Medical Policy
Hematopoietic Cell Transplantation for Solid Tumors of Childhood

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- Description
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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 Blue™ and Medicare PPO Blue™ 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.

<table>
<thead>
<tr>
<th>Outpatient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial Managed Care (HMO and POS)</td>
</tr>
<tr>
<td>Commercial PPO and Indemnity</td>
</tr>
<tr>
<td>Medicare HMO BlueSM</td>
</tr>
<tr>
<td>Medicare PPO BlueSM</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>CPT codes:</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>38241</td>
<td>Bone marrow or blood-derived peripheral stem-cell transplantation; autologous</td>
</tr>
<tr>
<td>38243</td>
<td>Hematopoietic progenitor cell (HPC); HPC boost</td>
</tr>
</tbody>
</table>

HCPCS Codes

<table>
<thead>
<tr>
<th>HCPCS codes:</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S2150</td>
<td>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)</td>
</tr>
</tbody>
</table>
## ICD-10 Procedure Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>30233G0</td>
<td>Transfusion of Autologous Bone Marrow into Peripheral Vein, Percutaneous Approach</td>
</tr>
<tr>
<td>30233X0</td>
<td>Transfusion of Autologous Cord Blood Stem Cells into Peripheral Vein, Percutaneous Approach</td>
</tr>
<tr>
<td>30233Y0</td>
<td>Transfusion of Autologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach</td>
</tr>
<tr>
<td>30243G0</td>
<td>Transfusion of Autologous Bone Marrow into Central Vein, Percutaneous Approach</td>
</tr>
<tr>
<td>30243X0</td>
<td>Transfusion of Autologous Cord Blood Stem Cells into Central Vein, Percutaneous Approach</td>
</tr>
<tr>
<td>30243Y0</td>
<td>Transfusion of Autologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach</td>
</tr>
<tr>
<td>30263G0</td>
<td>Transfusion of Autologous Bone Marrow into Central Artery, Percutaneous Approach</td>
</tr>
<tr>
<td>30263X0</td>
<td>Transfusion of Autologous Cord Blood Stem Cells into Central Artery, Percutaneous Approach</td>
</tr>
<tr>
<td>30263Y0</td>
<td>Transfusion of Autologous Hematopoietic Stem Cells into Central Artery, Percutaneous Approach</td>
</tr>
<tr>
<td>3E03305</td>
<td>Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach</td>
</tr>
<tr>
<td>3E04305</td>
<td>Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach</td>
</tr>
<tr>
<td>3E05305</td>
<td>Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach</td>
</tr>
<tr>
<td>3E06305</td>
<td>Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach</td>
</tr>
</tbody>
</table>

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

### CPT Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>38240</td>
<td>Bone marrow or blood-derived peripheral stem-cell transplantation; allogeneic</td>
</tr>
</tbody>
</table>

### HCPCS Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S2142</td>
<td>Cord blood derived stem-cell transplantation, allogeneic</td>
</tr>
</tbody>
</table>

### ICD-10 Procedure Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>30233G1</td>
<td>Transfusion of Nonautologous Bone Marrow into Peripheral Vein, Percutaneous Approach</td>
</tr>
<tr>
<td>30233X1</td>
<td>Transfusion of Nonautologous Cord Blood Stem Cells into Peripheral Vein, Percutaneous Approach</td>
</tr>
<tr>
<td>30233Y1</td>
<td>Transfusion of Nonautologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach</td>
</tr>
<tr>
<td>30243G1</td>
<td>Transfusion of Nonautologous Bone Marrow into Central Vein, Percutaneous Approach</td>
</tr>
<tr>
<td>30243X1</td>
<td>Transfusion of Nonautologous Cord Blood Stem Cells into Central Vein, Percutaneous Approach</td>
</tr>
</tbody>
</table>
**Description**

**Solid Tumors of Childhood**

Solid tumors of childhood arise from mesodermal, ectodermal, and endodermal cells of origin. 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). 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, 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. 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 frequently occurs 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 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.

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>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Localized tumor with complete gross excision, with or without microscopic residual disease; lymph nodes negative for tumor</td>
</tr>
<tr>
<td>2A</td>
<td>Localized tumor with incomplete gross excision; lymph nodes negative for tumor</td>
</tr>
<tr>
<td>Stage</td>
<td>Description</td>
</tr>
<tr>
<td>-------</td>
<td>-------------</td>
</tr>
<tr>
<td>2B</td>
<td>Localized tumor with or without complete gross excision, with ipsilateral lymph nodes positive for tumor</td>
</tr>
<tr>
<td>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>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>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 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>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1</td>
<td>Localized tumor not involving vital structures as defined by the list of Image-Defined Risk Factors and confined to one body compartment</td>
</tr>
<tr>
<td>L2</td>
<td>Locoregional tumor with presence of one or more Image-Defined Risk Factors</td>
</tr>
<tr>
<td>M</td>
<td>Distant metastatic disease (except stage MS)</td>
</tr>
<tr>
<td>MS</td>
<td>Metastatic disease in children younger than 18 months with metastases confined to skin, liver, and/or bone marrow</td>
</tr>
</tbody>
</table>

**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. 8

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, extrasosseous 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%. 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.

**Treatment**
Specific treatment is based on tumor location, resection, and node status, and may involve surgery, radiotherapy, and chemotherapy. 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.

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.

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.

**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).

**Table 3. National Wilms Tumor Study Staging**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>(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</td>
</tr>
<tr>
<td>II</td>
<td>(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</td>
</tr>
<tr>
<td>III</td>
<td>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</td>
</tr>
<tr>
<td>IV</td>
<td>Presence of hematogenous metastases or metastases to distant lymph nodes</td>
</tr>
<tr>
<td>V</td>
<td>Bilateral renal involvement at the time of initial diagnosis</td>
</tr>
</tbody>
</table>
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, DF, 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**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/2020</td>
<td>Bone marrow harvesting codes were removed. Outpatient prior authorization is not required.</td>
</tr>
</tbody>
</table>
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