

Corporate Medical Policy

Bone Marrow Transplant for Multiple Myeloma

File Name: bone_marrow_transplant_for_multiple_myeloma
Policy Number: SUR6090.14
Origination: 2/2001
Last Review: 11/2008
Next Review: 11/2010

Description of Procedure or Service

This policy addresses high-dose chemotherapy with [hematopoietic stem-cell](#) support as a treatment of multiple myeloma. Bone marrow transplants typically include high-dose chemotherapy (HDC).

"High-dose chemotherapy" (HDC) involves the administration of [cytotoxic agents](#) for the treatment of cancer. It uses doses several times greater than the standard therapeutic dose. In some cases, whole body or localized radiotherapy is also given and is included in the term HDC. The rationale for HDC is that many [cytotoxic agents](#) act according to a [steep dose-response curve](#). Thus, small increments in dosage will result in relatively large increases in tumor cell kill. Increasing the dosage also increases the incidence and severity of adverse effects related primarily to bone marrow [ablation](#) (e.g., [opportunistic](#) infections, hemorrhage, organ failure).

Various techniques have been developed to counter the [myelosuppressive](#) effects, and secondary susceptibility to infections of HDC regimens. The main technique is the infusion into the patient of [hematopoietic stem cells](#) to repopulate the bone marrow. [Hematopoietic stem cells](#) are primitive cells capable of replication and formation into mature blood cells. [Stem cells](#) can be [harvested](#) from three sources:

1. Bone marrow cells: Bone marrow [stem cells](#) can be [harvested](#) from a related or unrelated donor.
2. Peripheral [stem cells](#): [Stem cells](#) may be [harvested](#) from the peripheral blood circulation. This may involve several pheresis procedures. Pheresis involves withdrawing blood from a donor in which a portion containing [stem cells](#) is separated and retained with the remainder retransfused back to the donor.
3. [Umbilical cord](#): Blood [harvested](#) from the [umbilical cord](#) and [placenta](#) shortly after the delivery of neonates contains [stem cells](#). Although cord blood is an [allogeneic](#) source, these [stem cells](#) are associated with a lower incidence of rejection or graft versus host disease.

When [harvested](#) from and infused back into the same patient, [stem cells](#) are referred to as [autologous](#). [Stem cells harvested](#) from a healthy, [histocompatible](#) donor and infused into a patient are referred to as [allogeneic](#).

Multiple myeloma is a [neoplastic](#) disease characterized by the infiltration of bone and bone marrow by myeloma cells forming multiple tumor masses. Multiple myeloma is rarely curable with standard dose chemotherapy, prompting interest in high dose chemotherapy with either [autologous](#) or [allogeneic stem cell](#) support.

Policy

BCBSNC will provide coverage for Bone Marrow Transplant, high dose chemotherapy and stem cell support for Multiple Myeloma when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

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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

Please refer to certificate for availability of benefits. This policy relates only to the services or supplies described herein. Benefits may vary according to benefit design, therefore certificate language should be reviewed before applying the terms of the policy.

There may be certificates which exclude benefits for transplantation or for specific diagnoses.

Services for or related to the search for a donor are not covered.

When Bone Marrow Transplant for Multiple Myeloma

Note: The clinical indications and discussion of Bone Marrow Transplant for Multiple Myeloma is complex and technical. If you have any questions concerning this treatment, please talk with your physician.

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.

When Bone Marrow Transplant for Multiple Myeloma is not covered

1. When the medical criteria listed above are not met.
2. HDC and [autologous stem cell](#) support is considered investigational in the treatment of multiple myeloma in [refractory](#) relapse.
3. 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

1. Refer to the individual certificate for prior approval/precertification requirements.
2. Primary refractory disease is newly diagnosed myeloma that does not respond to conventional-dose

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chemotherapy.

3. Primary progressive disease is progression that occurs during or immediately after the first conventional dose induction regimen given to a newly-diagnosed myeloma patient, i.e., before any stem cell support, even before the first transplant cycle in a planned tandem transplant. (These are considered high risk or standard risk.)
4. Responsive multiple myeloma is defined as a tumor showing a complete or partial remission or minimal response.
5. Partial remission has at least a 50% reduction in tumor burden which is measured by blood levels of beta-2 microglobulin or monoclonal immunoglobulins (tumor markers for multiple myeloma).
6. Minimal response implies at least a 25% reduction in serum monoclonal paraprotein and no increase (in size or number) of lytic bone lesions.
7. Refractory multiple myeloma is a response of less than 50% tumor burden. Refractory multiple myeloma and resistant multiple myeloma are the same.
8. The reference to HLA-identical consists of an identical twin with a 6 of 6 HLA match.
9. While some HDC protocols can be administered on an outpatient basis, typically the patient is hospitalized for management of the marrow **ablative** complications of the therapy. All patients receiving whole body radiotherapy, typically those receiving an **allogeneic** transplant (from donor to patient), will require prolonged hospitalization.

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

Policy Key Words

Key Words: High Dose Chemotherapy, HDC, Stem Cell Support, SCS, Autologous, Allogeneic, Multiple Myeloma, Bone Marrow Transplant, BMT, Tandem, primary refractory myeloma, SUR6090.14

Medical Term Definitions

Ablation

the removal of tissue or an abnormal growth, usually by cutting; may also refer to a very high dose of treatment that is calculated to kill a tumor.

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Allogeneic

genetically dissimilar - involves a donor and a recipient; genes are not identical in each organism.

Autologous

derived from the same organism, i.e., self donation.

Cytotoxic agents

drugs which possess a specific destructive action on certain cells; often used to refer to drugs used to fight cancer, such as chemotherapy.

Harvesting

to remove tissues or cells from a donor and preserve for transplantation.

Hematopoietic

pertaining to or effecting the formation of blood cells.

Histocompatible

tissue compatible; donor and recipient are well enough matched that a transplant will be easily accepted.

Myelosuppressive

something that inhibits bone marrow activity, resulting in decreased production of blood cells and platelets.

Neoplasm

new and abnormal growth, specifically growth of tissue in which the growth is uncontrolled and progressive. May be benign or cancerous.

Opportunistic

a microorganism that does not usually cause disease but that, under certain circumstances such as impaired immune system due to other diseases or drug treatment becomes pathogenic.

Placenta

Temporary organ formed from both fetal and maternal tissues that provides nutrients and oxygen to the developing fetus, carries away fetal metabolic wastes, and produces the hormones of pregnancy.

Refractory

not responding to treatment.

Steep dose-response curve

a theory in delivery of cytotoxic agents that small increments in dosage will result in relatively large increases in tumor cell kill.

Stem cells

immature generic blood cells that will mature into the various types of blood cells in the body.

Tandem bone marrow transplants

two planned courses of high dose chemotherapy and stem cell support. Tandem transplants are typically administered at intervals of 2-6 months, contingent on recovery from prior toxicity.

Umbilical cord

a flexible structure through which the umbilical arteries and vein pass and which connects the fetus to the placenta.

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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

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.
- 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 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.

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.