MEDICAL POLICY – 8.01.21
Allogeneic Hematopoietic Cell Transplantation for Myelodysplastic Syndromes and Myeloproliferative Neoplasms

BCBSA Ref. Policy: 8.01.21
Effective Date: April 1, 2021
Last Revised: April 14, 2021
Replaces: N/A

RELATED MEDICAL POLICIES:
8.01.15 Hematopoietic Cell Transplantation for Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma
8.01.24 Hematopoietic Cell Transplantation for Miscellaneous Solid Tumors in Adults
8.01.25 Hematopoietic Cell Transplantation for Autoimmune Diseases
8.01.29 Hematopoietic Cell Transplantation for Hodgkin Lymphoma
8.01.42 Hematopoietic Cell Transplantation for Primary Amyloidosis
8.01.511 Hematopoietic Cell Transplantation for Solid Tumors of Childhood
8.01.520 Hematopoietic Cell Transplantation for Acute Lymphoblastic Leukemia
8.01.529 Hematopoietic Cell Transplantation for Non-Hodgkin Lymphomas
8.01.531 Hematopoietic Cell Transplantation for Waldenström Macroglobulinemia
8.01.532 Hematopoietic Cell Transplantation in the Treatment of Germ-Cell Tumors
8.01.538 Allogeneic Hematopoietic Cell Transplantation for Genetic Diseases and Acquired Anemias

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RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

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Introduction

Myelodysplastic syndromes (MDS) and myeloproliferative neoplasms (MPN) are diseases of bone marrow and the blood cells they produce. These disorders can turn into a certain type of leukemia (acute myelocytic leukemia, or AML). A type of treatment called a hematopoietic stem cell transplant is sometimes used to treat these conditions.

Hematopoietic stem cells are cells that are made within the bone marrow and can develop into many different types of blood cells. In a hematopoietic stem cell transplant, stem cells can be
taken from a donor and transplanted into the person with the MDS or MPN. When the stem cells are harvested from a donor, it is called an allogeneic hematopoietic stem cell transplant.

This policy discusses when a hematopoietic stem cell transplant may be medically necessary to treat myelodysplastic syndromes and myeloproliferative neoplasms.

**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>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Myeloablative allogeneic hematopoietic cell transplantation</strong></td>
<td>Myeloablative allogeneic hematopoietic cell transplantation (allo-HCT) may be considered medically necessary as a treatment of:</td>
</tr>
<tr>
<td></td>
<td>• Myelodysplastic syndromes (MDS)</td>
</tr>
<tr>
<td></td>
<td>• Myeloproliferative neoplasms (MPN)</td>
</tr>
<tr>
<td><strong>Reduced-intensity conditioning allogeneic hematopoietic cell transplantation</strong></td>
<td>Reduced-intensity conditioning allo-HCT may be considered medically necessary as a risk-adapted treatment of:</td>
</tr>
<tr>
<td></td>
<td>• Myelodysplastic syndromes</td>
</tr>
<tr>
<td></td>
<td>• Myeloproliferative neoplasms in patients who are at high-risk of intolerance of a myeloablative conditioning regimen</td>
</tr>
</tbody>
</table>

### Myeloid Neoplasms

Myeloid neoplasms are categorized according to criteria developed by the World Health Organization (WHO). Neoplasms are risk-stratified using the International Prognostic Scoring System (IPSS).

**2008 WHO Classification Scheme for Myeloid Neoplasms**

- Acute myeloid leukemia (AML)
### 2008 WHO Classification Scheme for Myeloid Neoplasms

- **Myelodysplastic syndromes (MDS)**
- **Myeloproliferative neoplasms**
  - Chronic myelogenous leukemia
  - Polycythemia vera
  - Essential thrombocythemia
  - Primary myelofibrosis
  - Chronic neutrophilic leukemia
  - Chronic eosinophilic leukemia, not otherwise categorized
  - Hypereosinophilic leukemia
  - Mast cell disease
  - MPNs, unclassifiable
- **MDS/Myeloproliferative neoplasm**
  - Chronic myelomonocytic leukemia
  - Juvenile myelomonocytic leukemia
  - Atypical chronic myeloid leukemia
  - MDS/Myeloproliferative neoplasm, unclassifiable
- **Myeloid neoplasms associated with eosinophilia and abnormalities of PDGFRA, PDGFRB, or FGFR1**
  - Myeloid neoplasms associate with PDGFRA rearrangement
  - Myeloid neoplasms associate with PDGFRB rearrangement
  - Myeloid neoplasms associate with FGFR1 rearrangement (8p11 myeloproliferative syndrome)

### 2008 WHO Classification of MDS

- Refractory anemia (RA)
- RA with ring sideroblasts (RARS)
- Refractory cytopenia with multilineage dysplasia
- Refractory cytopenia with multilineage dysplasia with ring sideroblasts
- RA with excess blasts 1 and 2 (RAEB 1 and 2)
- Del 5q syndrome
- Unclassified MDS

### Risk Stratification of Myelodysplastic Syndromes

Risk stratification for MDS is performed using the IPSS (see Table 1). This system was developed after pooling data from 7 studies that used independent, risk-based prognostic factors. The
prognostic model and the scoring system were based on blast count, degree of cytopenia, and blast percentage. Risk scores were weighted relative to their statistical power. This system is widely used to group patients into either low-risk and high-risk groups (see Table 2). The low-risk group includes low-risk and intermediate-1 IPSS groups; treatment goals in low-risk MDS patients are to improve quality of life and achieve transfusion independence. In the high-risk group, which includes intermediate-2 and high-risk IPSS groups, treatment goals are slowing disease progression to AML and improving survival. The IPSS is usually calculated on diagnosis. The role of lactate dehydrogenase, marrow fibrosis, and $\beta_2$-microglobulin also should be considered after establishing the IPSS. If elevated, the prognostic category worsens by one category level.

