

<b>Subject: Hematopoietic Stem Cell Transplantation for Ewing’s Sarcoma</b>		<b>Original Effective Date: 5/3/16</b>
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**DISCLAIMER**

*This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this Molina Clinical Policy (MCP) document and provide the directive for all Medicare members.<sup>1</sup>*

**DESCRIPTION OF PROCEDURE/SERVICE/PHARMACEUTICAL**

*Ewing’s sarcoma*<sup>27</sup>

The Ewing's sarcoma family of tumors (ESFT) is the second most common primary malignant bone tumor in children, adolescents and young adults. ESFTs include Ewing tumor of bone (classic Ewing sarcoma and primitive neuroectodermal tumor or PNET) and extraosseous Ewing (i.e., Ewing sarcoma in a site other than bone). The incidence of ESFT is approximately 3 cases per 1,000,000 persons per year. The incidence in the U.S. population is one per 1,000,000 in the population. The median age of patients is 15 years, and more than 50 percent of patients are adolescents. The majority of primary sites of bone disease are in the lower extremity followed by pelvis, chest wall, upper extremity, spine and skull. Primary sites of extraosseous Ewing's are mostly found in the trunk, followed by extremity, head and neck, retroperitoneum and other sites. Approximately 25 percent of patients will have metastatic disease at diagnosis. Certain adverse prognostic factors place some patients with ESFT into a high-risk category: relapsed or resistant disease, primary tumor site in the axial skeleton, including pelvis, large tumor volume, and the presence of metastatic disease (patients with isolated lung metastases are considered to have better prognosis than patients with metastases to bone and/or bone marrow). Standard treatment of ESFT includes systemic chemotherapy in conjunction with either surgery or radiation or both for local tumor control. The prognosis for patients with high-risk tumors treated with conventional chemotherapy, radiation and surgery remain poor, with long-term survival rates for patients with metastatic disease less than 35 percent. Dose-intensive chemotherapy regimens as well as HSCT have been investigated in patients with high-risk ESFT in an effort to improve survival.

Classification of Ewing’s Sarcoma is based on risk assignment:

- Low-risk: localized tumor when there is no spread beyond the primary site or regional lymph node involvement.
- Intermediate-risk: tumor has spread to lungs
- Advanced-risk: tumor has spread beyond to bone, bone marrow and/or other tissue

### *Stem Cell Transplantation*

Stem-cell transplantation refers to transplantation of hematopoietic stem cells (HSCs) from a donor into a patient. HSCs are immature cells that can develop into any of the three types of blood cells (red cells, white cells or platelets). HSCs are created in the bone marrow and are found in the bone marrow and peripheral blood. There is also a high concentration of HSCs in umbilical-cord blood. Hematopoietic stem-cell transplantation (HSCT) can be either autologous (using the person's own stem cells) or allogeneic (using stem cells from a donor). In allogeneic HSCT, it is preferable for donors to have a human leukocyte antigen (HLA) type that is identical to the recipient. Matching is performed on the basis of variability at three or more loci of the HLA gene (e.g., HLA-A, HLA-B, HLA-DRB1). As HLA variability increases, transplant-related morbidity and mortality, including graft rejection and graft-versus-host disease, also increase.

### RECOMMENDATION

**All transplants require prior authorization from the Corporate Transplant Department. Solid organ transplant requests will be reviewed by the Corporate Senior Medical Director or qualified clinical designee. All other transplants will be by the Corporate Senior Medical Director or covering Medical Director. If the criteria are met using appropriate NCD and/or LCD guidelines, state regulations and/or MCP policies the Corporate Senior Medical Director's designee can approve the requested transplant.**

**Members must meet UNOS guidelines for transplantation and the diagnosis must be made by a *Specialist in the Disease* and or Transplant Surgeon.**

### **Pre-Transplant Evaluation:** <sup>24-26 29 31</sup>

Criteria for transplant evaluation include all of the following:

- History and physical examination
- Psychosocial evaluation and clearance:
  - No behavioral health disorder by history or psychosocial issues:
    - if history of behavioral health disorder, no severe psychosis or personality disorder
    - mood/anxiety disorder must be excluded or treated
    - member has understanding of surgical risk and post procedure compliance and follow-up required
  - Adequate family and social support
- EKG
- Chest x-ray
- Cardiac clearance in the presence of any of the following:
  - chronic smokers
  - > 50 years age
  - those with a clinical or family history of heart disease or diabetes

