

MEDICAL POLICY – 8.01.529

Hematopoietic Cell Transplantation for Non-Hodgkin Lymphomas

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RELATED MEDICAL POLICIES:

- 7.01.50 Placental and Umbilical Cord Blood as a Source of Stem Cells
- 8.01.15 Hematopoietic Cell Transplantation for Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma
- 8.01.21 Allogeneic Hematopoietic Cell Transplantation for Myelodysplastic Syndromes and Myeloproliferative Neoplasms
- 8.01.22 Allogeneic Hematopoietic Cell Transplantation for Genetic Diseases and Acquired Anemias
- 8.01.24 Hematopoietic Cell Transplantation for Miscellaneous Solid Tumors in Adults
- 8.01.25 Hematopoietic Cell Transplantation for Autoimmune Diseases
- 8.01.29 Hematopoietic Cell Transplantation for Hodgkin Lymphoma
- 8.01.511 Hematopoietic Cell Transplantation for Solid Tumors of Childhood
- 8.01.532 Hematopoietic Cell Transplantation in the Treatment of Germ Cell Tumors

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Introduction

A hematopoietic cell is an immature cell that can mature into different types blood cells. Certain chemotherapy drugs can destroy the bone marrow, and bone marrow is where blood cells form. Infusing immature blood cells gives the body a chance to restore blood cell production in the bone marrow. When the immature blood cells are taken from the patient it’s known as an autologous hematopoietic cell transplant (HCT). Using immature cells from a donor is known as an allogeneic HCT. This policy discusses when hematopoietic cell transplants may be considered medically necessary for non-Hodgkin lymphoma, a type of immune system cancer.

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

Small lymphocytic lymphoma may be considered a node-based variant of chronic lymphocytic leukemia. Therefore, small lymphocytic lymphoma is considered along with chronic lymphocytic leukemia in a separate policy. Lymphoplasmacytic lymphoma and Waldenstrom macroglobulinemia are considered in separate policies (see [Related Policies](#)).

Indication	Coverage Statement
<p>Non-Hodgkin lymphoma (NHL) B-cell aggressive subtype (except mantle cell)</p>	<p>Myeloablative autologous, myeloablative allogeneic or reduced-intensity conditioning (RIC) allogeneic HCT with curative intent may be considered medically necessary:</p> <ul style="list-style-type: none"> As salvage for patients not in complete remission after first line chemotherapy induction <p>OR</p> <ul style="list-style-type: none"> To achieve or consolidate a complete remission in chemotherapy sensitive first or subsequent relapse <p>OR</p> <ul style="list-style-type: none"> To consolidate a complete remission in patients with an age-adjusted International Prognostic Index (IPI) that predicts a high or high-intermediate risk of relapse
<p>Mantle cell NHL B-cell subtype</p>	<p>Autologous HCT may be considered medically necessary to consolidate a first remission of mantle cell NHL B-cell subtype.</p> <p>Allogeneic and RIC allogeneic HCT are considered investigational to consolidate a first remission of mantle cell NHL B-cell subtype.</p> <p>Allogeneic or RIC allogeneic HCT with curative intent may be considered medically necessary as salvage for patients with</p>



Indication	Coverage Statement
	<p>mantle cell NHL B-cell subtype who are not in complete remission after first line chemotherapy.</p> <p>Myeloablative autologous HCT is considered investigational as salvage for patients with mantle cell NHL B-cell subtype who are not in complete remission after first line chemotherapy.</p>
<p>NHL B-cell indolent subtypes</p>	<p>Myeloablative autologous, allogeneic, or RIC allogeneic HCT with curative intent may be considered medically necessary:</p> <ul style="list-style-type: none"> As salvage for patients not in complete remission after first line (induction) chemotherapy <p>OR</p> <ul style="list-style-type: none"> To achieve or consolidate a complete remission in chemotherapy sensitive first or subsequent relapse (regardless of transformation) <p>Myeloablative autologous, allogeneic, and RIC allogeneic HCT are considered investigational:</p> <ul style="list-style-type: none"> As initial therapy (without standard induction chemotherapy) for all B-Cell NHL <p>OR</p> <ul style="list-style-type: none"> To consolidate a first complete remission for low or low-intermediate IPI score diffuse large B-Cell NHL <p>OR</p> <ul style="list-style-type: none"> To consolidate a first complete remission for indolent B-cell NHL
<p>Mature T-cell or NK (peripheral T-cell) lymphoma</p>	<p>Myeloablative autologous HCT may be considered medically necessary:</p> <ul style="list-style-type: none"> To consolidate a first complete remission in high-risk subtypes (see Table 1 below) <p>Myeloablative autologous, allogeneic, or reduced-intensity conditioning allogeneic HCT may be considered medically necessary as salvage therapy.</p> <p>Myeloablative and reduced-intensity conditioning allogeneic HCT are considered investigational to consolidate a first complete remission.</p>



Indication	Coverage Statement
Tandem transplants	Tandem transplants are considered investigational to treat patients with any stage, grade, or subtype of NHL.

Table 1: Allowable Treatment by NHL Type

NHL Type	Presenting Stage	Treatment Intent	Autologous HCT	Allogeneic HCT	RIC	Tandem Transplant
B-Cell aggressive (not mantle)	Not in CR post 1 st Line	Salvage	Medically Necessary	Medically Necessary	Medically Necessary	Investigational
	Chemo-sensitive 1st or later relapse	Consolidate (CR)	Medically Necessary	Medically Necessary	Medically Necessary	Investigational
High or high-intermediate IPI	CR	Consolidate	Medically Necessary	Medically Necessary	Medically Necessary	Investigational
Mantle cell	1st Remission	Consolidate	Medically Necessary	Investigational	Investigational	Investigational
	Not in CR post 1st Line	Salvage	Investigational	Medically Necessary	Medically Necessary	Investigational
Indolent	CR	Consolidate	Investigational	Investigational	Investigational	Investigational
	Not in CR post 1 st Line Chemo	Salvage	Medically Necessary	Medically Necessary	Medically Necessary	Investigational
	Chemo-sensitive 1 st or later relapse	Consolidate (CR)	Medically Necessary	Medically Necessary	Medically Necessary	Investigational
Mature T-cell or NK cell high risk	1 st CR	Consolidate	Medically Necessary	Investigational	Investigational	Investigational
	Not CR post Chemo	Salvage	Medically Necessary	Medically Necessary	Medically Necessary	Investigational
Mature T-cell or NK cell not high risk	1 st CR	Consolidate	Investigational	Investigational	Investigational	Investigational
All NHL low or low-intermediate IPI	1 st CR	Consolidate	Investigational	Investigational	Investigational	Investigational



Additional Information

Reduced-intensity conditioning (RIC) would be considered an option in patients who meet criteria for an allogeneic hematopoietic stem-cell transplant (HCT), but whose age (typically older than 55 years) or comorbidities (eg, liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy) preclude use of a standard conditioning regimen.

