Hematopoietic Cell Transplantation for Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma

Introduction

Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are two types of cancer that affect the white blood cells and the bone marrow. Many patients initially do not have any obvious symptoms of these diseases, and they may be discovered during an annual physical exam or by doing routine blood tests. Other patients may have symptoms and go to their doctor because they are worried and don’t feel well. A variety of medications can be used to treat these cancers, and the choice of treatment may depend on how bad a person’s symptoms are and how aggressive their cancer is. In some cases, a hematopoietic cell transplant may be used to treat these diseases. This policy discusses when a hematopoietic cell transplant may be medically necessary to treat CLL and SLL.

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.
**Transplant** | **Medical Necessity**
--- | ---
**Allogeneic hematopoietic cell transplantation** | Allogeneic hematopoietic cell transplantation is considered medically necessary to treat chronic lymphocytic leukemia or small lymphocytic lymphoma in patients with markers of poor-risk disease (see Table 2 below). Use of a myeloablative or reduced-intensity pretransplant conditioning regimen should be individualized based on factors that include patient age, the presence of comorbidities, and disease burden.

**Transplant** | **Investigational**
--- | ---
**Autologous hematopoietic cell transplantation** | Autologous hematopoietic cell transplantation is considered investigational to treat chronic lymphocytic leukemia or small lymphocytic lymphoma.

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**Staging and Prognosis of Chronic Lymphocytic Leukemia or Small Lymphocytic Leukemia**

Two scoring systems are used to determine stage and prognosis of patients with chronic lymphocytic leukemia (CLL) or small lymphocytic leukemia (SLL). As outlined in Table 1, the Rai and Binet staging systems classify patients into 3 risk groups with different prognoses and are used to make therapeutic decisions.

**Table 1. Rai and Binet Classification for CLL or SLL**

<table>
<thead>
<tr>
<th>Rai Stage</th>
<th>Risk</th>
<th>Description</th>
<th>Median Survival, y</th>
<th>Binet Stage</th>
<th>Description</th>
<th>Median Survival, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Low</td>
<td>Lymphocytosis</td>
<td>&gt;10</td>
<td>A</td>
<td>≤3 lymphoid areas, normal hemoglobin and platelets</td>
<td>&gt;10</td>
</tr>
<tr>
<td>I</td>
<td>Int</td>
<td>Lymphocytosis + lymphadenopathy</td>
<td>7-9</td>
<td>B</td>
<td>≥3 lymphoid areas, normal hemoglobin and platelets</td>
<td>7</td>
</tr>
<tr>
<td>Rai Stage</td>
<td>Risk</td>
<td>Description</td>
<td>Median Survival, y</td>
<td>Binet Stage</td>
<td>Description</td>
<td>Median Survival, y</td>
</tr>
<tr>
<td>-----------</td>
<td>------</td>
<td>-------------</td>
<td>-------------------</td>
<td>-------------</td>
<td>-------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>II</td>
<td>Int</td>
<td>Lymphocytosis + splenomegaly ± lymphadenopathy</td>
<td>7-9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>High</td>
<td>Lymphocytosis + anemia ± lymphadenopathy or splenomegaly</td>
<td>1.5-5</td>
<td>C</td>
<td>Any number of lymphoid areas, anemia, thrombocytopenia</td>
<td>5</td>
</tr>
<tr>
<td>IV</td>
<td>High</td>
<td>Lymphocytosis + thrombocytopenia ± anemia, splenomegaly, or lymphadenopathy</td>
<td>1.5-5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Because prognosis of patients varies within the different Rai and Binet classifications, other prognostic markers are used in conjunction with staging to determine clinical management. These are summarized in Table 2, according to availability in clinical centers.

