Hematopoietic Cell Transplantation for Solid Tumors of Childhood

BCBSA Ref. Policy: 8.01.34

Effective Date: Aug 1, 2017
Last Revised: July 18, 2017
Replaces: 8.01.34

RELATED MEDICAL POLICIES:
7.01.50 Placental and Umbilical Cord Blood as a Source of Stem Cells

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | CODING | RELATED INFORMATION
EVIDENCE REVIEW | REFERENCES | HISTORY

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

The bone marrow is filled with cells known as hematopoietic stem cells. These immature cells develop into different types of blood cells: white blood cells to fight infection, red blood cells to carry oxygen, and platelets to clot the blood. In some cases, treating cancer also means destroying the bone marrow’s natural ability to create healthy blood cells. Restoring this function means returning these immature cells — the hematopoietic stem cells — to the body. When the immature blood cells come from a donor it’s known as an allogeneic transplant. When the cells are collected from the patient, stored, and later given back to the same patient it’s called an autologous transplant (autologous means from the same person). This policy describes when these transplants may be considered medically necessary for specific types of solid tumors that usually develop during childhood.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
<table>
<thead>
<tr>
<th>Service</th>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| Autologous hematopoietic cell transplantation | 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’s sarcoma  
• Recurrent or refractory Ewing's sarcoma  
• Metastatic Retinoblastoma |
| Tandem autologous hematopoietic cell transplantation | Tandem autologous hematopoietic cell transplantation is considered medically necessary for high-risk, refractory or relapsed neuroblastoma. |

<table>
<thead>
<tr>
<th>Service</th>
<th>Investigational</th>
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</table>
| Autologous hematopoietic cell transplantation | Autologous hematopoietic 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:  
• Rhabdomyosarcoma  
• Osteosarcoma  
• Wilms Tumors |
| High-dose chemotherapy autologous cell support  | High-dose chemotherapy (with or without associated radiotherapy) and autologous cell support may be considered investigational for treatment of recurrent Wilms tumor |
| Tandem autologous hematopoietic cell transplantation | Tandem autologous hematopoietic cell transplantation is considered investigational for treatment of all other types of pediatric solid tumors. |
| Allogeneic hematopoietic cell transplantation | Allogeneic (myeloablative or nonmyeloablative) hematopoietic cell transplantation is considered investigational for treatment of pediatric solid tumors. |
| Salvage allogeneic hematopoietic cell transplantation | Salvage allogeneic hematopoietic cell transplantation for pediatric solid tumors that relapse after autologous transplant or fail to respond is considered investigational. |
### Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>CPT</strong></td>
<td></td>
</tr>
<tr>
<td>38230</td>
<td>Bone marrow harvesting for transplantation; allogeneic</td>
</tr>
<tr>
<td>38232</td>
<td>Bone marrow harvesting for transplantation; autologous</td>
</tr>
<tr>
<td>38240</td>
<td>Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor</td>
</tr>
<tr>
<td>38241</td>
<td>Hematopoietic progenitor cell (HPC); autologous transplantation</td>
</tr>
<tr>
<td><strong>HCPCS</strong></td>
<td></td>
</tr>
<tr>
<td>S2140</td>
<td>Cord blood harvesting for transplantation, allogeneic</td>
</tr>
<tr>
<td>S2142</td>
<td>Cord blood-derived stem-cell transplantation, allogeneic</td>
</tr>
<tr>
<td>S2150</td>
<td>Bone marrow or blood-derived stem cells (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, diagnostic, emergency, and rehabilitative services; and the number of days of pre and post transplant care in the global definition</td>
</tr>
</tbody>
</table>

**Note:** CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

### Related Information

This policy addresses peripheral neuroblastoma, those arising from the peripheral nervous system.

### Definition of Terms

**Hematopoietic cell transplantation (HCT):** This refers to any source of stem cells, i.e., autologous, allogeneic, syngeneic, or umbilical cord blood.

