Hematopoietic Cell Transplantation for Acute Lymphoblastic Leukemia

Policy # 00048
Original Effective Date: 01/28/2002
Current Effective Date: 10/11/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: BCR-ABL1 Testing in Chronic Myelogenous Leukemia and Acute Lymphoblastic Leukemia is addressed separately in medical policy 00428.

When Services Are Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Children

Based on review of available data, the Company may consider allogeneic or autologous hematopoietic cell transplantation (HCT) to treat childhood acute lymphoblastic leukemia (ALL) in first complete remission but at high risk of relapse to be **eligible for coverage.** **

Based on review of available data, the Company may consider autologous or allogeneic hematopoietic cell transplantation (HCT) to treat childhood acute lymphoblastic leukemia (ALL) in second or greater remission or refractory acute lymphoblastic leukemia (ALL) to be **eligible for coverage.****

Based on review of available data, the Company considers allogeneic hematopoietic cell transplantation (HCT) to treat relapsing acute lymphoblastic leukemia (ALL) after a prior autologous hematopoietic cell transplantation (HCT) to be **eligible for coverage.****

Adults

Based on review of available data, the Company may consider autologous hematopoietic cell transplantation (HCT) to treat adult acute lymphoblastic leukemia (ALL) in first complete remission but at high risk of relapse to be **eligible for coverage.****

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Based on review of available data, the Company may consider allogeneic hematopoietic cell transplantation (HCT) to treat adult acute lymphoblastic leukemia (ALL) in first complete remission for any risk level to be **eligible for coverage.****

Based on review of available data, the Company may consider allogeneic hematopoietic cell transplantation (HCT) to treat adult acute lymphoblastic leukemia (ALL) in second or greater remissions, or in adults with relapsed or refractory acute lymphoblastic leukemia (ALL) to be **eligible for coverage.****

Based on review of available data, the Company may consider reduced-intensity conditioning (RIC) allogeneic hematopoietic cell transplantation (HCT) as a treatment of acute lymphoblastic leukemia (ALL) in patients who are in complete marrow and extramedullary first or second remission, and who, for medical reasons, would be unable to tolerate a standard myeloablative conditioning regimen to be **eligible for coverage.****

Based on review of available data, the Company considers allogeneic hematopoietic cell transplantation (HCT) to treat relapsing acute lymphoblastic leukemia (ALL) after a prior autologous hematopoietic cell transplantation (HCT) to be **eligible for coverage.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers autologous hematopoietic cell transplantation (HCT) to treat adult acute lymphoblastic leukemia (ALL) in second or greater remission or those with refractory disease to be **investigational.***

Policy Guidelines

Relapse Risk Prognostic Factors

Childhood Acute Lymphoblastic Leukemia

Adverse prognostic factors in children include the following: age younger than 1 year or more than 9 years, male sex, white blood cell count at presentation above 50,000/μL, hypodiploidy (<45

chromosomes), translocation involving chromosomes 9 and 22 (t[9;22]) or *BCR-ABL* fusion, translocation involving chromosomes 4 and 11 (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 6 weeks with high-risk having 1% or higher 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) regardless of early response measures.

Adult Acute Lymphoblastic Leukemia
Risk factors for relapse are less well-defined in adults, but a patient with any of the following may be considered at high-risk for relapse: age older than 35 years, leukocytosis at presentation of greater than 30000/μL (B-cell lineage) or greater than 100000/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
Some patients for whom a conventional myeloablative allogeneic HCT could be curative may be considered candidates for reduced-intensity conditioning allogeneic HCT (see Background section). Such patients include those whose age (typically >60 years) or comorbidities (eg, liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy including autologous or allogeneic HCT, low Karnofsky Performance Status score) preclude the use of a standard myeloablative conditioning regimen.