**Table 2. Markers of Poor Prognosis in CLL or SLL**

<table>
<thead>
<tr>
<th>Community Center</th>
<th>Specialized Center</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Advanced Rai or Binet stage</td>
<td>• IgVH wild type</td>
</tr>
<tr>
<td>• Male sex</td>
<td>• Expression of ZAP-70 protein</td>
</tr>
<tr>
<td>• Atypical morphology or CLL or SLL</td>
<td>• Del(11q22-q23) (loss of ATM gene)</td>
</tr>
<tr>
<td>• Peripheral lymphocyte doubling time &lt;12 mo</td>
<td>• del(17p13)/variant TP53</td>
</tr>
<tr>
<td>• CD38-positive</td>
<td>• Trisomy 12</td>
</tr>
<tr>
<td>• Elevated β2-microglobulin level</td>
<td>• Elevated serum CD23</td>
</tr>
<tr>
<td>• Diffuse marrow histology</td>
<td>• Elevated serum tumor necrosis factor-α</td>
</tr>
<tr>
<td>• Elevated serum lactate dehydrogenase level</td>
<td>• Elevated serum thymidine kinase</td>
</tr>
<tr>
<td>• Fludarabine resistance</td>
<td></td>
</tr>
</tbody>
</table>

CLL: chronic lymphocytic leukemia; IgVH: immunoglobulin heavy-chain variable-region; SLL: small lymphocytic lymphoma.
An expert panel convened by the American Society for Blood and Marrow Transplantation was queried about criteria used to define high-risk CLL, as part of the process for developing 2016 guidelines. Panelists responded that criteria are presence of del17P and/or TP53 variants (100%) and presence of complex karyotype (67%).

Reduced-Intensity Conditioning for Allogeneic Hematopoietic Cell Transplantation

Some patients for whom a conventional myeloablative allotransplant could be curative may be considered candidates for reduced-intensity conditioning (RIC) allogeneic hematopoietic cell transplantation (allo-HCT). They include those patients whose age (typically >60 years) or comorbidities (eg, liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy, low Karnofsky Performance Status) preclude use of a standard myeloablative conditioning regimen. A patient who relapses following a conventional myeloablative allo-HCT could undergo a second myeloablative procedure if a suitable donor is available and his or her medical status would permit it. However, this type of patient would likely undergo RIC before a second allo-HCT if complete remission could be reinduced with chemotherapy.

The ideal allogeneic donors are human leukocyte antigen (HLA)-identical siblings, matched at the HLA-A, -B, and -DR loci on each arm of chromosome 6. Related donors mismatched at a single locus are also considered suitable donors. A matched, unrelated donor identified through the National Marrow Donor Registry is typically the next option considered. Recently, haploidentical donors—typically a parent or a child of the patient—with whom there is usually sharing of only 3 of the 6 major histocompatibility antigens, have been under investigation as a stem cell source. Most patients will have such a donor; however, the risk of graft-versus-host disease and overall morbidity of the procedure may be severe, and experience with these donors is not as extensive as that with matched donors.

Documentation Requirements

The patient’s medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:

- Diagnosis/condition
- History and physical examination documenting the severity of the condition
- Markers of poor-risk disease
### Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td><strong>CPT</strong></td>
<td></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>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><strong>HCPCS</strong></td>
<td></td>
</tr>
<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>

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### Related Information

### Benefit Application

The following considerations may supersede this policy:

- State mandates requiring coverage for autologous hematopoietic bone marrow transplantation offered as part of clinical trials of autologous bone marrow transplantation approved by the National Institutes of Health.
Some plans may participate in voluntary programs offering coverage for patients participating in National Institutes of Health-approved clinical trials of cancer chemotherapies, including autologous hematopoietic bone marrow transplantation.

Evidence Review

Description

Risk stratification of patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) guides therapy decisions, which may include hematopoietic cell transplantation (HCT) for those with poor-risk features.

Background

**Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma**

Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are neoplasms of hematopoietic origin characterized by the accumulation of lymphocytes with a mature, generally well-differentiated morphology. In CLL, these cells accumulate in blood, bone marrow, lymph nodes, and spleen; in SLL they are generally confined to lymph nodes. The Revised European-American/World Health Organization Classification of Lymphoid Neoplasms considers B-cell CLL and SLL a single disease entity.

