Hematopoietic Stem-Cell Transplantation for Miscellaneous Solid Tumors in Adults

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Description of Procedure or Service

Hematopoietic Cell Transplantation

Hematopoietic cell transplantation (HCT) 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 cells may be obtained from the transplant recipient (autologous HCT) or from a donor (allogeneic HCT). 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 stem cells and the recipient is not an issue in autologous HCT. However, immunologic compatibility between donor and patient is a critical factor for achieving a good outcome of allogeneic HCT. 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 HLA-A,-B, and -DR(antigen-D related) loci on each arm of 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 conventional (“classical”) practice of allogeneic HCT 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.

The success of autologous HCT is predicated on the ability of cytotoxic chemotherapy with or without radiation to eradicate cancerous cells from the blood and bone marrow. This permits
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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 HCT is typically performed as consolidation therapy when the patient’s disease is in complete remission. Patients who undergo autologous HCT are susceptible to chemotherapy-related toxicities and opportunistic infections prior to engraftment, but not GVHD.

Reduced-Intensity Conditioning for Allogeneic HCT

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 HCT 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.

HSCT in Solid Tumors in Adults

HCT is an established treatment for certain hematologic malignancies. Its use in solid tumors in adults is less well established, although it has been investigated for a variety of solid tumors. With the advent of nonmyeloablative 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.

HCT as a treatment of ovarian cancer, germ cell tumors, ependymoma, or malignant glioma is addressed in separate policies. HCT as a treatment of breast cancer is not addressed. This evidence review collectively addresses other solid tumors of adults for which SCT has been investigated, including lung cancer; malignant melanoma; tumors of the gastrointestinal tract (include colon, rectum, pancreas, stomach, esophagus, gallbladder, and bile duct); male and female genitourinary systems (e.g., renal cell carcinoma, cervical carcinoma, cancer of the uterus, fallopian tubes, and prostate gland); tumors of the head and neck; soft tissue sarcoma; thyroid tumors; tumors of the thymus; and tumors of unknown primary origin.

Related Policies:

Hematopoietic Stem-Cell Transplantation for Breast Cancer
Hematopoietic Stem-Cell Transplantation in the Treatment of Germ Cell Tumors
Hematopoietic Stem-Cell Transplantation for Epithelial Ovarian Cancer
Hematopoietic Stem-Cell Transplantation for CNS Embryonal Tumors and Ependymoma

***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.
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Hematopoietic stem-cell transplantation for miscellaneous solid tumors in adults is considered investigational. BCBSNC does not provide coverage for investigational services or procedures.

Some patients may be eligible for coverage under Clinical Trials. Refer to the policy, Clinical Trial Services.

Refer to Related Policies in the “Description of Procedure or Service” section for a listing of other medical policies regarding hematopoietic stem-cell transplantation for specific solid tumors.

Benefits Application

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.

When Hematopoietic Stem-Cell Transplantation for Miscellaneous Solid Tumors In Adults is covered

Hematopoietic stem-cell transplantation may be covered for members participating in a clinical trial, (see Clinical Trial Services policy).

Refer to Related Policies in the “Description of Procedure or Service” section for a listing of other medical policies regarding hematopoietic stem-cell transplantation for specific solid tumors.

When Hematopoietic Stem-Cell Transplantation for Miscellaneous Solid Tumors In Adults is not covered

Autologous or allogeneic hematopoietic stem-cell transplantation is considered investigational for miscellaneous solid tumors including, but not limited to the following, unless they are part of a clinical trial (see Clinical Trial Services policy):

- Lung cancer, any histology;
- Colon cancer;
- Rectal cancer;
- Pancreas cancer;
- Stomach cancer;
- Esophageal cancer;
- Gall bladder cancer;
- Cancer of the bile duct;
- Renal cell cancer;
- Cervical cancer;
- Uterine cancer;
- Cancer of the fallopian tubes;
- Prostate cancer;
- Nasopharyngeal cancer;
- Paranasal sinus cancer;
- Neuroendocrine tumors;
- Soft tissue sarcomas;
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- Thyroid tumors;
- Tumors of the thymus;
- Tumors of unknown primary origin;
- Malignant melanoma;
- Undifferentiated tumors.

Policy Guidelines

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

Hematopoietic cell transplantation (HCT) is an established treatment for certain hematologic malignancies. Interest continues in exploring non-myeloablative allogeneic HCT for a graft-versus-tumor effect of donor-derived T cells in metastatic solid tumors.