- Pulmonary clearance if evidence of pulmonary artery hypertension (PAH) or chronic pulmonary disease
- Neurological exam and clearance for transplant: [ONE]
  - Normal exam by H&P
  - Abnormal neurological exam with positive findings: [ONE]
    - Lumbar puncture normal cytology
    - Lumbar puncture with cytological exam abnormal: CNS disease treated prior to clearance
- Performance Status : [ONE]
  - Karnofsky score 70-100%; or
  - Eastern Cooperative Oncology Group (ECOG) grade 0-2
- Lab studies:
  - \*Complete blood count, Kidney profile (blood urea nitrogen, creatinine), electrolytes, calcium, phosphorous, albumin, liver function tests, Coagulation profile (prothrombin time, and partial thromboplastin time)
  - \*Serologic screening for HIV, Epstein Barr virus (EBV), Hepatitis virus B (HBV), and Hepatitis C(HCV), cytomegalovirus (CMV), RPR and/or FTA:
    - If HIV positive all of the following are met:
      - CD4 count >200 cells/mm-3 for >6 months
      - HIV-1 RNA undetectable
      - On stable anti-retroviral therapy >3 months
      - No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioides mycosis, resistant fungal infections, Kaposi's sarcoma, or other neoplasm)
    - If abnormal serology need physician plan to address and/or treatment as indicated
  - UDS (urine drug screen) if patient is current or gives a history of past drug abuse
- \*Colonoscopy (if indicated or if patient is 50 ≥ older should have had an initial screening colonoscopy, after initial negative screening requires follow up colonoscopy every ten years) with complete workup and treatment of abnormal results as indicated
- \*GYN examination with Pap smear for women ≥ 21 to ≤ 65 years of age or indicated (not indicated in women who have had a TAH or TVH) with in the last three year with complete workup and treatment of abnormal results as indicated

Within the last 12 months:

- Dental examination or oral exam showing good dentition and oral care or no abnormality on panorex or plan for treatment of problems pre or post-transplant
- \*Mammogram (if indicated or > age 40) with complete workup and treatment of abnormal results as indicated
- \*PSA if history of prostate cancer or previously elevated PSA with complete workup and treatment of abnormal results as indicated

*\*Participating Centers of Excellence may waive these criteria*

**Criteria for Hematopoietic Autologous Stem Cell transplantation (HSCT) Transplantation:** <sup>4-23 27-31</sup>

1. **Hematopoietic Autologous stem-cell transplantation (HSCT)** may be considered medically necessary and may be authorized for the treatment of Ewing's sarcoma when the following criteria are met: <sup>27</sup>

- ❑ All pre-transplant criteria are met; and [ONE]
  - Initial treatment of high risk Ewing's Sarcoma: Defined as metastatic disease, unfavorable tumor location (i.e. primary tumor site in the axial skeleton, including pelvis), larger tumor size, or older age of the patient; OR
  - As salvage therapy for recurrent or refractory Ewing's sarcoma: Defined as a tumor that does not achieve a complete remission after initial standard-dose chemotherapy

**AND**

- ❑ The requesting transplant recipient should not have any of the following **absolute contraindications**:
  - Cardiac, pulmonary, and nervous system disease that cannot be corrected and is a prohibitive risk for surgery
  - Malignant neoplasm with a high risk for reoccurrence, non-curable malignancy (excluding localized skin cancer)
  - Systemic and/or uncontrolled infection
  - AIDS (CD4 count < 200cells/mm<sup>3</sup>)
  - Unwilling or unable to follow post-transplant regimen
    - ◇ Documented history of non-compliance
    - ◇ Inability to follow through with medication adherence or office follow-up
  - Chronic illness with one year or less life expectancy
  - Limited, irreversible rehabilitation potential
  - Active untreated substance abuse issues, requires documentation supporting free from addiction for minimally 6 months if previous addiction was present
  - No adequate social/family support
  