The ideal allogeneic donors are human leukocyte antigen (HLA) 'identical siblings, matched at the HLA-A, -B, and DR (antigen-D related) loci on each arm of chromosome 6. Related donors mismatched at one locus are also considered suitable donors. A matched, unrelated donor identified through the National Marrow Donor Registry is typically the next option considered. Recently, there has been interest in haploidentical donors, typically a parent or a child of the patient, where usually there is sharing of only 3 of the 6 major histocompatibility antigens. Most patients will have such a donor. The risk of morbidity (eg, graft-versus-host disease) may be higher than with HLA-matched donors; however, as medical treatments improve, the risks of graft-versus-host disease with haploidentical donors are approaching those similar to HLA-matched donors.

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Background/Overview

Acute Lymphoblastic Leukemia

Childhood Acute Lymphoblastic Leukemia

ALL is the most common cancer diagnosed in children; it represents nearly 25% of cancers in children younger than 15 years. Remission of disease is now typically achieved with pediatric chemotherapy regimens in 98% of children with ALL, 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 presymptomatic central nervous system prophylaxis, and intensification and risk-based stratification of treatment. The prognosis after the 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 with 10% to 15% for those who relapse less than 3 years after treatment. Thus, HCT may be a strong consideration in those with short remissions. At present, the comparative outcomes with autologous or allogeneic HCT (allo-HCT) are unknown.

ALL is a heterogeneous disease with different genetic variations resulting in distinct biologic subtypes. Patients are stratified by certain clinical and genetic risk factors that predict an outcome, with risk-adapted therapy tailoring treatment based on the predicted risk of relapse. Two of the most important factors predictive of risk are patient age and white blood cell count at diagnosis. Certain genetic characteristics of leukemic cells strongly influence prognosis. Clinical and biologic factors predicting clinical outcomes and relapse risk are summarized in the Policy Guidelines section.

Adult ALL

ALL accounts for 20% of acute leukemias in adults. Between 60% and 80% of adults with ALL can be expected to achieve a complete response after induction chemotherapy; however, only 35% to 40% can be expected to survive 2 years. Differences in the frequency of genetic abnormalities that characterize adult ALL versus childhood ALL help, in part, explain differences in outcomes between the 2 groups. For example, the “good prognosis” genetic abnormalities, such as hyperdiploidy and translocation of chromosomes 12 and 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 such as the Philadelphia chromosome (translocation of chromosomes 9 and 22) are seen in 25% to 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 greater than 30000/μL (B-cell lineage) or greater than 100000/μL (T-cell lineage).

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

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

Conditioning for Hematopoietic Cell Transplantation
Conventional Conditioning
The conventional ("classical") practice of allo-HCT involves administration of cytotoxic agents (e.g., cyclophosphamide, busulfan) with or without toxisting disease in the absence of pretransplant conditioning. Intense conditioning regimens are limited to patients who are sufficiently medically fital body irradiation at doses sufficient to cause bone marrow ablation in the recipient. The beneficial treatment effect of this procedure is due to a combination of the initial eradication of malignant cells and subsequent graft-versus-malignancy effect mediated by non-self-immunologic effector cells. While the slower graft-versus-malignancy effect is considered the potentially curative component, it may be overwhelmed by et to tolerate substantial adverse effects. These include opportunistic infections secondary to loss of endogenous bone marrow function and organ damage or failure caused by cytotoxic drugs. Subsequent to graft infusion in allo-HCT, immunosuppressant drugs are required to minimize graft rejection and graft-versus-host disease, which increases susceptibility to opportunistic infections.

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

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

FDA or Other Governmental Regulatory Approval

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

Rationale/Source

Acute lymphoblastic leukemia is a heterogeneous disease with different genetic variations resulting in distinct biologic subtypes. Patients are stratified to risk-adapted therapy according to certain clinical and genetic risk factors that predict an outcome. Therapy may include HCT.

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Summary of Evidence
For individuals who have childhood ALL in first complete remission (CR1) at high-risk of relapse, remission, or refractory ALL who receive autologous HCT, the evidence includes RCTs and systematic reviews. Relevant outcomes are overall survival (OS), disease-specific survival (DSS), and treatment-related mortality (TRM) and morbidity. For children with high-risk ALL in 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, autologous 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 if the technology results in an improvement in the net health outcome.

