



MASSACHUSETTS

Blue Cross Blue Shield of Massachusetts is an independent
Licensee of the Blue Cross and Blue Shield Association

Medical Policy

Hematopoietic Cell Transplantation for Solid Tumors of Childhood

Table of Contents

- [Policy: Commercial](#)
- [Policy: Medicare](#)
- [Authorization Information](#)
- [Coding Information](#)
- [Description](#)
- [Policy History](#)
- [Information Pertaining to All Policies](#)
- [References](#)

Policy Number: 208

BCBSA Reference Number: 8.01.34

NCD/LCD: National Coverage Determination (NCD) for Stem Cell Transplantation (110.8.1)

Related Policies

Hematopoietic Cell Transplantation for CNS Embryonal Tumors and Ependymoma, #[205](#)

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Autologous hematopoietic cell transplantation may be considered **MEDICALLY NECESSARY** for:

- Initial treatment of high-risk neuroblastoma,
- Recurrent or refractory neuroblastoma,
- Initial treatment of high-risk Ewing sarcoma,
- Recurrent or refractory Ewing sarcoma, and
- Metastatic retinoblastoma.

Tandem autologous hematopoietic cell transplantation may be considered **MEDICALLY NECESSARY** for high-risk neuroblastoma.

Autologous hematopoietic cell transplantation is considered **INVESTIGATIONAL** as initial treatment of low- or intermediate-risk neuroblastoma, initial treatment of low- or intermediate-risk Ewing sarcoma, and for other solid tumors of childhood including, but not limited, to the following:

- Rhabdomyosarcoma,
- Wilms tumor,
- Osteosarcoma
- Retinoblastoma without metastasis.

Tandem autologous hematopoietic cell transplantation is **INVESTIGATIONAL** for the treatment of all other types of pediatric solid tumors except high-risk neuroblastoma, as noted above.

Allogeneic (myeloablative or nonmyeloablative) hematopoietic cell transplantation is **INVESTIGATIONAL** for treatment of pediatric solid tumors.

Salvage allogeneic (myeloablative or nonmyeloablative) hematopoietic cell transplantation for pediatric solid tumors that relapse after autologous transplant or fail to respond is considered [INVESTIGATIONAL](#).

Medicare HMO BlueSM and Medicare PPO BlueSM Members

Medical necessity criteria and coding guidance can be found through the link below.

[National Coverage Determinations \(NCDs\)](#)

National Coverage Determination (NCD) for Stem Cell Transplantation (110.8.1)

Note: To review the specific NCD, please remember to click “accept” on the CMS licensing agreement at the bottom of the CMS webpage.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is required .
Commercial PPO and Indemnity	Prior authorization is required .
Medicare HMO Blue SM	Prior authorization is required .
Medicare PPO Blue SM	Prior authorization is required .

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above **medical necessity criteria MUST** be met for the following codes to be covered for **Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue**

CPT Codes

CPT codes:	Code Description
38241	Bone marrow or blood-derived peripheral stem-cell transplantation; autologous
38243	Hematopoietic progenitor cell (HPC); HPC boost

HCPCS Codes

HCPCS codes:	Code Description
S2150	Bone marrow or blood-derived peripheral stem-cell harvesting and transplantation, allogeneic or autologous, including pheresis, high-dose chemotherapy, and the number of days of post-transplant care in the global definition (including drugs; hospitalization; medical surgical, diagnostic and emergency services)

ICD-10 Procedure Codes

ICD-10-PCS procedure codes:	Code Description
30233G0	Transfusion of Autologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30233X0	Transfusion of Autologous Cord Blood Stem Cells into Peripheral Vein, Percutaneous Approach
30233Y0	Transfusion of Autologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach
30243G0	Transfusion of Autologous Bone Marrow into Central Vein, Percutaneous Approach
30243X0	Transfusion of Autologous Cord Blood Stem Cells into Central Vein, Percutaneous Approach
30243Y0	Transfusion of Autologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach

The following CPT and HCPCS codes are considered investigational for **Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:**

CPT Codes

CPT codes:	Code Description
38240	Bone marrow or blood-derived peripheral stem-cell transplantation; allogeneic

HCPCS Codes

HCPCS codes:	Code Description
S2142	Cord blood derived stem-cell transplantation, allogeneic

Description

Solid Tumors of Childhood

Solid tumors of childhood arise from mesodermal, ectodermal, and endodermal cells of origin.¹ Some common solid tumors of childhood are neuroblastoma, Ewing sarcoma/Ewing sarcoma family of tumors (ESFT), Wilms tumor, rhabdomyosarcoma, osteosarcoma, and retinoblastoma.

General Treatment

The prognosis for pediatric solid tumors has improved more recently, mostly due to the application of multiagent chemotherapy and improvements in local control therapy (including aggressive surgery and advancements in radiotherapy).² 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 hematopoietic cell transplantation (HCT), to improve event-free survival and overall survival.