**Primary refractory disease:** This is defined as a tumor that does not achieve a complete remission after initial standard-dose chemotherapy.
**Relapse:** This is defined as tumor recurrence after a prior complete response.

**RIC:** This refers to reduced intensity conditioning.

**Salvage transplantation:** This is defined as a hematologic cell transplantation (HCT), either autologous, allogeneic, or RIC-allogeneic. It is used as a second-line therapy after failure of primary therapy of any type. Salvage transplantation is sometimes referred to as a “rescue” transplant. It implies that the original therapy has failed. A salvage second HCT is often an autologous HCT if the prior therapy is chemotherapy. If the prior therapy is a failed autologous transplant a salvage second HCT would more likely be an allogeneic HCT or an RIC-allogeneic HCT. Typically, a salvage transplantation is done after enough time has elapsed to identify that the primary therapy has failed, so the interval between the two transplants would be longer.

**Tandem transplantation:** This is defined as a HCT technique where the preplanned intent for therapy involves two sequential HCTs. These may be autologous followed by a second autologous (auto-auto) transplantation, autologous followed by allogeneic (auto-allo) transplantation, or autologous followed by RIC-allogeneic (auto–RIC-allo) transplantation. The “tandem” implies a very short preplanned interval between the two transplants, as well as the therapeutic intent to do two transplants from the outset of therapy.

**Benefit Application**

The following considerations may supersede this policy:

- State mandates requiring coverage for autologous bone marrow transplantation offered as part of clinical trials of autologous bone marrow transplantation approved by the National Institutes of Health (NIH).

- Some contracts or certificates of coverage may include specific conditions in which autologous bone marrow transplantation would be considered eligible for coverage.
Description

**Hematopoietic Cell Transplantation for Solid Tumors**

Hematopoietic cell transplantation (HCT) 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 HCT) or can be 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.

Autologous HCT 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 HCT for solid tumors relies on a graft-versus-tumor effect. Allogeneic HCT 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 (ESFT), Wilms tumor, rhabdomyosarcoma (RMS), 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).1

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 HCT, in an effort to improve event-free survival (EFS) and overall survival (OS).

**Notes:** Other solid tumors of childhood include germ cell tumors, which are considered separately in another medical policy. Solid tumors classified as embryonal tumors arising in the central nervous system (CNS) and tumors derived from glial cells (ie, astrocytoma, oligodendroglioma, or glioblastoma multiforme) are also addressed in separate medical policies. Cord blood is discussed in greater detail in a separate medical policy. (See Related Medical Policies)
Descriptions of the solid tumors of childhood that are addressed in this policy are as follows.

**Peripheral Neuroblastoma**

Neuroblastoma is the most common extra cranial solid tumor of childhood,² with two-thirds of the cases presenting in children younger than 5 years of age.³ 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.⁴ It is well established that MYCN amplification is associated with rapid tumor progression and a poor prognosis,⁵ even in the setting of other coexisting favorable factors. Loss of heterozygosity (LOH) at chromosome arms 1p and 11q occurs frequently in neuroblastoma.⁶ Although 1p LOH is associated with MYCN amplification, 11q is usually found in tumors without this abnormality.⁶ Some recent studies have shown that 1p LOH and unbalanced 11q LOH are strongly associated with outcome in patients with neuroblastoma,⁶ 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:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>Localized tumor with complete gross excision, with or without microscopic residual disease; lymph nodes negative for tumor</td>
</tr>
<tr>
<td>Stage 2A</td>
<td>Localized tumor with incomplete gross excision; lymph nodes negative for tumor</td>
</tr>
<tr>
<td>Stage 2B</td>
<td>Localized tumor with or without complete gross excision, with ipsilateral lymph nodes positive for tumor</td>
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<tr>
<td>Stage 3</td>
<td>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</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Any primary tumor with dissemination to distant lymph nodes, bone, bone marrow, liver, skin, and/or other organs, except as defined for stage 4S</td>
</tr>
<tr>
<td>Stage 4S</td>
<td>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</td>
</tr>
</tbody>
</table>