CLL and SLL share many common features and are often referred to as blood and tissue counterparts of each other, respectively. Both tend to present as asymptomatic enlargement of the lymph nodes, tend to be indolent, but can undergo transformation to a more aggressive form of disease (e.g., Richter transformation). The median age at diagnosis of CLL is approximately 72 years, but it may present in younger individuals, often as poor-risk disease with significantly reduced life expectancy.

Treatment regimens used for CLL are generally the same as those used for SLL, and treatment outcomes are comparable for both diseases. Both low- and intermediate-risk CLL and SLL demonstrate relatively good prognoses, with median survivals of 6 to 10 years; however, the median survival of high-risk CLL or SLL may only be 2 years. Although typically responsive to initial therapy, CLL and SLL are rarely cured by conventional therapy, and nearly all patients
ultimately die of their disease. This natural disease history prompted investigation of HCT as a possible curative regimen.

**Hematopoietic Cell Transplantation**

Hematopoietic cell transplantation (HCT) is a procedure in which hematopoietic stem cells are infused to restore bone marrow function in cancer patients who receive bone-marrow–toxic doses of drugs with or without whole body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or from a donor (allogeneic HCT [allo-HCT]). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after the 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 detail in 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 critical for achieving a good outcome of allo-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 HLA-A, -B, and -DR loci on each arm of chromosome 6. Depending on the disease being treated, an acceptable donor will match the patient at all or most of the HLA loci.

**Conditioning for HCT**

**Conventional Conditioning for HCT**

The conventional practice of allo-HCT involves administration of cytotoxic agents (eg, cyclophosphamide, busulfan) with or without total body irradiation at doses sufficient to destroy endogenous hematopoietic capability in the recipient. The beneficial treatment effect in this procedure is due to a combination of initial eradication of malignant cells and subsequent graft-versus-malignancy effect that develops after engraftment of allogeneic stem cells within the patient’s bone marrow space. The slower graft-versus-malignancy effect is considered the potentially curative component, but it may be overwhelmed by extant disease without the use of pretransplant conditioning. However, intense conditioning regimens are limited to patients who are sufficiently fit medically to tolerate substantial adverse effects that include pre-engraftment opportunistic infections secondary to loss of endogenous bone marrow function and organ damage and failure caused by the cytotoxic drugs. Furthermore, in any allo-HCT,
immunosuppressant drugs are required to minimize graft rejection and graft-versus-host disease, which also increases susceptibility of the patient to opportunistic infections.

The success of autologous HCT is predicated on the ability of cytotoxic chemotherapy with or without radiation to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of bone marrow space with presumably normal hematopoietic stem cells obtained from the patient before undergoing bone marrow ablation. As a consequence, autologous HCT is typically performed as consolidation therapy when the patient’s disease is in complete remission. Patients who undergo autologous HCT are susceptible to chemotherapy-related toxicities and opportunistic infections before engraftment, but not graft-versus-host disease.

**Reduced-Intensity Conditioning for Allo-HCT**

Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses or less intense regimens of cytotoxic drugs or radiation than are used in conventional full-dose myeloablative conditioning treatments. The goal of RIC is to reduce disease burden but also to minimize as much as possible associated treatment-related morbidity and non-relapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. Although the definition of RIC remains arbitrary, with numerous versions employed, all seek to balance the competing effects of NRM and relapse due to residual disease. RIC regimens can be viewed as a continuum in effects, from nearly totally myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allo-HCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full-donor chimerism, which may be supplemented with donor lymphocyte infusions to eradicate residual malignant cells. For this policy, the term “reduced-intensity conditioning” will refer to all conditioning regimens intended to be non-myeloablative, as opposed to fully myeloablative (conventional) regimens.

