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## **1.0 Description of the Procedure, Product, 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 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 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, immunosuppressant 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 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 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 non-myeloablative, as opposed to fully myeloablative (traditional) regimens.

### **Hodgkin Lymphoma**

Hodgkin Lymphoma (HL) is a relatively uncommon B-cell lymphoma. In 2008, an estimated 8,220 new diagnoses and 1,350 deaths will occur in the U.S. The disease has a bimodal distribution, with most patients diagnosed between the ages of 15 and 30 years, with a second peak in adults aged 55 and older.

The World Health Organization (WHO) classification divides HL into two main types:

1. "Classical" HL (CHL)
  - a. Nodular sclerosis
  - b. Mixed cellularity
  - c. Lymphocyte depleted
  - d. Lymphocyte rich
2. Nodular Lymphocyte-Predominant (NLPHL)

In Western countries, CHL accounts for 95% of cases of HL and NLPHL only 5%. (1) Classic HL is characterized by the presence of neoplastic Reed-Sternberg cells in a background of numerous non-neoplastic inflammatory cells. NLPHL lacks Reed-Sternberg cells, but is characterized by the presence of lymphocytic and histiocytic cells termed "popcorn cells."

The following staging system for HL recognizes the fact that the disease is thought to typically arise in a single lymph node and spread to contiguous lymph nodes with eventual involvement of extranodal sites. The staging system attempts to distinguish patients with localized HL who can be treated with extended field radiation from those who require systemic chemotherapy.

## **Staging for Hodgkin Lymphoma**

Staging for HL is based on the Ann Arbor staging system. Each stage is subdivided into A and B categories. “A” indicates no systemic symptoms are present and “B” indicates the presence of systemic symptoms including unexplained weight loss of more than 10% of body weight, unexplained fevers or drenching night sweats.

### **Stage I**

Involvement of a single lymph node region (I) or localized involvement of a single extralymphatic organ or site (IE).

### **Stage II**

Involvement of two or more lymph node regions on the same side of the diaphragm (II) or localized involvement of a single associated extralymphatic organ or site and its regional lymph node(s) with or without involvement of other lymph node regions on the same side of the diaphragm (IIE). The number of lymph node regions involved should be indicated by a subscript (e.g., II<sub>2</sub>)

### **Stage III**

Involvement of lymph node regions or structures on both sides of the diaphragm. These patients are further subdivided as follows:

- III-1: disease limited to spleen or upper abdomen
- III-2: periaortic or pelvic node involvement

### **Stage IV**

Disseminated (multifocal) involvement of one or more extralymphatic organs, with or without associated lymph node involvement, or isolated extralymphatic organ involvement with distant (nonregional) nodal involvement.

Patients with HL are generally classified into 3 groups: early-stage favorable (stage I–II with no B symptoms or large mediastinal lymphadenopathy), early-stage unfavorable (stage I–II with large mediastinal mass, with or without B symptoms; stage IB–IIB with bulky disease), and advanced-stage disease (stage III–IV).

Patients with nonbulky stage IA or IIA disease are considered to have clinical early stage disease. These patients are candidates for chemotherapy, combined modality therapy, or radiation therapy alone. Patients with obvious stage III or IV disease, bulky disease (defined as a 10-cm mass or mediastinal disease with a transverse diameter exceeding 33% of the transthoracic diameter), or the presence of B symptoms will require combination chemotherapy with or without additional radiation therapy.

HL is highly responsive to conventional chemotherapy, and up to 80% of newly diagnosed patients can be cured with combination chemotherapy and/or radiation therapy. Patients who prove refractory or who relapse after first-line therapy have a significantly worse prognosis. Primary refractory HL is defined as disease regression of less than 50% after 4–6 cycles of anthracycline-containing chemotherapy, disease progression during induction therapy, or progression within 90 days after the completion of first-line treatment.

In patients with relapse, the results of salvage therapy vary depending upon a number of prognostic factors, as follows: the length of the initial remission, stage at recurrence, and the severity of anemia at the time of relapse. Early and late relapse are defined as less or more than 12 months from the time of remission, respectively. Approximately 70% of patients with late first relapse can be salvaged by autologous HSCT, but not more than 40% with early first relapse.

Only approximately 25%-35% of patients with primary progressive or poor-risk recurrent HL achieve durable remission after autologous HSCT, with most failures being due to disease progression after transplant. Most relapses after transplant occur within 1–2 years and once relapse occurs post-transplant, median survival is less than 12 months.