Table 1. International Prognostic Scoring System: Myelodysplastic Syndrome Prognostic Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>0</th>
<th>0.5</th>
<th>1.0</th>
<th>1.5</th>
<th>2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marrow blasts, %</td>
<td>&lt;5%</td>
<td>5%-10%</td>
<td>–</td>
<td>11%-20%</td>
<td>21%-30%</td>
</tr>
<tr>
<td>Karyotype</td>
<td>Good</td>
<td>Intermediate</td>
<td>Poor</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Cytopenias</td>
<td>0/1</td>
<td>2/3</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Table 2. International Prognostic Scoring System: Myelodysplastic Syndrome Clinical Outcomes

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Total Score</th>
<th>Median Survival, y</th>
<th>Time for 25% of patients to Progress to AML</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>0</td>
<td>5.7</td>
<td>9.4 years</td>
</tr>
<tr>
<td>Intermediate-1</td>
<td>0.5-1.0</td>
<td>3.5</td>
<td>3.3 years</td>
</tr>
<tr>
<td>Intermediate-2</td>
<td>1.5-2.0</td>
<td>1.2</td>
<td>1.12 years</td>
</tr>
<tr>
<td>High</td>
<td>≥2.5</td>
<td>0.4</td>
<td>0.2 years</td>
</tr>
</tbody>
</table>

AML: acute myelocytic leukemia.

An updated 5-category IPSS has been proposed for prognosis in patients with primary MDS or secondary AML to account for chromosomal abnormalities frequently seen in MDS$^1$. This system
stratifies patients into 5 categories: very poor, poor, intermediate, good, and very good. There has also been an investigation into using the 5-category IPSS to better characterize risk in MDS.

Given the long natural history of MDS, allogeneic hematopoietic cell transplantation (allo-HCT) is typically considered in patients with increasing numbers of blasts, signaling a possible transformation to AML. Subtypes falling into this category include refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, or chronic myelomonocytic leukemia.

Patients with refractory anemia with or without ringed sideroblasts may be considered candidates for allo-HCT when chromosomal abnormalities are present, or when the disorder is associated with the development of significant cytopenias (eg, neutrophils <500/mm³, platelets <20,000/mm³).

Patients with myeloproliferative neoplasms may be considered candidates for allo-HCT when there is progression to myelofibrosis or toward acute leukemia. In addition, allo-HCT may be considered in patients with essential thrombocythemia with an associated thrombotic or hemorrhagic disorder. Use of allo-HCT should be based on the following criteria: cytopenias, transfusion dependence, increasing blast percentage over 5%, and age.

Some patients for whom a conventional myeloablative allo-HCT could be curative may be candidates for reduced-intensity conditioning (RIC) allo-HCT. They include patients whose age (typically >60 years) or comorbidities (eg, liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy, low Karnofsky Performance Status) preclude the use of a standard myeloablative conditioning regimen. The ideal allogeneic donors are human leukocyte antigen (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, there has been interest in haploidentical donors, typically a parent or a child of the patient, who usually share only 3 of the 6 major histocompatibility antigens. Most patients will have such a donor; however, the risk of graft-versus-host disease (GVHD) and overall morbidity of the procedure may be severe, and experience with these donors is not as extensive as that with matched donors.

Evidence and clinical guidelines suggest RIC allo-HCT may be considered as a risk-adapted strategy for high-risk patients of MAC-intolerance as follows:

**MDS**

- Older age
• IPSS intermediate-2 or high risk
• Multiple comorbidities (e.g., hematopoietic cell transplantation-comorbidity index (HCT-CI) score higher than 2)
• Red blood cell (RBC) transfusion dependence
• Neutropenia
• Thrombocytopenia
• High-risk cytogenetics
• Increasing blast percentage

**Myeloproliferative Neoplasm**

• Cytopenias
• Transfusion dependence
• Increasing blast percentage over 5%
• Age 60 to 65 years

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**Documentation Requirements**

The patient’s medical records submitted for review should document that medical necessity criteria are met. The record should include clinical documentation of:

• Diagnosis/condition
• History and physical examination documenting the severity of the condition
• Whether myeloablative or reduced intensity conditioning allo-HCT is planned
• Contraindications to myeloablative conditioning regimen, if applicable

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**Coding**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>CPT</td>
<td>Bone marrow harvesting for transplantation; autologous</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>-------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>38240</td>
<td>Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor</td>
</tr>
</tbody>
</table>

**HCPCS**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S2150</td>
<td>Bone marrow or blood-derived stem cells (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications; including: pheresis and cell preparation/storage; marrow ablative therapy; drugs, supplies, hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days of pre and post transplant care in the global definition</td>
</tr>
</tbody>
</table>

**Note:** CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

**Related Information**

**Consideration of Age**

In this policy, RIC allogeneic HCT may be considered medically necessary as a treatment of MPNs in patients who for medical reasons would be unable to tolerate a myeloablative conditioning regime. MPNs primarily occur in older individuals, with the majority of cases reported in patients aged 60 and older. HCT is at present the only potentially curative therapy. Since direct, prospective clinical trials of outcomes are not available, clinical input was obtained. The clinical input supported the use of allogeneic HCT using either a myeloablative or RIC regimens in patients when selection is guided by age and disease risk factors.