- ❑ The requesting transplant recipient should be evaluated carefully and potentially treated if the following **relative contraindications** are present:
  - Irreversible lung disease patients require consultation and clearance by a Pulmonologist prior to consideration of transplantation, this includes the following:
  - Smoking, documentation supporting free from smoking for 6 months
  - Active peptic ulcer disease
  - Active gastroesophageal reflux disease
  - CVA with long term impairment that is not amendable to rehabilitation or a patient with CVA/transient ischemic attack within past 6 months
  - Obesity with body mass index of >30 kg/m<sup>2</sup> may increase surgical risk
  - Chronic liver disease such as Hepatitis B/C/D, or cirrhosis which increases the risk of death from sepsis and hepatic failure requires consultation by a gastroenterologist or hepatologist
  - Gall bladder disease requires ultrasound of the gall bladder with treatment prior to transplantation

**Criteria for Subsequent Hematopoietic Stem Cell Transplantation:**

2. **Hematopoietic autologous stem cell transplantation** may be considered medically necessary and may be authorized after *the first prior stem cell transplantation* has occurred only one time for members with Ewing's sarcoma who meet all of the above criteria for transplant and have any of the following:**[ONE]**

- primary graft failure indicated by no signs of engraftment\* by 42 days after the transplant;
- OR**
- failure to engraft\*;
- AND**
- a suitable allogeneic donor has been identified if applicable (applies to allogeneic only)

*\*Note: Engraftment is defined as the first 3 consecutive days on which the absolute neutrophil count (ANC) exceeds  $5 \times 10^9/L$  or  $> ANC500$  at any time after transplantation.<sup>26</sup>*

#### CONTINUATION OF THERAPY

When extension of a previously approved transplant authorization is requested, review using updated clinical information is appropriate.

- If Molina Healthcare has authorized prior requests for transplantation, the following information is required for medical review: [ALL]
  - Presence of no absolute contraindication as listed above;
  - History and physical within the last 12 months;
  - Kidney profile within the last 12 months;
  - Cardiac update if history of cardiac disease within two years ( $\geq 50$  years of age);
  - Psychosocial evaluation or update within the last 12 months;
  - Per initial and updated history and physical, any other clinically indicated tests and/or scans as determined by transplant center physician or Molina Medical Director.
- If authorized prior requests for transplantation were obtained from another insurer, the following information is required for medical review: [ALL]
  - Authorization letter/documentation from previous insurer;
  - Presence of no absolute contraindication as listed above;
  - History and physical within the last 12 months;
  - Cardiac update if history of cardiac disease within two years ( $\geq 50$  years of age);
  - Psychosocial evaluation or update within the last 12 months;
  - Per initial and updated history and physical, any other clinically indicated tests and/or scans as determined by transplant center physician or Molina Medical Director.

#### COVERAGE EXCLUSIONS<sup>24-31</sup>

1. Autologous stem cell transplantation when the above criteria are not met
2. A second or repeat autologous transplant due to persistent, progressive or relapsed disease
3. Allogeneic hematopoietic stem cell transplantation
4. Hematopoietic stem cell collection, storage and freezing for a future unplanned transplant

**SUMMARY OF MEDICAL EVIDENCE**<sup>4-23</sup>

The published medical evidence and outcomes for hematopoietic stem cell transplantation for Ewing Sarcoma is limited to information from international bone marrow transplant registries and case series from individual institutions comparing treatment outcomes that suggest a survival benefit with the use of high dose chemotherapy followed by autologous hematopoietic stem cell transplantation. Several uncontrolled trials demonstrate improved or equivalent survival outcomes with autologous HSCT.<sup>5 11 12 16 19 22</sup>

One of the largest studies by Ferrari et al. (2011) reported results of the Italian Sarcoma Group/Scandinavian Sarcoma Group III protocol, a multicenter, multi-country clinical trial involving 300 participants with Ewing family of tumors. At a median follow-up of 64 months, five-year overall survival (OS) and event-free survival (EFS) were 75% and 69%, respectively. Five-year EFS for those treated with high-dose therapy (HDT) were 75% for good responders and 72% for partial responders, and 33% for partial responders who did not receive HDT.<sup>11</sup>

