**Protocol**

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

(80127)

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<th>Medical Benefit</th>
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<tr>
<td>Preauthorization*</td>
<td>Yes</td>
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The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. **Preauthorization is required and must be obtained through Case Management.** *Please note that payment for covered services is subject to eligibility and the limitations noted in the patient’s contract at the time the services are rendered.*

**Description**

The use of high-dose chemotherapy and hematopoietic stem cell transplantation, instead of standard dose chemotherapy, has been used in an attempt to prolong survival in women with high-risk nonmetastatic and metastatic breast cancer.

**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
gain 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 Protocol, 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 (GVT) effect of donor-derived T cells.

Corporate Medical Guideline

Single or tandem autologous 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.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are
considered investigational. For explanation of experimental and investigational, please refer to the Technology
Assessment Protocol.

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to
conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced
procedures. Some of this Protocol may not pertain to the patients you provide care to, as it may relate to
products that are not available in your geographic area.
References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.