In patients who qualify for a myeloablative allogeneic hematopoietic HCT on the basis of overall health and disease status, allogeneic HCT using either myeloablative or RIC may be considered. However, a myeloablative conditioning regimen with allogeneic HCT may benefit younger patients with good performance status and minimal comorbidities more than allogeneic HCT with RIC.

Coding

Code	Description
CPT	
38230	Bone marrow harvesting for transplantation; allogeneic
38232	Bone marrow harvesting for transplantation; autologous
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
38241	Hematopoietic progenitor cell (HPC); autologous transplantation
HCPCS	
S2140	Cord blood harvesting for transplantation, allogeneic
S2142	Cord blood-derived stem-cell transplantation, allogeneic
S2150	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

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

The ages stated in this policy for which reduced intensity conditioning would be considered an option in patients who meet other criteria for an allogeneic HSCT are based on the risk factors defined by the International Prognostic Index. See Evidence Review section and NCCN.

Definition of Terms

Allogeneic 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.

Autologous HCT: This involves the administration of cytotoxic chemotherapy with or without radiation to eradicate cancerous cells from the blood and bone marrow. It is typically performed as consolidation therapy when the patient’s disease is in complete remission.

Chemo-sensitive relapse: This is defined as relapsed non-Hodgkin lymphoma (NHL) that does not progress during or immediately after standard-dose induction chemotherapy (ie, achieves stable disease or a partial response).

Complete remission (CR): This is the disappearance of all the signs of cancer in response to treatment. Also called complete response.

Consolidation therapy: This is treatment that is given after cancer has disappeared following initial therapy with the goal of killing any cancer cells that may be left in the body. Also referred to as intensification therapy and post-remission therapy.

Disease-free survival: This is the length of time after primary treatment for a cancer that the patient survives free of any signs or symptoms of the cancer being treated. Also called relapse-free survival.

First-line therapy: This is the first treatment given for a disease and is often part of a standard set of treatments, which may include surgery followed by chemotherapy and radiation.

Hematopoietic stem-cell transplantation (HCT): This refers to a procedure in which hematopoietic cells are infused to restore bone marrow function in cancer patients who receive bone-marrow-toxic doses of cytotoxic drugs with or without whole-body radiation therapy.



Hematopoietic cells may be obtained from the transplant recipient (autologous HCT) or from a donor (allogeneic HCT).

International Prognostic Index (IPI): This model was developed for predicting outcomes in patients with aggressive non-Hodgkin's lymphoma based on the patients' clinical characteristics before treatment.

Myeloablative chemotherapy: This is high-dose chemotherapy that kills all cells in the bone marrow, including the cancer cells. It is generally followed by bone marrow or stem-cell transplant to rebuild the bone marrow.

Reduced-intensity conditioning (RIC): This 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.

Relapse: The return of a disease or the signs and symptoms after a period of improvement.

Salvage therapy: Chemotherapy given to patients who have either (1) failed to achieve complete remission after initial treatment for newly diagnosed lymphoma, or (2) relapsed after an initial complete remission.

Tandem transplants: These are usually defined as the planned administration of 2 successive cycles of high-dose myeloablative chemotherapy, each followed by infusion of autologous hematopoietic cells, whether or not there is evidence of persistent disease following the first treatment cycle. Sometimes, the second cycle may use non-myeloablative immunosuppressive conditioning followed by infusion of allogeneic cells.

Transformation: This term describes a lymphoma whose histologic pattern has evolved to a higher-grade lymphoma. Transformed lymphomas typically evolve from a nodular pattern to a diffuse pattern.

High-Risk (Aggressive) T-Cell and NK-Cell Neoplasms:

The T-cell and NK-cell neoplasms are a clinically heterogeneous group of rare disorders, most of which have an aggressive clinical course and poor prognosis. The exception would include the following subtypes which typically have a relatively indolent and protracted course:

- T-cell large granulocyte leukemia (T-LGL),
- Chronic lymphoproliferative disorder of NK cells,



- Early stage mycosis fungoides,
- Primary cutaneous ALCL, and
- ALK+ ALCL.¹¹

Benefit Application

The following considerations may supersede this policy:

- State mandates requiring coverage for autologous 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 chemotherapy, including autologous bone marrow transplantation.
- Some contracts or certificates of coverage (eg, FEP) may include specific conditions in which autologous bone marrow transplantation would be considered eligible for coverage.

Evidence Review

Description

Hematopoietic stem-cell transplantation (HCT) refers to a procedure in which hematopoietic cells are infused to restore bone marrow function in cancer patients who receive bone-marrow-toxic doses of cytotoxic drugs, with or without whole-body radiation therapy. Hematopoietic cells may be obtained from the transplant recipient (autologous HCT) or from a donor (allogeneic HCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates. Although cord blood is an allogeneic source, the cells in it are antigenically “naïve” and thus are associated with a lower incidence of rejection or graft-versus-host disease (GVHD). Cord blood is discussed in greater detail in another medical policy (see [Related Policies](#)).



Background

Non-Hodgkin Lymphoma

A heterogeneous group of lymphoproliferative malignancies, non-Hodgkin lymphoma (NHL) usually originates in lymphoid tissue. Historically, uniform treatment of patients with NHL was hampered by the lack of a uniform classification system. In 1982, the Working Formulation was developed to unify different classification systems into one.¹ The Working Formulation divided NHL into low-, intermediate-, and high-grade, with subgroups based on histologic cell type. Because our understanding of NHL has improved, the diagnosis has become more sophisticated and includes the incorporation of new immunophenotyping and genetic techniques. As a result, the Working Formulation has become outdated.

