MEDICAL POLICY – 8.01.25

Hematopoietic Cell Transplantation for Autoimmune Diseases

BCBSA Ref. Policy: 8.01.25

Effective Date: May 1, 2018
Last Revised: April 3, 2018
Replaces: N/A

RELATED MEDICAL POLICIES:
7.01.50 Placental and Umbilical Cord Blood as a Source of Stem Cells
8.01.21 Allogeneic Hematopoietic Cell Transplantation for Myelodysplastic Syndromes and Myeloproliferative Neoplasms
8.01.22 Allogeneic Hematopoietic Cell Transplantation for Genetic Diseases and Acquired Anemias
8.01.24 Hematopoietic Cell Transplantation for Miscellaneous Solid Tumors in Adults
8.01.26 Hematopoietic Cell Transplantation for Acute Myeloid Leukemia
8.01.29 Hematopoietic Cell Transplantation for Hodgkin Lymphoma
8.01.511 Hematopoietic Cell Transplantation for Solid Tumors of Childhood
8.01.529 Hematopoietic Cell Transplantation for Non-Hodgkin Lymphomas
8.01.530 Hematopoietic Cell Transplantation for Primary Amyloidosis
8.01.532 Hematopoietic Cell Transplantation in the Treatment of Germ Cell Tumors

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 body’s immune system fights against disease and infection. However, the immune system can sometimes mistake healthy cells for foreign cells and start attacking them. This is known as an autoimmune disorder. Examples of autoimmune disorders include rheumatoid arthritis, multiple sclerosis, and inflammatory bowel disease. Stem cells are like basic building blocks. They can develop into many different types of cells. Stem cells are being studied as a way to treat autoimmune diseases. The idea is to eliminate a certain type of white blood cell (lymphocyte) that is attacking normal, healthy cells. Stem cells are then given to the patient so that new lymphocytes could be formed. This treatment is investigational for autoimmune diseases. More studies are needed to find out if this treatment works.
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.

Policy Coverage Criteria

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Investigational</th>
</tr>
</thead>
</table>
| Autologous or allogeneic hematopoietic cell transplantation | Autologous or allogeneic hematopoietic cell transplantation is considered investigational as a treatment of autoimmune diseases, including, but not limited to the following:  
- Multiple sclerosis  
- Systemic sclerosis/scleroderma  
- Systemic lupus erythematosus  
- Juvenile idiopathic or rheumatoid arthritis  
- Chronic inflammatory demyelinating polyneuropathy  
- Type 1 diabetes |

Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tr>
<td>CPT</td>
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<tr>
<td>38230</td>
<td>Bone marrow harvesting for transplantation; allogeneic</td>
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<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>38242</td>
<td>Allogeneic lymphocyte infusions</td>
</tr>
<tr>
<td>HCPCS</td>
<td></td>
</tr>
<tr>
<td>S2150</td>
<td>Bone marrow or blood-derived peripheral stem cell (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications including: pheresis and cell preparation/storage, marrow ablative therapy, drugs,</td>
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</tbody>
</table>
Related Information

N/A

Evidence Review

Description

Most patients with autoimmune disorders respond to conventional drug therapies; however, conventional drug therapies are not curative—and a proportion of patients suffer from autoimmune diseases that range from the severe to the recalcitrant to the rapidly progressive. It is in this group of patients with severe autoimmune disease that alternative therapies have been sought, including hematopoietic cell transplantation (HCT).

Background

Autoimmune Diseases

Autoimmune diseases represent a heterogeneous group of immune-mediated disorders, including MS, rheumatoid arthritis (RA), SLE, systemic sclerosis/scleroderma, and chronic immune demyelinating polyneuropathy (CIDP). The National Institutes of Health (NIH) estimates that 5% to 8% of Americans have an autoimmune disorder.

