Clinical Policy: Nonmyeloablative Allogeneic Stem Cell Transplants
Reference Number: PA.CP.MP.141
Effective Date: 01/18
Last Review Date: 03/19

Description
Allogeneic hematopoietic stem cell transplants that do not destroy all of the hematopoietic cells in the bone marrow are termed reduced-intensity or nonmyeloablative conditioning regimens. Although there are no clear definitions, reduced-intensity conditioning (RIC) generally destroys more hematopoietic cells and is more toxic than nonmyeloablative conditioning, but less so than myeloablative conditioning. Both nonmyeloablative and RIC regimens are categorized as non-fully ablative regimens, and are used interchangeably in this policy, unless otherwise noted. RIC/nonmyeloablative approaches can circumvent the need for high-dose conditioning regimens that are associated with organ toxicity and mortality, while maintaining adequate response in certain cancers and blood disorders.

Policy/Criteria
I. It is the policy of Pennsylvania Health and Wellness® (PHW) that nonmyeloablative/RIC allogeneic transplants is medically necessary for members who meet all of the following criteria:
   A. Candidate for allogeneic stem cell transplantation for any of the following diagnoses:
      1. Acute lymphoblastic leukemia;
      2. Acute myelogenous leukemia;
      3. Aplastic anemia;
      4. Paroxysmal nocturnal hemoglobinuria;
      5. Chronic lymphoblastic leukemia;
      6. Chronic myelogenous leukemia;
      7. Congenital immunodeficiency syndromes: molecular remissions induced by Gleevec
      8. Hodgkin’s disease: primary refractory or relapsed, including those who have relapsed having an autologous bone marrow transplant;
      9. Non-Hodgkin’s disease, any of the following:
         a. Primary refractory or relapsed, including those who have relapsed having an autologous bone marrow transplant (excluding diffuse large B-cell lymphoma);
         b. Follicular lymphomas;
         c. Mantle cell lymphoma;
         d. Diffuse large cell lymphoma that is in remission following second-line therapy for relapsed or refractory disease;
      10. Multiple myeloma,, following autologous or fully myeloablative allogeneic stem cell transplant;
      11. Myelodysplastic syndromes;
      12. Myelofibrosis;
      13. Neuroblastoma, high risk;
   B. Unsuitable for conventional high-dose myeloablative allografting because of un treatable significant dysfunction of another major organ system and/or severe comorbidities, including, but not limited to, any of the following:
1. Bilirubin > 2 mg/dL;
2. Hemostasis: international normalized ratio (INR) > 1.6 (unless on oral anticoagulants);
3. Cardiac function: multigated acquisition scan (MUGA) or echocardiogram with ejection fraction (EF) < 45%;
4. Pulmonary function:
   a. Forced expiratory volume in 1 second (FEV1) ≤ 50% of predicted value; or
   b. Diffusing capacity of the lung for carbon monoxide (DLCO) ≤ 50% of predicted value;
5. Performance scale index:
   a. Karnofsky or Lansky score < 70%; or
   b. Eastern Cooperative Oncology Group (ECOG) performance score ≤ 2;

C. Does not have ANY of the following absolute contraindications:
   1. Chronic infection with highly virulent and/or resistant microbes that are poorly controlled pre-transplant;
   2. Current non-adherence to medical therapy or a history of repeated or prolonged episodes of non-adherence to medical therapy that are perceived to increase the risk of non-adherence after transplantation;
   3. Psychiatric or psychological condition associated with the inability to cooperate or comply with medical therapy;
   4. Absence of an adequate or reliable social support system;
   5. Substance abuse or dependence (including tobacco and alcohol) without convincing evidence of risk reduction behaviors, such as meaningful and/or long-term participation in therapy for substance abuse and/or dependence. Serial blood and urine testing may be used to verify abstinence from substances that are of concern.

II. It is the policy of PHW that nonmyeloablative/RIC allogeneic transplants are experimental/investigational for the following indications:
   A. Astrocytomas and gliomas
   B. Beta thalassemia
   C. Breast cancer
   D. Dermatomyositis
   E. Ewing sarcoma
   F. Germ cell Tumors
   G. Idiopathic thromboctopenic purpura
   H. Juvenile rheumatoid arthritis
   I. Lupus erythematosus
   J. Medulloblastoma
   K. Melanoma
   L. Multiple sclerosis
   M. Osteosarcoma
   N. Ovarian epithelia and mixed epithelia/germ cell cancers
   O. Polycythemias and leukaemia
   P. Polymyositis
   Q. Ovarian germ cell Tumors
Background
Allogeneic stem cell transplant (AlloBMT) has been used as a treatment for cancer and diseases of the blood system for many years. For this treatment, stem cells are collected from either related or unrelated donors. During the conditioning phase, high doses of chemotherapy (HDC), with or without radiation therapy, are used to eradicate the disease and this is followed by infusion of an allogeneic stem cell transplantation to rescue bone marrow and restore normal immune function. Major limitations of this technique are the associations with serious side effects and high mortality. All stem cell transplants (SCTs) preparative regimens have the potential for extensive toxicity. Loss of appetite and energy, alopecia, and nausea/vomiting are very frequent and add to poor physical and emotional tolerance of the transplant procedure. In addition, mucositis, diarrhea, and transient pancytopenia are inevitable side effects of most preparative regimens, and these complications are synergistic in dramatically increasing the risk of bacterial and fungal infections. Any decrease in toxicity, without concomitant loss of efficacy, would be desirable.

