

Table of Contents

1.0	Description of the Procedure, Product, or Service.....	1
2.0	Eligible Recipients.....	4
2.1	General Provisions.....	4
2.2	EPSDT Special Provision: Exception to Policy Limitations for Recipients under 21 Years of Age.....	5
3.0	When the Procedure, Product, or Service Is Covered.....	5
3.1	General Criteria.....	6
3.2	Specific Criteria.....	6
3.3	Other Medical Policy Guidelines.....	6
4.0	When the Procedure, Product, or Service Is Not Covered.....	6
4.1	General Criteria.....	7
4.2	Specific Criteria.....	7
4.3	Policy Guideline.....	7
5.0	Requirements for and Limitations on Coverage.....	8
5.1	Prior Approval.....	8
5.2	Prior Approval Requirements.....	8
6.0	Providers Eligible to Bill for the Procedure, Product, or Service.....	8
7.0	Additional Requirements.....	9
7.1	Compliance.....	9
8.0	Policy Implementation/Revision Information.....	9
Attachment A: Claims-Related Information.....		10
A.	Claim Type.....	10
B.	Diagnosis Codes.....	10
C.	Procedure Code(s).....	10
D.	Modifiers.....	10
E.	Billing Units.....	10
F.	Place of Service.....	11
G.	Co-payments.....	11
H.	Reimbursement.....	11
I.	Billing for Donor Expenses.....	11

1.0 Description of the Procedure, Product, or Service

Hematopoietic Stem-Cell Transplantation for Solid Tumors

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. Stem cells may be obtained from the transplant recipient (autologous HSCT) or can be harvested from a donor (allogeneic HSCT). Stem cells may be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates.

Autologous HSCT takes advantage of the steep dose-response relationship observed with many chemotherapeutic agents and allows for escalation of chemotherapy doses above those limited by myeloablation. The use of allogeneic HSCT for solid tumors relies 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.

Solid Tumors of Childhood

Solid tumors of childhood are defined as those not arising from myeloid or lymphoid cells. Some of the most common solid tumors of childhood are neuroblastoma, Ewing's sarcoma/Ewing's Sarcoma Family of Tumors, Wilms tumor, rhabdomyosarcoma, osteosarcoma, and retinoblastoma.

The prognosis for pediatric solid tumors has improved over the last 2 decades, mostly due to the application of multiagent chemotherapy and improvements in local control therapy (including aggressive surgery and advancements in radiation therapy). However, patients with metastatic, refractory, or recurrent disease continue to have poor prognoses, and these "high-risk" patients are candidates for more aggressive therapy, including autologous HSCT, in an effort to improve event-free survival (EFS) and overall survival (OS).

Descriptions of the solid tumors of childhood that are addressed in this policy are as follows:

Peripheral Neuroblastoma

Neuroblastoma is the most common extracranial solid tumor of childhood with two-thirds of the cases presenting in children younger than 5 years of age. These tumors originate where sympathetic nervous system tissue is present, within the adrenal medulla or paraspinal sympathetic ganglia. They are remarkable for their broad spectrum of clinical behavior, with some undergoing spontaneous regression, others differentiating into benign tumors, and still others progressing rapidly and resulting in patient death.

Patients with neuroblastoma are stratified into prognostic risk groups (low, intermediate, and high) that determine treatment plans. Risk variables include age at diagnosis, clinical stage of disease, tumor histology, and certain molecular characteristics, including the presence of the MYCN oncogene.

Tumor histology is categorized as favorable or unfavorable, according to the degree of tumor differentiation, proportion of tumor stromal component, and index of cellular proliferation. It is well established that MYCN amplification is associated with rapid tumor progression and a poor prognosis even in the setting of other coexisting favorable factors. Loss of heterozygosity (LOH) at chromosome arms 1p and 11q occurs frequently in neuroblastoma. Although 1p LOH is associated with MYCN amplification, 11q is usually found in tumors without this abnormality. Some recent studies have shown that 1p LOH and unbalanced 11q LOH are strongly associated with outcome in patients with neuroblastoma and both are independently predictive of worse progression-free survival (PFS) in patients with low- and intermediate-risk disease. Although the use of these LOH markers in assigning treatment in patients is evolving, they may prove useful to stratify treatment.