## **2.0 Eligible Recipients**

### **2.1 General Provisions**

To be eligible, NC Health Choice (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**

NCHC covers autologous or myeloablative allogeneic hematopoietic stem-cell transplantation (HSCT) in recipients with primary refractory Hodgkin's disease or relapsed Hodgkin lymphoma (HL) in the following situations:

Tandem autologous HSCT

- a. in recipients with primary refractory HL or
- b. in recipients with relapsed disease with poor risk features who do not attain a complete remission to cytoreductive chemotherapy prior to transplantation (**refer to Policy Guidelines**); or

Reduced-intensity conditioning (RIC)allogeneic HSCT

- a. in recipients who have failed a prior autologous HSCT used to treat primary refractory or relapsed disease; or
- b. in recipients who would otherwise qualify for a myeloablative allogeneic transplant, but would be unable to tolerate a standard myeloablative conditioning regimen (**refer to Policy Guidelines**); or
- c. when insufficient stem cells are collected for an autologous HSCT.

### 3.3 Policy Guidelines

Some patients for whom a conventional myeloablative allotransplant could be curative may be considered candidates for reduced-intensity conditioning (RIC) allogeneic HSCT. These include those with malignancies that are effectively treated with myeloablative allogeneic transplantation, but whose age (typically older than 55 years) or comorbidities (e.g., liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy, low Karnofsky Performance Status) preclude use of a standard myeloablative conditioning regimen.

Recent recipient history of substance abuse may require substance abuse testing and psychological evaluation.

## 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

- a. NCHC does not cover hematopoietic stem-cell or bone marrow transplantation for Hodgkin's disease in the following clinical situations:
  1. A second autologous stem-cell transplantation for relapsed lymphoma after a prior autologous HSCT;
  2. Other uses of HSCT in patients with HL including, but not limited to, initial therapy for newly diagnosed disease to consolidate a first complete remission.

- b. HSCT is not covered when the recipient's psychosocial history limits the recipient's ability to comply with pre- and post-transplant medical care.
- c. HSCT is not covered when current recipient or caretaker non-compliance would make compliance with a disciplined medical regime improbable.

## 5.0 Requirements for and Limitations on Coverage

### 5.1 Prior Approval

Prior approval is required for hematopoietic stem-cell transplantation for Hodgkin lymphoma.

If prior approval has been given for HSCT, actual donor expenses (**procuring, harvesting, short-term storing and all associated laboratory costs**) are covered.

### 5.2 Prior Approval Requirements

The provider(s) shall submit to DMA's designee the following:

- a. the prior approval request; and
- b. all health care records and any other records that support the NCHC recipient has met the specific criteria in **Subsection 3.2** of this policy

## 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 shall 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
7/1/2010		Policy Conversion: Implementation of Session Law 2009-451, <b>Section 10.32 “NC HEALTH CHOICE/PROCEDURES FOR CHANGING MEDICAL POLICY.”</b>
1/1/2012	Throughout	Policy updated to reflect current community standards and changing transplant protocols.

## Attachment A: Claims-Related Information

Reimbursement requires compliance with all NCHC guidelines.

### A. Claim Type

Professional (CMS-1500/837P transaction)

### B. Diagnosis Codes

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

### C. Procedure Code(s)

CPT Code(s)	Description
38205	Blood derived Hemopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38206	Blood derived Hemopoietic progenitor cell harvesting for transplantation, per collection; Autologous
38230	Bone Marrow harvesting for transplantation
38240	Bone marrow or peripheral stem cell transplantation; allogeneic
38241	Bone marrow or peripheral stem cell transplantation; Autologous
38242	Allogeneic donor lymphocyte infusions

ICD-9 Procedure Codes	Description
41.00	Bone marrow transplant
41.01	Autologous bone marrow transplant
41.03	Allogeneic bone marrow transplant
41.04	Autologous (hematopoietic) stem cell transplant
41.05	Allogeneic (hematopoietic) stem cell transplant

HCPCS Code(s)	Description
S2150	Bone Marrow or blood derived stem cell (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications including pheresis and cell preparation,/storage; marrow ablative therapy; drugs; supplies; hospitalization with outpatient follow-up; medical/surgical; and the number of days of pre and post transplant care in the global definition.

### 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

**G. Co-payments**

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

**H. Reimbursement**

Providers shall bill their usual and customary charges.

**I. Billing for Donor Expenses**

Donor expenses for non-NCHC donors are billed on the NCHC recipient's transplant claim using the recipient's Medicaid identification number. Donor expenses for NCHC donors are billed on the NCHC donor's claim using the donor's NCHC identification number.

NCHC reimburses only for the actual donor's expenses. NCHC does not reimburse for unsuccessful donor searches.