Allogeneic Hematopoietic Cell Transplantation for Genetic Diseases and Acquired Anemias

Policy # 00055
Original Effective Date: 01/28/2002
Current Effective Date: 07/12/2021

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: Hematopoietic Cell Transplantation for Autoimmune Diseases is addressed separately in medical policy 00050.

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.*

Based on review of available data, the Company may consider allogeneic hematopoietic cell transplantation (HCT) to be **eligible for coverage**** for selected patients with the following disorders:

Hemoglobinopathies

- Sickle cell anemia for children or young adults with either a history of prior stroke or at increased risk of stroke or end-organ damage.
- Homozygous beta-thalassemia (i.e., thalassemia major).

Bone marrow failure syndromes

- Aplastic anemia including hereditary (including Fanconi anemia, dyskeratosis congenita, Shwachman-Diamond syndrome, Diamond-Blackfan syndrome) or acquired (e.g., secondary to drug or toxin exposure) forms.

Primary immunodeficiencies

- Absent or defective T-cell function (e.g., severe combined immunodeficiency [SCID], Wiskott-Aldrich syndrome, X-linked lymphoproliferative syndrome).

- Absent or defective natural killer function (e.g. Chediak-Higashi syndrome).
- Absent or defective neutrophil function (e.g. Kostmann syndrome, chronic granulomatous disease (CGD), leukocyte adhesion defect).

(See Guideline 1.)

Inherited metabolic disease

- Lysosomal and peroxisomal storage disorders *except* Hunter, Sanfilippo and Morquio syndromes.

(See Guideline 2.)

Genetic disorders affecting skeletal tissue

- Infantile malignant osteopetrosis (Albers-Schonberg disease or marble bone disease).

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 allogeneic hematopoietic cell transplantation (HCT) for any other condition not listed above to be **investigational.***

Policy Guidelines

GUIDELINE 1

The following guideline lists immunodeficiencies that have been successfully treated by allogeneic hematopoietic cell transplantation (allo-HCT) (Gennery & Cant et al, 2008).

Lymphocyte Immunodeficiencies

- Adenosine deaminase deficiency
- Artemis deficiency
- Calcium channel deficiency
- CD40 ligand deficiency

- Cernunnos/X-linked lymphoproliferative disease deficiency
- CHARGE syndrome with immune deficiency
- Common gamma chain deficiency
- Deficiencies in CD45, CD3, CD8
- DiGeorge syndrome
- DNA ligase IV deficiency syndrome
- Interleukin-7 receptor alpha deficiency
- Janus-associated kinase 3 deficiency
- Major histocompatibility class II deficiency
- Omenn syndrome
- Purine nucleoside phosphorylase deficiency
- Recombinase-activating gene 1/2 deficiency
- Reticular dysgenesis
- Winged helix deficiency
- Wiskott-Aldrich syndrome
- X-linked lymphoproliferative disease
- Zeta-chain-associated protein-70 deficiency

Phagocytic Deficiencies

- Chédiak-Higashi syndrome
- Chronic granulomatous disease
- Griscelli syndrome type 2
- Hemophagocytic lymphohistiocytosis
- Interferon-gamma receptor deficiencies
- Leukocyte adhesion deficiency
- Severe congenital neutropenias
- Shwachman-Diamond syndrome

Other Immunodeficiencies

- Autoimmune lymphoproliferative syndrome
- Cartilage hair hypoplasia
- CD25 deficiency

- Hyper IgD and IgE syndromes
- Immunodeficiency, centromeric instability, and facial dysmorphism syndrome
- Immunodysregulation polyendocrinopathy enteropathy X-linked syndrome
- Nuclear factor-κ B (NF-κB) essential modulator deficiency
- NF-κB inhibitor, NF-κB-α deficiency
- Nijmegen breakage syndrome

GUIDELINE 2
For inherited metabolic disorders, allo-HCT has been proven effective in some cases of Hurler, Maroteaux-Lamy, and Sly syndromes, childhood onset cerebral X-linked adrenoleukodystrophy, globoid cell leukodystrophy, metachromatic leukodystrophy, alpha-mannosidosis, and aspartylglucosaminuria. Allogeneic HCT is possibly effective for fucosidosis, Gaucher types 1 and 3, Farber lipogranulomatosis, galactosialidosis, GM_1 gangliosidosis, mucolipidosis II (I-cell disease), multiple sulfatase deficiency, Niemann-Pick disease, neuronal ceroid lipofuscinosis, sialidosis, and Wolman disease. Allogeneic HCT has not been effective in Hunter, Sanfilippo, or Morquio syndromes (Mehta, 2004).