Clinical stage of disease is based on the International Neuroblastoma Staging System (INSS) as follows:

Stage 1: Localized tumor with complete gross excision, with or without microscopic residual disease; lymph nodes negative for tumor

Stage 2A: Localized tumor with incomplete gross excision; lymph nodes negative for tumor

Stage 2B: Localized tumor with or without complete gross excision, with ipsilateral lymph nodes positive for tumor

Stage 3: Unresectable unilateral tumor infiltrating across the midline, with or without regional lymph node involvement; or localized unilateral tumor with contralateral regional lymph node involvement; or midline tumor with bilateral extension by infiltration or by lymph node involvement

Stage 4: Any primary tumor with dissemination to distant lymph nodes, bone, bone marrow, liver, skin, and/or other organs, except as defined for stage 4S

Stage 4S: Localized primary tumor as defined for stage 1, 2A, or 2B, with dissemination limited to skin, liver, and/or bone marrow (marrow involvement less than 10%), limited to children younger than 1 year of age

The low-risk group includes patients less than 1 year of age with stage 1, 2, or 4S with favorable histopathologic findings and no MYCN oncogene amplification. High-risk neuroblastoma is characterized by an age older than 1 year, disseminated disease, MYCN oncogene amplification, and unfavorable histopathologic findings.

In general, most patients with low-stage disease have excellent outcomes with minimal therapy, and with INSS stage 1 disease, most patients can be treated by surgery alone. Most infants, even with disseminated disease, have favorable outcomes with chemotherapy and surgery. In contrast, most children older than 1 year with advanced-stage disease die due to progressive disease, despite intensive multimodality therapy and relapse remains common. Treatment of recurrent disease is determined by the risk group at the time of diagnosis, and the extent of disease and age of the patient at recurrence.

Ewing's Sarcoma and the Ewing Family of Tumors

Ewing's sarcoma family of tumors (ESFT) encompasses a group of tumors that have in common some degree of neuroglial differentiation and a characteristic underlying molecular pathogenesis (chromosomal translocation). The translocation usually involves chromosome 22 and results in fusion of the EWS gene with one of the members of the ETS family of transcription factors, either FLI1 (90–95%) or ERG (5–10%). These fusion products function as oncogenic aberrant transcription factors. Detection of these fusions is considered to be specific for the ESFT, and helps further validate the diagnosis. Included in ESFT are “classic” Ewing's sarcoma of bone, extraosseous Ewing's, peripheral primitive neuroectodermal tumor (pPNET), and Askin tumors (chest wall).

Most commonly diagnosed in adolescence, ESFT can be found in bone (most commonly) or soft tissue; however, the spectrum of ESFT has also been described in various organ systems. Ewing's is the second most common primary malignant bone tumor. The most common primary sites are the pelvic bones, the long bones of the lower extremities, and the bones of the chest wall. Current therapy for Ewing's sarcoma favors induction chemotherapy, with local control consisting of surgery and/or radiation (dependent on tumor size and location), followed by adjuvant chemotherapy. Multiagent chemotherapy, surgery, and radiation therapy have improved the PFS in patients with localized disease to 60%–70%. The presence of metastatic disease is the most unfavorable prognostic feature, and the outcome for patients presenting with metastatic disease is poor, with 20%–30% PFS. Other adverse prognostic factors that may categorize a patient as having “high-risk” Ewing's are tumor location (e.g., patients with pelvic primaries have worse outcomes), larger tumor size, and older age of the patient. However, “high-risk” Ewing's has not always been consistently defined in the literature. Thirty to forty percent of patients with ESFT experience disease recurrence and patients with recurrent disease have a 5-year EFS and OS rate of less than 10%.