The low-risk group includes patients younger 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, extra osseous 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 (eg, 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 (eg, parameningeal, orbital, 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 tumor, 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%. A clinical trial in 2008 with high-dose chemotherapy (HDC) and autologous HCT reported 3- or 4-year OS rates from 60–73%. Subsequent randomized trials have been abandoned due to low accrual rates and the rarity of the targeted disease state.
**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.\(^\text{15}\) However, 30–40% of patients with non-metastatic osteosarcoma of the extremities experience recurrent disease, most commonly in the lungs.\(^\text{15}\) 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%.\(^\text{16}\)

**Retinoblastoma**

Retinoblastoma is the most common primary tumor of the eye in children. It may occur as a heritable (40%) or nonheritable (60%) tumor.\(^\text{17}\) 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.\(^\text{17}\) 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, and stage 4b disease has been lethal in virtually all cases reported.\(^\text{18}\) 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.
Summary of Evidence

**Neuroblastoma**

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

- No studies directly comparing single autologous to tandem autologous HCT for high-risk neuroblastoma have been published; however, case series on the use of tandem autologous for high-risk neuroblastoma have reported EFS rates superior to those reported with the use of single autologous HCT (reported in randomized trials comparing single autologous HCT to conventional chemotherapy).

Some transplant centers use tandem autologous HCT as the preferred approach to the treatment of high-risk neuroblastoma.

A Phase III, randomized trial of single versus tandem autologous HCT for high-risk neuroblastoma is currently underway.

**Ewing’s sarcoma family of tumors (ESFT)**

- Evidence on the use of HCT in the initial treatment of high-risk or recurrent or refractory ESFT have shown varied results for a survival benefit with the use of HCT. Two Phase III trials are currently underway using risk-stratified approaches which will likely serve to guide future treatment options for ESFT.

**Rhabdomyosarcoma**

- The use of HCT for metastatic rhabdomyosarcoma has failed to show a survival benefit.

**Wilms Tumor**

- The use of HCT for high-risk relapsed Wilms tumor, in general, has failed to show a survival benefit, although a few reports have suggested some benefit in certain subpopulations (e.g., patients with advanced stage disease with lung-only metastases).
Osteosarcoma

- The use of HCT for osteosarcoma has failed to show a survival benefit.

Retinoblastoma

- Small case series and case reports have shown prolonged DFS in some patients with stage 4 disease, particularly those with stage 4a disease.

- A recent study of 15 patients showed that some patients with stage 4a retinoblastoma were cured with the use of HCT. A prospective multicenter trial (COG ARET 0321) is underway to better determine the role of HCT in patients with retinoblastoma.

Allogeneic HCT

Very little evidence is available on the use of allogeneic HCT for pediatric solid tumors, either upfront or as salvage therapy after a failed autologous HCT. A large retrospective review of the use of allogeneic HCT for high-risk neuroblastoma failed to show a survival benefit over autologous HCT and was associated with a higher risk of transplant-related mortality.

Clinical Input Received from Physician Specialty Societies and Academic Medical Centers

In response to requests, input was received from 3 academic medical centers and 2 Blue Distinction Centers for Transplants for review in April 2011. While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted. There was general agreement from all of the reviewers for most of the policy statements with a few exceptions. One of the reviewers did not consider autologous HCT for low- to intermediate-risk Ewing’s sarcoma investigational, but did state that the results of the Euro-Ewing’s phase III trial are awaited. Two reviewers agreed with the policy statement that tandem autologous HCT for pediatric solid tumors is investigational, two considered it medically necessary for high-risk neuroblastoma, and the fifth reviewer agreed...
that tandem autologous HCT is considered investigational for pediatric solid tumors but also stated that it is considered standard for high-risk neuroblastoma at some centers.

**2017 Input**

In 2017, clinical input was sought to help determine the appropriate use in clinical practice of hematopoietic cell transplantation (HCT) for children who have metastatic retinoblastoma, late-stage Wilms tumor, or osteosarcoma.