**Summary of Evidence**

For individuals who have chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) and markers of poor-risk disease who receive allo-HCT, the evidence includes single-arm prospective and registry-based studies as well as a TEC Assessment. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related mortality and morbidity. Data have suggested that allo-HCT can provide long-term disease
control and overall survival in patients with poor-risk CLL/SLL. High rates of treatment-related morbidity discourage this approach in lower risk disease, particularly among older patients whose health status typically precludes the use of myeloablative conditioning. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have CLL/SLL who receive autologous HCT, the evidence includes randomized controlled trials, systematic reviews, and a TEC Assessment. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related mortality and morbidity. Autologous HCT is feasible in younger patients but is not curative, particularly in those with poor-risk CLL. Studies of autologous HCT published to date have not shown improvement in overall survival in patients with CLL/SLL, and results must furthermore be considered in the context of improved outcomes with the use of newer chemo-immunotherapy agents. Furthermore, evidence from the European Intergroup randomized controlled trial has suggested quality-of-life issues are important in selecting patients for autologous HCT and may dictate the management course for patients who are otherwise candidates for this approach. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Ongoing and Unpublished Clinical Trials**

A search of ClinicalTrials.gov in February 2019 identified two ongoing trials that might affect this review (see Table 3).

**Table 3. 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>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02988466</td>
<td>Reduced Intensity (RIC) Conditioning And Transplantation of HLA-Haploidentical Related Hematopoietic Cells (Haplo-HCT) For Patients With Hematologic Malignancies</td>
<td>84</td>
<td>Jan 2021</td>
</tr>
<tr>
<td>NCT00104858</td>
<td>Nonmyeloablative Conditioning With Pre- and Post-Transplant Rituximab Followed by Related or Unrelated Donor Hematopoietic Cell Transplantation for Patients With Advanced Chronic Lymphocytic Leukemia: A Multi-Center Trial</td>
<td>94</td>
<td>Dec 2018</td>
</tr>
</tbody>
</table>
Clinical Input Received from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 1 specialty medical center reviewer, 1 academic medical center reviewer, and 2 Blue Distinction Center reviewers while this policy was under review in 2010. Three of 4 reviewers agreed that allogeneic hematopoietic cell transplantation was of value to patients with poor-risk chronic lymphocytic leukemia and that this procedure should be medically necessary for this setting. However, reviewers indicated that the specific approach (eg, reduced-intensity conditioning vs myeloablative conditioning) should be individualized based on criteria such as age and health status. All reviewers concurred with the policy statement that autologous HCT is investigational.

Practice Guidelines and Position Statements

American Society for Blood and Marrow Transplantation

In 2015, the American Society for Blood and Marrow Transplantation published guidelines on indications for allogeneic (allo-) and autologous hematopoietic cell transplantation (HCT) for chronic lymphocytic leukemia (CLL). Reccommendations described the current consensus on use of HCT in and out of the clinical trial setting. Treatment recommendations are shown in Table 4.

Table 4: 2015 Recommendations for Allogeneic and Autologous HCT for CLL

<table>
<thead>
<tr>
<th>Adult Indications</th>
<th>Allogeneic HCT</th>
<th>Autologous HCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk, first or greater remission</td>
<td>C</td>
<td>N</td>
</tr>
<tr>
<td>T cell, prolymphocytic leukemia</td>
<td>R</td>
<td>R</td>
</tr>
</tbody>
</table>
### Adult Indications

<table>
<thead>
<tr>
<th>Indications</th>
<th>Allogeneic HCT</th>
<th>Autologous HCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>B cell, prolymphocytic leukemia</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Transformation to high-grade lymphoma</td>
<td>C</td>
<td>C</td>
</tr>
</tbody>
</table>

C: standard of care, clinical evidence available; CLL: chronic lymphocytic leukemia; HCT: hematopoietic cell transplantation; N: Not generally recommended; R: standard of care, rare indication.

In 2016, the Society published clinical practice recommendations with additional detail on allo-HCT for CLL. Recommendations are shown in Table 5.