The pathogenesis of autoimmune diseases is not well-understood but appears to involve underlying genetic susceptibility and environmental factors that lead to loss of self-tolerance, culminating in tissue damage by the patient’s own immune system (T cells).
Treatment

Immune suppression is a common treatment strategy for many of these diseases, particularly the rheumatic diseases (e.g., RA, SLE, scleroderma). Most patients with autoimmune disorders respond to conventional therapies, which consist of anti-inflammatory agents, immunosuppressants, and immune-modulating drugs. However, these drugs are not curative, and a proportion of patients will have severe, recalcitrant, or rapidly progressive disease. It is in this group of patients with severe autoimmune disease that alternative therapies have been sought, including HCT. The primary concept underlying use of HCT for these diseases is that ablating and “resetting” the immune system can alter the disease process, first inducing a sustained remission that possibly leads to cure.¹

Hematopoietic Cell Transplantation HCT

HCT refers to a procedure in which hematopoietic stem cells are infused to restore bone marrow function in patients who receive bone-marrow-toxic doses of cytotoxic drugs with or without wholebody radiation therapy. Hematopoietic Stem cells may be obtained from the transplant recipient (autologous HCT) or from 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 (GVHD). Cord blood is discussed in greater detail in a separate medical policy (see Related Policies).

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 a critical factor for achieving a good outcome of allogeneic HCT. Compatibility is established by typing of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. HLA refers to the tissue type expressed at the class I and class II loci on chromosome 6. Depending on the disease being treated, an acceptable donor will match the patient at all or most of the HLA loci (with the exception of umbilical cord blood).

Autologous Cell Transplantation for Autoimmune Diseases

The goal of autologous HCT in patients with autoimmune diseases is to eliminate self-reactive lymphocytes (lymphoablation) and generate new self-tolerant lymphocytes.² This approach is in
contrast to destroying the entire hematopoietic bone marrow (myeloablation), as is often performed in autologous HCT for hematologic malignancies. However, no standard conditioning regimen exists for autoimmune diseases and both lymphoablative and myeloablative regimens are used. The efficacy of the different conditioning regimens has not been compared in clinical trials.

Currently, for autoimmune diseases, autologous transplant is preferred over allogeneic, in part because of the lower toxicity of autotransplant relative to allogeneic, the GVHD associated with allogeneic transplant, and the need to administer post-transplant immunosuppression after an allogeneic transplant.

**Allogeneic Cell Transplantation**

The experience of using allogeneic HCT for autoimmune diseases is currently limited but has two potential advantages over autologous transplant. First, the use of donor cells from a genetically different individual could possibly eliminate genetic susceptibility to the autoimmune disease and potentially result in a cure. Second, there exists a possible graft-versus-autoimmune effect, in which the donor T cells attack the transplant recipient’s autoreactive immune cells.