The experience with reduced-intensity conditioning and allo-HCT for the diseases listed in this evidence review has been limited to small numbers of patients and has yielded mixed results, depending on the disease category. In general, the results have been most promising in the bone marrow failure syndromes and primary immunodeficiencies. In the hemoglobinopathies, success has been hampered by difficulties with high rates of graft rejection, and in adults, severe graft-versus-host-disease. Phase 2/3 trials are ongoing or completed examining the role of this type of transplant for these diseases, as outlined in the Ongoing and Unpublished Clinical Trials.

Background/Overview

Genetic Diseases and Acquired Anemias

Hemoglobinopathies

Thalassemias result from variants in the globin genes, resulting in reduced or absent hemoglobin production, thereby reducing oxygen delivery. The supportive treatment of b-thalassemia major requires life-long red blood cell transfusions that lead to progressive iron overload and the potential for organ damage and impaired cardiac, hepatic, and endocrine function. Sickle cell disease is caused

by a single amino acid substitution in the beta chain of hemoglobin and, unlike thalassemia major, has a variable course of clinical severity. Sickle cell disease typically manifests clinically with anemia, severe painful crises, acute chest syndrome, stroke, chronic pulmonary and renal dysfunction, growth retardation, neurologic deficits, and premature death. The mean age of death for patients with sickle cell disease has been demonstrated as 42 years for men and 48 for women.

Treatment
The only definitive cure for thalassemia is to correct the genetic defect with allogeneic hematopoietic cell transplantation(allo-HCT).
Three major therapeutic options are available for sickle cell disease: chronic blood transfusions, hydroxyurea, and allo-HCT, the latter being the only possibility for cure.

Bone Marrow Failure Syndromes
Aplastic anemia in children is rare; most often, it is idiopathic and, less commonly, due to a hereditary disorder. Inherited syndromes include Fanconi anemia, a rare, autosomal recessive disease characterized by genomic instability, with congenital abnormalities, chromosome breakage, cancer susceptibility, and progressive bone marrow failure leading to pancytopenia and severe aplastic anemia. Frequently, this disease terminates in myelodysplastic syndrome or acute myeloid leukemia. Most patients with Fanconi anemia succumb to the complications of severe aplastic anemia, leukemia, or solid tumors, with a median survival of 30 years of age.

Dyskeratosis congenita is characterized by marked telomere dysregulation with clinical features of reticulated skin hyperpigmentation, nail dystrophy, and oral leukoplakia. Early mortality is associated with bone marrow failure, infections, pulmonary complications, or malignancy.

Variants affecting ribosome assembly and function are associated with Shwachman-Diamond syndrome and Diamond-Blackfan syndrome. Shwachman-Diamond has clinical features that include pancreatic exocrine insufficiency, skeletal abnormalities, and cytopenias, with some patients developing aplastic anemia. As with other bone marrow failure syndromes, patients are at increased risk of myelodysplastic syndrome and malignant transformation, especially acute myeloid leukemia. Diamond-Blackfan anemia is characterized by absent or decreased erythroid precursors in the bone marrow, with 30% of patients also having a variety of physical anomalies.

Treatment
In Fanconi anemia, HCT is currently the only treatment that definitively restores normal hematopoiesis. Excellent results have been observed with the use of human leukocyte antigen (HLA)-matched sibling allo-HCT, with cure of the marrow failure and amelioration of the risk of leukemia.

Primary Immunodeficiencies
The primary immunodeficiencies are a genetically heterogeneous group of diseases that affect distinct components of the immune system. More than 120 gene defects have been described, causing more than 150 disease phenotypes. The most severe defects (collectively known as severe combined immunodeficiency) cause an absence or dysfunction of T lymphocytes and sometimes B lymphocytes and natural killer cells.,

Treatment
Without treatment, patients with severe combined immunodeficiency usually die by 12 to 18 months of age. With supportive care, including prophylactic medication, the lifespan of these patients can be prolonged, but long-term outlook is still poor, with many dying from infectious or inflammatory complications or malignancy by early adulthood. Bone marrow transplantation is the only definitive cure, and the treatment of choice for severe combined immunodeficiency and other primary immunodeficiencies, including Wiskott-Aldrich syndrome and congenital defects of neutrophil function.,

Inherited Metabolic Diseases
Lysosomal storage disorders consist of many different rare diseases caused by a single gene defect, and most are inherited as an autosomal recessive trait. Lysosomal storage disorders are caused by specific enzyme deficiencies that result in defective lysosomal acid hydrolysis of endogenous macromolecules that subsequently accumulate as a toxic substance. Peroxisomal storage disorders arise due to a defect in a membrane transporter protein that leads to defects in the metabolism of long-chain fatty acids. Lysosomal storage disorders and peroxisomal storage disorders affect multiple organ systems, including the central and peripheral nervous systems. These disorders are progressive and often fatal in childhood due to both the accumulation of toxic substrate and a deficiency of the product of the enzyme reaction. Hurler syndrome usually leads to premature death by 5 years of age.