Rhabdomyosarcoma

Rhabdomyosarcoma (RMS), the most common soft tissue sarcoma of childhood, shows skeletal muscle differentiation. The most common primary sites are the head and neck (e.g., parameningeal, orbital, and pharyngeal), genitourinary tract, and extremities. Most children with RMS present with localized disease, and with conventional multimodal therapy, the cure rate in this group is 70%–80%. However, approximately 15% of children present with metastatic disease, and despite the introduction of new drugs and intensified treatment, the 5-year survival is 20%–30% for this “high-risk” group.

Wilms Tumor

Wilms tumor, the most common primary malignant renal tumor of childhood, is highly sensitive to chemotherapy and radiation, and current cure rates exceed 85%. Ten to 15% of patients with favorable histology and 50% of patients with anaplastic tumors experience tumor progression or relapse. Similar to newly diagnosed Wilms, relapsed Wilms tumor is a heterogeneous disease, and current treatment strategies stratify intensity and scheduling of the treatment modalities based on prognostic features. For newly diagnosed disease, the most important prognostic features are stage and histology. Similar risk-adapted strategies are being attempted for the 15% of patients who experience relapse. Success rates after relapse range from 25%–45%. For patients with adverse prognostic factors (histologically anaplastic tumors, relapse less than 6–12 months after nephrectomy, second or subsequent relapse, relapse within the radiation field, bone or brain metastases) event-free survival is less than 15%. However, recent trials with HDC and autologous HSCT have reported 3- or 4-year OS rates from 60%–73%.

Osteosarcoma

Osteosarcoma is a primary malignant bone tumor that is characterized by formation of bone or osteoid by the tumor cells. Osteosarcoma occurs predominantly in the appendicular skeleton of adolescents. In children and adolescents, more than 50% of these tumors arise from bones around the knee. The prognosis of localized osteosarcoma has greatly improved over the last 30 years with OS rates increasing from 10% with surgery alone (usually amputation) to 70% with the introduction of neoadjuvant chemotherapy and limb-sparing surgery. However, 30%–40% of patients with non-metastatic osteosarcoma of the extremities experience recurrent disease, most commonly in the lungs. Mean 5-year post-relapse survival rate is approximately 28%, with some groups having a 0% OS rate. Prognostic factors for recurrence include site and size of the primary tumor, presence of metastases at the time of diagnosis, resection adequacy, and tumor response to preoperative chemotherapy (measured as percent of tumor necrosis in the resection specimen). Overall EFS for patients with metastatic disease at diagnosis is about 20%–30%.

Retinoblastoma

Retinoblastoma is the most common primary tumor of the eye in children. It may occur as a heritable (40%) or nonheritable (60%) tumor. Cases may be unilateral or bilateral, with bilateral tumor almost always occurring in the heritable type. The type of treatment depends on the extent of disease. Retinoblastoma is usually confined to the eye, and with current therapy has at least a 90% cure rate. However, once disease has spread beyond the eye, survival rates drop significantly; 5-year disease-free survival is reported to be less than 10% in those with extraocular disease. Extraocular disease may be localized to the soft tissues surrounding the eye, or to the optic nerve, extending beyond the margin of resection. Further extension may result in involvement of the brain and meninges, with subsequent seeding of the cerebrospinal fluid, as well as distant metastases to the lungs, bone, and bone marrow. Stage 4a disease is defined as distant metastatic disease not involving the central nervous system (CNS), and stage 4b is defined as metastatic disease to the CNS.

Related Policies:

Cord Blood As a Source of Stem Cells.

Hematopoietic Stem-Cell Transplantation for Neuroectodermal Tumors and Ependymoma

Hematopoietic Stem-Cell Transplantation for Germ Cell Tumors

2.0 Eligible Recipients

2.1 General Provisions

Medicaid recipients may have service restrictions due to their eligibility category that would make them ineligible for this service.

