| NC Medicaid<br>Hematopoietic Stem-Cell Transplantation (HSCT) for Central Nervous System (CNS) Embryonal Tumors & Ependymoma | Medicaid<br>Clinical Coverage Policy No: 11A-10<br>Amended Date: August 15, 2023 |
|---|---|

**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.**

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**Related Clinical Coverage Policies**

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

11A-15, *Hematopoietic Stem-Cell Transplantation for Solid Tumors of Childhood*

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. Bone-marrow stem cells may be obtained from the transplant recipient (autologous SCT) or from a donor (allogeneic SCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood and placenta shortly after delivery of neonates.

### Hematopoietic Stem-Cell Transplantation for Brain Tumors

Autologous HSCT allows for escalation of chemotherapy doses above those limited by myeloablation and has been tried in patients with high-risk brain tumors in an attempt to eradicate residual tumor cells and improve cure rates. The use of allogeneic HSCT for solid tumors does not rely on escalation of chemotherapy intensity and tumor reduction, but rather on a graft-versus-tumor effect. Allogeneic HSCT is uncommonly used in solid tumors and may be used if an autologous source cannot be cleared of tumor or cannot be harvested.

### CNS Embryonal Tumors

Embryonal tumors are a collection of biologically heterogeneous lesions that share the tendency to disseminate throughout the nervous system via cerebrospinal fluid (CSF) pathways. Although there is significant variability, histologically these tumors are grouped together because they are at least partially composed of hyperchromatic cells (blue cell tumors on standard staining) with little cytoplasm, which are densely packed and demonstrate a high degree of mitotic activity. Other histologic and immunohistochemical features, such as the degree of apparent cellular transformation along identifiable cell lineages (ependymal, glial, etc.), can be used to separate these tumors to some degree. The classification also separates these tumors on the basis of presumed location of origin within the central nervous system (CNS). Molecular studies have substantiated the differences between tumors arising in different areas of the brain and give partial credence to this classification approach.

In 2016, the WHO proposed an integrated phenotypic and genotypic classification system for CNS tumors. The term *primitive neuroectodermal tumor (PNET)* has been removed from the newest WHO diagnostic lexicon, although some rare entities (e.g., medulloepithelioma) have remained. A molecularly distinct entity, embryonal tumor with multilayered rosettes (ETMR), *C19MC*-altered, has been added, encompassing embryonal tumor with abundant neuropil and true rosettes (ETANTR), ependymoblastoma, and medulloepithelioma. The WHO classification will be updated as other molecularly distinct entities are defined.

The pathologic diagnosis of embryonal tumors is based primarily on histological and immunohistological microscopic features. However, molecular genetic studies are employed increasingly to subclassify embryonal tumors. These molecular genetic findings are also being utilized for risk stratification and treatment planning. Embryonal tumors of the CNS include medulloblastoma, medulloepithelioma, CNS neuroblastoma, CNS ganglioneuroblastoma, CNS atypical teratoid/rhabdoid tumor (AT/RT), CNS embryonal tumor with rhabdoid features, and pineoblastoma.

**Note:** Due to their neuroepithelial origin, peripheral neuroblastoma and Ewing's sarcoma may be considered ETMRs. However, these peripheral tumors are considered separately in clinical coverage policy 11A-15, *Hematopoietic Stem-Cell Transplantation for Solid Tumors of Childhood*.