**Evidence Review**

**Description**

Myelodysplastic syndromes (MDS) and myeloproliferative neoplasms refer to a heterogeneous group of clonal hematopoietic disorders with the potential to transform into acute myelocytic leukemia. Allogeneic hematopoietic cell transplantation (HCT) has been proposed as a curative treatment option for patients with these disorders.
Background

Myelodysplastic Syndromes

Myelodysplastic syndromes (MDS) can occur as a primary (idiopathic) disease or can be secondary to cytotoxic therapy, ionizing radiation, or other environmental insults. Chromosomal abnormalities are seen in 40% to 60% of patients, frequently involving deletions of chromosome 5 or 7, or an extra chromosome as in trisomy 8. Most MDS diagnoses occur in individuals older than age 55-60 years, with an age-adjusted incidence of 62% among individuals older than age 70 years. Patients succumb either to disease progression to AML or to complications of pancytopenias. Patients with higher blast counts or complex cytogenetic abnormalities have a greater likelihood of progressing to AML than do other patients.

Myelodysplastic Syndrome Classification and Prognosis

The French-American-British system was used to classify MDS into five subtypes: (1) refractory anemia; (2) refractory anemia with ringed sideroblasts; (3) refractory anemia with excess blasts; (4) refractory anemia with excess blasts in transformation; and, (5) chronic myelomonocytic leukemia. The French-American-British system was supplanted by that of the World Health Organization (WHO), which records the number of lineages in which dysplasia is seen (unilineage versus multilineage), separates the 5q- syndrome, and reduces the threshold maximum blast percentage for the diagnosis of MDS from 30% to 20% (see the Policy Coverage Criteria section for WHO classification scheme for myeloid neoplasms).

The most commonly used prognostic scoring system for MDS is the International Prognostic Scoring System (IPSS), which groups patients into one of four prognostic categories based on the number of cytopenias, cytogenetic profile, and the percentage of blasts in the bone marrow. This system underweights the clinical importance of severe, life-threatening neutropenia and thrombocytopenia in therapeutic decisions and does not account for the rate of change in critical parameters (eg, peripheral blood counts, blast percentage). However, the IPSS has been useful in comparative analysis of clinical trial results and its utility confirmed at many institutions. An updated 5-category IPSS has been proposed for prognosis in patients with primary MDS or secondary AML to account for chromosomal abnormalities frequently seen in MDS. This system stratifies patients into 5 categories: very poor, poor, intermediate, good, and very good. There has been an investigation into using the 5-category IPSS to better characterize risk in MDS. A second prognostic scoring system incorporates the WHO subgroup classification that accounts for blast percentage, cytogenetics, and severity of cytopenias as assessed by transfusion requirements. The WHO Classification-based Prognostic Scoring System uses a 6-category
system, which allows more precise prognostication of overall survival (OS) duration, as well as risk for progression to AML. This system is not yet in widespread use in clinical trials.

**Myelodysplastic Syndrome Treatment**

Treatment of non-progressing MDS has involved best supportive care, including red blood cell and platelet transfusions and antibiotics. Active therapy was given only when MDS progressed to AML or resembled AML with severe cytopenias. An array of therapies are now available to treat MDS, including hematopoietic growth factors (eg, erythropoietin, darbepoetin, granulocyte colony-stimulating factor), transcriptional-modifying therapy (eg, U.S. Food and Drug Administration (FDA) approved hypomethylating agents, nonapproved histone deacetylase inhibitors), immunomodulators (eg, lenalidomide, thalidomide, antithymocyte globulin, cyclosporine A), low-dose chemotherapy (eg, cytarabine), and allogeneic hematopoietic cell transplantation (allo-HCT). Given the spectrum of treatments available, the goal of therapy must be decided upfront whether it is to improve anemia, thrombocytopenia, or neutropenia, to eliminate the need for red blood cell transfusion; to achieve complete remission, or to cure the disease.

Allo-HCT is the only approach with curative potential, but its use is governed by patient age, performance status, medical comorbidities, the patient’s risk preference, and severity of MDS at presentation. Allo-HCT is discussed in more detail in a subsequent section.

**Chronic Myeloproliferative Neoplasms**

Chronic myeloproliferative neoplasms are clonal bone marrow stem-cell disorders; as a group, approximately 8,400 myeloproliferative neoplasms are diagnosed annually in the United States. Like MDS, myeloproliferative neoplasms primarily occur in older individuals, with approximately 67% reported in patients aged 60 years and older.

Myeloproliferative neoplasms are characterized by the slow but progressive expansion of a clone of cells with the potential evolution into a blast crisis similar to AML. Myeloproliferative neoplasms share a common stem cell-derived clonal heritage, with phenotypic diversity attributed to abnormal variations in signal transduction as the result of a spectrum of variants that affect protein tyrosine kinases or related molecules. The unifying characteristic common to all myeloproliferative neoplasms is effective clonal myeloproliferation resulting in peripheral granulocytosis, thrombocytosis, or erythrocytosis that is devoid of dyserythropoiesis, granulocytic dysplasia, or monocytosis.
**Myeloproliferative Neoplasm Classification**

The WHO (2008) classification scheme replaced the term *chronic myeloproliferative disorder* with the term *myeloproliferative neoplasm*. Myeloproliferative neoplasms are a subdivision of myeloid neoplasms that includes the four classic disorders: chronic myeloid leukemia, polycythemia vera, essential thrombocytopenia, and primary myelofibrosis. The WHO classification also includes chronic neutrophilic leukemia, chronic eosinophilic leukemia/hypereosinophilic syndrome, mast cell disease, and myeloproliferative neoplasm unclassifiable.