For individuals who have childhood ALL in CR1 at high-risk of relapse, remission, or refractory ALL who receive allo-HCT, the evidence includes RCTs and systematic reviews. Relevant outcomes are OS, DSS, and TRM and morbidity. For children with high-risk ALL in CR1 or with relapsed ALL, studies have suggested that allo-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, allo-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 if the technology results in an improvement in the net health outcome.

For individuals who have adult ALL in CR1, subsequent remission, or refractory ALL who receive autologous HCT, the evidence includes RCTs and systematic reviews. Relevant outcomes are OS, DSS, and TRM and morbidity. Current evidence supports the use of autologous HCT for adults with high-risk ALL in CR1, whose health status is sufficient to tolerate the procedure. The evidence is sufficient to determine if the technology results in an improvement in the net health outcome.

For individuals who have adult ALL in CR1 or subsequent remission or refractory ALL who receive allo-HCT, the evidence includes RCTs and systematic reviews. The Relevant outcomes are OS, DSS, and TRM and morbidity. Current evidence supports the use of myeloablative allo-HCT for adults with any risk level ALL, whose health status is sufficient to tolerate the procedure. Reduced-intensity conditioning 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 if the technology results in an improvement in the net health outcome.

For individuals who have relapsed after a prior autologous HCT for ALL who receive allo-HCT, the evidence includes case series and systematic reviews. Relevant outcomes are OS, DSS, and TRM and morbidity. Evidence reviews have identified only small case series with short-term follow-up, which was considered inadequate evidence of benefit. The evidence is insufficient to determine if the technology results in an improvement in the net health outcome.

Additional Information

2013 Input
Given a scarcity of evidence on this topic - with no substantial trials likely to be forthcoming, that allo-HCT after failed autologous HCT has been shown to be of clinical benefit in other hematologic malignancies and is potentially curative, that reduced-intensity conditioning allo-HCT is considered medically necessary to treat ALL in second or greater remission or relapsed or refractory ALL, and the support from 2013 clinical input of this use, the policy statements were revised to medical necessity for this indication in children and adults.

Supplemental Information

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

In response to requests, input was received from 1 medical society, 2 academic medical centers, and 3 physicians from Blue Distinction Centers while this policy was under review in 2013. In general, input supported most existing policy statements. However, most reviewers disagreed that allo-HCT is considered investigational to treat relapsing ALL after a prior autologous HCT in either children or adults. Given a scarcity of evidence on this topic, with no substantial trials likely to be forthcoming, that allo-HCT after failed autologous HCT has been shown to be of clinical benefit in

other hematologic malignancies and is potentially curative, and that 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 were revised to medical necessity for this indication in children and adults.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network
Current National Comprehensive Cancer Network guidelines (v.2.2020) for ALL indicate allo-HCT is appropriate for consolidation treatment of most poor risk (eg, the Philadelphia chromosome-positive, relapsed, or refractory) patients with ALL. The guidelines state that for appropriately fit older adults with ALL who are achieving remission, "consideration of autologous or reduced-intensity allogeneic stem cell transplantation may be appropriate." In addition, the guidelines note that chronologic age is not a good surrogate for fitness for therapy and that patient should be evaluated on an individual basis.

Current National Comprehensive Cancer Network guidelines (v.2.2020) for pediatric ALL say that "Allogeneic HSCT has demonstrated improved clinical outcomes in pediatric ALL patients with evidence of certain high-risk features and/or persistent disease. In addition, survival rates appear to be comparable regardless of the stem cell source (matched related, matched unrelated, cord blood, or haploidentical donor)."

American Society for Blood and Marrow Transplantation
In 2015, the guidelines from the American Society for Blood and Marrow Transplantation were published on indications for autologous and allo- HCT. Recommendations were intended to describe the current consensus on the use of HCT in and out of the clinical trial setting. Recommendations on ALL are listed in Table 1.

