PREMERA | BLUE CROSS

MEDICAL POLICY – 8.01.520

Hematopoietic Cell Transplantation for Acute Lymphoblastic Leukemia

BCBSA Ref. Policy:	8.01.32
Effective Date:	May 1, 2018
Last Revised:	April 3, 2018
Replaces:	8.01.32

RELATED MEDICAL POLICIES:

8.01.01	Adoptive Immunotherapy
8.01.26	Hematopoietic Cell Transplantation for Acute Myeloid Leukemia
8.01.30	Hematopoietic Cell Transplantation for Chronic Myelogenous Leukemia

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | CODING | RELATED INFORMATION
EVIDENCE REVIEW | REFERENCES | HISTORY

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Acute lymphocytic leukemia (ALL) is a cancer that starts from a certain form of early white blood cells known as lymphocytes. One way of treating ALL is to do a hematopoietic stem cell transplant.

Hematopoietic stem cells are cells that form within the bone marrow and can become many different types of blood cells. In a hematopoietic stem cell transplant, stem cells can be taken from a donor or the patient before the patient receives high dose chemotherapy. The harvested stem cells are then given to the patient, just like in a transfusion. It is hoped that these new stem cells will then settle into the bone marrow and start producing normal blood cells. If the hematopoietic stem cells are harvested from another person, it is called an allogeneic transplant. If the cells come from the patient, it is called an autologous stem cell transplant. This policy discusses when different types of hematopoietic stem cell transplants might be medically necessary to treat ALL.

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

The use of donor leukocyte infusions to treat relapse after high-dose chemotherapy (HDC) with allogeneic HCT for either children or adults is addressed in a separate medical policy (see **Related Policies**).

Service	Medical Necessity
Autologous or allogeneic HCT for children	**Autologous or allogeneic hematopoietic cell transplantation (HCT) may be considered medically necessary to treat childhood acute lymphoblastic leukemia (ALL) for ANY of the following:** • First complete remission (CR1) but at high risk of relapse (see **Related Information** for high-risk factors) **OR** • Second or greater remission (CR2 or >2) **Allogeneic HCT may be considered medically necessary to treat relapsing ALL after a prior autologous HCT or prior chemotherapy.**
Autologous or allogeneic HCT for adults	**Autologous hematopoietic cell transplantation (HCT) may be considered medically necessary to treat adult acute lymphoblastic leukemia (ALL) in:** • First complete remission (CR1) for any relapse risk level (see **Related Information** for risk factors) **Allogeneic HCT may be considered medically necessary to treat adult ALL for ANY of the following:** • First complete remission (CR1) for any relapse risk level **OR** • Second or greater remission (CR2 or >) **OR** • Relapsing ALL after a prior autologous HCT or prior chemotherapy
Reduced-intensity conditioning allogeneic HCT	**Reduced-intensity conditioning (RIC) allogeneic HCT may be considered medically necessary as a treatment of ALL in patients who are in complete marrow and extramedullary first**

Service	Medical Necessity
	or second remission (CR1 or 2), and who for medical reasons (see Related Information), would be unable to tolerate a standard myeloablative conditioning regimen.

Service	Investigational
Autologous HCT for adults	**Autologous HCT is considered investigational to treat adult ALL for the following:** • Second or greater remission (CR2 or >) **OR** • Those with refractory disease

Coding

Code	Description
CPT	
38230	Bone marrow harvesting for transplantation; allogeneic
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
38241	Hematopoietic progenitor cell (HPC); autologous transplantation
38230	Bone marrow harvesting for transplantation; allogeneic
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 service; 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

Relapse Risk Prognostic Factors

Childhood ALL

Adverse prognostic factors include the following: age younger than one year or older than nine years, male gender, white blood cell count at presentation above 50,000/µL, hypodiploidy (<45 chromosomes), t(9:22) or BCR/ABL fusion, t(4;11) or MLL/AF4 fusion, and ProB or T-lineage immunophenotype. Several risk stratification schema exist, but, in general, the following findings help define children at high risk of relapse: 1) poor response to initial therapy including poor response to prednisone prophase defined as an absolute blast count of 1000/µL or greater, or poor treatment response to induction therapy at six weeks with high risk having ≥1% minimal residual disease measured by flow cytometry), 2) all children with T-cell phenotype and 3) patients with either the t(9;22) or t(4;11) are considered high risk regardless of early response measures.

Adult ALL

Risk factors for relapse are less well defined, but an adult patient with any of the following may be considered at high risk for relapse: age greater than 35 years, leukocytosis at presentation of >30,000/µL (B-cell lineage) and >100,000/µL (T-cell lineage), "poor prognosis" genetic abnormalities like the Philadelphia chromosome (t(9;22)), extramedullary disease and time to attain complete remission longer than 4 weeks.