**Myeloproliferative Neoplasm Treatment**

In indolent, nonprogressing cases, therapeutic approaches are based on relief of symptoms. Supportive therapy may include prevention of thromboembolic events. Hydroxyurea may be used in cases of high-risk essential thrombocytosis and polycythemia vera and intermediate- and high-risk primary myelofibrosis.

The FDA (2011) approved the orally administered selective Janus kinase 1 and 2 inhibitor ruxolitinib for the treatment of intermediate- or high-risk myelofibrosis. Ruxolitinib has been associated with improved OS, spleen size, and symptoms of myelofibrosis when compared with placebo. The Randomized Study of Ruxolitinib Tablets Compared to Best Available Therapy in Subjects With Primary Myelofibrosis, Post-Polycythemia Vera-Myelofibrosis or Post-Essential Thrombocythemia Myelofibrosis (COMFORT-II trial [2013]) compared ruxolitinib with best available therapy in patients who had intermediate- and high-risk myelofibrosis, and demonstrated improvements in spleen volume and OS. In a randomized trial comparing ruxolitinib with best available therapy (including antineoplastic agents, most commonly hydroxyurea, glucocorticoids), with no therapy for treatment of myelofibrosis, Harrison et al (2012) reported improvements in spleen size and quality of life, but not OS.

Myeloablative allo-HCT has been considered the only potentially curative therapy, but because most patients are of advanced age with attendant comorbidities, its use is limited to those who can tolerate often severe treatment-related adverse events of this procedure. However, the use of reduced-intensity conditioning for allo-HCT has extended the potential benefits of this procedure to selected individuals with these disorders. Allo-HCT is discussed in more detail in the next section.
Hematopoietic Cell Transplantation

Hematopoietic cell transplantation is a procedure in which hematopoietic stem cells are intravenously infused to restore bone marrow and immune function in cancer patients who receive bone marrow-toxic doses of cytotoxic drugs with or without whole-body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or from a donor (allo-HCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates. Cord blood transplantation is discussed in greater detail in a separate policy (see Related Policies).

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. In allogeneic stem cell transplantation, immunologic compatibility between donor and patient is a critical factor for achieving a successful outcome. Compatibility is established by typing of human leukocyte antigen (HLA) using cellular, serologic, or molecular techniques. HLA refers to the gene complex expressed at the HLA-A, -B, and -DR (antigen-D related) loci on each arm of chromosome 6. An acceptable donor will match the patient at all or most of the HLA loci.

Conditioning for Hematopoietic Cell Transplantation

Conventional Conditioning

The conventional (“classical”) practice of allo-HCT involves administration of cytotoxic agents (eg, cyclophosphamide, busulfan) with or without total body irradiation at doses sufficient to cause bone marrow ablation 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 mediated by non-self-immunologic effector cells. While the slower graft-versus-malignancy effect is considered the potentially curative component, it may be overwhelmed by existing disease in the absence of pretransplant conditioning. Intense conditioning regimens are limited to patients who are sufficiently fit to tolerate substantial adverse effects. These include opportunistic infections secondary to loss of endogenous bone marrow function and organ damage or failure caused by the cytotoxic drugs. Subsequent to graft infusion in allo-HCT, immunosuppressant drugs are required to minimize graft rejection and graft-versus-host disease, which also increases susceptibility to opportunistic infections.

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

**Reduced Intensity Conditioning for Allo Hematopoietic Cell Transplantation**

Reduced-intensity conditioning refers to the pre-transplant use of lower doses of cytotoxic drugs or less intense regimens of radiotherapy than are used in traditional full-dose myeloablative conditioning treatments. Although the definition of reduced-intensity conditioning is variable, with numerous versions employed, all regimens seek to balance the competing effects of relapse due to residual disease and non-relapse mortality. The goal of reduced-intensity conditioning is to reduce disease burden and to minimize associated treatment-related morbidity and nonrelapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. Reduced-intensity conditioning regimens range from nearly totally myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo reduced-intensity conditioning with allo-HCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full-donor chimerism. For the purposes of this policy, reduced-intensity conditioning will refer to all conditioning regimens intended to be nonmyeloablative.