Treatment

Exogenous enzyme replacement therapy is available for a limited number of the inherited metabolic diseases; however, these drugs do not cross the blood-brain barrier, which results in the ineffective treatment of the central nervous system. Stem cell transplantation provides a constant source of enzyme replacement from the engrafted donor cells, which are not impeded by the blood-brain barrier. The donor-derived cells can migrate and engraft in many organ systems, giving rise to different types of cells (eg, microglial cells in the brain and Kupffer cells in the liver).

Allo-HCT has been primarily used to treat the inherited metabolic diseases that belong to the lysosomal and peroxisomal storage disorders, as listed in Table 1. The first stem cell transplant for an inherited metabolic disease was performed in1980 in a patient with Hurler syndrome. Since that time, more than 1000 transplants have been performed worldwide.

Table 1. Lysosomal and Peroxisomal Storage Disorders

Category	Diagnosis	Other Names
Mucopolysaccharidosis	Mucopolysaccharidosis I H or H/S Mucopolysaccharidosis II Mucopolysaccharidosis III A-D Mucopolysaccharidosis IV A-B Mucopolysaccharidosis VI Mucopolysaccharidosis VII	Hurler syndrome or Hurler-Scheie syndrome Hunter syndrome Sanfilippo syndrome A-D Morquio syndrome A-B Maroteaux-Lamy syndrome Sly syndrome
Sphingolipidosis	Fabry disease Farber disease Gaucher disease types 1 and 3 GM1 gangliosidosis Niemann-Pick disease A and B Tay-Sachs disease Sandhoff disease Globoid cell leukodystrophy	Lipogranulomatosis Krabbe disease MLD

	Metachromatic leukodystrophy	
Glycoproteinosis	Aspartylglucosaminuria Fucosidosis Alpha-mannosidosis Beta-mannosidosis Mucolipidosis III and IV	Sialidosis
Other lipidoses	Niemann-Pick disease C Wolman disease Ceroid lipofuscinosis type III	Batten disease
Glycogen storage	Glycogen storage disease type II	Pompe disease
Multiple enzyme deficiency	Galactosialidosis Mucolipidosis type II	I-cell disease
Lysosomal transport defects	Cystinosis Sialic acid storage disease Salla disease	
Peroxisomal storage disorders	Adrenoleukodystrophy Adrenomyeloneuropathy	ALD AMN

Genetic Disorders Affecting Skeletal Tissue

Osteopetrosis is a condition caused by defects in osteoclast development and/or function. The osteoclast (the cell that functions in the breakdown and resorption of bone tissue) is known to be part of the hematopoietic family and shares a common progenitor with the macrophage in the bone marrow. Osteopetrosis is a heterogeneous group of heritable disorders, resulting in several different types of variable severity. The most severely affected patients are those with infantile malignant osteopetrosis (Albers-Schonberg disease or marble bone disease). Patients with infantile malignant osteopetrosis suffer from dense bone, including a heavy head with frontal bossing, exophthalmos, blindness by approximately 6 months of age, and severe hematologic malfunction with bone marrow failure. Seventy percent of these patients die before the age of 6 years, often of recurrent infections.

Treatment

HCT is the only curative therapy for this fatal disease.

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 total 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 existing disease in the absence of pretransplant conditioning. Intense conditioning regimens are limited to patients who are sufficiently medically fit to tolerate substantial adverse effects. These include opportunistic infections secondary to loss of endogenous bone marrow function and organ damage or failure caused by 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 incomplete remission. Patients who undergo autologous HCT are also susceptible to chemotherapy-related toxicities and opportunistic infections before engraftment, but not GVH disease.

Reduced-Intensity Conditioning Allogeneic Hematopoietic Cell Transplantation
Reduced-intensity conditioning (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 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, parts1270 and 1271. Hematopoietic stem cells are included in these regulations.

