To all beneficiaries enrolled in a Prepaid Health Plan (PHP): for questions about benefits and services available on or after implementation, please contact your PHP.

Table of Contents

NC Medicaid Hematopoietic Stem-Cell Transplantation for Hodgkin Lymphoma	Medicaid Clinical Coverage Policy No: 11A-7 Amended Date: August 15, 2023

Related Clinical Coverage Policies

Refer to https://medicaid.ncdhhs.gov/ for the related coverage policies listed below:

11A-14, Placental and Umbilical Cord Blood as a Source of Stem Cells

1A-39 Routine Costs in Clinical Trial Services for Life Threatening Conditions

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 2011, an estimated 8,830 new diagnoses and 1,300 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) Classical 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., II2)

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.

1.1 Definitions

1.1.1 Hematopoietic Stem Cell Transplantation (HSCT)

Refers to any source of stem cells, such as autologous, allogeneic, syngeneic, or umbilical cord blood.

1.1.2 Induction Therapy

The first treatment given for a disease. It is often part of a standard set of treatments, such as surgery followed by chemotherapy and radiation. When used by itself, induction therapy is the one accepted as the best treatment. If induction therapy doesn't cure the disease or causes severe side effects, other treatment may be added or used instead. Also called first-line therapy, primary therapy, and primary treatment.

1.1.3 Tandem Transplants

A transplant technique where the preplanned intent for therapy involves sequential hematopoietic stem cell transplants.

1.1.4 Donor Lymphocyte Infusion (DLI)

A type of therapy in which lymphocytes from the blood of a donor are given to a patient who has already received a stem cell transplant from the same donor. The donor lymphocytes may kill remaining cancer cells.

2.0 Eligibility Requirements

2.1 Provisions

2.1.1 General

(*The term "General" found throughout this policy applies to all Medicaid policies*)

a. An eligible beneficiary shall be enrolled in the NC Medicaid Program *(Medicaid is NC Medicaid program, unless context clearly indicates otherwise*).
b. Provider(s) shall verify each Medicaid beneficiary's eligibility each time a service is rendered.
c. The Medicaid beneficiary may have service restrictions due to their eligibility category that would make them ineligible for this service.

2.1.2 Specific

(***The term "Specific" found throughout this policy only applies to this policy***)

a. Medicaid

None Apply.

2.2 Special Provisions

2.2.1 EPSDT Special Provision: Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age

a. **42 U.S.C. § 1396d(r) [1905(r) of the Social Security Act]**

Early and Periodic Screening, Diagnostic, and Treatment (EPSDT) is a federal Medicaid requirement that requires the state Medicaid agency to cover services, products, or procedures for Medicaid beneficiary under 21 years of age **if** the service is **medically necessary health care** to correct or ameliorate a defect, physical or mental illness, or a condition [health problem] identified through a screening examination (includes any evaluation by a physician or other licensed practitioner).

This means EPSDT covers most of the medical or remedial care a child needs to improve or maintain his or her health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

Medically necessary services will be provided in the most economic mode, as long as the treatment made available is similarly efficacious to the service requested by the beneficiary's physician, therapist, or other licensed practitioner; the determination process does not delay the delivery of the needed service; and the determination does not limit the beneficiary's right to a free choice of providers.

EPSDT does not require the state Medicaid agency to provide any service, product or procedure:

1. that is unsafe, ineffective, or experimental or investigational.
2. that is not medical in nature or not generally recognized as an accepted method of medical practice or treatment.

Service limitations on scope, amount, duration, frequency, location of service, and other specific criteria described in clinical coverage policies may be exceeded or may not apply as long as the provider's documentation shows that the requested service is medically necessary "to correct or ameliorate a defect, physical or mental illness, or a condition" [health problem]; that is, provider documentation shows how the service, product, or procedure meets all EPSDT criteria, including to correct or improve or maintain the beneficiary's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

b. **EPSDT and Prior Approval Requirements**

1. If the service, product, or procedure requires prior approval, the fact that the beneficiary is under 21 years of age does **NOT** eliminate the requirement for prior approval.
2. **IMPORTANT ADDITIONAL INFORMATION** about EPSDT and prior approval is found in the *NCTracks Provider Claims and Billing Assistance Guide,* and on the EPSDT provider page. The Web addresses are specified below.