**Summary of Evidence**

For individuals who have MDS or myeloproliferative neoplasms who receive myeloablative conditioning allogeneic HCT, the evidence includes case series, which are often heterogeneous in terms of diseases included. The relevant outcomes are OS, disease-specific survival, and treatment-related mortality and morbidity. Primarily uncontrolled, observational studies of HCT for MDS have reported a relatively large range of overall and progression-free survival rates, which reflect the heterogeneity in patient populations, conditioning regimens, and other factors. Reported estimates for 3- to 5-year OS of 40% to 50% are typical. For HCT for myeloproliferative neoplasms, data are more limited. At least one comparative study of HCT for myelofibrosis has demonstrated improved survival with HCT compared with standard therapy. At present, HCT is the only potentially curative treatment option for patients with MDS and myeloproliferative neoplasms. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.
For individuals who have MDS or myeloproliferative neoplasms who receive reduced-intensity conditioning reduced-intensity conditioning allogeneic-HCT, the evidence includes randomized controlled trials (RCTs) and retrospective observational series. The relevant outcomes are OS, disease-specific survival, and treatment-related mortality and morbidity. Evidence from RCTs and retrospective, nonrandomized comparisons have suggested that reduced-intensity conditioning may be used as a risk-adapted strategy in high-risk patients who are older and have more comorbidities without significantly worsening OS. Reduced-intensity conditioning appears to be associated with lower rates of nonrelapse mortality but higher cancer relapse than myeloablative HCT. At present, HCT is the only potentially curative treatment option for patients with MDS and myeloproliferative neoplasms. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some currently ongoing trials that might influence this review are listed in 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>NCT00739141</td>
<td>Conditioning Regimen and the Transplantation of Unrelated Donor Umbilical Cord Blood in Patients with Hematologic Malignancies</td>
<td>86</td>
<td>Aug 2021</td>
</tr>
<tr>
<td>NCT01760655</td>
<td>Reduced Intensity Conditioning Before Donor Stem Cell Transplant in Treating Patients with High-Risk Hematologic Malignancies</td>
<td>72</td>
<td>Apr 2021</td>
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<tr>
<td>NCT02757989</td>
<td>Allogeneic Hematopoietic Stem Cell Transplantation in Patients with Myelodysplastic Syndrome Low Risk</td>
<td>105</td>
<td>June 2022</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.
Practice Guidelines and Position Statements

National Comprehensive Cancer Network

Current National Comprehensive Cancer Network clinical guidelines for myelodysplastic syndromes (v.1.2021) make the following general recommendation about allogeneic (allo) hematopoietic cell transplantation HCT:

For patients who are transplant candidates, an HLA-matched sibling, or HLA-matched unrelated donor can be considered. Results with HLA-matched unrelated donors have improved to levels comparable to those obtained with HLA-matched siblings. With the increasing use of cord blood or HLA-haploidentical related donors, HCT has become a viable option for many patients. High-dose conditioning is typically used for younger patients, whereas RIC [reduced-intensity conditioning] for HCT is generally the strategy in older individuals.

Specific National Comprehensive Cancer Network recommendations for HCT for treatment of myelodysplastic syndromes are outlined in Table 4.

Table 4: Guidelines for Allogeneic Hematopoietic Cell Transplantation for Myelodysplastic Syndromes

<table>
<thead>
<tr>
<th>Prognostic Category</th>
<th>Recommendations for HCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPSS low/intermediate-1 OR</td>
<td>• Consider allo-HCT for patients who have clinically relevant thrombocytopenia or neutropenia or increased marrow blasts, with disease progression or no response after azacitidine/decitabine or immunosuppressive therapy</td>
</tr>
<tr>
<td>IPSS-R very low, low, intermediate OR</td>
<td>• Consider allo-HCT for patients who have symptomatic anemia with no 5q deletion, with serum erythropoietin level &gt; 500 mU/mL, with poor probability of response to immunosuppressive therapy, and no response or intolerance to azacitidine/decitabine or immunosuppressive therapy</td>
</tr>
<tr>
<td>WPSS very low, low, intermediate</td>
<td></td>
</tr>
<tr>
<td>IPSS intermediate-2, high OR</td>
<td>• Recommend allo-HCT if a high-intensity therapy candidate and transplant candidate and donor stem cell source is available</td>
</tr>
<tr>
<td>IPSS-R intermediate, high, very high OR</td>
<td></td>
</tr>
<tr>
<td>WPSS high, very high</td>
<td></td>
</tr>
</tbody>
</table>

Table 4: Guidelines for Allogeneic Hematopoietic Cell Transplantation for Myelodysplastic Syndromes

Table 5 summarizes the National Comprehensive Cancer Network recommendations (v.1.2020) on the use of allo-HCT for the treatment of myeloproliferative neoplasms.52 The guidelines note that selection of allo-HCT should be based on age, performance status, major comorbid conditions, psychosocial status, patient preference, and availability of caregiver.

Table 5: Guidelines for Allogeneic Hematopoietic Cell Transplantation for Myeloproliferative Neoplasms

<table>
<thead>
<tr>
<th>Prognostic Category</th>
<th>Recommendations for Allo-HCT</th>
</tr>
</thead>
</table>
| Intermediate risk – 1 myelofibrosis | • Consider observation or ruxolitinib if symptomatic or allo-HCT  
IPSS=1  
DIPSS-Plus=1  
DIPSS=1 or 2 |  
• Evaluation for allo-HCT is recommended for patients with low platelet counts or complex cytogenetics |
| Intermediate risk – 2 myelofibrosis | • Consider allo-HCT immediately or bridging therapy can be used to decrease marrow blasts to an acceptable level prior to transplant  
IPSS=2  
DIPSS-Plus=2 or 3  
DIPSS=3 or 4 |  
• Evaluation for allo-HCT is recommended for patients with low platelet counts or complex cytogenetics |
| High-risk myelofibrosis |  
IPSS>3  
DIPSS-Plus=4 to 6  
DIPSS=5 or 6 |  |
| Disease progression to advanced stage/AML | • Induce remission with hypomethylating agents or intensive induction chemotherapy followed by allo-HCT |

allo: allogeneic; AML: acute myeloid leukemia; DIPSS: Dynamic International Prognostic Scoring System; HCT: hematopoietic cell transplantation; IPSS: International Prognostic Scoring System