Descriptions of pediatric-onset solid tumors addressed herein are as follows.

Peripheral Neuroblastoma

Neuroblastoma is the most common extracranial solid tumor of childhood,¹ with approximately 90% of 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, but have diverse clinical behavior depending on a variety of risk factors.

Patients with neuroblastoma are stratified into prognostic risk groups (low, intermediate, 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, the proportion of tumor stromal component, and index of cellular proliferation.³ It is well-established that *MYCN* amplification is associated with rapid tumor progression and a poor prognosis,⁴ even in the setting of other coexisting favorable factors. Loss of heterozygosity (LOH) at chromosome arms 1p and 11q frequently occurs in neuroblastoma.⁵ Although 1p LOH is associated with *MYCN* amplification, 11q is usually found in tumors without this abnormality.⁵ 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 in patients with low- and intermediate-risk disease.³ Although the use of these LOH markers in assigning treatment in patients is evolving, they may prove useful to stratify treatment.

In the early 1990s, a uniform clinical staging system based on surgical respectability and distant spread, the International Neuroblastoma Staging System, was adopted by pediatric cooperative groups (see Table 1).

Table 1. International Neuroblastoma Staging System

Stage	Description
1	Localized tumor with complete gross excision, with or without microscopic residual disease; lymph nodes negative for tumor
2A	Localized tumor with incomplete gross excision; lymph nodes negative for tumor
2B	Localized tumor with or without complete gross excision, with ipsilateral lymph nodes positive for tumor
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
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
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 younger than one year of age with stage 1, 2, or 4S with favorable histopathologic findings and no *MYCN* oncogene amplification. High-risk neuroblastoma is characterized by age older than one year, disseminated disease, *MYCN* oncogene amplification, and unfavorable histopathologic findings.

The International Neuroblastoma Risk Group (2009) proposed a revised staging system, which incorporated pretreatment imaging parameters instead of surgical findings (see Table 2).⁶

Table 2. International Neuroblastoma Risk Group Staging System⁶

Stage	Description
L1	Localized tumor not involving vital structures as defined by the list of Image-Defined Risk Factors and confined to one body compartment
L2	Locoregional tumor with presence of one or more Image-Defined Risk Factors
M	Distant metastatic disease (except stage MS)
MS	Metastatic disease in children younger than 18 months with metastases confined to skin, liver, and/or bone marrow

Treatment

In general, most patients with the low-stage disease have excellent outcomes with minimal therapy; and with International Neuroblastoma Staging System stage-1 disease, most patients can be treated by surgery alone.⁷ Most infants, even with disseminated disease, have favorable outcomes with chemotherapy and surgery.⁷

For intermediate-risk disease, moderately intensive multiagent chemotherapy is the mainstay of therapy.⁸ Surgery is needed to obtain a diagnosis, and the extent of resection necessary to obtain an optimal outcome is not established.⁹ Patients at high-risk have historically had very low (<15%) long-term overall survival. Current therapy for high-risk disease typically includes an aggressive multimodal approach with chemotherapy, surgical resection, and radiotherapy.¹⁰

Treatment of recurrent disease is determined by the risk group at diagnosis and the extent of disease and age of the patient at recurrence.

Ewing Sarcoma Family of Tumors

ESFT encompasses a group of tumors that share 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 (E26 transformation-specific) 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 diagnosis. Included in ESFT are “classic” Ewing sarcoma of bone, extraosseous Ewing, peripheral primitive neuroectodermal tumor, 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 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.

Treatment

Current therapy for Ewing sarcoma typically includes induction chemotherapy, followed by local control with surgery and/or radiotherapy (dependent on tumor size and location), followed by adjuvant chemotherapy. Multiagent chemotherapy, surgery, and radiotherapy have improved progression-free survival rates in patients with the localized disease to 60% to 70%.¹¹ The presence of metastatic disease is the most unfavorable prognostic feature, and the outcome for patients presenting with metastatic disease is poor, with 20% to 30% progression-free survival. Other adverse prognostic factors that may categorize a patient as having “high-risk” Ewing are tumor location (eg, patients with pelvic primaries have worse outcomes), larger tumor size, and older age of the patient. However, “high-risk” Ewing has not always been consistently defined in the literature.