European and American pathologists proposed a new classification, the Revised European-American Lymphoma (REAL) Classification² and an updated version of the REAL system, the new World Health Organization (WHO) classification.³ The WHO/REAL classification recognized three major categories of lymphoid malignancies based on morphology and cell lineage: B-cell neoplasms, T-cell/natural killer (NK) cell neoplasms, and Hodgkin lymphoma.

The most recent lymphoma classification is the 2016 WHO classification (see [Table 2](#)).⁴

Table 2. Updated WHO Classification (2016)

Classification of Non-Hodgkin Lymphoma	
Mature B-cell neoplasms	Chronic lymphocytic leukemia/small lymphocytic lymphoma
	Monoclonal B-cell lymphocytosis ^a
	B-cell prolymphocytic leukemia
	Splenic marginal zone lymphoma
	Hairy cell leukemia
	<i>Splenic lymphoma/leukemia, unclassifiable</i>
	<i>Splenic diffuse red pulp small B-cell lymphoma</i>
	<i>Hairy cell leukemia-variant</i>
	Lymphoplasmacytic lymphoma
	Waldenström macroglobulinemia
	Monoclonal gammopathy of undetermined significance, IgM ^a



Classification of Non-Hodgkin Lymphoma

Heavy chain diseases
Alpha heavy chain disease
Gamma heavy chain disease
Mu heavy chain disease
Monoclonal gammopathy of undetermined significance, IgG/IgA ^a
Plasma cell myeloma
Solitary plasmacytoma of bone
Extrasosseous plasmacytoma
Monoclonal immunoglobulin deposition diseases ^a
Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
Nodal marginal zone lymphoma (MZL)
<i>Pediatric nodal MZL</i>
Follicular lymphoma
<i>In situ follicular neoplasia^a</i>
<i>Duodenal-type follicular lymphoma^a</i>
Pediatric type follicular lymphoma ^a
<i>Large B-cell lymphoma with IRF4 rearrangement^a</i>
Primary cutaneous follicle center lymphoma
Mantle cell lymphoma
<i>In situ mantle cell neoplasia^a</i>
Diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS)
<i>Germinal center B-cell type^a</i>
<i>Activated B-cell type^a</i>
T-cell/histiocyte-rich large B-cell lymphoma
DLBCL associated with chronic inflammation
Lymphomatoid granulomatosis
Primary mediastinal (thymic) large B-cell lymphoma
Intravascular large B-cell lymphoma
<i>Primary cutaneous DLBCL, leg type</i>
ALK [anaplastic lymphoma kinase]-positive large B-cell lymphoma



Classification of Non-Hodgkin Lymphoma

	Plasmablastic lymphoma
	Primary effusion lymphoma
	<i>HHV8 DLBCL NOS^a</i>
	Burkitt lymphoma
	<i>Burkitt-like lymphoma with 11q aberration^a</i>
	High-grade B-cell lymphoma, with <i>MYC</i> and <i>BCL2</i> and/or <i>BCL6</i> rearrangements ^a
	High-grade B-cell lymphoma, NOS ^a
	B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma
Mature T-cell and NK-cell neoplasms	T-cell prolymphocytic leukemia
	T-cell large granular lymphocytic leukemia
	<i>Chronic lymphoproliferative disorder of NK cells</i>
	Aggressive NK-cell leukemia
	Systemic Epstein-Barr virus-positive T-cell lymphoproliferative of childhood ^a
	Hydroa vacciniforme-like lymphoproliferative disorder ^a
	Adult T-cell leukemia/ lymphoma
	Extranodal NK/T-cell lymphoma, nasal type
	Enteropathy-associated T-cell lymphoma
	Monomorphic epitheliotropic intestinal T-cell lymphoma ^a
	<i>Indolent T-cell lymphoproliferative disorder of the GI tract^a</i>
	Hepatosplenic T-cell lymphoma
	Subcutaneous panniculitis-like T-cell lymphoma
	Mycosis fungoides
	Sézary syndrome
	Primary cutaneous CD30-positive T-cell lymphoproliferative disorder
	Lymphomatoid papulosis
	Primary cutaneous anaplastic large-cell lymphoma
	Primary cutaneous gamma-delta T-cell lymphoma
	<i>Primary cutaneous aggressive epidermotropic CD8-positive cytotoxic T-cell lymphoma^a</i>
<i>Primary cutaneous acral CD8+ T-cell lymphoma^a</i>	
<i>Primary cutaneous small/medium CD4-positive T-cell lymphoproliferative disorder^a</i>	



Classification of Non-Hodgkin Lymphoma

	Peripheral T-cell lymphoma, NOS
	Angioimmunoblastic T-cell lymphoma
	<i>Follicular T-cell lymphoma^a</i>
	<i>Nodal peripheral T-cell lymphoma with TFH phenotype^a</i>
	Anaplastic large-cell lymphoma (ALCL), ALK-positive
	Anaplastic large-cell lymphoma (ALCL), ALK-negative ^a
	<i>Breast implant-associated anaplastic large-cell lymphoma^a</i>

ALK: anaplastic lymphoma kinase; NK: natural killer.

^a Changes from 2008 WHO classification. Provisional entities are listed in italics.

In the U.S., B-cell lymphomas represent 80% to 85% of cases of NHL, and T-cell lymphomas represent 15% to 20%. NK lymphomas are relatively rare.⁵

The International Lymphoma Classification Project identified the most common NHL subtypes as follows: diffuse large B-cell lymphoma (DLBCL) 31%, follicular lymphoma (FL) 22%, small lymphocytic lymphoma/chronic lymphocytic leukemia (SLL/CLL) 6%, mantle cell lymphoma (MCL) 6%, peripheral T-cell lymphoma (PTCL) 6%, and marginal zone B-cell lymphoma/MALT lymphoma 5%. All other subtypes each represent less than 2% of cases of NHL.⁵

Types of NHL

In general, the NHL can be divided into two prognostic groups, indolent and aggressive. Indolent NHL has a relatively good prognosis, with a median survival of 10 years; however, it is not curable in advanced clinical stages.¹ Early stage indolent NHL (stage 1 or 2) may be effectively treated with radiation alone.¹ Although indolent NHL is responsive to radiation and chemotherapy, a continuous rate of relapse is seen in advanced stages.¹ These patients can often be re-treated if their disease remains of the indolent type. Indolent NHL may transform into a more aggressive form, which is generally treated with regimens that are used for aggressive, recurrent NHL. Histologic transformation to higher grade lymphoma occurs in up to 70% of patients with low-grade lymphoma,⁶ and median survival with conventional chemotherapy is 1 year or less.