American Society of Transplantation and Cellular Therapy

In 2015, the American Society of Transplantation and Cellular Therapy (formerly The American Society for Blood and Marrow Transplantation) published guidelines on indications for HCT, based on the recommendations of a multiple-stakeholder task force.53 Table 6 summarizes categorizations for allo-HCT.
Table 6. Recommendations for the Use of Hematopoietic Cell Transplantation to Treat Myelodysplastic Syndromes, Myelofibrosis, and Myeloproliferative Neoplasms

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Myelodysplastic Syndromes</strong></td>
<td></td>
</tr>
<tr>
<td>Low/intermediate-1 risk</td>
<td>Standard of care, clinical evidence available (large clinical trials are not available; however, sufficiently large cohort studies have shown efficacy with &quot;acceptable risk of morbidity and mortality&quot;)</td>
</tr>
<tr>
<td>Intermediate-2/high risk</td>
<td>Standard of care (&quot;well defined and generally supported by evidence in the form of high quality clinical trials and/or observational studies&quot;)</td>
</tr>
<tr>
<td><strong>Myelofibrosis and Myeloproliferative Neoplasms</strong></td>
<td></td>
</tr>
<tr>
<td>Primary, low risk</td>
<td>Standard of care (&quot;well defined and generally supported by evidence in the form of high quality clinical trials and/or observational studies&quot;)</td>
</tr>
<tr>
<td>Primary, intermediate/high risk</td>
<td>Standard of care (&quot;well defined and generally supported by evidence in the form of high quality clinical trials and/or observational studies&quot;)</td>
</tr>
<tr>
<td>Secondary</td>
<td>Standard of care (&quot;well defined and generally supported by evidence in the form of high quality clinical trials and/or observational studies&quot;)</td>
</tr>
<tr>
<td>Hypereosinophilic syndromes, refractory</td>
<td>Standard of care, rare indication (clinical trials and observational studies are not feasible due to low incidence; small cohorts have shown efficacy with &quot;acceptable risk of morbidity and mortality&quot;)</td>
</tr>
</tbody>
</table>

HCT: hematopoietic cell transplantation

Medicare National Coverage

There is a national coverage determination for stem cell transplantation (110.23; formerly 110.81), portions of which are highlighted below:

Nationally Covered Indications

“I.  Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

   a.  Treatment of leukemia, leukemia in remission, or aplastic anemia when it is reasonable and necessary,
b. Treatment of severe combined immunodeficiency disease (SCID) and for the treatment of Wiskott-Aldrich syndrome.

c. Treatment of Myelodysplastic Syndromes (MDS) pursuant to Coverage with Evidence Development (CED) in the context of a Medicare-approved, prospective clinical study. Medicare payment for these beneficiaries will be restricted to patients enrolled in an approved clinical study.

d. Effective January 27, 2016, allogeneic HSCT for multiple myeloma is covered by Medicare only for beneficiaries with Durie-Salmon Stage II or III multiple myeloma, or International Staging System (ISS) Stage II or Stage III multiple myeloma, and participating in an approved prospective clinical study that meets the criteria below. There must be appropriate statistical techniques to control for selection bias and confounding by age, duration of diagnosis, disease classification, International Myeloma Working Group (IMWG) classification, ISS stage, comorbid conditions, type of preparative/conditioning regimen, graft vs. host disease (GVHD) prophylaxis, donor type and cell source....

e. Effective January 27, 2016, allogeneic HSCT for myelofibrosis (MF) is covered by Medicare only for beneficiaries with Dynamic International Prognostic Scoring System (DIPSSplus) intermediate-2 or High primary or secondary MF and participating in an approved prospective clinical study. All Medicare approved studies must use appropriate statistical techniques in the analysis to control for selection bias and potential confounding by age, duration of diagnosis, disease classification, DIPSS plus score, comorbid conditions, type of preparative/conditioning regimen, graft vs. host disease (GVHD) prophylaxis, donor type and cell source....

f. Effective January 27, 2016, allogeneic HSCT for sickle cell disease (SCD) is covered by Medicare only for beneficiaries with severe, symptomatic SCD who participate in an approved prospective clinical study...."

**Regulatory Status**

The FDA regulates human cells and tissues intended for implantation, transplantation or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation title 21, parts 1270 and 1271. Hematopoietic stem cells are included in these regulations.
References