Rhabdomyosarcoma

Rhabdomyosarcoma, the most common soft tissue sarcoma of childhood, shows skeletal muscle differentiation. The most common primary sites are the head and neck (eg, parameningeal, orbital, pharyngeal), genitourinary tract, and extremities.¹²

Treatment

Specific treatment is based on tumor location, resection, and node status, and may involve surgery, radiotherapy, and chemotherapy.¹³ Five-year survival rates for rhabdomyosarcoma increased between 1975 and 2010 from 53% to 67% in children younger than 15 years and from 30% to 51% in 15- to 19-year-olds.¹²

Approximately 15% of children present with metastatic disease, and despite the introduction of new drugs and intensified treatment, the 5-year survival is 20% to 30% for this “high-risk” group.^{14,15}

Similarly, postrelapse mortality is very high. The prognosis of the metastatic disease is affected by tumor histology, age at diagnosis, the site of metastatic disease, and the number of metastatic sites.¹²

Wilms Tumor

Wilms tumor is the most common primary malignant renal tumor of childhood. In the United States, Wilms tumor is staged using the National Wilms Tumor Study system, which is based on surgical evaluation before chemotherapy (see Table 3).¹⁶

Table 3. National Wilms Tumor Study Staging

Stage	Description
I	(a) Tumor is limited to the kidney and completely excised; (b) The tumor was not ruptured before or during removal; (c) The vessels of the renal sinus are not involved beyond 2 mm (d) There is no residual tumor apparent beyond the margins of excision
II	(a) Tumor extends beyond the kidney but is completely excised (b) No residual tumor is apparent at or beyond the margins of excision (c) Tumor thrombus in vessels outside the kidney is stage II if the thrombus is removed en bloc with the tumor
III	Residual tumor confined to the abdomen: (a) Lymph nodes in the renal hilum, the periaortic chains, or beyond are found to contain tumor (b) Diffuse peritoneal contamination by the tumor (c) Implants are found on the peritoneal surfaces (d) Tumor extends beyond the surgical margins either microscopically or grossly (e) Tumor is not completely resectable because of local infiltration into vital structures
IV	Presence of hematogenous metastases or metastases to distant lymph nodes
V	Bilateral renal involvement at the time of initial diagnosis

Adapted from Metzger and Dome (2005).¹⁶

Treatment

In the United States, National Wilms Tumor Study and Children's Oncology Group protocols are based on primary resection for unilateral tumors, followed by escalating levels of chemotherapy and radiotherapy depending on tumor stage and other prognostic factors. Tumor histology, tumor stage, molecular and genetic markers (eg, LOH at chromosome 16q), and age (>2 years) are all associated with increased risks of recurrence and death. Wilms tumors are highly sensitive to chemotherapy and radiotherapy, and current cure rates exceed 85%.¹⁷ Between 10% and 15% of patients with favorable histology and 50% of patients with anaplastic tumors, experience tumor progression or relapse.¹⁷

Similar risk-adapted strategies are being tested for the 15% of patients who experience a relapse. Success rates after relapse range from 25% to 45%. For patients with adverse prognostic factors (histologically anaplastic tumors, relapse <6 to 12 months after nephrectomy, second or subsequent relapse, relapse within the radiation field, bone or brain metastases), the event-free survival rate is less than 15%.¹⁸

Osteosarcoma

Osteosarcoma is a primary malignant bone tumor and the most common bone cancer in children and adolescents; it is characterized by infiltration of bone or osteoid by the tumor cells. Peak incidence occurs around puberty, most commonly in long bones such as the femur or humerus. Osteosarcomas are characterized by variants in the *TP53* tumor suppressor gene.

The prognosis of osteosarcoma has greatly improved, with 5-year survival rates increasing between 1975 and 2010 from 40% to 76% in children younger than 15 years and from 56% to 66% in 15- to 19-year-olds. Prognostic factors for patients with localized disease include site and size of the primary tumor, the presence of metastases at the time of diagnosis, resection adequacy, and tumor response to neoadjuvant chemotherapy.

Treatment

For patients with recurrent osteosarcoma, the most important prognostic factor is surgical resectability. There is a 5-year survival rate of 20% to 45% in patients who had a complete resection of metastatic pulmonary tumors and a 20% survival rate for patients with metastatic tumors at other sites.¹⁹

Retinoblastoma

Retinoblastoma is the most common primary tumor of the eye in children. It may occur as a heritable (25%-30%) or nonheritable (70%-75%) tumor.²⁰ Cases may be unilateral or bilateral, with bilateral tumors almost always being the heritable type.

Treatment

Treatment options depend on the extent of disease. Retinoblastoma is usually confined to the eye, and with current therapy has a high cure rate. However, once disease spreads beyond the eye, survival rates drop significantly; five-year disease-free survival is reported to be less than 10% in those with the extraocular disease, and stage 4B disease (ie, disease metastatic to the central nervous system) has been lethal in virtually all cases reported.²¹

The strategy for nonmetastatic disease depends on the disease extent but may include focal therapies (eg, laser photocoagulation, cryotherapy, plaque radiotherapy), intravitreal chemotherapy, intra-arterial chemotherapy, systemic chemotherapy, enucleation, or a combination.²² For metastatic disease, intensive multimodal therapy with high-dose chemotherapy, with or without radiotherapy, is standard care.