Reduced Intensity Conditioning (RIC)

Some patients for whom a conventional myeloablative allogeneic HCT could be curative may be considered candidates for RIC allogeneic HCT. These include those whose age (typically older than 60 years) or co morbidities (eg, liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy, low Karnofsky Performance Status) preclude use of a standard myeloablative conditioning regimen.

Note: Unless otherwise specified in the text of this Policy, it is assumed that the term "allogeneic HCT" refers to the use of a myeloablative pretransplant conditioning regimen.

The ideal allogeneic donors are HLA-identical siblings, matched at the LHA-A, B and DR loci (six of six). 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, where usually there is sharing of only three of the six major histocompatibility antigens. The majority of patients will have such a donor; however, the risk of GVHD and overall morbidity of the procedure may be severe, and experience with these donors is not as extensive as that with matched donors.

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 chemotherapies, including autologous bone marrow transplantation.
- Some contracts or certificates of coverage 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 stem 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. Bone-marrow stem cells may be obtained from the transplant recipient (ie, autologous HCT) or from a donor (ie, allogeneic HCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood and placenta shortly after delivery of neonates. Although cord blood is an allogeneic source, the stem 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 a separate policy (see **Related Policies**).

Background

Immunologic compatibility between infused stem cells and the recipient is not an issue in autologous HCT. However, immunologic compatibility between donor and patient is a critical factor for achieving a good outcome of allogeneic HCT. Compatibility is established by typing of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. HLA refers to the tissue type expressed at the HLA A, B, and DR loci on each leg of chromosome 6. Depending on the disease being treated, an acceptable donor will match the patient at all or most of the HLA loci.

Allo-HCT after failed autologous HCT has been shown to be of clinical benefit in other hematologic malignancies and is potentially curative. In addition, clinical input has supported use of allogeneic HCT to treat relapsing ALL after a failed prior autologous HCT, particularly with RIC regimens, in adults or children. Thus, this indication may be considered medically necessary.

Conventional Preparative Conditioning for HCT

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 prior to undergoing bone marrow ablation. As a consequence, autologous HCT is typically performed as consolidation therapy when the patient's disease is in complete remission. Patients who undergo autologous HCT are susceptible to chemotherapy-related toxicities and opportunistic infections prior to engraftment, but not GVHD.

The conventional ("classical") practice of allogeneic HCT involves administration of cytotoxic agents (eg, cyclophosphamide, busulfan) with or without total-body irradiation at doses sufficient to destroy endogenous hematopoietic capability in the recipient. The beneficial treatment effect in this procedure is due to a combination of initial eradication of malignant cells and subsequent graft-versus-malignancy (GVM) effect that develops after engraftment of allogeneic stem cells within the patient's bone marrow space. While the slower GVM effect is considered to be 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 sufficiently fit medically to tolerate substantial adverse effects that include pre-engraftment opportunistic infections secondary to loss of endogenous bone marrow function and organ damage and failure caused by the cytotoxic drugs. Furthermore, in any allogeneic HCT, immune suppressant drugs are required to minimize graft rejection and GVHD, which also increases susceptibility of the patient to opportunistic infections.

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 to reduce disease burden, but also to minimize as much as possible associated treatment-related morbidity and non-relapse mortality (NRM) in the period during which the beneficial GVM effect of allogeneic transplantation develops. Although the definition of RIC remains arbitrary, with numerous versions employed, all seek to balance the competing effects of NRM and relapse due to residual disease. RIC regimens can be viewed as a continuum in effects. They range from being nearly totally myeloablative, to minimally myeloablative with lymphoablation, with the intensity tailored to specific disease 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 the Policy, the term "reduced-intensity conditioning" will refer to all conditioning regimens intended to be non-myeloablative, as opposed to fully myeloablative (conventional) regimens.

Acute Lymphoblastic Leukemia (ALL)

Childhood ALL

ALL is the most common cancer diagnosed in children and represents almost 25% of cancers in children younger than 15 years.[1] Approximately 95% of children with ALL achieve remission with up to 85% long-term survival rates. Survival rates have improved with the identification of effective drugs and combination chemotherapy through large, randomized trials, integration of pre-symptomatic central nervous system prophylaxis, and intensification and risk-based stratification of treatment.[2] The prognosis after first relapse is related to the length of the original remission. For example, leukemia-free survival is 40% to 50% for children whose first remission was longer than 3 years compared to only 10% to 15% for those who relapse less than

3 years after treatment. Thus, hematopoietic cell transplantation (HCT) may be a strong consideration in those with short remissions. At present, the comparative outcomes with autologous or allogeneic HCT are unknown.