Follicular lymphoma (FL) is the most common indolent NHL (70%-80% of cases), and often the terms indolent lymphoma and FL are used synonymously. Also included in the indolent NHL are



SLL/CLL, lymphoplasmacytic lymphoma, marginal zone lymphomas, and cutaneous T-cell lymphoma.

Aggressive NHL has a shorter natural history; however, 30% to 60% of these patients can be cured with intensive combination chemotherapy regimens.¹ Aggressive lymphomas include DLBCL, MCL, PTCL, anaplastic large cell lymphoma, and Burkitt lymphoma.

Risk Assessment

Oncologists developed a clinical tool to aid in predicting the prognosis of patients with aggressive NHL (specifically DLBCL), referred to as the International Prognostic Index (IPI).⁷ Prior to the development of IPI in 1993, prognosis was predominantly based on disease stage.

Based on the number of risk factors present and adjusted for patient age, the IPI defines 4 risk groups: low, low intermediate, high intermediate, and high risk, based on 5 significant risk factors prognostic of overall survival (OS):

1. Age older than 60 years
2. Elevated serum lactate dehydrogenase (LDH) level
3. Ann Arbor stage III or IV disease
4. Eastern Cooperative Oncology Group (ECOG) performance status of 2, 3, or 4
5. Involvement of more than 1 extranodal site

Risk groups are stratified according to the number of adverse factors as follows: 0 or 1 is low risk, 2 is low intermediate, 3 is high intermediate, and 4 or 5 are high risk.

Patients with 2 or more risk factors have a less than 50% chance of relapse-free survival (RFS) and OS at 5 years. Age-adjusted IPI and stage-adjusted modifications of this IPI are used for younger patients with localized disease.

Adverse risk factors for age-adjusted IPI include stage III or IV disease, elevated LDH and ECOG performance status of 2 or greater and can be calculated as follows: 0 is low risk, 1 is low intermediate, 2 is high intermediate, and 3 is high risk.

With the success of the IPI, a separate prognostic index was developed for FL, which has multiple independent risk factors for relapse after a first complete remission. The proposed and



validated Follicular Lymphoma International Prognostic Index (FLIPI) contains 5 adverse prognostic factors:

1. Age older than 60 years
2. Ann Arbor stage III–IV
3. Hemoglobin level less than 12.0 g/dL
4. More than 4 lymph node areas involved
5. Elevated serum LDH level

These 5 factors are used to stratify patients into 3 categories of risk: low (0-1 risk factor), intermediate (2 risk factors), or poor (3 or more risk factors).⁸

Mantle Cell Lymphoma

Mantle Cell Lymphoma (MCL) comprises approximately 65% to 68% of NHL and has been recognized within the past 15 years as a unique lymphoma subtype with a particularly aggressive course. MCL is characterized by a chromosomal translocation t(11;14), and the term mantle cell lymphoma was proposed in 1992 by Banks et al.⁹ The number of therapeutic trials is not as numerous for MCL as for other NHL, as it was not widely recognized until the REAL classification. MCL shows a strong predilection for elderly men, and the majority of cases (70%) present with disseminated (stage 4) disease and extranodal involvement is common. Localized MCL is quite rare. MCL has a median survival of approximately 2 to 4 years, and although most patients achieve remission with first -line therapy, relapse inevitably occurs, often within 12 to 18 months. MCL is rarely, if ever, cured with conventional therapy, and no standardized therapeutic approach to MCL is used.

Risk Assessment

There had been no generally established prognostic index for patients with MCL. Application of the IPI or FLIPI system to patients with MCL showed limitations, which included no separation of some important risk groups. In addition, some of the individual IPI and FLIPI risk factors, including number of extranodal sites and number of involved nodal areas showed no prognostic relevance, and hemoglobin showed no independent prognostic relevance in patients with MCL.¹⁰ Therefore, a new prognostic index for patients with MCL was developed and should prove useful in comparing clinical trial results for MCL.



The MCL International Prognostic Index (MIPI) is based on the following risk factors prognostic for overall survival.

1. Age
2. ECOG performance status
3. Serum LDH (calculated as a ratio of LDH to a laboratory's upper limit of normal)
4. White blood cell (WBC) count
 - Zero points each are assigned for age younger than 50 years, ECOG performance 0-1, LDH ratio less than 0.67, WBC less than 6700
 - One point each for age 50 to 59 years, LDH ratio 0.67-0.99, WBC 6700-9999
 - Two points each for age 60 to 69 years, ECOG 2-4, LDH ratio 1.00-1.49, WBC 10,000-14,999
 - Three points each for age 70 years or older, LDH ratio 1.5 or greater, WBC 15,000 or more

MIPI allows separation of 3 groups with significantly different prognoses¹⁰:

- 0-3 points=low risk, 44% of patients, median OS not reached and a 5-year OS rate of 60%
- 4-5 points=intermediate risk, 35% of patients, median OS, 51 months
- 6-11 points=high risk, 21% of patients, median OS, 29 months

Peripheral T-Cell Lymphoma (PTCL)

The majority of peripheral T-cell lymphomas are aggressive and fall into the category of PTCL, unspecified (PTCL-u) or not otherwise specified (PTCL-NOS), angioimmunoblastic or anaplastic large cell which, combined make up approximately 60% to 70% of T-cell lymphomas. PTCLs are less responsive to standard chemotherapy than DLBCLs and carry a worse prognosis than aggressive Bcell counterparts. Survival rates at 5 years with standard chemotherapy regimens range from 20% to 35%. The poor results with conventional chemotherapy have prompted exploration of the role of HCT as therapy.



Staging

The Ann Arbor staging classification is commonly used for the staging of lymphomas and is the scheme defined in the American Joint Committee on Cancer (AJCC) Manual for Staging Cancer. Originally developed for Hodgkin disease, this staging scheme was later expanded to include non-Hodgkin lymphoma.