Notes: Other solid tumors of childhood include germ cell tumors, which are considered in policy #[247](#). For solid tumors classified as embryonal tumors arising in the central nervous system, see policy #[205](#) and for central nervous system tumors derived from glial cells (ie, astrocytoma, oligodendroglioma, or glioblastoma multiforme) see policy #[159](#).

Hematopoietic Cell Transplantation

HCT is a procedure in which hematopoietic stem cells are infused to restore bone marrow function in cancer patients who receive bone-marrow-toxic doses of drugs, with or without whole body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or 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 “naive” and thus are associated with a lower incidence of rejection or graft-versus-host disease.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. However, immunologic compatibility between donor and patient is critical for achieving a good outcome of allogeneic HCT. Compatibility is established by typing of human leukocyte antigens using cellular, serologic, or molecular techniques. Human leukocyte antigens refer to the tissue type expressed at class I and class II loci on chromosome 6. Depending on the disease being treated, an acceptable donor (except umbilical cord blood) will match the patient at all or most human leukocyte antigens loci.

Cord blood is discussed in detail in policy #[285](#).

Summary

Hematopoietic cell transplantation (HCT) is a procedure in which hematopoietic stem cells are infused to restore bone marrow function in cancer patients who receive bone-marrow-toxic doses of drugs, with or without whole body radiotherapy. Stem cells may be obtained from the transplant recipient (autologous HCT) or harvested from a donor (allogeneic HCT). Stem cells may be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates.

For individuals who have high-risk or relapsed peripheral neuroblastoma who receive single or tandem autologous HCT, the evidence includes randomized controlled trials, systematic reviews of those trials, and observational studies. The relevant outcomes are overall survival (OS), disease-specific survival

(DSS), and treatment-related mortality (TRM) and morbidity. In the pooled analysis, patients with high-risk neuroblastoma treated with first-line therapy with single autologous HCT with myeloablative conditioning had significantly improved event-free survival (EFS) compared with standard therapy. Similarly, well-designed randomized trials comparing tandem autologous HCT with conventional therapy showed improvements in EFS for children with high-risk neuroblastoma. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have high-risk Ewing sarcoma who receive single or tandem autologous HCT, the evidence includes single-arm studies. The relevant outcomes are OS, DSS, and TRM and morbidity. Although early nonrandomized studies were promising, more recent prospective nonrandomized study results have been inconsistent regarding whether HCT extends survival compared with typical conventional therapy. Additional studies, including a randomized trial, are ongoing, comparing HCT with conventional therapy. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input obtained in 2011 supported the use of single autologous HCT for high-risk Ewing sarcoma, and it is supported by national guidelines from the American Society for Blood and Marrow Transplantation. Also, the use of single autologous HCT is supported by national guidelines for recurrent or refractory Ewing sarcoma. Therefore, autologous HCT may be considered medically necessary for these indications.

For individuals who have rhabdomyosarcoma who receive single autologous HCT, the evidence includes nonrandomized comparative studies and case series. The relevant outcomes are OS, DSF, and TRM and morbidity. Available studies have not demonstrated improvements in OS or EFS with autologous HCT. Additional research is needed to demonstrate a benefit with autologous HCT for pediatric rhabdomyosarcoma. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have Wilms tumor who receive single autologous HCT, the evidence includes a retrospective analysis, meta-analysis of case series, and case reports. The relevant outcomes are OS, DSS, and TRM and morbidity. Overall four-year survival rates were similar between patients receiving HCT and receiving chemotherapy. There was a trend suggesting that patients with lung-only stage 3 or 4 relapse might benefit from autologous HCT. However, the overall body of evidence is limited. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input obtained in 2017 does not support whether the following indication provides a clinically meaningful improvement in the net health outcome or is consistent with generally accepted medical practice:

- Use of autologous HCT for children with advanced-stage Wilms tumor.

Thus, the above indication may be considered investigational.

For individuals who have osteosarcoma who receive single autologous HCT, the evidence includes case reports, case series, and a prospective single-arm study. The relevant outcomes are OS, DSF, and TRM and morbidity. An interim analysis of the prospective single-arm study showed that patients receiving autologous HCT were experiencing lower EFS rates than historical controls, resulting in all patients being enrolled in the standard of care chemotherapy. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input obtained in 2017 does not support whether the following indication provides a clinically meaningful improvement in the net health outcome or is consistent with generally accepted medical practice:

- Use of autologous HCT for children with osteosarcoma.

Thus, the above indication(s) may be considered investigational.

For individuals who have localized retinoblastoma who receive single autologous HCT, the evidence includes no studies. The relevant outcomes are OS, DSS, and TRM and morbidity. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have metastatic retinoblastoma who receive single autologous HCT, the evidence includes small case series and case reports and a systematic review and meta-analysis. The relevant outcomes are OS, DSS, and TRM and morbidity. Results from the limited data have suggested that autologous HCT may prolong disease-free survival, particularly in patients without central nervous system involvement (stage 4A). Given the poor prognosis for this indication with conventional therapies, the incremental improvement with autologous HCT might be considered a significant benefit. However, the overall body of evidence is limited. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input obtained in 2017 supports that the following indication provides a clinically meaningful improvement in net health outcome and is consistent with generally accepted medical practice:

- Use of autologous HCT for children with metastatic retinoblastoma.