ALL is a heterogeneous disease with different genetic alterations resulting in distinct biologic subtypes. Patients are stratified according to certain clinical and genetic risk factors that predict outcome, with risk-adapted therapy tailoring treatment based on the predicted risk of relapse.[3] Two of the most important factors predictive of risk are patient age and white blood cell count (WBC) at diagnosis.[3] Certain genetic characteristics of the leukemic cells strongly influence prognosis. Clinical and biologic factors predicting clinical outcome can be summarized as follows[2]:

Prognostic factor	Favorable	Unfavorable
Age at diagnosis	1-9 years	<1 or >9 years
Sex	Female	Male
WBC count	<50,000/µL	≥50,000/µL
Genotype	Hyperdiploidy (>50 chromosomes) t(12;21) or *TEL/AML1* fusion	Hypodiploidy (<45 chromosomes) t(9:22) or *BCR/ABL* fusion t(4;11) or *MLL/AF4* fusion
Immunophenotype	Common, preB	ProB, Tlineage

Adult ALL

ALL accounts for approximately 20% of acute leukemias in adults. Approximately 60-80% of adults with ALL can be expected to achieve complete remission after induction chemotherapy; however, only 35-40% can be expected to survive two years.[4] Differences in the frequency of genetic abnormalities that characterize adult ALL versus childhood ALL help, in part, to explain the outcome differences between the two groups. For example, the "good prognosis" genetic abnormalities like hyperdiploidy and t(12;21) are seen much less commonly in adult ALL, whereas they are some of the most common in childhood ALL. Conversely, "poor prognosis" genetic abnormalities like the Philadelphia chromosome (t(9;22)) are seen in 25-30% of adult ALL but infrequently in childhood ALL. Other adverse prognostic factors in adult ALL include age greater than 35 years, poor performance status, male sex, and leukocytosis at presentation of >30,000/µL (B-cell lineage) and >100,000/µL (T-cell lineage).

Note: The use of killer (LAK) cells in the treatment of malignancies is addressed in a separate policy (see **Related Policies**).

Summary of Evidence

For individuals who have childhood acute lymphoblastic leukemia (ALL) in their first complete remission at high risk of relapse, subsequent remission, or refractory ALL who receive autologous or allogeneic hematopoietic cell transplantation (HCT), the evidence includes randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, and treatment-related mortality and morbidity. For children with high risk ALL in first complete remission (CR1) or with relapsed ALL, studies have suggested that HCT is associated with fewer relapses but higher death rates due to treatment-related toxicity. However, for a subset of high-risk patients in second complete remission or beyond or with relapsed disease, HCT is a treatment option. This conclusion is further supported by an evidence-based systematic review and position statement from the American Society for Blood and Marrow Transplantation. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have adult ALL in first complete remission or subsequent remission, or refractory ALL who receive autologous or allogeneic HCT, the evidence includes RCTs and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, and treatment-related mortality and morbidity. Current evidence supports the use of autologous HCT for adults with high-risk ALL in first complete remission, or myeloablative allogeneic HCT (allo-HCT) for adults with any risk level ALL, whose health status is sufficient to tolerate the procedure. Reduced-intensity conditioning (RIC) allo-HCT may be considered for patients who demonstrate complete marrow and extramedullary first or second remission and who could be expected to benefit from a myeloablative allo-HCT, but for medical reasons would not tolerate a myeloablative conditioning regimen. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have relapse after a prior autologous HCT for ALL who receive allo-HCT, the evidence includes case series and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, and treatment-related mortality and morbidity. The evidence is sufficient to determine that the technology results in a meaningful improvement in net health outcome.

Ongoing and Unpublished Clinical Trials

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

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02042690	Haplo-identical HCT Versus Chemotherapy for Adult Acute Lymphoblastic Leukemia Patients	300	Dec 2018
NCT01700946	Therapy for Pediatric Relapsed or Refractory Precursor B-Cell Acute Lymphoblastic Leukemia and Lymphoma	40	Oct 2021

NCT: national clinical trial

Clinical Input Received from Physician Specialty Societies and Academic Medical Centers

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

In response to requests, input was received from 1 medical society, 2 academic medical centers, and 3 physicians from Blue Distinction Centers while this policy was under review in 2013. In general, clinical input supported most existing policy statements. However, most reviewers disagreed that allogeneic hematopoietic cell transplantation (allo-HCT) is considered investigational to treat relapsing acute lymphoblastic leukemia (ALL) after a prior autologous HCT in either children or adults. Evidence on this point is scare but evolving and substantial trials are likely to be slow in forthcoming. Given this background, reduced-intensity conditioning allo-HCT is considered medically necessary to treat ALL in second or greater remission or relapsed or refractory ALL, the policy statements reflect this for children and adults.

