Medical Policy
Hematopoietic Cell Transplantation for Hodgkin Lymphoma

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Policy Number: 207
BCBSA Reference Number: 8.01.29
NCD/LCD: National Coverage Determination (NCD) for Stem Cell Transplantation (110.8.1)

Related Policies
- Hematopoietic Stem Cell Transplantation for Non-Hodgkin Lymphomas, #143

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

Autologous hematopoietic cell transplantation (HCT) may be considered MEDICALLY NECESSARY in patients with primary refractory or relapsed Hodgkin lymphoma.

Allogeneic HCT, using either myeloablative or reduced-intensity conditioning regimens, may be considered MEDICALLY NECESSARY in patients with primary refractory or relapsed Hodgkin lymphoma.

Tandem autologous HCT may be considered MEDICALLY NECESSARY:
- In patients with primary refractory HL or
- In patients with relapsed disease with poor risk features who do not attain a complete remission to cytoreductive chemotherapy prior to transplantation.

Second autologous HCT for relapsed lymphoma after a prior autologous HCT is considered INVESTIGATIONAL.

Other uses of HCT in patients with HL are considered INVESTIGATIONAL, including, but not limited to, initial therapy for newly diagnosed disease to consolidate a first complete remission.

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

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>
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<tbody>
<tr>
<td>Commercial Managed Care (HMO and POS)</td>
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<tr>
<td>Commercial PPO and Indemnity</td>
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<tr>
<td>Medicare HMO Blue&lt;sup&gt;SM&lt;/sup&gt;</td>
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<tr>
<td>Medicare PPO Blue&lt;sup&gt;SM&lt;/sup&gt;</td>
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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>
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<tbody>
<tr>
<td>38205</td>
<td>Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic</td>
</tr>
<tr>
<td>38206</td>
<td>Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous</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>38241</td>
<td>Hematopoietic progenitor cell (HPC); autologous transplantation</td>
</tr>
</tbody>
</table>

### HCPCS Codes

<table>
<thead>
<tr>
<th>HCPCS codes:</th>
<th>Code Description</th>
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<tbody>
<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 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>ICD-10-PCS procedure codes:</th>
<th>Code Description</th>
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</table>
Description

HODGKIN LYMPHOMA

Hodgkin lymphoma (HL) is a relatively uncommon B-cell lymphoma. In 2017, the estimated number of new cases in the United States was approximately 8,260 and 1,070 estimated deaths.1 The disease has a bimodal distribution, with most patients diagnosed between the ages of 15 and 30 years, with a second peak in adults aged 55 years and older.

The 2008 World Health Organization classification divides HL into 2 main types2:
1. “Classical” HL (CHL)
   - Nodular sclerosis
   - Mixed cellularity
   - Lymphocyte depleted
   - Lymphocyte rich
2. Nodular lymphocyte-predominant HL.

In Western countries, CHL accounts for 95% of cases of HL and, for nodular lymphocyte-predominant HL, only 5%. CHL is characterized by the presence of neoplastic Reed-Sternberg cells in a background of numerous non-neoplastic inflammatory cells. Nodular lymphocyte-predominant HL lacks Reed-Sternberg cells but is characterized by the presence of lymphocytic and histiocytic cells termed “popcorn cells”.

**Staging**

The Ann Arbor staging system for HL recognizes that the disease is thought typically to arise in a single lymph node and spread to contiguous lymph nodes with eventual involvement of extranodal sites. The staging system attempts to distinguish patients with localized HL who can be treated with extended field radiation from those who require systemic chemotherapy.

Each stage is subdivided into A and B categories. “A” indicates no systemic symptoms are present and “B” indicates the presence of systemic symptoms, which include unexplained weight loss of more than 10% of body weight, unexplained fevers, or drenching night sweats (see Table 1).

| Table 1. Ann Arbor Staging System for Hodgkin Lymphoma |
|----------------------------------|----------------------------------|
| **Stage** | **Area of Concern** |
| I       | Single lymph node region (I) or localized involvement of a single extralymphatic organ or site (IE) |
| II      | 2 or more lymph node regions on the same side of the diaphragm (II) or localized involvement of a single associated extralymphatic organ or site and its regional lymph node(s) with or without involvement of other lymph node regions on the same side of the diaphragm (IIIE). The number of lymph node regions involved should be indicated by a subscript (eg, II3). |
| III     | Involvement of lymph node regions or structures on both sides of the diaphragm. These patients are further subdivided as follows:  
  - III-1: disease limited to spleen or upper abdomen  
  - III-2: periaortic or pelvic node involvement |
| IV      | Disseminated (multifocal) involvement of 1 or more extralymphatic organs, with or without associated lymph node involvement, or isolated extralymphatic organ involvement with distant (nonregional) nodal involvement |

Patients with Hodgkin lymphoma are generally classified into 3 groups: early-stage favorable (stage I-II with no B symptoms or large mediastinal lymphadenopathy), early-stage unfavorable (stage I-II with large mediastinal mass, with or without B symptoms; stage IB-IIB with bulky disease), and advanced-stage disease (stage III-IV).  

**TREATMENT**

Patients with nonbulky stage IA or IIA disease are considered to have clinically early-stage disease. These patients are candidates for chemotherapy, combined modality therapy, or radiotherapy alone.  