   NCTracks Provider Claims and Billing Assistance Guide: https://www.nctracks.nc.gov/content/public/providers/provider-manuals.html

   EPSDT provider page: https://medicaid.ncdhhs.gov/

3.0 When the Procedure, Product, or Service Is Covered

Note: Refer to Subsection 2.2.1 regarding EPSDT Exception to Policy Limitations for Medicaid Beneficiaries under 21 Years of Age.

3.1 General Criteria

Medicaid shall cover the procedure, product, or service related to this policy when 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 beneficiary'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 statewide; and
c. the procedure, product, or service is furnished in a manner not primarily intended for the convenience of the beneficiary, the beneficiary's caretaker, or the provider.

3.2 Specific Criteria Covered

3.2.1 Specific criteria covered by Medicaid

Medicaid shall cover Hematopoietic Stem Cell Transplantation (HSCT) for Hodgkin Lymphoma in **ANY** the following situations:

a. Single autologous HSCT in beneficiaries with primary refractory Hodgkin disease (refer to **Section 1.0**) or relapsed Hodgkin lymphoma;
b. Allogeneic HSCT, using either myeloablative or reduced-intensity conditioning regimens in beneficiaries with primary refractory (refer to **Section 1.0)** or relapsed Hodgkin lymphoma;
c. Tandem autologous HSCT for **ANY** of the following:
   1. Beneficiaries with primary refractory Hodgkin lymphoma; or
   2. Beneficiaries with relapsed disease with poor risk features who do not attain a complete remission to cytoreductive chemotherapy prior to transplantation (refer to **Section 1.0**).
d. Donor lymphocyte infusion (DLI) (refer to **Section 1.1**) is considered medically necessary and, therefore, covered following allogeneic hematopoietic stem cell transplantation (HSCT) that is medically necessary

for the treatment of Hodgkin lymphoma that has relapsed or is refractory, to prevent relapse in the setting of a high risk of relapse, or to convert an individual from mixed to full donor chimerism.

3.2.2 Medicaid Additional Criteria Covered

None Apply.

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

Note: Refer to Subsection 2.2.1 regarding EPSDT Exception to Policy Limitations for Medicaid Beneficiaries under 21 Years of Age.

4.1 General Criteria Not Covered

Medicaid shall not cover the procedure, product, or service related to this policy when:

a. the beneficiary does not meet the eligibility requirements listed in **Section 2.0;**
b. the beneficiary does not meet the criteria listed in **Section 3.0;**
c. the procedure, product, or service duplicates another provider's procedure, product, or service; or
d. the procedure, product, or service is experimental, investigational, or part of a clinical trial.

4.2 Specific Criteria Not Covered

4.2.1 Specific Criteria Not Covered by Medicaid

a. Medicaid shall not cover Hematopoietic Stem Cell Transplantation (HSCT) for Hodgkin Lymphoma in the following clinical situations:
    1. A second autologous stem cell transplantation for relapsed lymphoma after a prior autologous HSCT; and
    2. Other uses of HSCT in beneficiaries with Hodgkin Lymphoma, including initial therapy for newly diagnosed disease to consolidate a first complete remission.
b. Medicaid shall not cover HSCT when the beneficiary's psychosocial history limits the beneficiary's ability to comply with pre- and post-transplant medical care.
c. Medicaid shall not cover HSCT when current beneficiary or caretaker non-compliance would make compliance with a disciplined medical regime improbable.

4.2.2 Medicaid Additional Criteria Not Covered

None Apply.

5.0 Requirements for and Limitations on Coverage

Note: Refer to Subsection 2.2.1 regarding EPSDT Exception to Policy Limitations for Medicaid Beneficiaries under 21 Years of Age.

5.1 Prior Approval

Medicaid shall not require prior approval for Hematopoietic Stem Cell Transplantation for Hodgkin Lymphoma.