National Comprehensive Cancer Network Guidelines

The 2013 National Comprehensive Cancer Network clinical practice guidelines for acute lymphoblastic leukemia indicate allogeneic HCT is appropriate for consolidation treatment of most poor-risk (eg, Ph1+, relapsed or refractory) patients with ALL.[32] These guidelines are

generally consistent with this policy. However, the NCCN guidelines now stratify treatment according to the categories of adolescent and young adult (age 15-39 years) and adult (age 40 or more years), rather than the more traditional categories of children (18 years or younger) and adults (18 or more years).

American Society for Blood and Marrow Transplantation

In 2015, the American Society for Blood and Marrow Transplantation published guidelines on indications for autologous and allogeneic HCT. Recommendations were intended to describe the current consensus on the use of HCT within and outside of the clinical trial setting.[33] Recommendations on ALL are listed in **Table 2**.

Table 2. ASBMT Guidelines for Autologous and Allogeneic HCT

Indication	Allogeneic HCT	Autologous HCT
First complete response, standard risk	N	N
First complete response, high risk	S	N
Second complete response	S	N
At least third complete response	C	N
Not in remission	C	N

ASBMT: American Society for Blood and Marrow Transplantation; C: clinical evidence available; HCT: hematopoietic cell transplantation; N: not generally recommended; S: standard of care.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

Regulatory Status

The U.S. Food and Drug Administration regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and

Research, under Code of Federal Regulation (CFR) title 21, parts 1270 and 1271. Hematopoietic stem cells are included in these regulations.

References

1. Physician Data Query (PDQ). Childhood acute lymphoblastic leukemia. 2008. **https://www.cancer.gov/types/leukemia/hp/child-all-treatment-pdq**. Accessed April 2018.
2. Pieters R, Carroll WL. Biology and treatment of acute lymphoblastic leukemia. Pediatr Clin North Am. Feb 2008;55(1):1-20, ix. PMID 18242313
3. Carroll WL, Bhojwani D, Min DJ, et al. Pediatric acute lymphoblastic leukemia. Hematology Am Soc Hematol Educ Program. 2003:102-131. PMID 14633779
4. Physician Data Query (PDQ). Adult acute lymphoblastic leukemia treatment. 2008. **https://www.cancer.gov/types/leukemia/hp/adult-all-treatment-pdq**. Accessed April 2018.
5. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). 1987 TEC Evaluations.Page 243.
6. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). 1990 TEC Evaluations.Page 254.
7. Harrison G, Richards S, Lawson S, et al. Comparison of allogeneic transplant versus chemotherapy for relapsed childhood acute lymphoblastic leukaemia in the MRC UKALL R1 trial. MRC Childhood Leukaemia Working Party. Ann Oncol. Aug 2000;11(8):999-1006. PMID 11038037
8. Lawson SE, Harrison G, Richards S, et al. The UK experience in treating relapsed childhood acute lymphoblastic leukaemia: a report on the Medical Research Council UKALLR1 study. Br J Haematol. Mar 2000;108(3):531-543. PMID 10759711
9. Wheeler KA, Richards SM, Bailey CC, et al. Bone marrow transplantation versus chemotherapy in the treatment of very high-risk childhood acute lymphoblastic leukemia in first remission: results from Medical Research Council UKALL X and XI. Blood. Oct 1 2000;96(7):2412-2418. PMID 11001892
10. Ribera JM, Ortega JJ, Oriol A, et al. Comparison of intensive chemotherapy, allogeneic, or autologous stem-cell transplantation as postremission treatment for children with very high risk acute lymphoblastic leukemia: PETHEMA ALL-93 Trial. J Clin Oncol. Jan 1 2007;25(1):16-24. PMID 17194902
11. Oliansky DM, Camitta B, Gaynon P, et al. Role of cytotoxic therapy with hematopoietic stem cell transplantation in the treatment of pediatric acute lymphoblastic leukemia: update of the 2005 evidence-based review. Biol Blood Marrow Transplant. Apr 2012;18(4):505-522. PMID 22209888
12. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). High-dose chemotherapy with autologous stem-cell support in the treatment of adult acute lymphoblastic leukemia. TEC Assessments. 1997;Volume 12:Tab 25.
13. Yanada M, Matsuo K, Suzuki T, et al. Allogeneic hematopoietic stem cell transplantation as part of postremission therapy improves survival for adult patients with high-risk acute lymphoblastic leukemia: a metaanalysis. Cancer. Jun 15 2006;106(12):2657-2663. PMID 16703597
14. Hahn T, Wall D, Camitta B, et al. The role of cytotoxic therapy with hematopoietic stem cell transplantation in the therapy of acute lymphoblastic leukemia in adults: an evidence-based review. Biol Blood Marrow Transplant. Jan 2006;12(1):1-30. PMID 16399566
15. Attal M, Blaise D, Marit G, et al. Consolidation treatment of adult acute lymphoblastic leukemia: a prospective, randomized trial comparing allogeneic versus autologous bone marrow transplantation and testing the impact of recombinant interleukin-2 after autologous bone marrow transplantation. BGMT Group. Blood. Aug 15 1995;86(4):1619-1628. PMID 7632972