**Medulloblastomas** account for 20% of all childhood CNS tumors. Surgical resection is the mainstay of therapy with the goal being gross total resection with adjuvant radiation therapy, as medulloblastomas are very radiosensitive. Treatment protocols are based on risk stratification, as average or high risk. The **average-risk group** includes children older than three years, without metastatic disease, and with tumors that are totally or near totally resected (less than 1.5 $cm^2$ of residual disease). The **high-risk group** includes children aged three years or younger, or with metastatic disease, and/or subtotal resection (greater than 1.5 $cm^2$ of residual disease). Current standard treatment regimens for **average-risk medulloblastoma** (postoperative craniospinal irradiation with boost to the posterior fossa followed by 12 months of chemotherapy) have resulted in five-year overall survival (OS) rates of 80% or better. For **high-risk medulloblastoma** treated with conventional doses of chemotherapy and radiotherapy, the average event-free survival at five years ranges from 34%–40% across studies. Fewer than 55% of children with high-risk disease survive longer than five years. The treatment of newly diagnosed medulloblastoma continues to evolve, and in children under the age of three years, because of the concern of the deleterious effects of craniospinal radiation on the immature nervous system, therapeutic approaches have attempted to delay and sometimes avoid the use of radiation and have included trials of higher-dose chemotherapeutic regimens with autologous HSCT.

The other types of embryonal tumors are rare by comparison. The prognosis for these tumors is worse than for medulloblastoma, despite identical therapies. After surgery, children are usually treated similarly to children with high-risk medulloblastoma. Three- to five-year OS rates of 40%–50% have been reported, and for patients with disseminated disease, survival rates at five years range from 10%–30%.

Recurrent childhood CNS embryonal tumor is not uncommon and depending on which type of treatment the patient initially received, autologous HSCT may be an option. For patients who receive high-dose chemotherapy and autologous HSCT for recurrent embryonal tumors, objective response is 50%–75%; however, long-term disease control is obtained in fewer than 30% of patients and is seen primarily in patients in first relapse with localized disease at the time of relapse.

## Ependymoma

Ependymomas arise from ependymal cells that line the ventricles and passageways in the brain and the center of the spinal cord. Ependymal cells produce cerebrospinal fluid (CSF). These

tumors are classified as supratentorial or infratentorial. In children, most ependymomas are infratentorial tumors that arise in or around the fourth ventricle. Childhood ependymoma comprises approximately 9% of all childhood brain tumors, representing about 200 cases per year in the United States. According to the 2016 revision to the World Health Organization (WHO) classification of tumors of the central nervous system, ependymal tumors are classified into subependymoma, myxopapillary ependymoma, ependymoma, ependymoma (RELA fusion–positive), and anaplastic ependymoma. Initial treatment of ependymoma consists of maximal surgical resection followed by radiotherapy. Chemotherapy usually does not play a role in the initial treatment of ependymoma. However, disease relapse is common, typically occurring at the site of origin. Treatment of recurrence is problematic; further surgical resection or radiation therapy is usually not possible. Given the poor response to conventional-dose chemotherapy, high-dose chemotherapy with autologous HSCT has been investigated as a possible salvage therapy.

## 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 Consolidation Therapy

Treatment that is given after cancer has disappeared following the initial therapy. Consolidation therapy is used to kill any cancer cells that may be left in the body. It may include radiation therapy, a stem cell transplant, or treatment with drugs that kill cancer cells. Also called intensification therapy and post remission therapy.

### 1.1.4 Rescue Transplant

A method of replacing blood-forming stem cells that were destroyed by treatment with high doses of anticancer drugs or radiation therapy. The stem cells help the bone marrow recover and make healthy blood cells. A rescue transplant may allow more chemotherapy or radiation therapy to be given so that more cancer cells are killed. It is usually done using the patient's own stem cells that were saved before treatment. Also called stem cell rescue.

### 1.1.5 Salvage Therapy

Treatment that is given after the cancer has not responded to other treatments.

### 1.1.6 Tandem Transplants

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

# 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. <u>Medicaid</u>**
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 Covered

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

a. Medicaid shall cover **single** autologous HSCT when it is determined to be medically necessary as:

1. Consolidation therapy for previously untreated embryonal tumors of the central nervous system (CNS) that show partial or complete response to induction chemotherapy, or stable disease after induction therapy (refer to **Section 1.0**); or
2. Treatment for recurrent CNS embryonal tumors.

b. Medicaid shall cover **tandem** autologous HSCT when it is determined to be medically necessary as treatment for **high-risk** embryonal tumors of the CNS (refer to **Section 1.0**).