5.2 Prior Approval Requirements

5.2.1 General

None Apply.

5.2.2 Specific

None Apply.

6.0 Provider(s) Eligible to Bill for the Procedure, Product, or Service

To be eligible to bill for the procedure, product, or service related to this policy, the provider(s) shall:

a. meet Medicaid qualifications for participation;
b. have a current and signed Department of Health and Human Services (DHHS) Provider Administrative Participation Agreement; 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.

6.1 Provider Qualifications and Occupational Licensing Entity Regulations

None Apply.

6.2 Provider Certifications

None Apply.

7.0 Additional Requirements

Note: Refer to Subsection 2.2.1 regarding EPSDT Exception to Policy Limitations for Medicaid Beneficiaries under 21 Years of Age.

7.1 Compliance

Provider(s) shall comply with the following in effect at the time the service is rendered:

a. All applicable agreements, federal, state and local laws and regulations including the Health Insurance Portability and Accountability Act (HIPAA) and record retention requirements; and
b. All NC Medicaid's clinical (medical) coverage policies, guidelines, policies, provider manuals, implementation updates, and bulletins published by the Centers for Medicare and Medicaid Services (CMS), DHHS, DHHS division(s) or fiscal contractor(s).

8.0 Policy Implementation/Revision Information

Original Effective Date: January 1, 1994

Revision Information:

Date	Section Revised	Change
07/01/2005	Entire Policy	Policy was updated to include coverage criteria effective with approved date of State Plan amendment 4/1/05.
09/01/2005	Section 2.2	The special provision related to EPSDT was revised.
12/01/2005	Section 2.2	The web address for DMA's EDPST policy instructions was added to this section.
12/01/2006	Sections 2.2	The special provision related to EPSDT was revised.
12/01/2006	Sections 3.0 and 4.0	A note regarding EPSDT was added to these sections.
05/01/2007	Sections 2 through 4	EPSDT information was revised to clarify exceptions to policy limitations for recipients under 21 years of age.
05/01/2007	Attachment A	Added the UB-04 as an accepted claims form.
07/01/2010	Throughout	Session Law 2009-451, Section 10.31(a) Transition of NC Health Choice Program administrative oversight from the State Health Plan to the Division of Medical Assistance (DMA) in the NC Department of Health and Human Services.
01/01/2012	Throughout	Policy updated to reflect current community standards and changing transplant protocols.
03/12/2012	Throughout	To be equivalent where applicable to NC DMA's Clinical Coverage Policy # 11A-7 under Session Law 2011-145, § 10.41.(b)
03/12/2012	Throughout	Technical changes to merge Medicaid and NCHC current coverage into one policy.
10/01/2015	All Sections and Attachments	Updated policy template language and added ICD-10 codes to comply with federally mandated 10/1/2015 implementation where applicable.
03/01/2017	Attachment A, Section B	ICD-10 update revisions
03/15/2019	Table of Contents	Added, "To all beneficiaries enrolled in a Prepaid Health Plan (PHP): for questions about benefits and services available on or after November 1, 2019, please contact your PHP."
03/15/2019	All Sections and Attachments	Updated policy template language.
10/01/2019	Throughout	Removed "& Bone Marrow" from policy title.
10/01/2019	Section 1.0	Updated Hodgkin lymphoma statistics.
10/01/2019	Section 1.1	Added definitions for Hematopoietic Stem Cell Transplantation, induction therapy, tandem transplants, and donor lymphocyte infusion.
10/01/2019	Section 3.2.1	Removed specific situations when reduced intensity conditioning (RIC) is covered. This is discussed in Section 1.0. Criteria added for DLI coverage.