**Table 5: 2016 Recommendations for Allogeneic HCT for CLL**

<table>
<thead>
<tr>
<th>Indications</th>
<th>Allogeneic HCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk CLL</td>
<td>Not recommended in the first-line consolidation setting</td>
</tr>
<tr>
<td></td>
<td>Not recommended for patients who relapse after first-line therapy and demonstrate sensitive disease after second line therapy (not BCR inhibitors)</td>
</tr>
<tr>
<td></td>
<td>Recommended for patients who relapse after first-line therapy, have refractory disease after second-line therapy (not BCR inhibitors) and show an objective response to BCR inhibitors or to a clinical trial</td>
</tr>
<tr>
<td></td>
<td>Recommended for patients who relapse after first-line therapy, have refractory disease after second-line therapy (including BCR inhibitors but not BCL-2 inhibitors) and show an objective response to BCL-2 inhibitors or to a clinical trial</td>
</tr>
<tr>
<td></td>
<td>Recommended when there is a lack of response or there is progression after BCL-2 inhibitors</td>
</tr>
<tr>
<td>Richter transformation</td>
<td>Recommended after achieving an objective response to anthracycline-based chemotherapy</td>
</tr>
<tr>
<td>Purine analogue relapsed and/or refractory disease</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

BCR: B cell receptor; BCL-2: B cell lymphoma 2; CLL: chronic lymphocytic leukemia; HCT: hematopoietic cell transplantation.
**National Comprehensive Cancer Network Guidelines**

Current National Comprehensive Cancer Network (NCCN) guidelines (v.2.2019) for CLL and small lymphocytic lymphoma (SLL) state that allogeneic HCT may be considered for patients:

- Without significant comorbidities and CLL refractory to small molecule inhibitor therapy
- With relapsed CLL or SLL and without a17p deletion or TP53 variant
- With CLL or SLL, a response to treatment and with a complex karyotype
- With CLL (Rai stages 0-IV) or SLL (Lugano stages II-IV), after histologic transformation to diffuse large B-cell/Hodgkin lymphoma.

**Medicare National Coverage**

There is no national coverage determination.

**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 the Code of Federal Regulation title 21, parts 1270 and 1271. Hematopoietic cells are included in these regulations.

**References**

2. Blue Cross and Blue Shield Association (TEC). High-dose chemotherapy plus allogeneic stem cells to treat chronic lymphocytic leukemia or small lymphocytic lymphoma. TEC Assessments. 2002;Volume 17:Tab 4.


### History

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>03/10/14</td>
<td>New Policy. Policy replaces 8.01.514. Policy updated with literature review through December, 2013; reference 11 added. In new policy, policy statement regarding autologous HCT changed from medically necessary to investigational. Policy statement regarding allogeneic HCT changed to medically necessary only in patients with markers of poor-risk disease as defined in Policy Guidelines.</td>
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<tr>
<td>04/18/14</td>
<td>Update Related Policies. Delete 8.01.20 and replace with 8.01.529.</td>
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<tr>
<td>06/27/14</td>
<td>Update Related Policies. Remove 8.01.35 and add 8.01.532.</td>
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<tr>
<td>12/03/14</td>
<td>Update Related Policies. Remove 8.01.17.</td>
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<tr>
<td>03/10/15</td>
<td>Annual Review. Policy updated with literature review through December 22, 2014; no new references added; no change to policy statements. ICD-9 and ICD-10 diagnosis codes removed; not utilized in adjudication. HCPCS Q and J code ranges removed.</td>
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<td>07/01/16</td>
<td>Annual Review, approved June 14, 2016. Literature review. No change to policy statement.</td>
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<td>11/04/16</td>
<td>Coding update. Removed codes that are transplant benefit related.</td>
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<tr>
<td>04/01/17</td>
<td>Annual Review, approved March 14, 2017. Policy updated with literature review through November 9, 2016; references 22-23 added. Policy statements unchanged.</td>
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<td>10/24/17</td>
<td>Policy moved to new format; no change to policy statements.</td>
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<tr>
<td>04/01/18</td>
<td>Annual Review, approved March 13, 2018. Policy updated with literature review through November 2017; Note added that American Society for Blood and Marrow Transplantation guidelines were updated - allo-HSCT no longer recommended for high-risk CLL as consolidation in first remission or immune-chemotherapy sensitive first relapse. No references added; reference 24 updated. Policy statements unchanged.</td>
</tr>
<tr>
<td>04/01/19</td>
<td>Annual Review, approved March 5, 2019. Policy updated with literature review through...</td>
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  - Information written in other languages

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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)

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يجب أن يكون هذا الإشعار معلومة هامة. قد يكون هذا الإشعار معلوماتًا مهمة لبعضك أو بعضك. غمَّنَت هذه المعلومات من خلال وسائل الإعلام المتاحة. إذا كنت ترغب في الحصول على هذه المعلومات، يمكنك الاتصال بنا مجانًا تTTY: 800-842-5357.