Table 3. Ann Arbor Classification

Stage	Involvement
I	Involvement of a single lymph node region (I) or of a single extralymphatic organ or site (IE)
II	Involvement of 2 or more lymph node regions on the same side of the diaphragm (II) or localized involvement of extralymphatic organ or site and of one or more lymph node regions on the same side of the diaphragm (IIE)
III	Involvement of lymph node regions on both sides of the diaphragm (III), which may also be accompanied by localized involvement of extralymphatic organ or site (IIIE) or by involvement of the spleen (IIIS) or both (IIISE)
IV	Diffuse or disseminated involvement of one or more extralymphatic organs or tissues with or without associated lymph node enlargement

Treatment for NHL

Hematopoietic Cell Transplantation

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 with allogeneic HCT. Compatibility is established by typing of human leukocyte antigens (HLAs) 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 (with the exception of umbilical cord blood).

Conventional Preparative Conditioning for HCT

The conventional practice of allogeneic HCT involves administration of cytotoxic agents (eg, cyclophosphamide, busulfan) with or without total body irradiation; this is performed at doses



sufficient to destroy endogenous hematopoietic capability in the recipient. The beneficial treatment effect of this procedure is due to a combination of initial eradication of malignant cells and subsequent graft-versus-malignancy effect that is mediated by non-self-immunologic effector cells that develop after engraftment of allogeneic stem cells within the patient's bone marrow space. While the slower graft-versus-malignancy effect is considered the potentially curative component, it may be overwhelmed by extant disease without the use of pretransplant conditioning. However, intense conditioning regimens are limited to patients who are medically fit to tolerate substantial adverse events that include preengraftment 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, immunosuppressant drugs are required to minimize graft rejection and graft-versus-host disease, which also increase susceptibility to opportunistic infections. The immune reactivity between donor T cells and malignant cells is responsible for the graft-versus-malignancy effect; it also leads to acute and chronic graft-versus-host disease.

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 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 Allogeneic 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 2-fold: to reduce disease burden, and to minimize treatment-related morbidity and nonrelapse 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 nonrelapse mortality and relapse due to residual disease. RIC regimens can be viewed as a continuum—from nearly totally myeloablative to minimally myeloablative with lymphoablation—because it tailors its intensity 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 evidence review, reduced-intensity conditioning will refer to all conditioning regimens intended to be nonmyeloablative, as opposed to fully myeloablative (traditional) regimens.

Summary of Evidence

For individuals who have indolent B-cell non-Hodgkin lymphomas who receive autologous HCT as first-line therapy, the evidence includes randomized trials and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related mortality and morbidity. Randomized trials have not shown a survival advantage with HCT as first-line therapy for indolent B-cell lymphomas; however, randomized studies have shown a survival benefit for relapsed disease. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have aggressive B-cell non-Hodgkin lymphomas who receive autologous HCT as consolidation therapy after first complete remission, the evidence includes randomized trials and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related mortality and morbidity. While the data from the randomized trials offer conflicting results, some of the data has revealed an overall survival benefit in patients with aggressive B-cell lymphomas (at high or high-intermediate risk of relapse) who receive HCT to consolidate a first complete remission. Randomized studies of HCT for relapsed aggressive B-cell lymphomas have shown an overall survival benefit with the previously described approach. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have non-Hodgkin lymphomas who receive tandem autologous and allogeneic HCT, the evidence includes several nonrandomized trials. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related mortality and morbidity. No randomized studies have been conducted on the use of tandem HCT for the treatment of non-Hodgkin lymphoma, and the published evidence comprises a limited number of patients. Presently, conclusions on the use of tandem transplants cannot be made about autologous and allogeneic HCT. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have mantle cell lymphoma who receive autologous, allogeneic, or tandem HCT, the evidence includes case series. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related mortality and morbidity. Due in part to the rarity of this disease, randomized trials on the use of HCT in mantle cell



lymphoma have not been conducted. Case series have shown long-term disease control of this aggressive lymphoma with autologous HCT (with rituximab) to consolidate a first remission; however, the use of autologous HCT in the relapsed setting has not shown improved outcomes. Allogeneic HCT has shown prolonged disease control in the relapsed or refractory setting. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have peripheral T-cell lymphoma (PTCL) who receive autologous or allogeneic HCT, the evidence includes prospective trials and case reports. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related mortality and morbidity. The role of HCT in PTCL is not well-defined. Few studies have been conducted, and most were performed retrospectively, with a limited number of patients; further the patient populations were heterogeneous and included good- and poor-risk patients in the same study. Patient population and characteristics of the studies can be explained partially by the rarity and heterogeneity of the particular group of lymphomas in which the study addresses. Additionally, studies of this nature often mix of three types of patients: one type of patient has PTCL not otherwise specified, which has a poorer prognosis; another type has anaplastic lymphoma kinase (ALK)-positive anaplastic large-cell lymphomas (ALCL), which has a better prognosis—even with conventional chemotherapy regimens; and a third type has ALK-negative ALCL, which has a worse prognosis than ALK-positive ALCL (but better than patients with PTCL not otherwise specified). There have been no randomized studies comparing chemotherapy regimens solely in patients with PTCL (ie, some randomized studies have included PTCL with aggressive B-cell lymphomas). For front-line therapy, results from recent phase 2 studies with autologous HCT as consolidation offers the best survival outcomes for patients with high-risk features; randomized trials to confirm this have not been performed. No relevant data for the use of allogeneic HCT in the first-line setting are available. Patients with relapsed or refractory PTCL are generally considered incurable with chemotherapy alone. In the salvage setting, data have shown that the use of HCT may improve survival outcomes similar to the results seen in corresponding aggressive B-cell lymphomas in the same treatment setting. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Practice Guidelines and Position Statements

*National Comprehensive Cancer Network Guidelines*⁶⁶

Current National Comprehensive Cancer Network guidelines on B-cell lymphomas (v.3.2017) include the following recommendations⁶⁵:



Second-line chemotherapy ... followed by high-dose therapy and autologous HSCT [hematopoietic stem cell transplantation] or allogeneic HSCT ... may be considered in selected patients with a reasonable remission duration.”