Rationale/Source

Description
A number of inherited and acquired conditions have the potential for severe and/or progressive disease. For some conditions, allogeneic hematopoietic cell transplantation (allo-HCT) has been used to alter the natural history of the disease or potentially offer a cure.

Summary of Evidence
For individuals who have a hemoglobinopathy, bone marrow failure syndrome, primary immunodeficiency, inherited metabolic syndrome disease (specifically those other than Hunter, Sanfilippo, or Morquio syndromes), or a genetic disorder affecting skeletal tissue who receive allo-HCT, the evidence includes mostly case series, case reports, and registry data. Relevant outcomes are overall survival, disease-specific survival, symptoms, quality of life, and treatment-related morbidity. The evidence has shown that, for most of these disorders, there is a demonstrable improvement in overall survival and other disease-specific outcomes. Allo-HCT is likely to improve health outcomes in select patients with certain inherited and acquired diseases. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have an inherited metabolic syndrome disease (specifically those including Hunter, Sanfilippo, and Morquio syndromes) who receive allo-HCT, the evidence includes case reports. Relevant outcomes are overall survival, disease-specific survival, symptoms, quality of life, and treatment-related morbidity. Use of allo-HCT to treat patients with Hunter, Sanfilippo, or Morquio syndromes does not result in improvements in neurologic, neuropsychologic, and neurophysiologic function. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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 physician specialty society (3 reviewers) and 3 academic medical centers while this policy was under review in 2009. There was general agreement with the policy statements. In particular, the reviewers were specifically asked to comment on the use of hematopoietic cell transplant in the inherited metabolic diseases, except for Hunter, Sanfilippo, and Morquio syndromes; 4 reviewers agreed with the current policy statement, 1 disagreed, and 1 did not address this specific question.

Practice Guidelines and Position Statements

American Society for Blood and Marrow Transplantation
In 2015, the American Society for Blood and Marrow Transplantation published consensus guidelines on the use of hematopoietic cell transplantation to treat specific conditions in and out of the clinical trial settings. Specific to this review Table 2 provides the allogeneic guidelines for specific indications.

Table 2. Recommendations for Use of Allogeneic HCT to Treat Genetic Diseases and Acquired Anemias

Indications	Allogeneic HCT <18 Years
Severe aplastic anemia, new diagnosis	S
Severe aplastic anemia, relapse/refractory	S
Fanconi anemia	R
Dyskeratosis congenita	R
Blackfan-Diamond anemia	R
Sickle cell disease	C
Thalassemia	S
Congenital amegakaryocytic thrombocytopenia	R
Severe combined immunodeficiency	R
T-cell immunodeficiency, severe combined immunodeficiency variants	R
Wiskott-Aldrich syndrome	R
Hemophagocytic disorders	R
Lymphoproliferative disorders	R
Severe congenital neutropenia	R
Chronic granulomatous disease	R
Other phagocytic cell disorders	R
Immunodysregulation polyendocrinopathy enteropathy X-linked syndrome	R
Juvenile rheumatoid arthritis	D
Systemic sclerosis	D

Other autoimmune and immune dysregulation disorders	R
Mucopolysaccharidoses (MPS-I and MPS-VI)	R
Other metabolic diseases	R
Osteopetrosis	R
Globoid cell leukodystrophy (Krabbe)	R
Metachromatic leukodystrophy	R
Cerebral X-linked adrenoleukodystrophy	R
Indications	Allogeneic HCT >18 Years
Severe aplastic anemia, new diagnosis	S
Severe aplastic anemia, relapse/refractory	S
Fanconi anemia	R
Dyskeratosis congenita	R
Sickle cell disease	C
Thalassemia	D
Hemophagocytic syndromes, refractory	R
Mast cell diseases	R
Common variable immunodeficiency	R
Wiskott-Aldrich syndrome	R
Chronic granulomatous disease	R
Multiple sclerosis	N
Systemic sclerosis	N
Rheumatoid arthritis	N

C: clinical evidence available; D: developmental; HCT: hematopoietic cell transplantation; N: not generally recommended; R: standard of care, rare indication; S: standard of care.

British Committee for Standards in Haematology

In 2015, the British Committee for Standards in Haematology published guidelines on the diagnosis and management of adult aplastic anemia. The following key recommendations on HCT were included in the guidelines:

Matched sibling donor (allogeneic) HCT is the treatment of choice for severe aplastic anemia; however, for patients aged 35 to 50 years, patients need to be assessed for comorbidities before being considered for HCT.

For adults, unrelated donor HCT should be considered if patients fail to respond to a single course of immunosuppressive therapy.