**Respondents**

Clinical input was provided by the following physicians identified by the associated medical specialty societies (listed alphabetically):

- Carrie L. Kitko, MD, Pediatric Hematology/Oncology, BMT, Vanderbilt University Medical Center (American Society for Blood and Marrow Transplantation [ASBMT])
- Maxim Yankelevich, MD, Pediatric Hematology/Oncology, BMT, Wayne State University (American Society of Clinical Oncology [ASCO])

Clinical input provided by the specialty society at an aggregate level is attributed to the specialty society. Clinical input provided by a physician member designated by the specialty society is attributed to the individual physician and is not a statement from the specialty society. Specialty society and physician respondents participating in the Evidence Street® clinical input process provide review, input, and feedback on topics being evaluated by Evidence Street. However, participation in the clinical input process by a specialty society and/or physician member designated by the specialty society or clinical health system does not imply an endorsement or explicit agreement with the Evidence Opinion published by BCBSA or any Blue Plan.

One reviewer (Kitko) regarded HCT for metastatic retinoblastoma as generally accepted medical practice which was only intermediately supported (3/5) by the scientific evidence while the second reviewer regarded these as only weakly supported (2/5). HCT for late stage Wilms tumor was weakly supported (2/5) by one reviewer (Kitko) and not supported by another (Yankelevich).