National Comprehensive Cancer Network guidelines on T-cell lymphomas (v.2.2017) include the following recommendations⁶⁶:

Second-line systematic therapy followed by consolidation with HDT [high-dose therapy]/ASCR [autologous stem cell rescue] or allogeneic HSCT for those with a CR [complete response] or PR [partial response] is recommended for patients who are candidates for transplant.

Allogeneic HSCT (using myeloablative or non-myeloablative conditioning) may improve outcomes for some patients with ATLL [adult T-cell leukemia/lymphoma].

Although the available data are based on retrospective evaluations, allogeneic HSCT may be the best chance for long-term disease control in a subgroup of patients with T-PLL [T-cell prolymphocytic leukemia]. Only limited data have been published on the use of autologous HSCT in patients with T-PLL.

Regulatory Status

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

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History

Date	Comments
04/14/14	New PR policy; replaces 8.01.20. Policy updated with literature search through December 23, 2013. Policy section reworded and reformatted. Policy statements changed as follows: NHL B-cell – RIC is now medically necessary; B-cell Indolent – RIC is now investigational (previously medically necessary); Mature T-cell or NK – RIC is now investigational to consolidate CR (previously medically necessary). References 37 and 42 added; reference 66 updated.
06/24/14	Update Related Policies. Remove 8.01.35, 8.01.42 and 8.01.54, then add 8.01.532
12/03/14	Update Related Policies. Remove 8.01.17 and 8.01.26.



Date	Comments
04/24/15	Annual Review. Policy updated with literature review; no change in policy statements.
08/09/16	Update Related Policies. Remove 8.01.27 as it was archived.
11/04/16	Coding update. Removed codes that are transplant benefit related.
12/01/16	Annual review, approved November 8, 2016. Added references 68 and 69. No changes to policy statement.
04/01/17	Updated titles in Related Policies.
08/01/17	Updated title of Related Policy 8.01.511.
12/01/17	Annual Review, approved November 9, 2017. Updated WHO classifications and Summary of Evidence section. No changes to policy statement.
05/01/18	Annual Review, approved April 3, 2018. Policy updated with literature review through November 2017. Policy statements unchanged.
09/01/18	Minor update. Re-adding Consideration of Age information which was inadvertently removed during a previous update.

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ይህ ማስታወቂያ አስፈላጊ መረጃ ይዟል። ይህ ማስታወቂያ ስለ ማመልከቻዎ ወይም የ Premera Blue Cross ሽፋን አስፈላጊ መረጃ ሊኖረው ይችላል። በዚህ ማስታወቂያ ውስጥ ቁልፍ ቀናት ሊኖሩ ይችላሉ። የጤና ሽፋንዎን ለመጠበቅና በአስፋፈል እርዳታ ለማግኘት በተውሰኑ የጊዜ ገደቦች እርምጃ መውሰድ ይገባዎት ይሆናል። ይህን መረጃ እንዲያገኙ እና የለምንም ክፍያ በቋንቋዎ እርዳታ እንዲያገኙ መሰታ አለዎት። በስልክ ቁጥር 800-722-1471 (TTY: 800-842-5357) ይደውሉ።

العربية (Arabic):

يحتوي هذا الإشعار على معلومات هامة. قد يحوي هذا الإشعار معلومات مهمة بخصوص طلبك أو التغطية التي تزيد الحصول عليها من خلال Premera Blue Cross. قد تكون هناك تواريخ مهمة في هذا الإشعار. وقد تحتاج لاتخاذ إجراء في تاريخ معينه للحفاظ على تغطيتك الصحية أو المساعدة في دفع التكاليف. يحق لك الحصول على هذه المعلومات والمساعدة بلغتك دون تكبد أية تكلفة. اتصل بـ 800-722-1471 (TTY: 800-842-5357)

中文 (Chinese):

本通知有重要的訊息。本通知可能有關於您透過 Premera Blue Cross 提交的申請或保險的重要訊息。本通知內可能有重要日期。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者費用補貼。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)。

Oromoo (Cushite):

Beeksisni kun odeeffannoo barbaachisaa qaba. Beeksisti kun sagantaa yookan karaa Premera Blue Cross tiin tajaajila keessan ilaalchisee odeeffannoo barbaachisaa qabaachuu danda'a. Guyyaawwan murteessaa ta'an beeksisa kana keessatti ilaalaa. Tarii kaffaltiidhaan deeggaramuuf yookan tajaajila fayyaa keessaniif guyyaa dhumaa irratti wanti raawwattan jiraachuu danda'a. Kaffaltii irraa bilisa haala ta'een afaan keessaniin odeeffannoo argachuu fi deeggarsa argachuuf mirga ni qabaattu. Lakkoofsa bilbilaa 800-722-1471 (TTY: 800-842-5357) tii bilbilaa.

Français (French):

Cet avis a d'importantes informations. Cet avis peut avoir d'importantes informations sur votre demande ou la couverture par l'intermédiaire de Premera Blue Cross. Le présent avis peut contenir des dates clés. Vous devez peut-être prendre des mesures par certains délais pour maintenir votre couverture de santé ou d'aide avec les coûts. Vous avez le droit d'obtenir cette information et de l'aide dans votre langue à aucun coût. Appelez le 800-722-1471 (TTY: 800-842-5357).

Kreyòl ayisyen (Creole):

Avi sila a gen Enfòmasyon Enpòtan ladann. Avi sila a kapab genyen enfòmasyon enpòtan konsènan aplikasyon w lan oswa konsènan kouvèti asirans lan atravè Premera Blue Cross. Kapab genyen dat ki enpòtan nan avi sila a. Ou ka gen pou pran kèk aksyon avan sèten dat limit pou ka kenbe kouvèti asirans sante w la oswa pou yo ka ede w avèk depans yo. Se dwa w pou resewva enfòmasyon sa a ak asistans nan lang ou pale a, san ou pa gen pou peye pou sa. Rele nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):

Diese Benachrichtigung enthält wichtige Informationen. Diese Benachrichtigung enthält unter Umständen wichtige Informationen bezüglich Ihres Antrags auf Krankenversicherungsschutz durch Premera Blue Cross. Suchen Sie nach eventuellen wichtigen Terminen in dieser Benachrichtigung. Sie könnten bis zu bestimmten Stichtagen handeln müssen, um Ihren Krankenversicherungsschutz oder Hilfe mit den Kosten zu behalten. Sie haben das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Rufen Sie an unter 800-722-1471 (TTY: 800-842-5357).