Thus, the above indication may be considered medically necessary considering the suggestive evidence and clinical input support.

Policy History

Date	Action
10/2020	Clarified coding information
4/2020	Bone marrow harvesting codes were removed. Outpatient prior authorization is not required.
3/2020	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
3/2019	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
1/2019	Outpatient prior authorization is required for all commercial products including Medicare Advantage. Effective 1/1/2019.
2/2018	Coding information clarified.
10/2017	BCBSA National policy review. "Metastatic retinoblastoma" added to first medically necessary statement. In first investigational statement, "retinoblastoma" changed to "retinoblastoma without metastases." Title changed. Effective 10/1/2017.
6/2015	New references added from BCBSA National medical policy.
1/2015	Clarified coding information.
7/2014	New references added from BCBSA National medical policy.
6/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
6/2013	New references from BCBSA National medical policy.
2/2013	BCBSA National medical policy review. New medically necessary and investigational indications described. Effective 2/4/2013.
12/2012	Updated to add new CPT code 38243.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
7/2011	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
5/2011	Reviewed - Medical Policy Group - Pediatrics and Endocrinology. No changes to policy statements.
3/22/2011	BCBSA National medical policy review. Changes to policy statements.
9/2010	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.

8/1/2010	New policy, effective 8/1/2010, describing covered and non-covered indications.
----------	---

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

[Medical Policy Terms of Use](#)

[Managed Care Guidelines](#)

[Indemnity/PPO Guidelines](#)

[Clinical Exception Process](#)

[Medical Technology Assessment Guidelines](#)

References

1. Stewart E, Federico S, Karlstrom A, et al. The Childhood Solid Tumor Network: A new resource for the developmental biology and oncology research communities. *Dev Biol*. Mar 15 2016;411(2):287-293. PMID 26068307
2. Hale GA. Autologous hematopoietic stem cell transplantation for pediatric solid tumors. *Expert Rev Anticancer Ther*. Oct 2005;5(5):835-846. PMID 16221053
3. Shimada H, Ambros IM, Dehner LP, et al. Terminology and morphologic criteria of neuroblastic tumors: recommendations by the International Neuroblastoma Pathology Committee. *Cancer*. Jul 15 1999;86(2):349-363. PMID 10421272
4. Tang XX, Zhao H, Kung B, et al. The MYCN enigma: significance of MYCN expression in neuroblastoma. *Cancer Res*. Mar 1 2006;66(5):2826-2833. PMID 16510605
5. Attiyeh EF, London WB, Mosse YP, et al. Chromosome 1p and 11q deletions and outcome in neuroblastoma. *N Engl J Med*. Nov 24 2005;353(21):2243-2253. PMID 16306521
6. Monclair T, Brodeur GM, Ambros PF, et al. The International Neuroblastoma Risk Group (INRG) staging system: an INRG Task Force report. *J Clin Oncol*. Jan 10 2009;27(2):298-303. PMID 19047290
7. Weinstein JL, Katzenstein HM, Cohn SL. Advances in the diagnosis and treatment of neuroblastoma. *Oncologist*. 2003;8(3):278-292. PMID 12773750
8. Baker DL, Schmidt ML, Cohn SL, et al. Outcome after reduced chemotherapy for intermediate-risk neuroblastoma. *N Engl J Med*. Sep 30 2010;363(14):1313-1323. PMID 20879880
9. Mullassery D, Farrelly P, Losty PD. Does aggressive surgical resection improve survival in advanced stage 3 and 4 neuroblastoma? A systematic review and meta-analysis. *Pediatr Hematol Oncol*. Nov 2014;31(8):703-716. PMID 25247398
10. Laprie A, Michon J, Hartmann O, et al. High-dose chemotherapy followed by locoregional irradiation improves the outcome of patients with international neuroblastoma staging system Stage II and III neuroblastoma with MYCN amplification. *Cancer*. Sep 01 2004;101(5):1081-1089. PMID 15329919
11. Barker LM, Pendergrass TW, Sanders JE, et al. Survival after recurrence of Ewing's sarcoma family of tumors. *J Clin Oncol*. Jul 1 2005;23(19):4354-4362. PMID 15781881
12. National Cancer Institute (NCI). Physician Data Query (PDQ): Childhood rhabdomyosarcoma treatment. 2017; <https://www.cancer.gov/types/soft-tissue-sarcoma/hp/rhabdomyosarcoma-treatment-pdq>. Accessed November 1, 2019.
13. Raney RB, Anderson JR, Barr FG, et al. Rhabdomyosarcoma and undifferentiated sarcoma in the first two decades of life: a selective review of intergroup rhabdomyosarcoma study group experience and rationale for Intergroup Rhabdomyosarcoma Study V. *J Pediatr Hematol Oncol*. May 2001;23(4):215-220. PMID 11846299
14. Admiraal R, van der Paardt M, Kobes J, et al. High-dose chemotherapy for children and young adults with stage IV rhabdomyosarcoma. *Cochrane Database Syst Rev*. Dec 8 2010(12):CD006669. PMID 21154373
15. Koscielniak E, Klingebiel TH, Peters C, et al. Do patients with metastatic and recurrent rhabdomyosarcoma benefit from high-dose therapy with hematopoietic rescue? Report of the German/Austrian Pediatric Bone Marrow Transplantation Group. *Bone Marrow Transplant*. Feb 1997;19(3):227-231. PMID 9028550
16. Metzger ML, Dome JS. Current therapy for Wilms' tumor. *Oncologist*. Nov-Dec 2005;10(10):815-826. PMID 16314292

