MEDICAL POLICY – 8.01.15
Hematopoietic Cell Transplantation for Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma

BCBSA Ref. Policy: 8.01.15
Effective Date: April 1, 2017
Last Revised: Oct. 24, 2017
Replaces: 8.01.514

RELATED MEDICAL POLICIES:
7.01.50 Placental and Umbilical Cord Blood as a Source of Stem Cells
8.01.529 Hematopoietic Cell Transplantation for Non-Hodgkin Lymphomas
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

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.
Policy Coverage Criteria

<table>
<thead>
<tr>
<th>Transplant</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allogeneic hematopoietic cell transplantation</td>
<td>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.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Transplant</th>
<th>Investigational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autologous hematopoietic cell transplantation</td>
<td>Autologous hematopoietic cell transplantation is considered investigational to treat chronic lymphocytic leukemia or small lymphocytic lymphoma in patients without markers of poor-risk disease.</td>
</tr>
</tbody>
</table>

Staging and Prognosis of Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia

Two scoring systems are used to determine stage and prognosis of patients with chronic lymphocytic leukemia (CLL)/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 Chronic Lymphocytic Leukemia / Small Lymphocytic Leukemia

<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>Rai Stage</td>
<td>Risk Description</td>
<td>Median Survival, y</td>
<td>Binet Stage</td>
<td>Description</td>
<td>Median Survival, y</td>
<td></td>
</tr>
<tr>
<td>----------</td>
<td>------------------</td>
<td>--------------------</td>
<td>-------------</td>
<td>-------------</td>
<td>--------------------</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Intermediate</td>
<td>7-9</td>
<td>B</td>
<td>≥3 lymphoid areas, normal hemoglobin and platelets</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Intermediate</td>
<td>7-9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>High</td>
<td>1.5-5</td>
<td>C</td>
<td>Any number of lymphoid areas, anemia, thrombocytopenia</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>High</td>
<td>1.5-5</td>
<td></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 Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia**

<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⁺</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>
</tbody>
</table>
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 the criteria are the presence of del17P and/or TP53 mutations (100%) and presence of complex karyotype (67%).

**Reduced-Intensity Conditioning for Allogeneic HCT**

Some patients for whom a conventional myeloablative allotransplant could be curative may be considered candidates for reduced-intensity conditioning (RIC) allogeneic HCT. These 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 allogeneic 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 allogeneic HCT if a complete remission could be reinduced with chemotherapy.

The ideal allogeneic donors are HLA-identical siblings, matched at the HLA-A, B, and DR loci (6/6). Related donors mismatched at one 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 GVHD and overall morbidity of the procedure may be severe, and experience with these donors is not as extensive as that with matched donors.
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</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>HCPCS</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 (NIH).

- Some plans may participate in voluntary programs offering coverage for patients participating in NIH-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 in nature, 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 (“classical”) practice of allogeneic 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 (GVM) effect that develops after engraftment of allogeneic stem cells within the patient’s bone marrow space. The slower GVM 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 medically sufficiently fit and can tolerate substantial adverse effects. These effects 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 allogeneic HCT, immune suppressant drugs are required to minimize graft rejection and GVHD, 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 (CR). Patients who undergo autologous HCT are susceptible to chemotherapy-related toxicities and opportunistic infections before engraftment, but not GVHD.

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

RIC refers to the pre-transplant 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 (TRM) and non-relapse mortality (NRM) in the period during which the beneficial GVM 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 allogeneic 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 the purposes of 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 allogeneic hematopoietic cell transplantation (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 (RCTs), 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 be considered in the context of improved outcomes with the use of newer chemoimmunotherapy agents. Furthermore, evidence from the European Intergroup RCT 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 December 2016 did not identify any ongoing or unpublished trials that would likely influence this review.

**Clinical Input Received from Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may provide appropriate reviewers who collaborate with and make recommendations during this process, 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 2009. Three of 4 reviewers agreed that allogeneic hematopoietic cell transplantation (HCT) was of value to patients with poor-risk chronic lymphocytic leukemia (see Policy Guidelines section), and that this procedure should be medically necessary in this setting. However, the reviewers indicate 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 (ASBMT) published guidelines on indications for autologous and allogeneic hematopoietic cell transplantation (allo-HCT) for chronic lymphocytic leukemia (CLL). Recommendations described the current consensus on use of HCT within and outside of the clinical trial setting. Treatment recommendations are shown in Table 3.

**Table 3: ASBMT 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>
<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>

ASBMT: American Society for Blood and Marrow Transplantation; 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, ASBMT published clinical practice recommendations with additional detail on allo-HCT for CLL. Recommendations are shown in Table 4.

**Table 4: ASBMT 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>
</tbody>
</table>
Indications | Allogeneic HCT
---|---
| 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
| Recommended when there is a lack of response or there is progression after BCL-2 inhibitors
| Richter transformation | Recommended after achieving an objective response to anthracycline-based chemotherapy
| Purine analogue relapsed and/or refractory disease | Not recommended

ASBMT: American Society for Blood and Marrow Transplantation; 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.1.2017) for CLL and small lymphocytic lymphoma (SLL) state that allogeneic HCT may be considered for patients:

- With relapsed CLL or SLL and without a17p deletion or TP53 mutation
- 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 (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

**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>
</tr>
<tr>
<td>04/18/14</td>
<td>Update Related Policies. Delete 8.01.20 and replace with 8.01.529.</td>
</tr>
<tr>
<td>06/27/14</td>
<td>Update Related Policies. Remove 8.01.35 and add 8.01.532.</td>
</tr>
<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>
</tr>
<tr>
<td>07/01/16</td>
<td>Annual Review, approved June 14, 2016. Literature review. No change to policy statement.</td>
</tr>
<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>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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</tbody>
</table>
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- U.S. Department of Health and Human Services
  - 200 Independence Avenue SW, Room S09F, HHH Building
  - Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
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Hmoob (Hmong):

Iloko (Ilocano):
Daytoy a pakdaar ket naglaon iti Napateg nga Imporman. Daytoy a pakdaar mabalay nga adda ket naglaon iti napateg nga imporman maihanggep iti aplikasyonawen no coverage babaen iti Premera Blue Cross. Daytoy ket mabalay dagiti importante a pelsa iti daytoy a pakdaar. Mabalay nga adda rumng awen aramidney nga addang sakbay dagiti partikular a naituding nga aladaw tapno mapagtalaineyd a coverage ti salay-ayowo yen toloung kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga imporman ken toloung iti bukodyo a pagasasaw nga awan ti bayadanyo. Tumawag ti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):
Premera Blue Cross reminder.

This notice contains important information. Este aviso contiene información importante. Сховіште цю інформацію.

Premera Blue Cross reminder.

This notice contains important information. Esta notificación contiene información importante. Отрадиайте цю інформацію в місці, де не можна або неможливо зберегти її.

Premera Blue Cross reminder.

This notice contains important information. هذه الرمزية تنتمي إلى معلومات مهمة.

Premera Blue Cross reminder.

This notice contains important information. Deze herinnering bevat belangrijke informatie.

Premera Blue Cross reminder.

This notice contains important information. Diese Mitteilung enthält wichtige Informationen.

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