Hmoob (Hmong):

Tsawb ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb. Tej zaum tsawb ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb txog koj daim ntawv thov kev pab los yog koj qhov kev pab cuam hnu ntawm Premera Blue Cross. Tej zaum muaj cov hnuv tseem ceeb uas sau rau hauv daim ntawv no. Tej zaum koj kuj yuav tau ua qee yam uas pab kom koj ua tsis pub dhau cov caij nyoog uas teev tseg rau hauv daim ntawv no mas koj thiaj yuav tau txais kev pab cuam kho mob los yog kev pab them tej nqi kho mob ntawd. Koj muaj cai kom lawv muab cov ntshiab lus no uas tau muab sau ua koj hom lus pub dawb rau koj. Hu rau 800-722-1471 (TTY: 800-842-5357).

Iloko (Ilocano):

Daytoy a Pakdaar ket naglaon iti Napateg nga Impormasion. Daytoy a pakdaar mabalin nga adda ket naglaon iti napateg nga impormasion maipanggep iti aplikasyonyo wenna coverage babaen iti Premera Blue Cross. Daytoy ket mabalin dagiti importante a petsa iti daytoy a pakdaar. Mabalin nga adda rumbeng nga aramidenyo nga addang sakbay dagiti partikular a naituding nga aldaw tapno mapagtalinaedyo ti coverage ti salun-ato wenna tulong kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga impormasion ken tulong iti bukodyo a pagsasao nga awan ti bayadanyo. Tumawag iti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):

Questo avviso contiene informazioni importanti. Questo avviso può contenere informazioni importanti sulla tua domanda o copertura attraverso Premera Blue Cross. Potrebbero esserci date chiave in questo avviso. Potrebbe essere necessario un tuo intervento entro una scadenza determinata per consentirti di mantenere la tua copertura o sovvenzione. Hai il diritto di ottenere queste informazioni e assistenza nella tua lingua gratuitamente. Chiama 800-722-1471 (TTY: 800-842-5357).

日本語 (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 の申請または補償範囲に関する重要な情報が含まれている場合があります。この通知に記載されている可能性がある重要な日付をご確認ください。健康保険や有料サポートを維持するには、特定の期日までに行動を取らなければならない場合があります。ご希望の言語による情報とサポート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。

한국어 (Korean):

본 통지서에는 중요한 정보가 들어 있습니다. 즉 이 통지서는 귀하의 신청에 관하여 그리고 Premera Blue Cross 를 통한 커버리지에 관한 정보를 포함하고 있을 수 있습니다. 본 통지서에는 핵심이 되는 날짜들이 있을 수 있습니다. 귀하의 건강 커버리지를 계속 유지하거나 비용을 절감하기 위해서 일정한 마감일까지 조치를 취해야 할 필요가 있을 수 있습니다. 귀하의 이러한 정보와 도움을 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 800-722-1471 (TTY: 800-842-5357) 로 전화하십시오.

ລາວ (Lao):

ແຈງການນີ້ມີຂໍ້ມູນສໍາຄັນ. ແຈງການນີ້ອາດຈະມີຂໍ້ມູນສໍາຄັນກ່ຽວກັບຄໍາຮ້ອງສະໝັກ ຫຼື ຄວາມຄົມຄອງປະກັນໄພຂອງທ່ານຜ່ານ Premera Blue Cross. ອາດຈະມີວັນທີ່ສໍາຄັນໃນແຈງການນີ້. ທ່ານອາດຈະຈຳເປັນຕ້ອງດໍາເນີນການຕາມກຳນົດ ເວລາສະເພາະເພື່ອຮັກສາຄວາມຄົມຄອງປະກັນສະພາບ ຫຼື ຄວາມຊ່ວຍເຫຼືອເວັ້ນເວົ້ອງຄ່າໃຊ້ຈ່າຍຂອງທ່ານໄດ້. ທ່ານມີສິດໄດ້ຮັບຂໍ້ມູນນີ້ ແລະ ຄວາມຊ່ວຍເຫຼືອເປັນພາສາຂອງທ່ານໂດຍບໍ່ເສຍຄ່າ. ໃຫ້ໃບທາ 800-722-1471 (TTY: 800-842-5357).

ភាសាខ្មែរ (Khmer):

សេចក្តីជូនដំណឹងនេះមានព័ត៌មានយ៉ាងសំខាន់។ សេចក្តីជូនដំណឹងនេះប្រហែលជាមានព័ត៌មានយ៉ាងសំខាន់អំពីទម្រង់បែបបទ ឬការរៀបចំរបស់អ្នកកាមរយ: Premera Blue Cross ។ ប្រហែលជាមាន កាលបរិច្ឆេទសំខាន់នៅក្នុងសេចក្តីជូនដំណឹងនេះ។ អ្នកប្រហែលជាត្រូវការបញ្ជាក់សមត្ថភាព ដល់កិច្ចការផ្ទៃក្នុងដូចជា ឆ្លើយតបនឹងសំណួរ ឬប្រាកដថា អ្នកបានអាននូវព័ត៌មាននេះ និងដំណើរការនៅក្នុងភាសារបស់អ្នកដោយមិនអស់លុយឡើយ។ សូមទូរស័ព្ទ 800-722-1471 (TTY: 800-842-5357)។

ਪੰਜਾਬੀ (Punjabi):