Although there have been improvements in outcomes after alternative donor HCT, these transplants are still experimental, and expert consultation should be sought before considering their use.

European Blood and Marrow Transplantation
In 2014, the European Blood and Marrow Transplantation provided consensus-based recommendations on indications for HCT and transplant management in the hemoglobinopathies.

Pediatric Haemato-Oncology Italian Association
In 2015, the Pediatric Haemato-Oncology Italian Association issued guidelines on the diagnosis and treatment of acquired aplastic anemia in childhood.

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

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 3.

Table 3. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			

NCT02766465	A Study to Compare Bone Marrow Transplantation to Standard Care in Adolescents and Young Adults With Severe Sickle Cell Disease	200	Mar 2023
NCT02356653	Expanded Access Protocol Using CD3+/CD19+ Depleted Unrelated Donor or Partially Matched Related Donor Peripheral Stem Cells	100	Jan 2021
NCT02986698	A Single-Center, Non-Randomized Study of the Safety and Efficacy of In Utero Hematopoietic Stem Cell Transplantation for the Treatment of Fetuses With Alpha Thalassemia Major	10	Feb 2024
Unpublished			
NCT00176826	In-vivo T-cell Depletion and Hematopoietic Stem Cell Transplantation for Life-Threatening Immune Deficiencies and Histiocytic Disorders	22	Aug 2015(Terminated)

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Policy History

Original Effective Date: 01/28/2002
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12/06/2000	Medical Policy Committee review
01/28/2002	Managed Care Advisory Council approval
06/24/2002	Format revision
03/31/2004	Medical Director review
04/20/2004	Medical Policy Committee review. Format revision. No substance change to policy.
04/26/2004	Managed Care Advisory Council approval

04/05/2005	Medical Director review
04/27/2005	Medical Policy Committee review. Format revisions. Policy unchanged.
05/23/2005	Managed Care Advisory Council approval
05/03/2006	Medical Director review
05/17/2006	Medical Policy Committee approval. Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
04/04/2007	Medical Director review
04/18/2007	Medical Policy Committee approval. Coverage eligibility unchanged.
04/02/2008	Medical Director review
04/16/2008	Medical Policy Committee approval. Coverage eligibility unchanged.
04/02/2009	Medical Director review
04/15/2009	Medical Policy Committee approval. Coverage eligibility unchanged
04/08/2010	Medical Policy Committee approval
04/21/2010	Medical Policy Implementation Committee approval. Entire policy redone.
04/07/2011	Medical Policy Committee approval
04/13/2011	Medical Policy Implementation Committee approval. No change to coverage.
04/12/2012	Medical Policy Committee review
04/25/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/04/2013	Coding updated
04/04/2013	Medical Policy Committee review
04/24/2013	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/03/2014	Medical Policy Committee review
04/23/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
10/29/2015	Medical Policy Committee review
11/16/2015	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/01/2016	Medical Policy Committee review

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12/21/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
12/07/2017	Medical Policy Committee review
12/20/2017	Medical Policy Implementation Committee approval. "Stem" removed from title and Policy. HSCT changed to HCT in Policy and Policy Guidelines and text. Coverage eligibility unchanged.
12/06/2018	Medical Policy Committee review
12/19/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/05/2019	Medical Policy Committee review
12/11/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/07/2020	Medical Policy Committee review
05/13/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/03/2021	Medical Policy Committee review
06/09/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Indicated that Shwachman-Diamond and Diamond-Blackfan are both syndromes under the Bone Marrow Failure Syndromes section that are eligible for coverage.

Next Scheduled Review Date: 06/2022

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.

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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, 38207, 38208, 38209, 38210, 38211, 38212, 38213, 38214, 38215, 38230, 38240, 38242, 38243
HCPCS	S2140, S2142, S2150
ICD-10 Diagnosis	D56.0-D56.8, D57.00-D57.03, D57.09, D57.1, D57.20-D57.219, D57.40-D57.419, D57.42, D57.431-D57.439, D57.44, D57.451-D57.459, D57.80, D57.811-D57.819, D60.0-D60.9, D61.01-D61.09, D61.1-D61.3, D61.810-D61.818, D61.82, D61.89, D61.9, D70.0, D82.0, E75.21-E75.22, E75.240-E75.249, E75.3, E76.01-E76.03, E76.1, E76.210-E76.219, E76.22, E76.29, E76.3, E76.8-E76.9, E77.0-E77.9, Q78.2

*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.

Allogeneic Hematopoietic Cell Transplantation for Genetic Diseases and Acquired Anemias

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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.