10/01/2019	Section 3.2.4	Section removed as the information contained is discussed in Section 1.0.
10/01/2019	Section 5.1	Added text that if PA has been given for allogeneic HSCT and DLI is later indicated, separate PA is not required for the DLI procedure.
10/01/2019	Section 5.3	"Indications for transplant" added to letter of medical necessity requirements. Added "panel" to Hepatitis panel to reflect verbiage in the State Plan.
10/01/2019	Section 7.0	Removed the following statements: FDA approved procedures, products, and devices for implantation must be utilized. A statement signed by the surgeon certifying all FDA requirements for the implants, products, and devices must be retained in the beneficiary's medical record and made available for review upon request. This text is not applicable to this policy.
10/01/2019	Attachment A	Added the UB-04 as an accepted claims form. Removed all CPT, HCPCS, and ICD-10 codes.
01/15/2020	Table of Contents	Updated policy template language, "To all beneficiaries enrolled in a Prepaid Health Plan (PHP): for questions about benefits and services available on or after implementation, please contact your PHP."
01/15/2020	Attachment A	Added, "Unless directed otherwise, Institutional Claims must be billed according to the National Uniform Billing Guidelines. All claims must comply with National Coding Guidelines".
07/01/2021	Section 5.0	Prior approval requirement removed.
8/15/2023	All Sections and Attachments	Updated policy template language due to North Carolina Health Choice Program's move to Medicaid. Policy posted 8/15/2023 with an effective date of 4/1/2023.

Attachment A: Claims-Related Information

Provider(s) shall comply with the, *NCTracks Provider Claims and Billing Assistance Guide*, Medicaid bulletins, fee schedules, NC Medicaid's clinical coverage policies and any other relevant documents for specific coverage and reimbursement for Medicaid:

A. Claim Type

Professional (CMS-1500/837P transaction)

Institutional (UB-04/83711)

Unless directed otherwise, Institutional Claims must be billed according to the National Uniform Billing Guidelines. All claims must comply with National Coding Guidelines.

B. International Classification of Diseases and Related Health Problems, Tenth Revisions, Clinical Modification (ICD-10-CM) and Procedural Coding System (PCS)

Provider(s) shall report the ICD-10-CM and Procedural Coding System (PCS) to the highest level of specificity that supports medical necessity. Provider(s) shall use the current ICD-10 edition and any subsequent editions in effect at the time of service. Provider(s) shall refer to the applicable edition for code description, as it is no longer documented in the policy.

C. Code(s)

Provider(s) shall report the most specific billing code that accurately and completely describes the procedure, product or service provided. Provider(s) shall use the Current Procedural Terminology (CPT), Health Care Procedure Coding System (HCPCS), and UB-04 Data Specifications Manual (for a complete listing of valid revenue codes) and any subsequent editions in effect at the time of service. Provider(s) shall refer to the applicable edition for the code description, as it is no longer documented in the policy.

If no such specific CPT or HCPCS code exists, then the provider(s) shall report the procedure, product or service using the appropriate unlisted procedure or service code.

Unlisted Procedure or Service
CPT: The provider(s) shall refer to and comply with the Instructions for Use of the CPT Codebook, Unlisted Procedure or Service, and Special Report as documented in the current CPT in effect at the time of service.

HCPCS: The provider(s) shall refer to and comply with the Instructions for Use of HCPCS National Level II codes, Unlisted Procedure or Service and Special Report as documented in the current HCPCS edition in effect at the time of service.

D. Modifiers

Provider(s) shall follow applicable modifier guidelines.

E. Billing Units

Provider(s) shall report the appropriate code(s) used which determines the billing unit(s).

F. Place of Service

Inpatient Hospital, Outpatient Hospital

G. Co-payments

For Medicaid refer to Medicaid State Plan:
https://medicaid.ncdhhs.gov/meetings-notices/medicaid-state-plan-public-notices

H. Reimbursement

Provider(s) shall bill their usual and customary charges.
For a schedule of rates, refer to: https://medicaid.ncdhhs.gov/

I. Billing for Donor Expenses

Billing for Donor Expenses for Medicaid Beneficiaries
Donor transplant-related medical expenses are billed on the Medicaid beneficiary's transplant claim using the beneficiary's Medicaid identification number.

Medicaid reimburses only for the actual donor's transplant-related medical expenses. Medicaid does not reimburse for unsuccessful donor searches.