### History

<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. Policy represents revision of 7.03.10 to focus on myelodysplasia and myelofibrosis. New policy statement on HDC for myelofibrosis.</td>
</tr>
<tr>
<td>11/12/02</td>
<td>Replace policy - Policy reviewed with no criteria changes.</td>
</tr>
<tr>
<td>07/13/04</td>
<td>Replace policy - Policy reviewed with literature; policy statement also now includes “mini-transplant.” References added; cross-reference to BC.8.01.38 on mini-transplants added.</td>
</tr>
<tr>
<td>07/12/05</td>
<td>Replace policy - Policy reviewed with literature search; no change in policy statement. No further review scheduled.</td>
</tr>
<tr>
<td>02/06/06</td>
<td>Codes updated - No other changes.</td>
</tr>
<tr>
<td>06/02/06</td>
<td>Disclaimer and Scope Updates - No other changes.</td>
</tr>
<tr>
<td>10/09/07</td>
<td>Replace policy - Policy updated with literature review. Status changed from AR to BC. References added. No change in policy statement.</td>
</tr>
<tr>
<td>11/12/07</td>
<td>Codes updated - CPT code 86817 removed as directed by RPIW.</td>
</tr>
<tr>
<td>05/13/08</td>
<td>Cross Reference Update - No other changes</td>
</tr>
<tr>
<td>03/10/09</td>
<td>Replace policy - Policy updated with literature search. Minor terminology changes to policy statements; the intent of the policy statements remain unchanged. Additional policy statements include Reduced intensity conditioning allogeneic SCT is considered investigational as a treatment of myeloproliferative disorders and myelodysplastic syndrome. References and codes added. “High-Dose Chemotherapy” removed from the title and throughout the body of the policy and &quot;myeloproliferative&quot; diseases added to the policy title.</td>
</tr>
<tr>
<td>12/08/09</td>
<td>Code Update - 86817 code added back to the policy.</td>
</tr>
<tr>
<td>Date</td>
<td>Comments</td>
</tr>
<tr>
<td>------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>02/09/10</td>
<td>Code Update - New 2010 codes added.</td>
</tr>
<tr>
<td>03/08/11</td>
<td>Replace policy - Policy updated with literature search, reference numbers 14-17 added. Myeloproliferative Disorders” replaced with “Myeloproliferative Neoplasms” in title and text. Policy statements revised to indicate that RIC HCT, previously investigational, may now be considered medically necessary as a treatment of myelodysplastic syndrome and myeloproliferative neoplasms in patients who for medical reasons would be unable to tolerate a myeloablative conditioning regimen. Reviewed and recommended by OAP in February 2011.</td>
</tr>
<tr>
<td>10/19/11</td>
<td>Related Policies updated; links refreshed.</td>
</tr>
<tr>
<td>01/06/12</td>
<td>Replace policy – Policy updated with literature search; references 15-18 and 20 added. Policy statements unchanged. ICD-10 codes added.</td>
</tr>
<tr>
<td>01/24/12</td>
<td>Code 38232 added.</td>
</tr>
<tr>
<td>02/09/12</td>
<td>CPT code 38204 was removed from the policy.</td>
</tr>
<tr>
<td>06/20/12</td>
<td>Minor update: Related Policies updated; 8.01.17 replaced 8.01.507 effective June 12, 2012.</td>
</tr>
<tr>
<td>08/01/12</td>
<td>Update Related Policies Titles: 8.01.17, 8.01.22, 8.01.30, 8.01.35, and 8.01.520. Removed Related Policy 8.01.38 as it was archived.</td>
</tr>
<tr>
<td>10/01/12</td>
<td>Update Coding Section – ICD-10 codes are now effective 10/01/2014.</td>
</tr>
<tr>
<td>01/29/13</td>
<td>Replace policy. Title revised with addition of the word “Hematopoietic”. Policy rationale updated based on a literature review through September 2012. Reference 26 added; others renumbered or removed. Policy statements unchanged.</td>
</tr>
<tr>
<td>09/30/13</td>
<td>Update Related Policies. Change title to 8.01.31.</td>
</tr>
<tr>
<td>10/18/13</td>
<td>Update Related Policies. Change title to 8.01.17.</td>
</tr>
<tr>
<td>01/21/14</td>
<td>Replace policy. Policy updated with literature search through October 8, 2013; reference 14 added. Policy statements unchanged. CPT code 38230 removed from policy; it does not apply.</td>
</tr>
<tr>
<td>02/27/14</td>
<td>Update Related Policies. Change title to 8.01.30.</td>
</tr>
<tr>
<td>03/21/14</td>
<td>Update Related Policies. Add 8.01.15 and 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 and 8.01.54, then add 8.01.530, 8.01.531 and 8.01.532.</td>
</tr>
<tr>
<td>12/03/14</td>
<td>Update Related Policies. Remove 8.01.21 and 8.01.26.</td>
</tr>
<tr>
<td>01/28/15</td>
<td>Annual Review. Policy updated with literature review through September 30, 2014. References 1-3, 5-6, 26-32, and 37 added. Policy statements unchanged. Remove ICD-9 and ICD-10 diagnosis codes; these are not utilized in policy adjudication.</td>
</tr>
<tr>
<td>Date</td>
<td>Comments</td>
</tr>
<tr>
<td>------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>02/19/15</td>
<td>Update Related Policies. Remove 8.01.30.</td>
</tr>
<tr>
<td>09/01/16</td>
<td>Update Related Policies. Remove 8.01.27 as it was archived.</td>
</tr>
<tr>
<td>09/30/16</td>
<td>Coding Update. Remove CPT 86817 from coding section.</td>
</tr>
<tr>
<td>11/04/16</td>
<td>Coding update. Removed codes that are transplant benefit related.</td>
</tr>
<tr>
<td>08/01/17</td>
<td>Updated title of Related Policy 8.01.511.</td>
</tr>
<tr>
<td>11/10/17</td>
<td>Policy moved to new format; no changes to policy statement.</td>
</tr>
<tr>
<td>05/01/18</td>
<td>Annual Review, approved April 3, 2018. Policy updated with literature review through November 2017; references updated. Removed investigational policy statements.</td>
</tr>
<tr>
<td>09/01/18</td>
<td>Minor update. Re-added Consideration of Age information, which was in advertently removed during a previous update.</td>
</tr>
<tr>
<td>04/01/19</td>
<td>Annual Review, approved March 19, 2019. Policy updated with literature review through October 2018; no references added. Policy statements unchanged.</td>
</tr>
<tr>
<td>04/01/20</td>
<td>Delete policy, approved March 10, 2020. This policy will be deleted effective July 2, 2020, and replaced with InterQual criteria for dates of service on or after July 2, 2020.</td>
</tr>
<tr>
<td>05/01/20</td>
<td>Annual Review, approved April 14, 2020. Policy updated with literature review through November 2019; references added; new description of HCT added; Policy statement for RIC allo-HCT changed to specify it as a risk-adapted strategy for patients at high-risk of MAC intolerance, which is meant to encompass both older age and medical co-occurring conditions; RCT evidence review and updates to Policy Coverage Criteria section support the existing medically necessary policy statement for RIC allo-HCT and supplants the 2009 clinical input which has been removed.</td>
</tr>
<tr>
<td>06/10/20</td>
<td>Interim Review, approved June 9, 2020, effective June 10, 2020. This policy is reinstated immediately and will no longer be deleted or replaced with InterQual criteria on July 2, 2020.</td>
</tr>
<tr>
<td>5/01/21</td>
<td>Update Related Policies. Removed policy 7.01.50 as it was archived.</td>
</tr>
</tbody>
</table>
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). ©2021 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 AppealsDepartmentinquines@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)