**Summary of Evidence**

For individuals with multiple sclerosis who receive hematopoietic cell transplantation (HCT), the evidence includes a randomized controlled trial (RCT) and several case series. Relevant outcomes are overall survival, health status measures, quality of life, and treatment-related mortality and morbidity. The phase 2 RCT compared HCT with mitoxantrone, and the trial reported intermediate outcomes (number of new T2 magnetic resonance imaging lesions); the group randomized to HCT developed significantly fewer lesions than the group receiving conventional therapy. The findings of the case series revealed improvements in clinical parameters following HCT compared with baseline. Adverse event rates were high, and most studies reported treatment-related deaths. Controlled trials (with appropriate comparator therapies) that report on clinical outcomes are needed to demonstrate efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with systemic sclerosis/scleroderma who receive HCT, the evidence includes RCTs and observational studies. Relevant outcomes are overall survival, symptoms, health status measures, quality of life, and treatment-related mortality and morbidity. The results of the ASTIS trial (N=156) have suggested high-dose chemotherapy plus autologous HCT might improve
survival among patients with diffuse cutaneous systemic sclerosis compared with pulsed intravenous cyclophosphamide. However, analysis of the internal validity of the trial using U.S. Preventive Services Task Force criteria showed fatal flaws and a poor study rating due to attrition in the control group that could have skewed the survival curve to show better survival for HCT recipients than for controls. A smaller RCT (N=19) found that the rate of improvement at 12 months was significantly higher in the HCT group than in the conventional therapy group. Data from these trials, however, are inconclusive, and additional studies are needed to confirm safety and efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with systemic lupus erythematosus who receive HCT, the evidence includes case series. Relevant outcomes are overall survival, symptoms, quality of life, and treatment-related mortality and morbidity. Several case series (total N=91 patients) have been published. The largest series (N=50) reported an overall 5-year survival rate of 84% and the probability of disease-free survival was 50%. Additional data are needed from controlled studies to demonstrate efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with juvenile idiopathic or rheumatoid arthritis who receive HCT, the evidence includes registry data. Relevant outcomes are symptoms, quality of life, medication use, and treatment-related mortality and morbidity. The registry included 50 patients with juvenile idiopathic or rheumatoid arthritis. The overall drug-free remission rate was approximately 50%. Additional data are needed from controlled studies to demonstrate efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with chronic inflammatory demyelinating polyneuropathy who receive HCT, the evidence includes case reports. Relevant outcomes are overall survival, symptoms, health status measures, quality of life, and treatment-related mortality and morbidity. Additional data are needed from controlled studies to demonstrate efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with type 1 diabetes who receive HCT, the evidence includes case series and a meta-analysis of 22 studies. Relevant outcomes are overall survival, symptoms, health status measures, quality of life, and treatment-related mortality and morbidity. While a substantial proportion of patients tended to become insulin-free after HCT, remission rates were still high. The meta-analysis further revealed that HCT is more effective in patients with type 1 diabetes and when HCT is administered soon after the diagnosis. Certain factors limit the conclusions that can be drawn about the overall effectiveness of HCT in treating diabetes; those factors are: heterogeneity in the stem cell types, cell number infused, and infusion methods. The evidence is insufficient to determine the effects of the technology on health outcomes.
For individuals with other autoimmune diseases (eg, Crohn disease, immune cytopenias, relapsing polychondritis) who receive HCT, the evidence includes small retrospective studies. Relevant outcomes are overall survival, symptoms, health status measures, quality of life, and treatment-related mortality and morbidity. Additional data are needed from controlled studies to demonstrate efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 1.