#### 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

Medicaid shall not cover HSCT for **ANY** of the following:

a. Allogenic HSCT to treat embryonal tumors of the CNS;
b. Tandem autologous HSCT for the treatment of **average-risk** embryonal tumors of the CNS (refer to **Section 1.0**);
c. Autologous, tandem autologous and allogeneic HSCT to treat ependymoma; or
d. Autologous, tandem autologous and allogeneic HSCT to treat other CNS tumors, such as astrocytoma, oligodendroglioma, and glioblastoma multiforme, as these tumors arise from glial cells and not neuroepithelial cells.

#### 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 (HSCT) for Central Nervous System (CNS) Embryonal Tumors & Ependymoma.

### 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 a Medicaid Beneficiary 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 | Medicaid: Policy was updated to include coverage criteria effective with approved date of State Plan amendment 4/1/05. |
| 09/01/2105 | Section 2.2 | Medicaid: The special provision related to EPSDT was revised. |
| 12/01/2005 | Section 2.2 | Medicaid: The web address for DMA's EDPST policy instructions was added to this section. |
| 12/01/2006 | Sections 2.2 | Medicaid: The special provision related to EPSDT was revised. |
| 12/01/2006 | Sections 3.0 and 4.0 | Medicaid: A note regarding EPSDT was added to these sections. |
| 05/01/2007 | Sections 2 through 4 | Medicaid: EPSDT information was revised to clarify exceptions to policy limitations for recipients under 21 years of age. |
| 05/01/2007 | Attachment A | Medicaid: Added the UB-04 as an accepted claims form. |
| 07/01/2010 | Throughout | NCHC: 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. |
| 03/12/2012 | Throughout | NCHC: To be equivalent where applicable to NC DMA's Clinical Coverage Policy # 11A-10 under Session Law 2011-145, § 10.41. (b) |
| 03/12/2012 | Throughout | Policy updated to reflect Current Community standards and changing transplant protocols. |
| 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 updated codes revised. |
| 11/01/2018 | Throughout | Name of policy changed to Hematopoietic Stem-Cell Transplantation (HSCT) for Central Nervous System (CNS) Embryonal Tumors & Ependymoma. |
| 11/01/2018 | Section 1.0 | Updated text regarding CNS embryonal tumors and ependymoma along with updated 2016 WHO classifications. |

| Date | Section Revised | Change |
|---|---|---|
| 11/01/2018 | Section 1.1 | Added definitions for HSCT, induction therapy, consolidation therapy, rescue transplant, salvage therapy, and tandem transplants. |
| 11/01/2018 | Section 3.2.1 | Added coverage for tandem autologous HSCT for high-risk CNS embryonal tumors. |
| 11/01/2018 | Section 3.2.4 | Section removed as information is now out of date. |
| 11/01/2018 | Section 4.2.1 | Added tandem autologous HSCT for the treatment of average-risk CNS embryonal tumors to non-coverage. |
| 11/01/2018 | Section 5.3 | Added "panel" after Hepatitis to reflect terminology in the State Plan. Added "indications for transplant" to the letter of medical necessity requirements. |
| 11/01/2018 | Section 7.1 | Removed requirement that a statement signed by the surgeon certifying all FDA requirements for the implants, products, and devices be retained. Removed statement that FDA approved procedures, products, and devices for implantation must be utilized. |
| 11/01/2018 | Attachment A, Section A | Added Institutional (UB-04/83711) as claim type. |
| 11/01/2018 | Attachment A, Section B | ICD-10 codes removed. |
| 11/01/2018 | Attachment A, Section C | CPT and HCPCS codes removed. |
| 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. |
| 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. |
| 07/01/2021 | Attachment A | Section I. Billing for Donor Expenses removed as donors do not apply to this policy (allogeneic transplant not covered). |
| 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/