

Corporate Medical Policy

Hematopoietic Stem-Cell Transplantation for Multiple Myeloma

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Description of Procedure or Service

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). Cord blood is discussed in greater detail in the Cord Blood as a Source of Stem Cells medical policy.

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 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 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 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.

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.

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Patients who undergo autologous HSCT are susceptible to chemotherapy-related toxicities and opportunistic infections prior to engraftment, but not GVHD.

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 conventional 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 total 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 nonmyeloablative, as opposed to fully myeloablative (traditional) regimens.

Multiple Myeloma

Multiple myeloma is a systemic malignancy of plasma cells that represents approximately 10% of all hematologic cancers. It is treatable but rarely curable, with estimated new cases and deaths in 2010 in the United States 20,180 and 10,650, respectively. At the time of diagnosis most patients have generalized disease, and, the selection of treatment is influenced by patient age, general health, prior therapy, and the presence of complications of the disease.

The disease is staged by estimating tumor mass, based on various clinical parameters like hemoglobin, serum calcium, number of lytic bone lesions, and the presence or absence of renal failure. Multiple myeloma usually evolves from an asymptomatic premalignant stage (termed “monoclonal gammopathy of undetermined significance” or MGUS). Treatment is usually reserved for patients with symptomatic disease (usually progressive myeloma), whereas asymptomatic patients are observed, as there is little evidence that early treatment of asymptomatic multiple myeloma prolongs survival when compared to therapy delivered at the time of symptoms or end-organ damage. In some patients, an intermediate asymptomatic but more advanced premalignant stage is recognized, and referred to as smoldering multiple myeloma. The overall risk of disease progression from smoldering to symptomatic multiple myeloma is 10% per year for the first 5 years, approximately 3% per year for the next 5 years, and 1% for the next 10 years.

*****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.**

Policy

BCBSNC will provide coverage for Hematopoietic Stem-Cell Transplantation for Multiple Myeloma when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

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.

Benefits Application

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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 Multiple Myeloma is covered

1. A single or second (salvage) autologous hematopoietic stem-cell transplantation may be considered medically necessary to treat multiple myeloma.
2. Tandem autologous-autologous hematopoietic stem-cell transplantation may be considered medically necessary to treat multiple myeloma in patients who fail to achieve at least a near-complete or very good partial response after the first transplant in tandem sequence. (For definitions of near-complete response and very good partial response, see Policy Guidelines).
3. Tandem transplantation with an initial round of autologous hematopoietic stem-cell transplantation followed by a non-marrow-ablative conditioning regimen and allogeneic hematopoietic stem-cell transplantation (i.e., reduced-intensity conditioning transplant) may be considered medically necessary to treat newly diagnosed multiple myeloma patients.

When Hematopoietic Stem-Cell Transplantation for Multiple Myeloma is not covered

1. When the medical criteria listed above are not met.
2. Allogeneic hematopoietic stem-cell transplantation, myeloablative or nonmyeloablative, as upfront therapy of newly diagnosed multiple myeloma or as salvage therapy, is considered investigational.

Policy Guidelines

1. Refer to the individual member's benefit booklet for prior review requirements.
2. A near complete response, as defined by the European Group for Blood and Marrow Transplant (EBMT) is the disappearance of M protein at routine electrophoresis, but positive immunofixation.
3. A very good partial response has been defined as a 90% decrease in the serum paraprotein level.
4. The reference to HLA-identical consists of an identical twin with a 6 of 6 HLA match.

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 codes: 38205, 38206, 38230, 38232, 38240, 38241, 38242, S2150

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

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specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Bone Marrow Transplant for Multiple Myeloma and Primary Amyloidosis

Barlogie B, et.al. Superiority of Tandem Autologous Transplantation Over Standard Therapy for Previously Untreated Multiple Myeloma. *Blood*, Volume 89, No. 3, February 11, 1997; pp. 789-793.

BCBSA TEC Evaluation, May 1998; Tab 8

Barlogie B, et.al. Total Therapy with Tandem Transplants for Newly Diagnosed Multiple Myeloma. *Blood*, Volume 93, No. 1, January 1, 1999; pp. 55-65.

BCBSA TEC Evaluation, March 1999; Tab 26

BCBSA Medical Policy Reference Manual, 12/1/1999; 8.01.17

Lemoli R, et.al. Engraftment, clinical and molecular follow-up of patients with multiple myeloma who were reinfused with highly purified CD34+ cells to support single or tandem high-dose chemotherapy. *Blood*, Volume 95, No. 7, April 1, 2000.

BCBSA Medical Policy Reference Manual, 8/18/2000; 8.01.17

BCBSA Medical Policy Reference Manual, 11/20/01; 8.01.17

Specialty Matched Consultant Advisory Panel - 11/2002

Bone Marrow Transplant for Multiple Myeloma

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.17, 4/16/2004

Specialty Matched Consultant Advisory Panel 11/2004

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.17, 7/20/2006

Specialty Matched Consultant Advisory Panel 11/2006

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.17, 7/10/2008

Specialty Matched Consultant Advisory Panel 11/2008

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BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.17, 1/14/2010

Specialty Matched Consultant Advisory Panel – 11/2010

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.17, 3/10/2011

Specialty Matched Consultant Advisory Panel – 11/2011

Policy Implementation/Update Information

Bone Marrow Transplant for Multiple Myeloma and Primary Amyloidosis

1/01 Specialty Matched Consultant Advisory Group. Under the Policy Guidelines section, adopted recommendation that tandem transplants be considered for specific criteria.

