cited 03/17/2014]; Available from: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf

CROSS REFERENCES

Donor Lymphocyte Infusion for Malignancies Treated with an Allogeneic Hematopoietic Stem-Cell Transplant, Transplant, Policy No. 45.03

Placental and Umbilical Cord Blood as a Source of Stem Cells, Transplant, Policy No. 45.16

Hematopoietic Stem-Cell Transplantation for Miscellaneous Solid Tumors in Adults, Transplant, Policy No. 45.27

CODES	NUMBER	DESCRIPTION
CPT	38204	Management of recipient hematopoietic cell donor search and cell acquisition
	38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection, allogeneic
	38206	;autologous
	38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
	38208	;thawing of previously frozen harvest, without washing, per donor
	38209	;thawing of previously frozen harvest with washing, per donor
	38210	;specific cell depletion with harvest, T cell depletion
	38211	;tumor cell depletion
	38212	;red blood cell removal
	38213	;platelet depletion
	38214	;plasma (volume) depletion
	38215	;cell concentration in plasma, mononuclear, or buffy coat layer
	38220	Bone marrow; aspiration only
	38221	Bone marrow; biopsy, needle or trocar
	38230	Bone marrow harvesting for transplantation; allogeneic
	38232	Bone marrow harvesting for transplantation; autologous
	38240	Bone marrow or blood-derived peripheral stem-cell transplantation; allogeneic

CODES	NUMBER	DESCRIPTION
	38241	;autologous
	38242	Allogeneic donor lymphocyte infusions
	38243	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor, HPC boost
HCPCS	J9000–J9999	Chemotherapy drugs code range
	Q0083–Q0085	Chemotherapy administration code range
	S2140	Cord blood harvesting for transplantation; allogeneic
	S2142	Cord blood derived stem-cell transplantation, allogeneic
	S2150	Bone marrow or blood-derived peripheral stem-cell harvesting and transplantation, allogeneic or autologous, including pheresis, high-dose chemotherapy, and the number of days of post-transplant care in the global definition (including drugs; hospitalization; medical surgical, diagnostic and emergency services)