Myeloablative means that the treatment kills (ablates) the myeloid stem cells in the bone marrow, the cells that produce new blood cells. Several less intense conditioning regimens have been developed recently and rely more on immuno-suppression than cytotoxic effects to permit engraftment of donor cells. These regimens are collectively termed non-myeloablative. Studies have shown that donor allogeneic stem cells can engraft in recipients using less-intensive conditioning regimens that are sufficiently immunosuppressive to permit graft-host tolerance. This manifests as a stable mixed donor-host hematopoetic chimerism, a term which means the coexistence of donor and recipient cells. Once chimerism has developed, a further infusion of donor leukocytes may be given to eradicate malignant cells by inducing a graft vs. tumor effect. Non-myeloablative allogeneic transplants, also referred to as “mini-transplant” or “transplant lite”, are thought to be potentially as effective as conventional HDC followed by an allogeneic stem cell transplantation, but with decreased morbidity and mortality related to the less intense nonmyeloablative chemotherapy conditioning regimen. Consequently, for patients with malignancies who are eligible for conventional HDC/AlloBMT, conditioning with milder, nonmyeloablative regimens represents a variation of an established procedure.

Coding Implications
## Clinical Policy
### Nonmyeloablative Allogeneic Stem Cell Transplants

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<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>38204</td>
<td>Management of recipient hematopoietic progenitor cell donor search and cell acquisition</td>
</tr>
<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>38207</td>
<td>Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage</td>
</tr>
<tr>
<td>38208</td>
<td>Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor</td>
</tr>
<tr>
<td>38209</td>
<td>Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing, per donor</td>
</tr>
<tr>
<td>38210</td>
<td>Transplant preparation of hematopoietic progenitor cells; specific cell deletion within harvest. T-cell depletion</td>
</tr>
<tr>
<td>38211</td>
<td>Transplant preparation of hematopoietic progenitor cells; tumor depletion</td>
</tr>
<tr>
<td>38212</td>
<td>Transplant preparation of hematopoietic progenitor cells; red blood cell removal</td>
</tr>
<tr>
<td>38213</td>
<td>Transplant preparation of hematopoietic progenitor cells; platelet depletion</td>
</tr>
<tr>
<td>38214</td>
<td>Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion</td>
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<td>38215</td>
<td>Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear, or buffy coat layer</td>
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<tr>
<td>38230</td>
<td>Bone marrow harvesting for transplantation; allogeneic</td>
</tr>
<tr>
<td>38240</td>
<td>Hematopoietic progenitor cell (HPC), allogeneic transplantation per donor</td>
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CLINICAL POLICY
Nonmyeloablative Allogeneic Stem Cell Transplants

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<thead>
<tr>
<th>HCPSC Codes</th>
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<tr>
<td>S2142</td>
<td>Cord blood-derived stem cell transplantation, allogeneic</td>
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<tr>
<td>S2150</td>
<td>Bone marrow or blood-derived peripheral 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>
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ICD-10-CM Diagnosis Codes that Support Coverage Criteria

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<thead>
<tr>
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<th>Description</th>
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<tbody>
<tr>
<td>C74.00-C74.02</td>
<td>Malignant neoplasm of adrenal gland</td>
</tr>
<tr>
<td>C81.0-C96.9</td>
<td>Malignant neoplasm of lymphoid, hematopoietic and related tissue</td>
</tr>
<tr>
<td>D46.0-D46.9</td>
<td>Myeloplastic syndromes</td>
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<tr>
<td>D56.0-D56.9</td>
<td>Thalassemia</td>
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<tr>
<td>D57.00-D57.819</td>
<td>Sickle-cell disorders</td>
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<tr>
<td>D61.01-D61.09</td>
<td>Constitutional aplastic anemia</td>
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<tr>
<td>Z51.11</td>
<td>Encounter for antineoplastic chemotherapy</td>
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<tr>
<td>Z94.84</td>
<td>Stem cells transplant status</td>
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Reviews, Revisions, and Approvals

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<th>Description</th>
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<td>Updated description. Moved beta thalassemia and sickle cell anemia from the list of approved indications to the list of E/I indications. Removed age restriction from myelodysplastic syndromes. Added to the multiple myeloma indication that an RIC/NMA approach is appropriate post – autologous or fully myeloablative stem cell transplant. Removed diffuse large b-cell lymphoma from E/I list. Clarified that diffuse large cell lymphoma is diffuse large b-cell lymphoma, and added requirement that the patient is in remission following second-line therapy for relapsed or refractory disease. Specialist reviewed. References reviewed and updated.</td>
<td>03/19</td>
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References
5. BlueCross BlueShield Association (BCBSA), Technology Evaluation Center (TEC). Nonmyeloablative allogeneic stem-cell transplantation for malignancy. TEC Assessment Program. Chicago, IL: BCBSA; May 2001;16(3).


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