16. Dombret H, Gabert J, Boiron JM, et al. Outcome of treatment in adults with Philadelphia chromosome-positive acute lymphoblastic leukemia--results of the prospective multicenter LALA-94 trial. Blood. Oct 1 2002;100(7):2357-2366. PMID 12239143

17. Hunault M, Harousseau JL, Delain M, et al. Better outcome of adult acute lymphoblastic leukemia after early genoidentical allogeneic bone marrow transplantation (BMT) than after late high-dose therapy and autologous BMT: a GOELAMS trial. Blood. Nov 15 2004;104(10):3028-3037. PMID 15256423

18. Gupta V, Richards S, Rowe J, et al. Allogeneic, but not autologous, hematopoietic cell transplantation improves survival only among younger adults with acute lymphoblastic leukemia in first remission: an individual patient data meta-analysis. Blood. Jan 10 2013;121(2):339-350. PMID 23165481

19. Ribera JM, Oriol A, Bethencourt C, et al. Comparison of intensive chemotherapy, allogeneic or autologous stem cell transplantation as post-remission treatment for adult patients with high-risk acute lymphoblastic leukemia. Results of the PETHEMA ALL-93 trial. Haematologica. Oct 2005;90(10):1346-1356. PMID 16219571

20. Goldstone AH, Richards SM, Lazarus HM, et al. In adults with standard-risk acute lymphoblastic leukemia, the greatest benefit is achieved from a matched sibling allogeneic transplantation in first complete remission, and an autologous transplantation is less effective than conventional consolidation/maintenance chemotherapy in all patients: final results of the International ALL Trial (MRC UKALL XII/ECOG E2993). Blood. Feb 15 2008;111(4):1827-1833. PMID 18048644

21. Fielding AK, Rowe JM, Richards SM, et al. Prospective outcome data on 267 unselected adult patients with Philadelphia chromosome-positive acute lymphoblastic leukemia confirms superiority of allogeneic transplantation over chemotherapy in the pre-imatinib era: results from the International ALL Trial MRC UKALLXII/ECOG2993. Blood. May 7 2009;113(19):4489-4496. PMID 19244158

22. Cornelissen JJ, van der Holt B, Verhoef GE, et al. Myeloablative allogeneic versus autologous stem cell transplantation in adult patients with acute lymphoblastic leukemia in first remission: a prospective sibling donor versus no-donor comparison. Blood. Feb 5 2009;113(6):1375-1382. PMID 18988865

23. Giebel S, Labopin M, Socie G, et al. Improving results of allogeneic hematopoietic cell transplantation for adults with acute lymphoblastic leukemia in first complete remission: an analysis from the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation. Haematologica. Jan 2017;102(1):139-149. PMID 27686376

24. Dinmohamed AG, Szabo A, van der Mark M, et al. Improved survival in adult patients with acute lymphoblastic leukemia in the Netherlands: a population-based study on treatment, trial participation and survival. Leukemia. Feb 2016;30(2):310-317. PMID 26286115

25. Pidala J, Djulbegovic B, Anasetti C, et al. Allogeneic hematopoietic cell transplantation for adult acute lymphoblastic leukemia (ALL) in first complete remission. Cochrane Database Syst Rev. 2011(10):CD008818. PMID 21975786

26. Abdul Wahid SF, Ismail NA, Mohd-Idris MR, et al. Comparison of reduced-intensity and myeloablative conditioning regimens for allogeneic hematopoietic stem cell transplantation in patients with acute myeloid leukemia and acute lymphoblastic leukemia: a meta-analysis. Stem Cells Dev. Nov 1 2014;23(21):2535-2552. PMID 25072307