Another large study by Ladenstein et al (2010) called the EURO-EWING-Intergroup-EE99 R3 trial enrolled 281 patients with primary disseminated metastatic Ewing sarcoma. Patients were treated with six cycles of vincristine, ifosfamide, doxorubicin, and etoposide followed by high-dose therapy and autologous stem cell transplant and after a median follow-up of 3.8 years, event-free survival (EFS) and overall survival (OS) at 3 years for all 281 patients were 27% +/- 3% and 34% +/- 4% respectively. Factors such as the presence and number of bone lesions, primary tumor volume greater than 200 mL, and age older than 14 years, additional pulmonary metastases, and bone marrow involvement were identified as independent prognostic factors.<sup>16</sup>

A comparative effectiveness review was conducted on the use of hematopoietic stem cell transplantation in the pediatric population by the Blue Cross and Blue Shield Association Technology Evaluation Center for the Agency for Healthcare Research and Quality (AHRQ). Conclusions for Ewing Sarcoma Family of Tumors (ESFT) indicated the following: Low strength evidence on overall survival suggests no benefit with single hematopoietic stem cell transplantation compared to conventional therapy for the treatment of high-risk ESFT. The body of evidence on overall survival with tandem hematopoietic stem cell transplantation compared to single hematopoietic stem cell transplantation for the treatment of high-risk ESFT and overall survival is insufficient to draw conclusions.<sup>4</sup>

A case series of 33 individuals with recurrent or progressive Ewing sarcoma by McTiernan et al. reported treatment outcomes of hematopoietic stem cell transplants with different preparatory regimens. Two of the individuals received autologous bone marrow, 1 received autologous bone marrow and stem cells, 29 received autologous peripheral blood stem cells, and 1 received an allogeneic bone marrow transplant due to an unsuccessful autologous harvest. Event-free survival was 42.5% (95% CI, 26-59%) at 2 years and 38.2% at 5 years (95% CI, 21-55%). Although this treatment demonstrated the potential for long-term survival with high-dose therapy (HDT) for recurrent or refractory Ewing sarcoma, it was associated with significant toxicity. One treatment-related death was reported and 2 participants experienced grade IV infections.<sup>19</sup>

Gardner et al. (2008) reported on 116 individuals with Ewing sarcoma who underwent autologous hematopoietic stem cell transplantation (80 [69%] as first-line therapy and 36 [31%] for recurrent disease) between 1989 and 2000. Five-year probabilities of PFS in individuals who received hematopoietic stem cell transplantation as first-line therapy were 49% (95% CI, 30-69%) for those with localized disease at diagnosis and 34% (95% CI, 22-47%) for those with metastatic disease at diagnosis. For those with localized disease at diagnosis and recurrent disease, 5-year probability of PFS was 14% (95% CI, 3-30%). The reviewers concluded that PFS rates after autologous hematopoietic stem cell transplantation were comparable to rates seen in those with similar disease characteristics treated with conventional therapy. <sup>12</sup>

**CODING INFORMATION** THE CODES LISTED IN THIS POLICY ARE FOR REFERENCE PURPOSES ONLY. LISTING OF A SERVICE OR DEVICE CODE IN THIS POLICY DOES NOT IMPLY THAT THE SERVICE DESCRIBED BY THIS CODE IS COVERED OR NON-COVERED. COVERAGE IS DETERMINED BY THE BENEFIT DOCUMENT. THIS LIST OF CODES MAY NOT BE ALL INCLUSIVE.

<b>CPT</b>	<b>Description</b>
	<b>Collection Codes</b>
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38230	Bone marrow harvesting for transplantation; allogeneic
38232	Bone marrow harvesting for transplantation; autologous
	<b>Cell Processing Services</b>
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing
38210	Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-cell depletion
38211	Transplant preparation of hematopoietic progenitor cells; tumor cell depletion
38212	Transplant preparation of hematopoietic progenitor cells; red blood cell removal
38213	Transplant preparation of hematopoietic progenitor cells; platelet depletion
38214	Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion
38215	Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear, or buffy coat layer
	<b>Cell infusion codes</b>
38240	Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic
38241	Bone marrow or blood-derived peripheral stem cell transplantation; autologous
38242	Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic donor lymphocyte infusions
38243	Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic hematopoietic cellular transplant boost

<b>HCPCS</b>	<b>Description</b>
S2140	Cord blood harvesting for transplantation, allogeneic