Table 1. Guidelines for Autologous and Allogeneic HCT in ALL

Indication	**Children (Age <18 Years)**		**Adults (Age ≥18 Years)**	
	Allogeneic HCT	**Autologous HCT**	**Allogeneic HCT**	**Autologous HCT**

First complete response, standard-risk	N	N	S	C
First complete response, high-risk	S	N	S	N
Second complete response	S	N	S	C
At least third complete response	C	N	C	N
Not in remission	C	N	C	N

ALL: acute lymphoblastic leukemia; C: clinical evidence available; HCT: hematopoietic cell transplantation; N: not generally recommended; S: standard of care.

U.S. Preventive Services Task Force Recommendations
Not applicable.

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

Nationally Covered Indications

"I. Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

a) Effective … 1978, for the treatment of leukemia, leukemia in remission, or aplastic anemia when it is reasonable and necessary,
b) Effective … 1985, for the treatment of severe combined immunodeficiency disease (SCID) and for the treatment of Wiskott-Aldrich syndrome.
c) Effective … 2010, for the treatment of Myelodysplastic Syndromes (MDS) pursuant to Coverage with Evidence Development (CED) in the context of a Medicare-approved, prospective clinical study…
d) Effective for claims with dates of service on or after January 27, 2016, allogeneic HSCT for multiple myeloma is covered by Medicare only for beneficiaries with Durie-Salmon Stage II or III multiple myeloma, or International Staging System (ISS) Stage II or Stage III multiple myeloma, and participating in an approved prospective clinical study that meets the criteria below. There must

be appropriate statistical techniques to control for selection bias and confounding by age, duration of diagnosis, disease classification, International Myeloma Working Group (IMWG) classification, ISS stage, comorbid conditions, type of preparative/conditioning regimen, graft vs. host disease (GVHD) prophylaxis, donor type and cell source…
e) Effective for claims with dates of service on or after January 27, 2016, allogeneic HSCT for myelofibrosis (MF) is covered by Medicare only for beneficiaries with Dynamic International Prognostic Scoring System (DIPSSplus) intermediate-2 or High primary or secondary MF and participating in an approved prospective clinical study. All Medicare-approved studies must use appropriate statistical techniques in the analysis to control for selection bias and potential confounding by age, duration of diagnosis, disease classification, DIPSSplus score, comorbid conditions, type of preparative/conditioning regimen, graft vs. host disease (GVHD) prophylaxis, donor type and cell source…
f) Effective for claims with dates of service on or after January 27, 2016, allogeneic HSCT for sickle cell disease (SCD) is covered by Medicare only for beneficiaries with severe, symptomatic SCD who participate in an approved prospective clinical study....

II. Autologous Stem Cell Transplantation (AuSCT)
a) Effective … 1989, AuSCT is considered reasonable and necessary … for the following conditions and is covered under Medicare for patients with:

1. Acute leukemia in remission who have a high probability of relapse and who have no HLA-matched;
2. Resistant non-Hodgkin's lymphomas or those presenting with poor prognostic features following an initial response;
3. Recurrent or refractory neuroblastoma; or,
4. Advanced Hodgkin's disease who have failed conventional therapy and have no HLA-matched donor.

b) Effective … 2000, single AuSCT is only covered for Durie-Salmon Stage II or III patients that fit the following requirements:

- Newly diagnosed or responsive multiple myeloma. This includes those patients with previously untreated disease, those with at least a partial response to prior chemotherapy (defined as a 50% decrease either in measurable paraprotein [serum and/or urine] or in bone marrow infiltration, sustained for at least 1 month), and those in responsive relapse; and
- Adequate cardiac, renal, pulmonary, and hepatic function.

c) Effective … 2005, when recognized clinical risk factors are employed to select patients for transplantation, high dose melphalan (HDM) together with AuSCT is reasonable and necessary for Medicare beneficiaries of any age group with primary amyloid light chain (AL) amyloidosis who meet the following criteria:
   - Amyloid deposition in 2 or fewer organs; and,
   - Cardiac left ventricular ejection fraction (EF) greater than 45%."