**Table 1. Summary of Key Trials**

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
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<tr>
<td>NCT02516124</td>
<td>Autologous Stem Cell Transplantation for Progressive Systemic Sclerosis: a Prospective Non-interventional Approach Across Europe (NISSC) for the Autoimmune Diseases Working Party of the EBMT</td>
<td>82</td>
<td>Jan 2018</td>
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<tr>
<td>NCT01445821</td>
<td>Randomized Study of Different Non-myeloablative Conditioning Regimens with Hematopoietic Stem Cell Support in Patients with Scleroderma (ASSIST-IIb)</td>
<td>160</td>
<td>Sep 2018</td>
</tr>
<tr>
<td>NCT00273364</td>
<td>Hematopoietic Stem Cell Therapy for Patients With Inflammatory Multiple Sclerosis Failing Alternate Approved Therapy: A Randomized Study</td>
<td>110</td>
<td>Dec 2018</td>
</tr>
<tr>
<td>NCT00278629</td>
<td>Non-myeloablative Autologous Hematopoietic Stem Cell Transplantation in Patients With Chronic Inflammatory Demyelinating Polyneuropathy: A Phase II Trial</td>
<td>80</td>
<td>Dec 2018</td>
</tr>
<tr>
<td>NCT02225795</td>
<td>A Pilot Study of Autologous Stem Cell Transplantation with Post-transplant Cyclophosphamide for Children and Young Adults with Refractory Crohn's Disease</td>
<td>15</td>
<td>Dec 2019</td>
</tr>
<tr>
<td>NCT02674217</td>
<td>Outpatient Hematopoietic Grafting in Patients with Multiple Sclerosis Employing Autologous Non-cryopreserved Peripheral Blood Stem Cells: a Feasibility Study</td>
<td>200</td>
<td>Dec 2019</td>
</tr>
<tr>
<td>NCT03113162</td>
<td>Evaluation of the Safety and Efficacy of Reduced-Intensity Immunoablation and Autologous Hematopoietic Stem Cell</td>
<td>15</td>
<td>May 2020</td>
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<tr>
<td>NCT No.</td>
<td>Trial Name</td>
<td>Planned Enrollment</td>
<td>Completion Date</td>
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<tr>
<td>NCT00750971</td>
<td>An Open-Label, Phase II Multicenter Cohort Study of Immunoablation with Cyclophosphamide and Antithymocyte-Globulin and Transplantation of Autologous CD34-Enriched Hematopoietic Stem Cells versus Currently Available Immunosuppressive /Immunomodulatory Therapy for Treatment of Refractory Systemic Lupus Erythematosus</td>
<td>30</td>
<td>Aug 2020</td>
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<tr>
<td>NCT00114530</td>
<td>A Randomized, Open-label, Phase II Multicenter Study of High-Dose Immunosuppressive Therapy Using Total Body Irradiation, Cyclophosphamide, ATGAM, and Autologous Stem Cell Transplantation with Auto-CD34+HPC versus Intravenous Pulse Cyclophosphamide for the Treatment of Severe Systemic Sclerosis</td>
<td>75</td>
<td>Apr 2016 (completed)</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

**Practice Guidelines and Position Statements**

*American Academy of Neurology et al*

A review of guidelines from the American Academy of Neurology and the American College of Rheumatology found no mention of stem cell transplantation for multiple sclerosis, lupus, rheumatoid arthritis, or juvenile idiopathic arthritis. In 2016, the Academy affirmed the statements in the Myasthenia Gravis Foundation of America’s consensus guidelines for the management of myasthenia gravis. The consensus guidelines did not discuss hematopoietic cell transplantation (HCT) as a therapeutic option.

*American Society for Blood and Marrow Transplantation*

In 2015, the American Society for Blood and Marrow Transplantation published consensus guidelines on the use of HCT to treat specific conditions in and out of the clinical trial setting. Table 2 lists guidelines for specific indications addressed in this evidence review.
Table 1. Recommendations for the Use of HCT to Treat Autoimmune Diseases

<table>
<thead>
<tr>
<th>Indications for HCT in Pediatric Patients (Generally &lt;18 y)</th>
<th>Allogeneic HCT</th>
<th>Autologous HCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Juvenile rheumatoid arthritis</td>
<td>D</td>
<td>R</td>
</tr>
<tr>
<td>Systemic sclerosis</td>
<td>D</td>
<td>R</td>
</tr>
<tr>
<td>Other autoimmune and immune dysregulation disorders</td>
<td>R</td>
<td>N</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Indications for HCT in Adults &gt;18 y</th>
<th>Allogeneic HCT</th>
<th>Autologous HCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple sclerosis</td>
<td>N</td>
<td>D</td>
</tr>
<tr>
<td>Systemic sclerosis</td>
<td>N</td>
<td>D</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>N</td>
<td>D</td>
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<tr>
<td>Systemic lupus erythematosus</td>
<td>N</td>
<td>D</td>
</tr>
<tr>
<td>Crohn disease</td>
<td>N</td>
<td>D</td>
</tr>
<tr>
<td>Polymyositis-dermatomyositis</td>
<td>N</td>
<td>D</td>
</tr>
</tbody>
</table>

D: developmental; HCT: hematopoietic cell transplantation; N: not generally recommended; R: standard of care, rare indication.