S2142	Cord blood derived stem-cell transplantation, allogeneic
S2150	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

<b>ICD-9</b>	<b>Description: [For dates of service prior to 10/01/2015]</b>
170.0-170.9	Malignant neoplasm of bone and articular cartilage [specified as Ewing's sarcoma]

<b>ICD-10</b>	<b>Description: [For dates of service on or after 10/01/2015]</b>
C40.00-C40.92	Malignant neoplasm of bone and articular cartilage or limbs [specified as Ewing's sarcoma]
C41.0-C41.9	Malignant neoplasm of bone and articular cartilage of other and unspecified sites [specified as Ewing's sarcoma]

## RESOURCE REFERENCES

### Government Agency

- Centers for Medicare & Medicaid Services. NCD for Stem Cell Transplantation (Formerly 110.8.1) 110.23. Effective date 1/27/2016. Accessed at: <http://www.cms.gov/medicare-coverage-database/>
- National Bone Marrow Donor Program HLA Matching Requirements. Accessed at: [http://marrow.org/Patient/Transplant\\_Process/Search\\_Process/HLA\\_Matching\\_Finding\\_the\\_Best\\_Donor\\_or\\_Cord\\_Blood\\_Unit.aspx](http://marrow.org/Patient/Transplant_Process/Search_Process/HLA_Matching_Finding_the_Best_Donor_or_Cord_Blood_Unit.aspx)
- Eastern Cooperative Oncology Group (ECOG) Performance Status. Accessed at: [http://www.ecog.org/general/perf\\_stat.html](http://www.ecog.org/general/perf_stat.html)
- Ratko TA, Belinson SE, Brown HM, et al. Hematopoietic Stem-Cell Transplantation in the Pediatric Population [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2012. Available at: <http://www.ncbi.nlm.nih.gov/books/NBK84626/>.

### Peer Reviewed Publications

- Barker L, Pendergrass T, Sanders J, Hawkins J. Survival after recurrence of Ewing's sarcoma family of tumors. *J Clin Oncol*. 2005 Jul 1;23(19):4354-62. Epub 2005 Mar 21.
- Burdach S, Meyer-Bahlburg A, Laws HJ, et al.: High-dose therapy for patients with primary multifocal and early relapsed Ewing's tumors: results of two consecutive regimens assessing the role of total-body irradiation. *J Clin Oncol* 21 (16): 3072-8, 2003.
- Burdach S, Thiel U, Schöniger M, et al.: Total body MRI-governed involved compartment irradiation combined with high-dose chemotherapy and stem cell rescue improves long-term survival in Ewing tumor patients with multiple primary bone metastases. *Bone Marrow Transplant* 45 (3): 483-9, 2010.
- Burdach S, van Kaick B, Laws HJ, et al.: Allogeneic and autologous stem-cell transplantation in advanced Ewing tumors. An update after long-term follow-up from two centers of the European Intergroup study EICESS. *Stem-Cell Transplant Programs at Düsseldorf University Medical Center, Germany and St. Anna Kinderspital, Vienna, Austria. Ann Oncol* 11 (11): 1451-62, 2000.
- Burdach S: Treatment of advanced Ewing tumors by combined radiochemotherapy and engineered cellular transplants. *Pediatr Transplant* 8 (Suppl 5): 67-82, 2004.