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 2.

Table 2. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01700946	A Phase II Study of Therapy for Pediatric Relapsed or Refractory Precursor B-Cell Acute Lymphoblastic Leukemia and Lymphoma	94	Apr 2021
NCT03314974	Myeloablative Allogeneic Hematopoietic Cell Transplantation Using a Related or Unrelated Donor for the Treatment of Hematological Diseases	40	Nov 2025
NCT01949129	Allogeneic Stem Cell Transplantation for Children and Adolescents With Acute Lymphoblastic Leukaemia	1000	Apr 2026

NCT: national clinical trial.

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Policy History

Original Effective Date: 01/28/2002
Current Effective Date: 10/11/2021
12/06/2001 Medical Policy Committee review
03/25/2002 Managed Care Advisory Council approval

Policy # 00048
Original Effective Date: 01/28/2002
Current Effective Date: 10/11/2021

06/24/2002	Format revision. Policy addresses only Acute Lymphocytic Leukemia. Replaces High Dose Chemotherapy with Hematopoietic Stem Cell Support.
03/31/2004	Medical Director review
04/20/2004	Medical Policy Committee review. Format revision. No changes to coverage eligibility.
04/26/2004	Managed Care Advisory Council approval
04/05/2005	Medical Director review
04/19/2005	Medical Policy Committee review. Format revisions only. Coverage eligibility unchanged. 05/23/2005 Managed Care Advisory Council approval
09/06/2006	Medical Director review
09/20/2006	Medical Policy Committee approval. Format changes only. Coverage eligibility unchanged.
07/11/2007	Medical Director review
07/18/2007	Medical Policy Committee approval. Format revision only. Coverage eligibility unchanged.
07/02/2008	Medical Director review
07/16/2008	Medical Policy Committee approval. No change to coverage eligibility.
07/02/2009	Medical Director review
07/22/2009	Medical Policy Committee approval. Title changed to Hematopoietic Stem-Cell Transplantation for Acute Lymphoblastic Leukemia. Revised policy based on updated research.
07/01/2010	Medical Policy Committee approval.
07/21/2010	Medical Policy Implementation Committee approval. Policy statement regarding treatment of adult ALL in first complete remission but at high risk of relapse split to address allogeneic and autologous transplant separately.
07/07/2011	Medical Policy Committee approval.
07/20/2011	Medical Policy Implementation Committee approval. No change to coverage eligibility.
06/28/2012	Medical Policy Committee review.
07/27/2012	Medical Policy Implementation Committee approval. No change to coverage eligibility.
03/04/2013	Coding updated
08/01/2013	Medical Policy Committee review

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08/21/2013	Medical Policy Implementation Committee approval. Revised coverage statements so that allogeneic HSCT may be considered eligible for coverage following a failed autologous HSCT in children or adult patients.
09/04/2014	Medical Policy Committee review
09/17/2014	Medical Policy Implementation Committee approval. No change to coverage.
09/03/2015	Medical Policy Committee review
09/23/2015	Medical Policy Implementation Committee approval. No change to coverage.
09/08/2016	Medical Policy Committee review
09/21/2016	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
09/07/2017	Medical Policy Committee review
09/20/2017	Medical Policy Implementation Committee approval. The word stem was removed from title and body of policy.
09/06/2018	Medical Policy Committee review
09/19/2018	Medical Policy Implementation Committee approval. No change to coverage.
09/05/2019	Medical Policy Committee review
09/11/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/03/2020	Medical Policy Committee review
09/09/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/02/2021	Medical Policy Committee review
09/08/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 09/2022

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2020 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

Hematopoietic Cell Transplantation for Acute Lymphoblastic Leukemia

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	38204, 38205, 38206, 38207, 38208, 38209, 38210, 38211, 38212, 38213, 38214, 38215, 38230, 38240, 38241, 38242, 38243
HCPCS	S2140, S2142, S2150
ICD-10 Diagnosis	C91.00-C91.02

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety,

effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company

recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.