European Group for Blood and Marrow Transplantation

In 2012, the European Group for Blood and Marrow Transplantation (EBMT) updated its guidelines on HCT for severe autoimmune diseases.\(^38\) EBMT recommended as follows: “HSCT [hematopoietic stem cell transplantation] should be considered as a therapeutic option at second line or beyond for patients with severe ADs [autoimmune diseases] progressing despite standard established and/or approved therapy” (level of evidence II). The following conditions should be met if HCT is chosen for treatment: referral to a center with JACIE (Joint Accreditation Committee of International Society for Cellular Therapy and EBMT) accreditation; when possible, HCT should be conducted within a phase 2 or 3 trial; if such a trial is not available, then a multidisciplinary team should meet with patients to discuss HCT and non-HCT treatment options.

In 2015, EBMT issued additional guidelines on HCT for severe autoimmune diseases, focusing on immune monitoring and biobanking.\(^39\) To standardize clinical HCT protocols, EBMT developed guidelines for “good laboratory practice” in relation to procuring, processing, storing, and analyzing biologic specimens of patients with autoimmune diseases undergoing HCT. The
guidance provides a table that specifies the type of biologic sample (eg, serum, biopsy, cerebrospinal fluid), sample tests, testing methods (eg, enzyme linked immunosorbent assay, fluorescent activated cell sorter), and timing of testing for the following autoimmune diseases: multiple sclerosis, systemic sclerosis, systemic lupus erythematosus, Crohn disease, type 1 diabetes, and arthritis.

**Medicare National Coverage**

There are numerous autoimmune diseases and the Centers for Medicare and Medicaid Services have not issued a national coverage determination (NCD) for stem cell transplantation for each individual disease. A general NCD for stem cell transplantation (110.8.1) states the following:

**Stem Cell Transplantation**

**Nationally Covered Indications**

The following uses of allogeneic HSCT [hematopoietic stem-cell transplantation] are covered under Medicare:

- Effective for services performed on or after August 1, 1978, for the treatment of leukemia, leukemia in remission, or aplastic anemia when it is reasonable and necessary,
- Effective for services performed on or after June 3, 1985, for the treatment of severe combined immunodeficiency disease (SCID) and for the treatment of Wiskott-Aldrich syndrome.
- Effective for services performed on or after August 4, 2010, for the treatment of Myelodysplastic Syndromes (MDS) pursuant to Coverage with Evidence Development (CED) in the context of a Medicare-approved, prospective clinical study.

**Autologous Stem-Cell Transplantation (AuSCT)**

**Nationally Covered Indications**

- Effective for services performed on or after April 28, 1989, AuSCT is considered reasonable and necessary under §1862(a)(1)(A) of the Social Security Act (the Act) for the following conditions and is covered under Medicare for patients with:
Acute leukemia in remission who have a high probability of relapse and who have no human leucocyte antigens (HLA)-matched;

Resistant non-Hodgkin's lymphomas or those presenting with poor prognostic features following an initial response;

Recurrent or refractory neuroblastoma; or

Advanced Hodgkin’s disease who have failed conventional therapy and have no HLA-matched donor.

- Effective October 1, 2000, single AuSCT is only covered for Durie-Salmon Stage II or III patients that fit the following requirements:
  - Newly diagnosed or responsive multiple myeloma. This includes those patients with previously untreated disease, those with at least a partial response to prior chemotherapy (defined as a 50% decrease either in measurable paraprotein [serum and/or urine] or in bone marrow infiltration, sustained for at least 1 month), and those in responsive relapse; and,
  - Adequate cardiac, renal, pulmonary, and hepatic function.

- Effective for services performed on or after March 15, 2005, when recognized clinical risk factors are employed to select patients for transplantation, high-dose melphalan (HDM) together with AuSCT is reasonable and necessary for Medicare beneficiaries of any age group with primary amyloid light chain (AL) amyloidosis who meet the following criteria:
  - Amyloid deposition in 2 or fewer organs; and,
  - Cardiac left ventricular ejection fraction (EF) greater than 45%.