Chinese (Chinese):
本通知有重要訊息。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。本通知中可能有重要日期。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):
Lakkoofsa bilbilaa 800-722-1471 (TTY: 800-842-5357) tii bilbilaa.

Français (French):
Appelez le 800-722-1471 (TTY: 800-842-5357).

Kreyòl ayisyen (Creole):

Deutsche (German):

Hmoob (Hmong):
Tsbab ntwaw tshaj xo no muaj covy ntsiab lus tseem ceeb. Tey zaum tsab ntwaw tshaj xo no muaj covy ntsiab lus tseem ceeb koj daim ntwaw thov kiev pad los yoj koj chov kiev pad cuam los ntsaw Premera Blue Cross. Tey zaum muaj covy huub tseem ceeb cuam sau rau hauv daim ntwaw no. Tey zaum koj kiu yuv taa uu qee yam uab pek koj uu tsip hub dhuu cov caj nyog uas teev tseg rau hauv daim ntwaw no mas koj tshaj yuv tuu bas kiev pad cuam kohmob los yoj kiev pab teem tar nqji kho mob ntwaw. Koj muaj cai kom laww muab cov ntsiab lus no uas taw muab sau koj hom lub pub dwaw rau koj. Hu rau 800-722-1471 (TTY: 800-842-5357).

Ilokano (Ilocano):
Daytoy a Pakdaar kat naglion iti Napateg nga Impormsyon. Daytoy a pakdaar mabalin nga adda kat naglion iti napateg nga impormsyon maipangee iti aplikasyono yowo coverage babaen iti Premera Blue Cross. Daytoy ket mabalin dagiti importante a petaa iti daytoy a pakdaar. Mabalin nga adda rumbeng nga aramideny nga addang sakbay dagiti partikul a naituding nga adlaw tapno mapagtalinayed nga coverage tii salan-atyo yowo tulong kadagiti gastos. Adda karbenganyo a mangala a daytoy nga impormsyon ken tulong iti bukody a pagasago nga awan ti bayadanyo. Tumawg ti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):
To og kluczowe daty, które mogą pomóc zrozumieć, mogą przekroczyć Português (Portuguese):


Talvez seja necessário que você tome providências dentro de termes limitados para evitar perder as informações importantes a respeito de sua aplicação ou cobertura por meio de Premera Blue Cross. Maaaring may mga mahalagang petsa dito sa paunawa. Maaring haya nang fechas clave envuelta al aviso de Premera Blue Cross. Es posible que haya fechas claves en este aviso. Es posible que debo tomar alguna medida antes de determinadas fechas para mantenimiento de esta cobertura médica y ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).

Lao (Lao):

Redirect the망사_Products to og kluczowe daty, które mogą pomóc zrozumieć, mogą przekroczyć.

 TAGALOG (Tagalog):

Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon. Ang paunawa na ito ay maaaring naglalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa pamamagitan ng Premera Blue Cross. Maaaring haya nang fechas clave envuelta al aviso de Premera Blue Cross. Es posible que haya fechas claves en este aviso. Es posible que debo tomar alguna medida antes de determinadas fechas para mantenimiento de esta cobertura médica y ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).

Spanish (Spanish):

Este Aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud o cobertura a través de Premera Blue Cross. Es posible que haya fechas clave en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica y ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).

Japanese (Japanese):

この通知には重要な情報が含まれています。この通知には、Premera Blue Crossの申請または補償情報に関する重要な情報が含まれている場合があります。この通知には記載されている情報が重要な場合をご確認ください。健康保険やクレジットカードを維持するには、特定の期日までに行動を取りなければならない場合があります。ご用意の言語による情報とサポーテーが無料で提供されます。800-722-1471 (TTY: 800-842-5357)までお電話ください。