### History

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/16/00</td>
<td>Add to Therapy Section - New Policy</td>
</tr>
<tr>
<td>12/21/00</td>
<td>Replace Policy - Additional minor changes recommended by Oncology Committee</td>
</tr>
<tr>
<td>12/10/02</td>
<td>Replace Policy - Policy reviewed; no criteria changes.</td>
</tr>
<tr>
<td>06/17/03</td>
<td>Replace Policy - Update CPT codes only.</td>
</tr>
<tr>
<td>08/12/03</td>
<td>Replace Policy - Policy updated; no criteria changes. Additional rationale language and references added.</td>
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<td>Comments</td>
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<td>09/01/04</td>
<td>Replace Policy - Policy renumbered from PR.8.01.111. No changes to dates.</td>
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<tr>
<td>12/14/04</td>
<td>Replace Policy - Scheduled review; codes updated; no criteria changes. Approved by OAP 10/29/04.</td>
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<tr>
<td>11/11/05</td>
<td>Replace Policy - Scheduled review; rationale and references updated; no change to policy statement. Recommended by OAP 10/27/05.</td>
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<td>06/02/06</td>
<td>Disclaimer and Scope update - No other changes.</td>
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<tr>
<td>11/14/06</td>
<td>Replace Policy - Policy updated with literature search; no change in policy statement.</td>
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<td>12/11/07</td>
<td>Replace Policy - Policy updated with literature review. Policy statement updated to include: High-dose chemotherapy and hematopoietic stem-cell support is considered investigational as initial treatment of low- or intermediate-risk neuroblastoma. Multiple cycle high-dose chemotherapy and hematopoietic stem-cell support (i.e., tandem or multiple transplants) is considered investigational for treatment of neuroblastoma. References added. Recommended and reviewed by OAP 11/15/07.</td>
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<td>12/31/07</td>
<td>Codes Updated - CPT code 86817 removed as directed by RPIW.</td>
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<tr>
<td>06/10/08</td>
<td>Replace Policy - Policy extensively consolidated and rewritten; updated with literature search. References also extensively revised; no changes to policy statements</td>
</tr>
<tr>
<td>12/08/09</td>
<td>Replace Policy - Policy updated with literature search; no change to the policy statement. Recommended and reviewed by OAP August 21, 2009. Code 86817 added back to the policy.</td>
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<tr>
<td>02/09/10</td>
<td>Code Update - New 2010 codes added.</td>
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<tr>
<td>06/08/10</td>
<td>Replace Policy - Policy updated with NCCN 2010 Guidelines. No change to policy statement. Reviewed and recommended by OAP Feb 2010.</td>
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<tr>
<td>06/13/11</td>
<td>Replace Policy - Policy presented to OAP for review May 12, 2011. Policy title changed to &quot;Hematopoietic Stem-Cell Transplantation for Solid Tumors of Childhood&quot; from &quot;HDC with Hematopoietic Stem-Cell Support for Solid Tumors in Childhood.&quot; ICD-10 codes added to policy.</td>
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<tr>
<td>01/25/12</td>
<td>Code 38232 added.</td>
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<td>02/09/12</td>
<td>CPT code 38204 was removed from the policy.</td>
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<tr>
<td>06/12/12</td>
<td>Replace Policy. Policy updated with literature search. Policy statement changed: Tandem autologous HSCT, previously considered investigational, may now be considered medically necessary for high risk neuroblastoma.</td>
</tr>
<tr>
<td>09/19/12</td>
<td>Update Coding Section – ICD-10 codes are now effective 10/01/2014.</td>
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<tr>
<td>09/28/12</td>
<td>Update Related Policies – Add 8.01.20-30, 8.01.514 and 8.01.520.</td>
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<td>11/15/12</td>
<td>Reviewed and recommended by OAP, November 2012.</td>
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<tr>
<td>02/01/13</td>
<td>Update Related Policies, change title of policy 8.01.21.</td>
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<tr>
<td>Date</td>
<td>Comments</td>
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<tr>
<td>02/15/13</td>
<td>Update Related Policies, change title of policy 8.01.30.</td>
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<td>03/20/13</td>
<td>The following codes were removed from the policy, as they were not suspending and just informational: HCPCS J9000-J9999 and Q0083 – Q0085.</td>
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<td>07/24/13</td>
<td>Replace policy. Policy updated with literature review; Rationale reorganized. References updated, added and renumbered. No change in policy statements.</td>
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<tr>
<td>09/30/13</td>
<td>Update Related Policies. Change title to policy 8.01.31.</td>
</tr>
<tr>
<td>10/18/13</td>
<td>Update Related Policies. Change title to policy 8.01.17.</td>
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<td>12/06/13</td>
<td>Update Related Policies. Remove 8.01.31 as it was archived.</td>
</tr>
<tr>
<td>01/30/14</td>
<td>Update Related Policies. Change title to 8.01.21.</td>
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<tr>
<td>02/27/14</td>
<td>Update Related Policies. Change title to 8.01.30.</td>
</tr>
<tr>
<td>03/21/14</td>
<td>Update Related Policies. Remove 8.01.514 as it was deleted.</td>
</tr>
<tr>
<td>04/18/14</td>
<td>Update Related Policies. Delete 8.01.20 and replace with 8.01.529.</td>
</tr>
<tr>
<td>06/09/14</td>
<td>Annual Review. Policy updated with literature search. Policy statements changed. Retinoblastoma added to the list of conditions for which autologous HSCT is considered medically necessary; treatment of recurrent Wilms tumor with HDC or autologous HSCT and tandem autologous HSCT for high-risk neuroblastoma remain medically necessary, but now much be conducted as part of a clinical trial.</td>
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<tr>
<td>06/24/14</td>
<td>Update Related Policies. Remove 8.01.35, 8.01.42, 8.01.54, then add 8.01.530 and 8.01.532</td>
</tr>
<tr>
<td>02/03/15</td>
<td>Update Related Polices. Remove 8.01.23, 8.01.28 and 8.01.30.</td>
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<tr>
<td>06/09/15</td>
<td>Annual Review. Policy updated with literature review; no change in policy statements. Related Policies removed except 7.01.50. ICD-9 and ICD-10 codes removed; these were informational only.</td>
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<tr>
<td>09/30/16</td>
<td>Coding Update. Remove CPT 86817 from coding table near end of policy.</td>
</tr>
<tr>
<td>11/04/16</td>
<td>Coding Update. Removed codes that are transplant benefit related.</td>
</tr>
<tr>
<td>12/01/16</td>
<td>Annual review, approved November 8, 2016. No changes to policy statement.</td>
</tr>
<tr>
<td>08/01/17</td>
<td>Annual Review, approved July 18, 2017. Policy moved into new format. The word stem dropped from the policy title. Retinoblastoma was divided into metastatic retinoblastoma and retinoblastoma without metastases. HCT for metastatic retinoblastoma is now medically necessary. HCT for retinoblastoma without metastases was added as investigational. HCT for late stage Wilms Tumor previously covered as medically necessary is now investigational based upon input from BC/BS association, guidelines from the American Society for Bone Marrow Transplant, UpToDate review, and weak support for use from a single clinician. Tandem autologous HCT for high risk or relapsed neuroblastoma is now covered as medically necessary based upon BCBS coverage and literature review.</td>
</tr>
</tbody>
</table>
Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2017 Premera All Rights Reserved.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.
Discrimination is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:
• Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  • Qualified sign language interpreters
  • Written information in other formats (large print, audio, accessible electronic formats, other formats)
• Provides free language services to people whose primary language is not English, such as:
  • Qualified interpreters
  • Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5592. TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at:
https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:
U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost.