2.2 EPSDT Special Provision: Exception to Policy Limitations for Recipients under 21 Years of Age

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 recipients 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 clinician). This means EPSDT covers most of the medical or remedial care a child needs to improve or maintain his/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 recipient'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 recipient's right to a free choice of providers.

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

- a. that is unsafe, ineffective, or experimental/investigational.
- b. 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/or 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 will correct or improve or maintain the recipient's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

**EPSDT and Prior Approval Requirements

- a. If the service, product, or procedure requires prior approval, the fact that the recipient is under 21 years of age does **NOT** eliminate the requirement for prior approval.
- b. **IMPORTANT ADDITIONAL INFORMATION** about EPSDT and prior approval is found in the *Basic Medicaid Billing Guide*, sections 2 and 6, and on the EPSDT provider page. The Web addresses are specified below.

Basic Medicaid Billing Guide: <http://www.ncdhhs.gov/dma/basicmed/>

EPSDT provider page: <http://www.ncdhhs.gov/dma/epsdt/>

3.0 When the Procedure, Product, or Service Is Covered

IMPORTANT NOTE: EPSDT allows a recipient less than 21 years of age to receive services in excess of the limitations or restrictions below and without meeting the specific criteria in this section when such services are **medically necessary health care services** to correct or ameliorate a defect, physical or mental illness, or a condition [health problem]; that is, documentation shows

how the service, product, or procedure will correct or improve or maintain the recipient's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

EPSDT DOES NOT ELIMINATE THE REQUIREMENT FOR PRIOR APPROVAL IF PRIOR APPROVAL IS REQUIRED. For additional information about EPSDT and prior approval requirements, refer to **Subsection 2.2** of this policy.

3.1 General Criteria

Medicaid 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 statewide; 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

Medicaid covers autologous hematopoietic stem-cell transplantation (HSCT) when it is determined to be medically necessary in the following situations for:

- a. initial treatment of high-risk neuroblastoma; or
- b. recurrent or refractory neuroblastoma; or
- c. initial treatment of high-risk Ewing's sarcoma; or
- d. recurrent or refractory Ewing's sarcoma

3.3 Other Medical Policy Guidelines

HSCT refers to any source of stem cells, i.e., autologous, allogeneic, syngeneic, or umbilical cord blood.

The policy statement regarding multiple hematopoietic stem-cell transplants (i.e., tandem or multiple) only mentions neuroblastoma, as that is the only indication in this policy in which studies regarding multiple-cycle therapy have been published.

Relapse is defined as tumor recurrence after a prior complete response.

Primary refractory disease is defined as a tumor that does not achieve a complete remission after initial standard-dose chemotherapy.

The use of autologous HSCT has become the preferred treatment for children with "high-risk" neuroblastoma, after randomized studies have shown improved EFS and OS.

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

IMPORTANT NOTE: EPSDT allows a recipient less than 21 years of age to receive services in excess of the limitations or restrictions below and without meeting the specific criteria in this

section when such services are **medically necessary health care services** to correct or ameliorate a defect, physical or mental illness, or a condition [health problem]; that is, documentation shows how the service, product, or procedure will correct or improve or maintain the recipient's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

EPSDT DOES NOT ELIMINATE THE REQUIREMENT FOR PRIOR APPROVAL IF PRIOR APPROVAL IS REQUIRED. For additional information about EPSDT and prior approval requirements, refer to **Subsection 2.2** of this policy.

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, investigational, or part of a clinical trial.