17. Campbell AD, Cohn SL, Reynolds M, et al. Treatment of relapsed Wilms' tumor with high-dose therapy and autologous hematopoietic stem-cell rescue: the experience at Children's Memorial Hospital. *J Clin Oncol.* Jul 15 2004;22(14):2885-2890. PMID 15254057
18. Dallorso S, Dini G, Faraci M, et al. SCT for Wilms' tumour. *Bone Marrow Transplant.* Jun 2008;41 Suppl 2:S128- 130. PMID 18545233
19. National Cancer Institute (NCI). Physician Data Query (PDQ): Neuroblastoma treatment. 2017; <https://www.cancer.gov/types/neuroblastoma/hp/neuroblastoma-treatment-pdq>. Accessed November 2, 2019.
20. National Cancer Institute (NCI). Physician Data Query (PDQ): Retinoblastoma treatment: health professional version. 2017; <https://www.cancer.gov/types/retinoblastoma/hp/retinoblastoma-treatment-pdq>. Accessed November 4, 2019.
21. Dunkel IJ, Chan HS, Jubran R, et al. High-dose chemotherapy with autologous hematopoietic stem cell rescue for stage 4B retinoblastoma. *Pediatr Blood Cancer.* Jul 15 2010;55(1):149-152. PMID 20486181
22. Abramson DH, Shields CL, Munier FL, et al. Treatment of retinoblastoma in 2015: agreement and disagreement. *JAMA Ophthalmol.* Nov 2015;133(11):1341-1347. PMID 26378747
23. Yalcin B, Kremer LC, Caron HN, et al. High-dose chemotherapy and autologous haematopoietic stem cell rescue for children with high-risk neuroblastoma. *Cochrane Database Syst Rev.* Aug 22 2013;8(8):CD006301. PMID 23970444
24. Matthay KK, Villablanca JG, Seeger RC, et al. Treatment of high-risk neuroblastoma with intensive chemotherapy, radiotherapy, autologous bone marrow transplantation, and 13-cis-retinoic acid. Children's Cancer Group. *N Engl J Med.* Oct 14 1999;341(16):1165-1173. PMID 10519894
25. Berthold F, Boos J, Burdach S, et al. Myeloablative megatherapy with autologous stem-cell rescue versus oral maintenance chemotherapy as consolidation treatment in patients with high-risk neuroblastoma: a randomised controlled trial. *Lancet Oncol.* Sep 2005;6(9):649-658. PMID 16129365
26. Pritchard J, Cotterill SJ, Germond SM, et al. High dose melphalan in the treatment of advanced neuroblastoma: results of a randomised trial (ENSG-1) by the European Neuroblastoma Study Group. *Pediatr Blood Cancer.* Apr 2005;44(4):348-357. PMID 15546135
27. Yalcin B, Kremer LC, van Dalen EC. High-dose chemotherapy and autologous haematopoietic stem cell rescue for children with high-risk neuroblastoma. *Cochrane Database Syst Rev.* Oct 05 2015(10):CD006301. PMID 26436598
28. Matthay KK, Reynolds CP, Seeger RC, et al. Long-term results for children with high-risk neuroblastoma treated on a randomized trial of myeloablative therapy followed by 13-cis-retinoic acid: a children's oncology group study. *J Clin Oncol.* Mar 1 2009;27(7):1007-1013. PMID 19171716
29. Proust-Houdemont S, Pasqualini C, Blanchard P, et al. Busulfan-melphalan in high-risk neuroblastoma: the 30- year experience of a single institution. *Bone Marrow Transplant.* Aug 2016;51(8):1076-1081. PMID 27042850
30. Sung KW, Ahn HS, Cho B, et al. Efficacy of tandem high-dose chemotherapy and autologous stem cell rescue in patients over 1 year of age with stage 4 neuroblastoma: the Korean Society of Pediatric Hematology-Oncology experience over 6 years (2000-2005). *J Korean Med Sci.* May 2010;25(5):691-697. PMID 20436703
31. Ladenstein R, Potschger U, Hartman O, et al. 28 years of high-dose therapy and SCT for neuroblastoma in Europe: lessons from more than 4000 procedures. *Bone Marrow Transplant.* Jun 2008;41 Suppl 2:S118-127. PMID 18545256
32. George RE, Li S, Medeiros-Nancarrow C, et al. High-risk neuroblastoma treated with tandem autologous peripheral-blood stem cell-supported transplantation: long-term survival update. *J Clin Oncol.* Jun 20 2006;24(18):2891-2896. PMID 16782928
33. Kletzel M, Katzenstein HM, Haut PR, et al. Treatment of high-risk neuroblastoma with triple-tandem high-dose therapy and stem-cell rescue: results of the Chicago Pilot II Study. *J Clin Oncol.* May 1 2002;20(9):2284-2292. PMID 11980999
34. Grupp SA, Stern JW, Bunin N, et al. Rapid-sequence tandem transplant for children with high-risk neuroblastoma. *Med Pediatr Oncol.* Dec 2000;35(6):696-700. PMID 11107149
35. Pasqualini C, Dufour C, Goma G, et al. Tandem high-dose chemotherapy with thiotepa and busulfan-melphalan and autologous stem cell transplantation in very high-risk neuroblastoma patients. *Bone Marrow Transplant.* Feb 2016;51(2):227-231. PMID 26524264