Call 800-722-1471 (TTY: 800-842-5357).

Arabic (Arabic):
يحتوي هذا الإشعار معلومات هامة. قد يحتوي هذا الإشعار معلومات مهمة بخصوص طبيك أو طبيتك و جملة تدعم أهداف تأسيس و развития في هذا الإشعار. تتألف هذه المعلومات من محتوى مصمم للمساعدة على تعلم اللغة العربية في دفع الألفاظ. يحقق كل الحوصل على هذه المعلومات والمساعدة بإمكانك نحن زبان كتبية إملاء، عالمية، عالمية
800-722-1471 (TTY: 800-842-5357).

中文 (Chinese):
本通知有重要的訊息。本通知可能有關於您透過 Premera Blue Cross 提交的申請或保險的重要訊息。本通知可能有重要日期。您可能需要在截止日期之前採取行動，以保留您的健康保險或費用補貼。您有權利免費以您的母語得到本訊息和幫助。請拔電話 800-722-1471 (TTY: 800-842-5357).

Oromo (Cushite):

Français (French):

Kreyòl ayisyen (Creole):
Avi sila a gen Enfòmasyon Enpòtan ladann. Avi sila a kapab genyen enfòmasyon enpòtan konsènan aplikasyon w lan oswa konvesan yon ou sa. Rele nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):

Hmoob (Hmong):

Iloko (Ilocano):
Daytoy a Pakdaar ket naglaon iti Napateg nga Impormasjon. Daytoy a pakdaar mabalini nga adda ket naglaon iti napateg nga impormasjon maipanggepi iti aplikasyonowi woyen coverage babaen iti Premera Blue Cross. Daytoy ket mabalini dagiti importante a pelsa iti daytoy a pakdaar. Mabalini nga adda rumbeng sa a amarideng nga adda sakkay dagiti partikular a naituding nga lantuing nga adlaw tapno mapagtalinaedyo ti coverage ti salun-ayowo yenwo tulong kadagit gastos. Adda karbenganyo a mangala ti daytoy nga impormasjon ken tulong ti bukodyo a pagasasao nga awan ti bayadanyo. Tumawag ti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):

037338 (07-2016)
Premera Blue Cross's decision to end coverage on a specific date may be important for determining your eligibility for coverage and how it will be affected. It is important to understand that you may need to take steps to maintain your coverage or avoid a lapse in coverage. This notice contains important information about dates that may affect your coverage. It is important to review these dates to ensure that your coverage will continue as expected.

If you have questions about the information in this notice or need assistance with language support, please contact Premera Blue Cross at 800-722-1471 (TTY: 800-842-5357).

Please note that some dates may be important for not only your coverage but also for your taxes and other personal reasons. It is important to review these dates carefully to ensure that you are prepared for any changes to your coverage.

If you have questions about the information in this notice or need assistance with language support, please contact Premera Blue Cross at 800-722-1471 (TTY: 800-842-5357).