**Nationally Non-Covered Indications**

Insufficient data exist to establish definite conclusions regarding the efficacy of AuSCT for the following conditions:

- Acute leukemia not in remission;
- Chronic granulocytic leukemia;
- Solid tumors (other than neuroblastoma);
• Up to October 1, 2000, multiple myeloma;
• Tandem transplantation (multiple rounds of AuSCT) for patients with multiple myeloma;
• Effective October 1, 2000, non-primary AL amyloidosis; and,
• Effective October 1, 2000, thru March 14, 2005, primary AL amyloidosis for Medicare beneficiaries age 64 or older.

In these cases, AuSCT is not considered reasonable and necessary within the meaning of §1862(a)(1)(A) of the Act and is not covered under Medicare.

Regulatory Status

The U.S. Food and Drug Administration regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation (CFR) title 21, parts 1270 and 1271. Hematopoietic stem cells are included in these regulations.

References


<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>02/01/00</td>
<td>Add to Therapy Section - New Policy</td>
</tr>
<tr>
<td>12/21/00</td>
<td>Replace policy - Policy statement revised to state that allogeneic transplant after a prior failed autotransplant is considered investigational, based on 2000 TEC Assessment.</td>
</tr>
<tr>
<td>05/14/02</td>
<td>Replace policy - Policy updated based on 2002 TEC Assessment; policy statement unchanged.</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 - Reviewed and recommended for adoption without any changes by Company Oncology Advisory Panel July 22, 2003.</td>
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<tr>
<td>10/12/04</td>
<td>Replace policy - Policy reviewed with literature search; no change to policy statement. Approved by OAP 10/29/04, no need to go back to MPC.</td>
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<td>08/09/05</td>
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<td>07/11/06</td>
<td>Replace policy - Policy updated with literature review; references added; no changes to policy statement.</td>
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<td>12/11/07</td>
<td>Replace policy - Policy updated with literature review; references added; no change in policy statement.</td>
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<td>05/13/08</td>
<td>Cross Reference Update - No other changes</td>
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<tr>
<td>11/11/08</td>
<td>Replace policy - Policy updated with literature search. Minor change to the policy statement to align with new title. Hematopoietic and Transplantation added to the title and incorporated throughout the policy. References added.</td>
</tr>
<tr>
<td>11/10/09</td>
<td>Replace policy - Policy updated with literature search; “hematopoietic” added to the policy statement, intent unchanged. References added.</td>
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<tr>
<td>02/09/10</td>
<td>Code Update - New 2010 codes added.</td>
</tr>
<tr>
<td>12/14/10</td>
<td>Replace policy - Policy updated and extensively revised with literature search; reference numbers 5–12, 14–18, and 20 and 21 added. Added indications of juvenile idiopathic arthritis and diabetes mellitus to policy statement as investigational.</td>
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<td>10/11/11</td>
<td>Replace policy – Policy updated with literature search; reference numbers 8, 16 and 17 added; references renumbered. Policy statements unchanged. ICD-10 codes added; codes 38220 and 38221 removed from policy.</td>
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<td>01/24/12</td>
<td>Code 38232 added.</td>
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<td>06/20/12</td>
<td>Minor update: Related Policies updated; 8.01.17 replaced 8.01.507 effective June 12, 2012.</td>
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<td>Related policy updates to titles of 8.01.17, 8.01.21, 8.01.26, 8.01.27, 8.01.29, 8.01.30, 8.01.31, 8.01.514, 8.01.520</td>
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<tr>
<td>------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
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<td>Update Related Policies, change title of policy 8.01.21.</td>
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<tr>
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<td>The following codes were removed from the policy, as they were not suspending and just informational: HCPCS J9000-J999 and Q0083 – Q0085.</td>
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<tr>
<td>09/30/13</td>
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<td>10/18/13</td>
<td>Update Related Policies. Change title to 8.01.17.</td>
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<tr>
<td>03/11/14</td>
<td>Coding Update. Codes 41.06 and 41.08 were removed per ICD-10 mapping project; these codes are not utilized for adjudication of policy.</td>
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<tr>
<td>03/21/14</td>
<td>Update Related Policies. Delete 8.01.514.</td>
</tr>
<tr>
<td>04/18/14</td>
<td>Update Related Policies. Remove 8.01.20 and add 8.01.529.</td>
</tr>
<tr>
<td>06/24/14</td>
<td>Update Related Policies. Remove 8.01.35, 8.01.42, then add 8.01.530 and 8.01.532.</td>
</tr>
<tr>
<td>12/17/14</td>
<td>Annual Review. Policy updated with literature review through September 15, 2014; references 3-4 deleted and 18, 31 added. Policy statements unchanged. ICD-9 and ICD-10 diagnosis and procedure codes removed; these do not relate to policy adjudication.</td>
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<tr>
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<td>08/19/15</td>
<td>Update Related Policies. Remove 8.02.02.</td>
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<tr>
<td>12/08/15</td>
<td>Annual Review. Literature review performed; no change in policy statements.</td>
</tr>
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<td>04/01/16</td>
<td>Annual Review, approved March 8, 2016. Policy updated with literature review through December 10, 2015; references 5, 9, 11, 13, 26-27, 29 and 31 added. Policy statements unchanged.</td>
</tr>
<tr>
<td>08/09/16</td>
<td>Update Related Policies. Remove 8.01.27 as it was archived.</td>
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<tr>
<td>11/04/16</td>
<td>Coding update. Removed codes that are transplant benefit related.</td>
</tr>
<tr>
<td>04/01/17</td>
<td>Update Related Policies; updated some titles. Minor formatting update.</td>
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<tr>
<td>06/09/17</td>
<td>Coding update, updated description for CPT codes 38240 and 38241.</td>
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<tr>
<td>08/01/17</td>
<td>Updated title of Related Policy 8.01.511.</td>
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<tr>
<td>05/01/18</td>
<td>Annual Review, approved April 3, 2018. Policy updated with literature review through November 2017; reference 37 added; note 40 updated. Policy statement unchanged</td>
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**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). ©2018 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)