2/01 Original policy issued.

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- 1/02 Policy named changed from Bone Marrow Transplant for Multiple Myeloma. Policy statement revised to include Primary Amyloidosis as investigational.
- 2/03 Specialty Matched Consultant Advisory Panel meeting 11/2002. Revised the Policy statement to include the statement that, "Some patients may be eligible for coverage under Clinical Trials. Refer to the policy on Clinical Trial Services for Life-Threatening Conditions." 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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- 12/23/04 Specialty Matched Consultant Advisory Panel review 11/29/2004. Split policy to remove reference to Primary Amyloidosis and changed name. Created new policy for Primary Amyloidosis/SUR6090.18. Revised Description of Procedure or Service section. Added new indications (bullets 2 and 3) to "When covered section" which states; "A second course of high-dose chemotherapy with autologous stem-cell support may be considered medically necessary to treat responsive multiple myeloma that has relapsed after a durable complete or partial remission following an autologous transplant or" "tandem high-dose chemotherapy with autologous stem-cell support may be considered medically necessary to treat newly diagnosed or responsive multiple myeloma". Added the 3rd and 4th bullet under "When not covered" which states; "Non-marrow ablative chemotherapy and allogeneic stem cell support following high-dose chemotherapy with autologous stem-cell support is considered investigational as the initial therapy of multiple myeloma." "Monotherapy using high-dose chemotherapy with allogeneic stem-cell support is considered investigational, either as initial therapy or after a prior failed course of high dose chemotherapy and autologous stem cell support." Added additional information regarding "responsive multiple myeloma", "partial remission", and "refractory multiple myeloma" to Policy Guidelines section. Removed reference to tandem autologous bone marrow transplants from the Policy Guidelines section. Added policy number to Policy Key Words. "Hematopoietic" and "Opportunistic" added to Definitions. References added. Notice given 12/23/2004. Effective date 3/3/2005.
- 11/3/05 Added "including primary refractory myeloma" to first bullet under the "When covered" section. Added explanation of "primary refractory myeloma" to "Policy Guidelines" and to "Policy Key Words" section.
- 12/11/06 Specialty Matched Consultant Advisory Panel review 11/6/2006. 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." No changes to policy statement. References added.
- 12/22/08 Specialty Matched Consultant Advisory Panel review 11/13/2008. Added "2. HDC and autologous stem cell support may be considered medically necessary in the treatment of multiple myeloma patients with primary progressive disease who are not at high risk." and "5. Tandem transplantation with an initial round of autologous stem cell support followed by a non- marrow-ablative conditioning regimen and allogeneic stem cell

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transplant may be considered medically necessary to treat newly diagnosed multiple myeloma patients with an Human leukocyte antigens (HLA)-identical sibling donor and who are in otherwise reasonably good health." to the "When Covered" section. Removed "Non-marrow ablative chemotherapy and allogeneic stem cell support following high-dose chemotherapy with autologous stem-cell support is considered investigational as the initial therapy of multiple myeloma." from the "When Not Covered" section. Updated "Policy Guidelines" section. References added. (btw)

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- 8/31/10 Policy name changed from "Bone Marrow Transplantation for Multiple Myeloma" to Hematopoietic Stem-Cell Transplantation for Multiple Myeloma. The policy has been extensively revised. Policy number removed. "Description" revised. The policy statements have been updated to reflect current practice. Removed the statement in the "Benefit Application" section that indicated "Services for or related to the search for a donor are not covered." Deleted the following "When Covered" statements: "1. HDC and autologous stem cell support may be considered medically necessary in the treatment of newly diagnosed or responsive multiple myeloma. OR 2.HDC and autologous stem cell support may be considered medically necessary in the treatment of multiple myeloma patients with primary progressive disease who are not at high risk. OR 3.A second course of high-dose chemotherapy with autologous stem-cell support may be considered medically necessary to treat responsive multiple myeloma that has relapsed after a durable complete or partial remission following an autologous transplant. OR 4 .Tandem high-dose chemotherapy with autologous stem-cell support may be considered medically necessary to treat newly diagnosed or responsive multiple myeloma. OR 5.Tandem transplantation with an initial round of autologous stem cell support followed by a non-marrow-ablative conditioning regimen and allogeneic stem cell transplant may be considered medically necessary to treat newly diagnosed multiple myeloma patients with an Human leukocyte antigens (HLA)-identical sibling donor and who are in otherwise reasonably good health." Removed the following "When Not Covered" statements: "HDC and autologous stem cell support is considered investigational in the treatment of multiple myeloma in refractory relapse." and "Monotherapy using high-dose chemotherapy with allogeneic stem-cell support is considered investigational, either as initial therapy or after a prior failed course of high dose chemotherapy and autologous stem cell support." Policy Guidelines revised. Senior Medical Director review 5/3/10 References added. (btw)
- 1/4/11 Specialty Matched Consultant Advisory Panel review 11/29/2010. No change to policy statement. (btw)
- 5/24/11 "Description" section revised to show 2010 updated statistics regarding estimated new cases and deaths. Added "in the tandem sequence" to statement "2. Tandem autologous – autologous..."under the When Covered" section Medical Director review 5/12/11. Reference added. (btw)
- 1/10/12 "Description" section revised. Specialty Matched Consultant Advisory Panel review 11/30/2011. No change to policy intent. (btw)
- 2/21/12 Added new 2012 CPT code, 38232, to Billing/Coding section. (btw)

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

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disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.