27. Gutierrez-Aguirre CH, Gomez-Almaguer D, Cantu-Rodriguez OG, et al. Non-myeloablative stem cell transplantation in patients with relapsed acute lymphoblastic leukemia: results of a multicenter study. Bone Marrow Transplant. Sep 2007;40(6):535-539. PMID 17618317

28. Mohty M, Labopin M, Tabrizzi R, et al. Reduced intensity conditioning allogeneic stem cell transplantation for adult patients with acute lymphoblastic leukemia: a retrospective study from the European Group for Blood and Marrow Transplantation. Haematologica. Feb 2008;93(2):303-306. PMID 18245655

29. Cho BS, Lee S, Kim YJ, et al. Reduced-intensity conditioning allogeneic stem cell transplantation is a potential therapeutic approach for adults with high-risk acute lymphoblastic leukemia in remission: results of a prospective phase 2 study. Leukemia. Oct 2009;23(10):1763-1770. PMID 19440217

30. Pulsipher MA, Boucher KM, Wall D, et al. Reduced-intensity allogeneic transplantation in pediatric patients ineligible for myeloablative therapy: results of the Pediatric Blood and Marrow Transplant Consortium Study ONC0313. Blood. Aug 13 2009;114(7):1429-1436. PMID 19528536

31. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Salvage high-dose chemotherapy with allogeneic stem-cell support for relapse or incomplete remission following high-dose chemotherapy with autologous stem-cell transplantation for hematologic malignancies. TEC Assessments. 2000;Volume 15:Tab 9. PMID

32. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute lymphoblastic leukemia. Version 2.2016. **https://www.nccn.org/professionals/physician_gls/pdf/all.pdf**. Accessed March 2017.

33. Majhail NS, Farnia SH, Carpenter PA, et al. Indications for autologous and allogeneic hematopoietic cell transplantation: guidelines from the American Society for Blood and Marrow Transplantation. Biol Blood Marrow Transplant. Nov 2015;21(11):1863-1869. PMID 26256941.

34. Pavlu J, et al. Allogeneic hematopoietic cell transplantation for primary refractory acute lymphoblastic leukemia: a report from the Acute Leukemia Working Party of the EBMT. 2017, Cancer 123(11):1965-1970

35. Rosko A, et al. Reduced intensity conditioned allograft yields favorable survival for older adults with B-cell acute lymphoblastic leukemia. 2017, Am. J Hematol 92(1):42-49.

History

Date	Comments
06/27/00	Add to Therapy Section - New Policy — replaces 8.01.15, original master policy on HDC for miscellaneous malignancies. However, policy statement is unchanged.
12/21/00	Replace Policy - Policy statement revised to state that allogeneic transplant after a prior failed autotransplant is considered investigational, based on 2000 Tec Assessment.
06/17/03	Replace Policy - Policy updated w/expanded rationale and new references; policy statement unchanged.
08/12/03	Replace Policy - Reviewed and recommended for adoption without any changes by Company Oncology Advisory Panel July 22, 2003.
12/14/04	Replace Policy - Policy reviewed w/literature search; update added on clinical trials and NCCN guidelines; policy statement unchanged.
01/10/06	Replace Policy - Policy reviewed with literature search; no change to policy statement.
06/02/06	Disclaimer and Scope update - No other changes
10/09/07	Replace Policy - Policy reviewed with BCBSA literature update through March 2007. NCI clinical trials updated; NCCN guidelines information unchanged. New references added; Policy statement unchanged.
11/12/07	Code updated - CPT code 86817 removed as directed by RPIW.
05/13/08	New PR status - Policy statement regarding HDC and allogeneic SCT to treat relapsing

