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1.0 Description of the Procedure, Product, 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 recipient 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:

- a. Bone marrow cells: Bone marrow stem cells can be harvested from a related or unrelated donor.
- b. 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.
- c. 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.

1.1 Medical Term Definitions

- a. 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.
- b. Allogeneic: genetically dissimilar - involves a donor and a recipient; genes are not identical in each organism
- c. Autologous: derived from the same organism, i.e., self donation.

- d. 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.
- e. Harvesting: to remove tissues or cells from a donor and preserve for transplantation.
- f. Hematopoietic: pertaining to or effecting the formation of blood cells.
- g. Histocompatible: tissue compatible; donor and recipient are well enough matched that a transplant will be easily accepted.
- h. Myelosuppressive: something that inhibits bone marrow activity, resulting in decreased production of blood cells and platelets.
- i. Neoplasm: new and abnormal growth, specifically growth of tissue in which the growth is uncontrolled and progressive. May be benign or cancerous.
- j. 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.
- k. 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.
- l. Refractory: not responding to treatment
- m. 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.
- n. Stem cells: immature generic blood cells that will mature into the various types of blood cells in the body.
- o. Tandem bone marrow transplants: two planned courses of high dose chemotherapy and stem cell support. Tandem transplants are typically administered at intervals of two(2) to six (6) months, contingent on recovery from prior toxicity.
- p. Umbilical cord: a flexible structure through which the umbilical arteries and vein pass and which connects the fetus to the placenta.

2.0 Eligible Recipients

2.1 General Provisions

To be eligible, NCHC recipients must be enrolled on the date of service.

3.0 When the Procedure, Product, or Service Is Covered

3.1 General Criteria

NCHC covers procedures, products, and services related to this policy when they are medically necessary and

- a. the procedure, product, or service is individualized, specific, and consistent with symptoms or confirmed diagnosis of the illness or injury under treatment, and not in excess of the recipient's needs;
- b. the procedure, product, or service can be safely furnished, and no equally effective and more conservative or less costly treatment is available; **AND**
- c. the procedure, product, or service is furnished in a manner not primarily intended for the convenience of the recipient, the recipient's caretaker, or the provider.

3.2 Specific Criteria

Bone marrow transplant, high dose chemotherapy and stem cell support for multiple myeloma are covered under the NCHC Program when they are determined to be medically necessary because the following medical criteria are met:

- a. HDC and autologous stem cell support may be considered medically necessary in the treatment of newly diagnosed or responsive multiple myeloma;
- b. HDC and autologous stem cell support may be considered medically necessary in the treatment of multiple myeloma recipients with primary progressive disease who are not at high risk;
- c. 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;
- d. Tandem high-dose chemotherapy with autologous stem-cell support may be considered medically necessary to treat newly diagnosed or responsive multiple myeloma; **OR**
- e. 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 recipients with an Human leukocyte antigens (HLA)-identical sibling donor and who are in otherwise reasonably good health.

3.3 Other Medical Policy Guidelines

- a. Primary refractory disease is newly diagnosed myeloma that does not respond to conventional-dose chemotherapy.
- b. Primary progressive disease is progression that occurs during or immediately after the first conventional dose induction regimen given to a newly-diagnosed myeloma recipient, 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.)
- c. Responsive multiple myeloma is defined as a tumor showing a complete or partial remission or minimal response.
- d. 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).
- e. Minimal response implies at least a 25% reduction in serum monoclonal paraprotein and no increase (in size or number) of lytic bone lesions.

- f. Refractory multiple myeloma is a response of less than 50% tumor burden. Refractory multiple myeloma and resistant multiple myeloma are the same.
- g. The reference to HLA-identical consists of an identical twin with a 6 of 6 HLA match.
- h. While some HDC protocols can be administered on an outpatient basis, typically the recipient is hospitalized for management of the marrow ablative complications of the therapy. All recipients receiving whole body radiotherapy, typically those receiving an allogeneic transplant (from donor to recipient), will require prolonged hospitalization.

4.0 When the Procedure, Product, or Service Is Not Covered

4.1 General Criteria

Procedures, products, and services related to this policy are not covered when

- a. the recipient does not meet the eligibility requirements listed in **Section 2.0**;
- b. the recipient does not meet the medical necessity criteria listed in **Section 3.0**;
- c. the procedure, product, or service unnecessarily duplicates another provider's procedure, product, or service; or
- d. the procedure, product, or service is experimental or investigational.

4.2 Specific Criteria

Bone marrow transplant for multiple myeloma is not covered for the following:

- a. When the criteria listed in **Subsection 3.2** are not met.
- b. HDC and autologous stem cell support is considered investigational in the treatment of multiple myeloma in refractory relapse.
- c. 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.
- d. Services for or related to the search.

Note: If the medical criteria and guidelines are not met, some recipients may be eligible for coverage in a clinical trial.

5.0 Requirements for and Limitations on Coverage

5.1 Prior Approval

Prior approval is required for all bone marrow transplant for multiple myeloma.

6.0 Providers Eligible to Bill for the Procedure, Product, or Service

To be eligible to bill for procedures, products, and services related to this policy, providers shall

- a. meet NCHC qualifications for participation;

- b. be currently enrolled with NCHC; **AND**
- c. bill only for procedures, products, and services that are within the scope of their clinical practice, as defined by the appropriate licensing entity.

7.0 Additional Requirements

7.1 Compliance

Providers must comply with all applicable federal, state, and local laws and regulations, including the Health Insurance Portability and Accountability Act (HIPAA) and record retention requirements.

8.0 Policy Implementation/Revision Information

Original Effective Date: July 1, 2010

Revision Information:

Date	Section Revised	Change
July 1, 2010		Policy Conversion: Implementation of Session Law 2009-451, Section 10.32 “NC HEALTH CHOICE/PROCEDURES FOR CHANGING MEDICAL POLICY.”

Attachment A: Claims-Related Information

Reimbursement requires compliance with all NCHC guidelines.

A. Claim Type

Professional (CMS-1500/837P transaction)

Institutional (UB-04/837I transaction)

B. Diagnosis Codes

Providers must bill the ICD-9-CM diagnosis codes(s) to the highest level of specificity that supports medical necessity.

C. Procedure Code(s)

CPT Codes				
38205	38206	38230	38240	38241
38242				

HCPCS Code
S2150

Note: If prior approval has not been obtained, claims will deny.

D. Modifiers

Providers are required to follow applicable modifier guidelines.

E. Billing Units

The appropriate procedure code(s) used determines the billing unit(s).

F. Place of Service

Inpatient Hospital and Outpatient Hospital

G. Co-payments

Co-payment(s) may apply to covered prescription drugs and services.

H. Reimbursement

Providers must bill their usual and customary charges.