For individuals who have adult soft tissue sarcomas who receive HCT, the evidence includes 2 TEC Assessments, 1 randomized controlled trial (RCT) and a number of phase 2 single arm studies, a number of which have been summarized in a Cochrane review. Relevant outcomes include overall survival, disease specific survival, and treatment related morbidity and mortality. 1995 and 1999 TEC Assessments focusing on HCT as primary and salvage therapy for a variety of solid tumors found that the available evidence did not permit conclusions about the effect of HCT on patient survival. Although 1 small phase 2 study reported longer survival for patients treated with HCT. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have small cell lung cancer (SCLC) who receive HCT, the evidence includes 2 TEC Assessments, several RCTs, and systematic reviews of these studies. Relevant outcomes are overall survival, disease-specific survival, and treatment-related morbidity and mortality. The 1995 and 1999 TEC Assessments, focusing on HCT as primary and salvage therapy for a variety of solid tumors, found that the available evidence did not permit conclusions about the effect of HCT on patient survival. Studies published since the TEC Assessments have not reported increased overall survival for patients with SCLC treated with HCT. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have renal cell carcinoma, colorectal cancer, pancreatic cancer, or nasopharyngeal cancer who receive HCT, the evidence includes a TEC Assessment and small single-arm series. Relevant outcomes are overall survival, disease-specific survival, and treatment-related morbidity and mortality. The 1995 and 1999 TEC Assessments, focusing on HCT as primary and salvage therapy for a variety of solid tumors, found that the available evidence did not permit conclusions about the effect of HCT on patient survival. Since publication of the TEC Assessments, the evidence for HCT to treat adult soft tissue sarcomas, renal cell carcinoma, colorectal cancer, pancreatic cancer, and nasopharyngeal cancer has been limited to small case series. The evidence is insufficient to determine the effects of the technology on health outcomes.

Billing/Coding/Physician Documentation Information

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. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 38205, 38206, 38230, 38232, 38240, 38241, 38242, 38243, S2150
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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

**Bone Marrow Transplant for Miscellaneous Solid Tumors in Adults**

TEC Assessment, July, 1999; Volume 14; No. 11


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Policy Implementation/Update Information

**Bone Marrow Transplant for Miscellaneous Solid Tumors in Adults**


2/01 Original policy issued.

1/02 Policy statement revised under when it is covered and removed reference to acute lymphocytic amyloidosis. This is addressed in our policy on BMT for multiple myeloma and primary amyloidosis.

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" section. Revised under "when it is not covered" section. 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.
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12/11/06 Specialty Matched Consultant Advisory Panel review 11/6/2006. No changes to policy statement. Added the following statement to the "Policy" section: "If the medical criteria and guidelines are not met, some patients may be eligible for coverage under Clinical Trials. Refer to the policy, Clinical Trial Services for Life-Threatening Conditions." Added "Malignant Melanoma" to the "When Not Covered" section for clarification. Updated rationale in "Policy Guidelines" section. References added.


6/22/10 Policy Number(s) removed (amw)

Bone Marrow Transplant for Miscellaneous Solid Tumors in Adults

1/4/11 Policy name changed from Bone Marrow Transplant for Miscellaneous Solid Tumors in Adults to Hematopoietic Stem-Cell Transplantation for Miscellaneous Solid Tumors In Adults. Specialty Matched Consultant Advisory Panel review 11/29/2010. “Description” section revised. Reference to bone marrow transplant with high dose chemotherapy changed to hematopoietic stem-cell transplantation throughout the policy as appropriate. Removed statement in the “Benefits Application” section which indicated; “Services for or related to the search for a donor are not covered.” No change to policy intent. References added. (btw)


12/9/14 Specialty Matched Consultant Advisory Panel review 11/24/2014. No change to policy intent. Reference added. (lpr)

12/30/15 Specialty Matched Consultant Advisory Panel review 11/18/2015. Reference added. No change to policy statement. (lpr)

4/1/2016 Updated Description and Policy Guidelines sections. No change to policy intent. Reference added. (lpr)

12/30/16 Specialty Matched Consultant Advisory Panel review 11/30/2016. No change to policy intent. (lpr)
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2/24/17   Revised Policy Guidelines and Description sections. Reference added. No change to policy intent. (lpr)

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.