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):
لا يجوز رفض الخدمات أو المعاملات التي تتعلق بالশرايط على أساس عرقية أو
العربية

Chinese (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。請撥電話 800-722-1471 (TTY: 800-842-5357).

Oromo (Cushite):

Italiano (Italian):
Informação importante:
Este aviso poderá conter informações importantes acerca do seu contrato de cobertura através de Premera Blue Cross. É possível que haja datas-chave no aviso.

Este aviso poderá conter informações importantes.

Talvez seja necessário que você tome providências dentro de um determinado prazo para manter sua cobertura de saúde e ajudar a custos. Você tem o direito de obter esta informação e ajudar em seu idioma sem custo.

Pokhri (Kharai):
ما زیاده به پیشنهادات دوستانه و خانوادگی گفته می‌شود. بازخوردهای ممکن این اطلاعات محدود می‌شناسند. هر چیزی که در این متن اشاره شده است به‌طور مشابه در تمامی اطلاعات ممکن مطرح می‌شود.

English (English):
To obtain information and assistance without charge, please call 800-722-1471 (TTY: 800-842-5357). For more information, please visit PremeraBlueCross.com.

Polskie (Polish):

Português (Portuguese):
Este aviso contém informações importantes. Este aviso poderá conter informações importantes a respeito de sua aplicação ou cobertura por meio do Premera Blue Cross. Poderão existir datas importantes neste aviso. Talvez seja necessário que você tome providências dentro de determinados prazos para manter sua cobertura de saúde e ajudar a custos. Você tem o direito de obter esta informação e ajudar em seu idioma e sem custos. Ligue para 800-722-1471 (TTY: 800-842-5357).