Date	Comments
	ALL after a prior course of HDC and autologous SCT changed from investigational to medically necessary for children and adults. Reviewed and recommended by the OAP on February 21, 2008. Replaces BC.8.01.32, status changed from BC to PR.
05/12/09	Replace Policy - Policy revised with literature search. Clinical input received. New policy statement added that RIC allogeneic SCT may be considered medically necessary in select patients in complete remission. Policy titles changed to: "Hematopoietic Stem Cell Transplantation for Acute Lymphocytic Leukemia". Reviewed and recommended by the OAP on February 19, 2009.
12/08/09	Code Update - 86817 added back to the policy.
02/09/10	Code Update - New 2010 codes added.
11/09/10	Replace Policy - Policy statement updated. Allogeneic HCT considered medically necessary for any risk level in first complete remission. Updated with literature review and references. References added. Reviewed by the OAP on August 19, 2010.
09/15/11	Replace Policy – Policy updated with literature review; no change in policy statement.
03/23/12	Replace policy. Policy updated with literature review; no change in policy statement. References added, removed and reordered. Reviewed and recommended by OAP on February 16, 2012.
08/01/12	Update Related Policies Titles: 8.01.21, 8.01.22, 8.01.29, 8.01.30, 8.01.31, 8.01.35, 8.01.514. Policy 8.01.507 was changed to 8.01.17.
02/01/13	Update Related Policies, change title of policy 8.01.21.
03/20/13	The following codes were removed from the policy, as they were not suspending and just informational: HCPCS J9000-J9999 and Q0083 – Q0085.
07/24/13	Replace policy. Policy statements formatted for readability. References 13,22,34,28 added; others renumbered/removed. Policy statement unchanged.
09/30/13	Update Related Policies. Change title to policy 8.01.31.
10/18/13	Update Related Policies. Change title to policy 8.01.17.
12/03/13	Coding Update. Add ICD-10 codes.
02/27/14	Update Related Policies. Change title to 8.01.30.
03/21/14	Update Related Policies. Remove 8.01.514 as it was deleted.
04/18/14	Update Related Policies. Delete 8.01.20 and replace with 8.01.529.
07/31/14	Annual Review. Policy updated with literature review; no change in policy statements. Related Policies updated; only those related to leukemia remain; all others removed.
03/13/15	Update Related Policies. Add 8.01.01
07/14/15	Annual Review. Policy updated with literature search; no change to policy statement. References updated. ICD-9 and ICD-10 procedure codes removed; they were listed for

Date	Comments
	informational purposes only.
07/01/16	Annual Review,approved June 14, 2016. Literature review. No change to policy statement. Discussion wording updated. Clinical trial reviews updated.
09/30/16	Coding Update. Remove CPT 86817 from coding section.
11/04/16	Coding update. Removed codes that are transplant benefit related.
04/01/17	Annual Review, approved March 14, 2017. Policy updated with literature review through November 9, 2016; references 28-29 and 32 added. Policy statements unchanged.
06/09/17	Coding update; updated description for CPT codes 38230, 38240, and 38241.
11/10/17	Policy moved into new format; no change to policy statements.
05/01/18	Annual Review, approved April 3, 2018. Policy updated with literature review through November 2017; references updated. Reference 35* added. Policy statements unchanged.

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.

PREMERA | BLUE CROSS

An Independent Licensee of the Blue Cross Blue Shield Association

Discrimination is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:

- Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  - Qualified sign language interpreters
  - Written information in other formats (large print, audio, accessible electronic formats, other formats)
- Provides free language services to people whose primary language is not English, such as:
  - Qualified interpreters
  - Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:
Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5592, TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:
U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

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).

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

العربية (Arabic):
يحوي هذا الإشعار معلومات هامة. قد يحوي هذا الإشعار معلومات مهمة بخصوص طلبك أو التغطية التي تريد الحصول عليها من خلال Premera Blue Cross. قد تكون هناك تواريخ مهمة في هذا الإشعار. وقد تحتاج لاتخاذ إجراء في تواريخ معينة للحفاظ على تغطيتك الصحية أو للمساعدة في دفع التكاليف. يحق لك الحصول على هذه المعلومات والمساعدة بلغتك دون تكبد أية تكلفة. اتصل بـ800-722-1471 (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 devrez 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 resevwa 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):
Tsab ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb. Tej zaum tsab ntawv tshaj xo no muaj cov ntsiab lus tseem ceeb txog koj daim ntawv thov kev pab los yog koj qhov kev pab cuam los ntawm Premera Blue Cross. Tej zaum muaj cov hnub tseem ceeb uas sau rau hauv daim ntawv no. Tej zaum koj kuj yuav tau ua qee yam uas peb 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 apliksayonyo wenno 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-atyo wenno 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. 귀하는 귀하의 건강 커버리지를 계속 유지하거나 비용을 절감하기 위해서 일정한 마감일까지 조치를 취해야 할 필요가 있을 수 있습니다. 귀하는 이러한 정보와 도움을 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 800-722-1471 (TTY: 800-842-5357) 로 전화하십시오.