10. Drabko K, Raciborska A, Bilska K, et al.: Consolidation of first-line therapy with busulphan and melphalan, and autologous stem cell rescue in children with Ewing's sarcoma. *Bone Marrow Transplant* 47 (12): 1530-4, 2012.
11. Ferrari S, Sundby Hall K, Luksch R, Tienghi A, Wiebe T, Fagioli F, et al. Nonmetastatic Ewing family tumors: high-dose chemotherapy with stem cell rescue in poor responder patients. Results of the Italian Sarcoma Group/Scandinavian Sarcoma Group III protocol. *Ann Oncol*. 2011 May;22(5):1221-7.
12. Gardner SL, Carreras J, Boudreau C, et al. Myeloablative therapy with autologous stem cell rescue for patients with Ewing sarcoma. *Bone Marrow Transplant*. 2008; 41(10):867-872.
13. Gaspar N, Rey A, Bérard PM, et al.: Risk adapted chemotherapy for localized Ewing's sarcoma of bone: the French EW93 study. *Eur J Cancer* 48 (9): 1376-85, 2012.
14. Hawkins D, Barnett T, Bensinger W, et al.: Busulfan, melphalan, and thiotepa with or without total marrow irradiation with hematopoietic stem cell rescue for poor-risk Ewing-Sarcoma-Family tumors. *Med Pediatr Oncol* 34 (5): 328-37, 2000.
15. Kushner BH, Meyers PA: How effective is dose-intensive/myeloablative therapy against Ewing's sarcoma/primitive neuroectodermal tumor metastatic to bone or bone marrow? The Memorial Sloan-Kettering experience and a literature review. *J Clin Oncol* 19 (3): 870-80, 2001.
16. Ladenstein R, Pötschger U, Le Deley MC, et al.: Primary disseminated multifocal Ewing sarcoma: results of the Euro-EWING 99 trial. *J Clin Oncol* 28 (20): 3284-91, 2010.
17. 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* 50 (8): 1083-8, 2015.
18. Marina N, Meyers PA: High-dose therapy and stem-cell rescue for Ewing's family of tumors in second remission. *J Clin Oncol* 23 (19): 4262-4, 2005.
19. McTiernan A, Driver D, Michelagnoli MP, et al. High dose chemotherapy with bone marrow or peripheral stem cell rescue is an effective treatment option for patients with relapsed or progressive Ewing's sarcoma family of tumours. *Ann Oncol*. 2006; 17(8):1301-1305.
20. 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* 19 (11): 2812-20, 2001.
21. Oberlin O, Rey A, Desfachelles AS, et al.: Impact of high-dose busulfan plus melphalan as consolidation in metastatic Ewing tumors: a study by the Société Française des Cancers de l'Enfant. *J Clin Oncol* 24 (24): 3997-4002, 2006.
22. Rosenthal J, Bolotin E, Shakhnovits M, et al.: High-dose therapy with hematopoietic stem cell rescue in patients with poor prognosis Ewing family tumors. *Bone Marrow Transplant* 42 (5): 311-8, 2008.
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### Professional Society Guidelines

24. National Marrow Donor Program<sup>®</sup> (NMDP) and the American Society for Blood and Marrow Transplantation (ASBMT) referral guidelines: Recommended Timing for Transplant Consultation. Accessed at: <https://bethematchclinical.org/Transplant-Indications-and-Outcomes/Referral-Timing-Guidelines/>
25. National Marrow Donor Program<sup>®</sup> (NMDP). Patient Eligibility for HCT. Accessed at: <https://bethematchclinical.org/Transplant-Indications-and-Outcomes/Eligibility/>
26. National Bone Marrow Donor Program. Measuring Engraftment. Accessed at: [http://marrow.org/Patient/Transplant\\_Process/Days\\_0-30/Measuring\\_Engraftment.aspx](http://marrow.org/Patient/Transplant_Process/Days_0-30/Measuring_Engraftment.aspx)

27. National Cancer Institute. Ewing Sarcoma Treatment – for health professionals. (PDQ). Updated 2019. Accessed at: <http://www.cancer.gov/types/bone/hp/ewing-treatment-pdq>
28. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Bone Cancer version 1.2019. Accessed at: <http://www.nccn.org/>

### **Other Resources**

29. McKesson InterQual Criteria for Procedures: Adult 2018 InterQual Transplantation, Autologous Stem Cell; 2018.
30. DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995-2019. Ewing’s Sarcoma. Updated 2019
31. UpToDate: [website]. Waltham, MA: Walters Kluwer Health; 2019.
  - Holmberg L, Deeg H, Sandmaier B. Determining eligibility for autologous/allogenic hematopoietic cell transplantation. 2019.
  - Harmon D, Gebhardt M. Treatment of the Ewing sarcoma family of tumors. 2019.
32. Advanced Medical Review (AMR): Policy reviewed by practicing MD board certified in Internal Medicine, Oncology, Hematology. 4/18/19.

### **Revision/Review History:**

3/8/18: Policy reviewed, clinical criteria has not changed.

9/18/19: Policy reviewed, clinical criteria has not changed. Updated guidelines and references.