36. Kim EK, Kang HJ, Park JA, et al. Retrospective analysis of peripheral blood stem cell transplantation for the treatment of high-risk neuroblastoma. *J Korean Med Sci.* Sep 2007;22 Suppl:S66-72. PMID 17923758
37. Marcus KJ, Shamberger R, Litman H, et al. Primary tumor control in patients with stage 3/4 unfavorable neuroblastoma treated with tandem double autologous stem cell transplants. *J Pediatr Hematol Oncol.* Dec 2003;25(12):934-940. PMID 14663275
38. von Allmen D, Grupp S, Diller L, et al. Aggressive surgical therapy and radiotherapy for patients with high-risk neuroblastoma treated with rapid sequence tandem transplant. *J Pediatr Surg.* Jun 2005;40(6):936-941; discussion 941. PMID 15991174
39. Meyers PA. High-dose therapy with autologous stem cell rescue for pediatric sarcomas. *Curr Opin Oncol.* Mar 2004;16(2):120-125. PMID 15075902
40. Meyers PA, Krailo MD, Ladanyi M, et al. High-dose melphalan, etoposide, total-body irradiation, and autologous stem-cell reconstitution as consolidation therapy for high-risk Ewing's sarcoma does not improve prognosis. *J Clin Oncol.* Jun 1 2001;19(11):2812-2820. PMID 11387352
41. Gardner SL, Carreras J, Boudreau C, et al. Myeloablative therapy with autologous stem cell rescue for patients with Ewing sarcoma. *Bone Marrow Transplant.* May 2008;41(10):867-872. PMID 18246113
42. Ladenstein R, Potschger U, Le Deley MC, et al. Primary disseminated multifocal Ewing sarcoma: results of the Euro-EWING 99 trial. *J Clin Oncol.* Jul 10 2010;28(20):3284-3291. PMID 20547982
43. Loschi S, Dufour C, Oberlin O, et al. Tandem high-dose chemotherapy strategy as first-line treatment of primary disseminated multifocal Ewing sarcomas in children, adolescents and young adults. *Bone Marrow Transplant.* Aug 2015;50(8):1083-1088. PMID 26030048
44. Weigel BJ, Breitfeld PP, Hawkins D, et al. Role of high-dose chemotherapy with hematopoietic stem cell rescue in the treatment of metastatic or recurrent rhabdomyosarcoma. *J Pediatr Hematol Oncol.* Jun-Jul 2001;23(5):272-276. PMID 11464981
45. McDowell HP, Foot AB, Ellershaw C, et al. Outcomes in paediatric metastatic rhabdomyosarcoma: results of The International Society of Paediatric Oncology (SIOP) study MMT-98. *Eur J Cancer.* Jun 2010;46(9):1588-1595. PMID 20338746
46. Klingebiel T, Boos J, Beske F, et al. Treatment of children with metastatic soft tissue sarcoma with oral maintenance compared to high dose chemotherapy: report of the HD CWS-96 trial. *Pediatr Blood Cancer.* Apr 2008;50(4):739-745. PMID 18286501
47. Carli M, Colombatti R, Oberlin O, et al. High-dose melphalan with autologous stem-cell rescue in metastatic rhabdomyosarcoma. *J Clin Oncol.* Sep 1999;17(9):2796-2803. PMID 10561355
48. Presson A, Moore TB, Kempert P. Efficacy of high-dose chemotherapy and autologous stem cell transplant for recurrent Wilms' tumor: a meta-analysis. *J Pediatr Hematol Oncol.* Aug 2010;32(6):454-461. PMID 20505538
49. Garaventa A, Hartmann O, Bernard JL, et al. Autologous bone marrow transplantation for pediatric Wilms' tumor: the experience of the European Bone Marrow Transplantation Solid Tumor Registry. *Med Pediatr Oncol.* Jan 1994;22(1):11-14. PMID 8232074
50. Kremens B, Gruhn B, Klingebiel T, et al. High-dose chemotherapy with autologous stem cell rescue in children with neuroblastoma. *Bone Marrow Transplant.* Dec 2002;30(12):893-898. PMID 12476282
51. Kullendorff CM, Bekassy AN. Salvage treatment of relapsing Wilms' tumour by autologous bone marrow transplantation. *Eur J Pediatr Surg.* Jun 1997;7(3):177-179. PMID 9241510
52. Pein F, Michon J, Valteau-Couanet D, et al. High-dose melphalan, etoposide, and carboplatin followed by autologous stem-cell rescue in pediatric high-risk recurrent Wilms' tumor: a French Society of Pediatric Oncology study. *J Clin Oncol.* Oct 1998;16(10):3295-3301. PMID 9779704
53. Spreafico F, Bisogno G, Collini P, et al. Treatment of high-risk relapsed Wilms tumor with dose-intensive chemotherapy, marrow-ablative chemotherapy, and autologous hematopoietic stem cell support: experience by the Italian Association of Pediatric Hematology and Oncology. *Pediatr Blood Cancer.* Jul 2008;51(1):23-28. PMID 18293386
54. Malogolowkin MH, Hemmer MT, Le-Rademacher J, et al. Outcomes following autologous hematopoietic stem cell transplant for patients with relapsed Wilms' tumor: a CIBMTR retrospective analysis. *Bone Marrow Transplant.* Nov 2017;52(11):1549-1555. PMID 28869618
55. Venkatramani R, Murray J, Helman L, et al. Risk-based therapy for localized osteosarcoma. *Pediatr Blood Cancer.* Mar 2016;63(3):412-417. PMID 26501936