4.2 Specific Criteria

Medicaid does not cover HSCT for solid tumors of childhood in the following situations:

- a. Autologous hematopoietic stem-cell transplantation is considered investigational as initial treatment of low- or intermediate-risk neuroblastoma, initial treatment of low- or intermediate-risk Ewing's sarcoma, and for other solid tumors of childhood including, but not limited, to the following:
 1. rhabdomyosarcoma
 2. Wilms tumor
 3. osteosarcoma
 4. retinoblastoma.
- b. Tandem or multiple hematopoietic stem-cell transplantations is considered investigational for treatment of neuroblastoma.
- c. Salvage allogeneic hematopoietic stem-cell transplantation for neuroblastoma or other pediatric solid tumors that relapse after autologous transplant or fail to respond is considered investigational.

4.3 Policy Guideline

The National Comprehensive Cancer Network (NCCN) Guidelines for Bone Cancer and Sarcoma do not list high dose chemotherapy (HDC) with stem-cell support as a treatment option.

5.0 Requirements for and Limitations on Coverage

IMPORTANT NOTE: EPSDT allows a recipient less than 21 years of age to receive services in excess of the limitations or restrictions below and without meeting the specific criteria in this section when such services are **medically necessary health care services** to correct or ameliorate a defect, physical or mental illness, or a condition [health problem]; that is, documentation shows how the service, product, or procedure will correct or improve or maintain the recipient's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

EPSDT DOES NOT ELIMINATE THE REQUIREMENT FOR PRIOR APPROVAL IF PRIOR APPROVAL IS REQUIRED. For additional information about EPSDT and prior approval requirements, refer to **Subsection 2.2** of this policy.

5.1 Prior Approval

Prior approval is required for bone marrow transplant for solid tumors of childhood.

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

All applicable N.C. Medicaid policies and procedures must be followed in addition to the ones listed in this procedure.

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 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 Medicaid's qualifications for participation;
- b. be currently enrolled with N.C. Medicaid; 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

IMPORTANT NOTE: EPSDT allows a recipient less than 21 years of age to receive services in excess of the limitations or restrictions below and without meeting the specific criteria in this section when such services are **medically necessary health care services** to correct or ameliorate a defect, physical or mental illness, or a condition [health problem]; that is, documentation shows how the service, product, or procedure will correct or improve or maintain the recipient's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

EPSDT DOES NOT ELIMINATE THE REQUIREMENT FOR PRIOR APPROVAL IF PRIOR APPROVAL IS REQUIRED. For additional information about EPSDT and prior approval requirements, refer to **Subsection 2.2** of this policy.

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: January 1, 1994

Revision Information:

Date	Section Revised	Change
7/1/05	Entire Policy	Policy was updated to include coverage criteria effective with approved date of State Plan amendment 4/1/05.
9/1/05	Section 2.2	The special provision related to EPSDT was revised.
12/1/05	Section 2.2	The web address for DMA's EDPST policy instructions was added to this section.
12/1/06	Sections 2.2	The special provision related to EPSDT was revised.
12/1/06	Sections 3.0 and 4.0	A note regarding EPSDT was added to these sections.
5/1/07	Sections 2 through 4	EPSDT information was revised to clarify exceptions to policy limitations for recipients under 21 years of age.
5/1/07	Attachment A	Added the UB-04 as an accepted claim form
12/1/05	Section 2.2	The web address for DMA's EDPST policy instructions was added to this section.
12/1/06	Sections 2.2	The special provision related to EPSDT was revised.
12/1/06	Sections 3.0 and 4.0	A note regarding EPSDT was added to these sections.
3/1/12	Entire Policy	Policy updated to reflect current community standards and changing transplant protocols.

Attachment A: Claims-Related Information

Reimbursement requires compliance with all Medicaid guidelines, including obtaining appropriate referrals for recipients enrolled in the Medicaid managed care programs.

A. Claim Type

Professional (CMS-1500/837P 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 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, Outpatient 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-Medicaid donors are billed on the Medicaid recipient's transplant claim using the recipient's Medicaid identification number. Donor expenses for Medicaid donors are billed on the Medicaid donor's claim using the donor's Medicaid identification number.

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