ລາວ (Lao):
ແຈ້ງການນີ້ມີຂໍ້ມູນສຳຄັນ. ແຈ້ງການນີ້ອາດຈະມີຂໍ້ມູນສຳຄັນກ່ຽວກັບຄຳຮ້ອງສະໝັກ ຫຼື ຄວາມຄຸ້ມຄອງປະກັນໄພຂອງທ່ານຜ່ານ Premera Blue Cross. ອາດຈະມີວັນທີສຳຄັນໃນແຈ້ງການນີ້. ທ່ານອາດຈະຈຳເປັນຕ້ອງດຳເນີນການຕາມກຳນົດເວລາສະເພາະເພື່ອຮັກສາຄວາມຄຸ້ມຄອງປະກັນສຸຂະພາບ ຫຼື ຄວາມຊ່ວຍເຫຼືອເລື່ອງຄ່າໃຊ້ຈ່າຍຂອງທ່ານໄວ້. ທ່ານມີສິດໄດ້ຮັບຂໍ້ມູນນີ້ ແລະ ຄວາມຊ່ວຍເຫຼືອເປັນພາສາຂອງທ່ານໂດຍບໍ່ເສຍຄ່າ. ໃຫ້ໂທຫາ 800-722-1471 (TTY: 800-842-5357).

ភាសាខ្មែរ (Khmer):
សេចក្តីជូនដំណឹងនេះមានព័ត៌មានយ៉ាងសំខាន់។ សេចក្តីជូនដំណឹងនេះប្រហែលជាមានព័ត៌មានយ៉ាងសំខាន់អំពីទម្រង់បែបបទ ឬការរ៉ាប់រងរបស់អ្នកតាមរយៈ Premera Blue Cross ។ ប្រហែលជាមាន កាលបរិច្ឆេទសំខាន់នៅក្នុងសេចក្តីជូនដំណឹងនេះ។ អ្នកប្រហែលជាត្រូវការបញ្ចេញសមត្ថភាព ដល់កំណត់ថ្ងៃជាក់ច្បាស់នានា ដើម្បីនឹងរក្សាទុកការជានាវ៉ាប់រងសុខភាពរបស់អ្នក ឬប្រាក់ជំនួយចេញផ្លែ។ អ្នកមានសិទ្ធិទទួលព័ត៌មាននេះ និងជំនួយនៅក្នុងភាសារបស់អ្នកដោយមិនអស់លុយឡើយ។ 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 ਨੋਜਿਸ ਜਵਚ ਖਾਸ ਤਾਰੀਖਾ ਹੋ ਸਕਦੀਆਂ ਹਨ. ਜੇਕਰ ਤੁਸੀ ਜਸਹਤ ਕਵਰੇਜ ਰਿੱਖਣੀ ਹੋਵੇ ਜਾ ਓਸ ਦੀ ਲਾਗਤ ਜਵਿੱਚ ਮਦਦ ਦੇ ਇਛੁੱਕ ਹੋ ਤਾਂ ਤੁਹਾਨੂੰ ਅੰਤਮ ਤਾਰੀਖ਼ ਤੋਂ ਪਹਿਲਾਂ ਕੁੱਝ ਖਾਸ ਕਦਮ ਚੁੱਕਣ ਦੀ ਲੋੜ ਹੋ ਸਕਦੀ ਹੈ ,ਤੁਹਾਨੂੰ ਮੁਫ਼ਤ ਵਿੱਚ ਤੇ ਆਪਣੀ 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 (کاربران 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 zwrócic 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 dumneavoastre 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 privitoare 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'amatalaga 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. Ang paunawa na ito ay maaaring 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 ganitong impormasyon at tulong sa iyong wika ng walang gastos. Tumawag sa 800-722-1471 (TTY: 800-842-5357).

ไทย (Thai):
ประกาศนี้มีข้อมูลสำคัญ ประกาศนี้อาจมีข้อมูลที่สำคัญเกี่ยวกับการการสมัครหรือขอบเขตประกันสุขภาพของคุณผ่าน Premera Blue Cross และอาจมีกำหนดการในประกาศนี้ คุณอาจจะต้องดำเนินการภายในกำหนดระยะเวลาที่แน่นอนเพื่อจะรักษาการประกันสุขภาพของคุณหรือการช่วยเหลือที่มีค่าใช้จ่าย คุณมีสิทธิที่จะได้รับข้อมูลและความช่วยเหลือนี้ในภาษาของคุณโดยไม่มีค่าใช้จ่าย 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 страхувального 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):
Thông báo này cung cấp thông tin quan trọng. Thông báo này có thông tin quan trọng về đơn xin tham gia hoặc hợp đồng bảo hiểm của quý vị qua chương trình Premera Blue Cross. Xin xem ngày quan trọng trong thông báo này. Quý vị có thể phải thực hiện theo thông báo đúng trong thời hạn để duy trì bảo hiểm sức khỏe hoặc được trợ giúp thêm về chi phí. Quý vị có quyền được biết thông tin này và được trợ giúp bằng ngôn ngữ của mình miễn phí. Xin gọi số 800-722-1471 (TTY: 800-842-5357).