ਇਸ ਨੋਟਿਸ ਵਿਚ ਖਾਸ ਜਾਣਕਾਰੀ ਹੈ. ਇਸ ਨੋਟਿਸ ਵਿਚ Premera Blue Cross ਵਲੋਂ ਤੁਹਾਡੀ ਕਵਰੇਜ ਅਤੇ ਅਰਜੀ ਬਾਰੇ ਮਹੱਤਵਪੂਰਨ ਜਾਣਕਾਰੀ ਹੋ ਸਕਦੀ ਹੈ . ਇਸ ਨੋਟਿਸ ਨਵ ਖਾਸ ਤਾਰੀਖਾਂ ਹੋ ਸਕਦੀਆਂ ਹਨ. ਜੇਕਰ ਤੁਸੀਂ ਜਸਰਤ ਕਵਰੇਜ ਰਿੱਖਣੀ ਹੋਵੇ ਜਾਂ ਓਸ ਦੀ ਲਾਗਤ ਜਵਿੱਚ ਮਦਦ ਦੇ ਇਕੱਠ ਹੋ ਤਾਂ ਤੁਹਾਨੂੰ ਅੰਤਮ ਤਾਰੀਖ ਤੋਂ ਪਹਿਲਾਂ ਢੁੱਝ ਖਾਸ ਕਰਮ ਚੁੱਕਣ ਦੀ ਲੋੜ ਹੋ ਸਕਦੀ ਹੈ ,ਤੁਹਾਨੂੰ ਮੁਫਤ ਵਿੱਚ ਤੋਂ ਅਪਣੀ ਭਾਸ਼ਾ ਵਿੱਚ ਜਾਣਕਾਰੀ ਅਤੇ ਮਦਦ ਪ੍ਰਾਪਤ ਕਰਨ ਦਾ ਅਧਿਕਾਰ ਹੈ ,ਕਾਲ 800-722-1471 (TTY: 800-842-5357).

فارسی (Farsi):

این اعلامیه حاوی اطلاعات مهم میباشد. این اعلامیه ممکن است حاوی اطلاعات مهم درباره فرم تقاضا و یا پوشش بیمه ای شما از طریق Premera Blue Cross باشد. به تاریخ های مهم در این اعلامیه توجه نمایید. شما ممکن است برای حفظ پوشش بیمه تان یا کمک در پرداخت هزینه های درمانی تان، به تاریخ های مشخصی برای انجام کارهای خاصی احتیاج داشته باشید. شما حق این را دارید که این اطلاعات و کمک را به زبان خود به طور رایگان دریافت نمایید. برای کسب اطلاعات با شماره 800-722-1471 (کلیران TTY تماس باشماره 800-842-5357) تماس برقرار نمایید.

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 kluczowe daty, które mogą być zawarte w tym ogłoszeniu aby nie przekroczyć terminów w przypadku utrzymania polisy ubezpieczeniowej lub pomocy związanej z kosztami. Macie Państwo prawo do bezpłatnej informacji we własnym języku. Zadzwońcie 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).

Română (Romanian):

Prezenta notificare conține informații importante. Această notificare poate conține informații importante privind cererea sau acoperirea asigurării dumneavoastră de sănătate prin Premera Blue Cross. Pot exista date cheie în această notificare. Este posibil să fie nevoie să acționați până la anumite termene limită pentru a vă menține acoperirea asigurării de sănătate sau asistența provizorie la costuri. Aveți dreptul de a obține gratuit aceste informații și ajutor în limba dumneavoastră. Sunați la 800-722-1471 (TTY: 800-842-5357).

Русский (Russian):

Настоящее уведомление содержит важную информацию. Это уведомление может содержать важную информацию о вашем заявлении или страховом покрытии через Premera Blue Cross. В настоящем уведомлении могут быть указаны ключевые даты. Вам, возможно, потребуется принять меры к определенным предельным срокам для сохранения страхового покрытия или помощи с расходами. Вы имеете право на бесплатное получение этой информации и помощь на вашем языке. Звоните по телефону 800-722-1471 (TTY: 800-842-5357).

Fa'asamoa (Samoan):

Atonu ua iai i lenei fa'asilasilaga ni fa'amatalaga e sili ona taua e tatau ona e malamalama i ai. O lenei fa'asilasilaga o se fesoasoani e fa'amatala atili i ai i le tulaga o le polokalame, Premera Blue Cross, ua e tau fia maua atu i ai. Fa'amolemole, ia e iloilo fa'alelei i aso fa'apitoa olo'o iai i lenei fa'asilasilaga taua. Masalo o le'a iai ni feau e tatau ona e faia ao le'i aulia le aso ua ta'ua i lenei fa'asilasilaga ina ia e iai pea ma maua fesoasoani mai ai i le polokalame a le Malo olo'o e iai i ai. Olo'o iai iate oe le aia tatau e maua atu i lenei fa'asilasilaga ma lenei fa'matalaga i legagana e te malamalama i ai aunoa ma se togiga tupe. Vili atu i le telefoni 800-722-1471 (TTY: 800-842-5357).

Español (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 o 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).

Tagalog (Tagalog):

Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa pamamagitan ng Premera Blue Cross. Maaaring may mga mahalagang petsa dito sa paunawa. Maaring mangailangan ka na magsagawa ng hakbang sa ilang mga itinakdang panahon upang mapanatili ang iyong pagsakop sa kalusugan o tulong na walang gastos. May karapatan ka na makakuha ng ganiitong impormasyon at tulong sa iyong wika ng walang gastos. Tumawag sa 800-722-1471 (TTY: 800-842-5357).

ไทย (Thai):

ประกาศนี้มีข้อมูลสำคัญ ประกาศนี้อาจมีข้อมูลที่สำคัญเกี่ยวกับกาการสมัครหรือขอบเขตประกันสุขภาพของคุณผ่าน Premera Blue Cross และอาจมีกำหนดการในประกาศนี้ คุณอาจจะต้องดำเนินการภายในกำหนดระยะเวลาที่แน่นอนเพื่อจะรักษาการประกันสุขภาพของคุณหรือการช่วยเหลือที่มีค่าใช้จ่าย คุณมีสิทธิที่จะได้รับข้อมูลและความช่วยเหลือในภาษาของคุณโดยไม่มีค่าใช้จ่าย โทร 800-722-1471 (TTY: 800-842-5357)

Український (Ukrainian):

Це повідомлення містить важливу інформацію. Це повідомлення може містити важливу інформацію про Ваше звернення щодо страховального покриття через Premera Blue Cross. Зверніть увагу на ключові дати, які можуть бути вказані у цьому повідомленні. Існує імовірність того, що Вам треба буде здійснити певні кроки у конкретні кінцеві строки для того, щоб зберегти Ваше медичне страхування або отримати фінансову допомогу. У Вас є право на отримання цієї інформації та допомоги безкоштовно на Вашій рідній мові. Дзвоніть за номером телефону 800-722-1471 (TTY: 800-842-5357).

Tiếng Việt (Vietnamese):

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