Complaint forms are available at

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).

Oromo (Oromo)


Français (French)


Kreyòl ayisyen (Creole)

Avi sila a gen Enfòmasyon Enpòtan ladann. Avi sila a kapab genyen enfòmasyon enpòtan konsèn a aplikasyon w lan oswa konse a kouvètis a sairisan lan atraver Premera Blue Cross. Kapab genyen dat ki eptpan nan avi sila a. Ou ka gen pou pran kék aksyon avan sèt la tazit pou pou kantebi kouvètis a sairisan sante w lan oswa pou yo ka ede w ak depans yo. Se de w pou resesu enfòmasiyon sa a ak asistans nan lang ou pa ake, san ou pa gen pou peye pou sa. Rate nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German)


Illoko (Ilocano)

Daytoy a Pakdaar ket naglaon iti Napateg nga Impormasion. Daytoy a pakdaar mabalini nga adda ket naglaon iti napateg nga impormasion maipanggep iti aplikasyon weno coverag babaen ti Premera Blue Cross. Daytoy ket mabalini dagiti importante a petsa iti daytoy a pakdaar. Mabalini nga adda rumbeng nga arimideny weno adda sabbay dagiti particular a naituding a petsa nga adda daway tapno mapagtalaiday odjo ti coverag iti salan-aty weno tulong kadagiti gastos. Adda karbenganyo a mangala nga daytoy nga impormasion ken tulong iti bukodyo a pagasao nga awan ti bayadanyo. Tumawag iti numero nga osa 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian)

Premera Blue Cross

Key dates that may be important to you are those that are revealed in your insurance
coverage information. It is possible that you may need to take some action within
a certain period for certain reasons. You may refer to these dates in your
information.

800-722-1471 (TTY: 800-842-5357)

Laos (Lao):

คำศัพท์และอัตราภาษีที่มีบริการที่เกี่ยวข้องกับการรักษา
คุณต้องรู้.

800-722-1471 (TTY: 800-842-5357)

Khmer (Khmer):

តូចចិត្តបានដ៏សំខាន់ៗ។

800-722-1471 (TTY: 800-842-5357)

Punjabi (Punjabi):

ਨਿਹਾਲੀ ਪਿੱਤੇ ਦਾ ਹਿੱਸਾ ਹੋਣਾ ਚਾਹਿੰਦੇ ਹਨ।

800-722-1471 (TTY: 800-842-5357)

Farsi (Farsi):

امکان حذف اطلاعات مربوط به برنامه تأمین در حال حاضر نداریم. اگر اطلاعات
همین اطلاعات الرسمی از طریق پرداخت

800-722-1471 (TTY: 800-842-5357)

Polskie (Polish):

To ogłoszenie może zawierać ważne informacje. To ogłoszenie może
zawierać ważne informacje odnośnie Państwa wniosku lub zakresu
świadczeń poprzez Premera Blue Cross. Prosimy zwrócić uwagę na
kłuczowe daty, które mogą być zawarte w tym ogłoszeniu aby
przekroczyć terminów w przypadku utrzymania polisy ubezpieczeniowej lub
informacji związanej z kosztami. Macie Państwo prawo do bezpłatnej
informacji we własnym języku. Zadbowicie pod 800-722-1471
(TTY: 800-842-5357)

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 ou ajuda de
custos. Você tem o direito de obter esta informação e ajuda em seu idioma
e sem custos. Ligue para 800-722-1471 (TTY: 800-842-5357)

Tiếng Việt (Vietnamese):

Thống báo này cung cấp thông tin quan trọng. Thông báo này có thông
tin quan trọng về đơn tin tham gia hoặc hợp đồng bảo hiểm của quý vị qua
chương trình Premera Blue Cross. Xin xem ngay quan trọng trong thông
báo này. Quý vị có thể phải thực hiện một hoặc bốn trong thời hạn
dề dự tri bảo hiểm sự khởi hoặc được trợ giúp thêm về chi phí. Quý vị có
thể được biết thông tin này và được trợ giúp bằng ngôn ngữ của mình
phí. Xin gọi số 800-722-1471 (TTY: 800-842-5357)