Patients with obvious stage III or IV disease, bulky disease (defined as a 10-cm mass or mediastinal disease with a transverse diameter exceeding 33% of the transthoracic diameter), or the presence of B symptoms will require combination chemotherapy with or without additional radiotherapy.

Hodgkin lymphoma is highly responsive to conventional chemotherapy, and up to 80% of newly diagnosed patients can be cured with chemotherapy and/or radiotherapy. Patients who prove refractory or who relapse after first-line therapy have a significantly worse prognosis. Primary refractory Hodgkin lymphoma is defined as disease regression of less than 50% after 4 to 6 cycles of anthracycline-containing chemotherapy, disease progression during induction therapy, or progression within 90 days after the completion of first-line treatment.

In patients with relapse, the results of salvage therapy vary depending on a number of prognostic factors, as follows: the length of the initial remission, stage at recurrence, and the severity of anemia at the time of
relapse. Early and late relapse are defined as less or more than 12 months from the time of remission, respectively. Approximately 70% of patients with late first relapse can be salvaged by autologous HCT but not more than 40% with early first relapse.

Only approximately 25% to 35% of patients with primary progressive or poor-risk recurrent Hodgkin lymphoma achieve durable remission after autologous HCT, with most failures being due to disease progression after transplant. Most relapses after transplant occur within 1 to 2 years, and once relapse occurs posttransplant, median survival is less than 12 months.

Summary
Hodgkin lymphoma (HL) results from a clonal expansion of a B-cell lineage, characterized by the presence of Reed-Sternberg cells on pathology. Standard treatment is based on the stage at presentation and may involve chemotherapy with or without radiotherapy. Hematopoietic cell transplantation (HCT) has been used for Hodgkin lymphoma, particularly in the setting of relapse or refractory disease.

Autologous HCT
For individuals who have Hodgkin lymphoma who receive autologous HCT as initial therapy, the evidence includes randomized controlled trials (RCTs). Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related mortality and morbidity. RCTs of autologous HCT as first-line treatment have reported that this therapy does not provide additional benefit compared to conventional chemotherapy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have relapsed or refractory Hodgkin lymphoma who receive autologous HCT, the evidence includes RCTs, nonrandomized comparative studies, and case series. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related mortality and morbidity. Two RCTs in patients with relapsed or refractory disease have reported a benefit in progression-free survival and a trend toward a benefit in overall survival. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have relapsed Hodgkin lymphoma after an autologous HCT who receive a second autologous HCT, the evidence includes case series. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related mortality and morbidity. No RCTs or nonrandomized comparative studies were identified. In 1 case series, treatment-related mortality at 100 days was 11%; at a median follow-up of 72 months, the mortality rate was 73%. The evidence is insufficient to determine the effects of the technology on health outcomes.

Allogeneic HCT
For individuals who have Hodgkin lymphoma who receive allogeneic HCT (allo-HCT) as first-line therapy, the evidence includes no published studies. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related mortality and morbidity. No studies specifically addressing allo-HCT as first-line treatment for (HL) were identified. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have relapsed or refractory (HL) who receive allo-HCT, the evidence includes a number of case series and a meta-analysis. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related mortality and morbidity. A 2016 meta-analysis identified 38 case series evaluating allo-HCT for relapsed or refractory (HL). The pooled analysis found a 6-month overall survival rate of 83% and a 3-year overall survival rate of 50%. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have relapsed (HL) after autologous HCT who receive allo-HCT, the evidence includes case series and a meta-analysis. Relevant outcomes are overall survival, disease-specific
survival, change in disease status, morbid events, and treatment-related mortality and morbidity. A 2016 meta-analysis of 38 case series found that a previous autologous HCT was significantly associated with higher 1- and 2-year overall survival rates and significantly higher recurrence-free survival rates at 1 year compared with no previous autologous HCT. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have relapsed or refractory (HL) who receive reduced-intensity conditioning (RIC) with allo-HCT, the evidence includes case series, cohort studies, and a systematic review. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related mortality and morbidity. A 2015 systematic review cited a number of studies, including some with comparison groups, showing acceptable outcomes after RIC allo-HCT in patients with relapsed or refractory (HL). The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

**Tandem Autologous HCT**

For individuals who have (HL) who receive tandem autologous HCT, the evidence includes nonrandomized comparative studies and case series. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related mortality and morbidity. One prospective, nonrandomized study reported that, in patients with poor prognostic markers, response to tandem autologous HCT may be higher than that for single autologous HCT. This study was not definitive due to potential selection bias; RCTs are needed to determine the impact of tandem autologous HCT on health outcomes in this population. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input obtained in 2009 supported the use of tandem autologous HCT in specific situations, including primary refractory HL and relapsed disease with poor risk features, not in remission. Tandem autologous HCT may be considered medically necessary for these situations.

**Policy History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>1/2019</td>
<td>Outpatient prior authorization is required for all commercial products including Medicare Advantage. Effective 1/1/2019.</td>
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<tr>
<td>3/2018</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
<tr>
<td>2/2018</td>
<td>Coding information clarified.</td>
</tr>
<tr>
<td>9/2015</td>
<td>Clarified coding information.</td>
</tr>
<tr>
<td>6/2014</td>
<td>Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.</td>
</tr>
<tr>
<td>12/2012</td>
<td>Updated to add new CPT code 38243.</td>
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**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](#)
References