56. Hong CR, Kang HJ, Kim MS, et al. High-dose chemotherapy and autologous stem cell transplantation with melphalan, etoposide and carboplatin for high-risk osteosarcoma. *Bone Marrow Transplant.* Oct 2015;50(10):1375-1378. PMID 26098952
57. Fagioli F, Aglietta M, Tienghi A, et al. High-dose chemotherapy in the treatment of relapsed osteosarcoma: an Italian sarcoma group study. *J Clin Oncol.* Apr 15 2002;20(8):2150-2156. PMID 11956277
58. Fagioli F, Biasin E, Mereuta OM, et al. Poor prognosis osteosarcoma: new therapeutic approach. *Bone Marrow Transplant.* Jun 2008;41 Suppl 2:S131-134. PMID 18545234
59. Dunkel IJ, Aledo A, Kernan NA, et al. Successful treatment of metastatic retinoblastoma. *Cancer.* Nov 15 2000;89(10):2117-2121. PMID 11066053
60. Kremens B, Wieland R, Reinhard H, et al. High-dose chemotherapy with autologous stem cell rescue in children with retinoblastoma. *Bone Marrow Transplant.* Feb 2003;31(4):281-284. PMID 12621463
61. Matsubara H, Makimoto A, Higa T, et al. A multidisciplinary treatment strategy that includes high-dose chemotherapy for metastatic retinoblastoma without CNS involvement. *Bone Marrow Transplant.* Apr 2005;35(8):763-766. PMID 15750608
62. Rodriguez-Galindo C, Wilson MW, Haik BG, et al. Treatment of metastatic retinoblastoma. *Ophthalmology.* Jun 2003;110(6):1237-1240. PMID 12799253
63. Dunkel IJ, Khakoo Y, Kernan NA, et al. Intensive multimodality therapy for patients with stage 4a metastatic retinoblastoma. *Pediatr Blood Cancer.* Jul 15 2010;55(1):55-59. PMID 20486171
64. Ratko TA, Belinson SE, Brown HM, et al. Hematopoietic Stem-Cell Transplantation in the Pediatric Population (Report No. 12-EHC018-EF). Rockville, MD: Agency for Healthcare Research and Quality; 2012.
65. Majhail NS, Farnia SH, Carpenter PA, et al. Indications for autologous and allogeneic hematopoietic cell transplantation: guidelines from the American Society for Blood and Marrow Transplantation. *Biol Blood Marrow Transplant.* Nov 2015;21(11):1863-1869. PMID 26256941
66. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Bone Cancer. Version 1.2018. https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf. Accessed November 1, 2019.
67. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Soft Tissue Sarcoma. Version 1.2018. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed November 2, 2019.