

Hematopoietic Cell Transplantation for Acute Myeloid Leukemia

Policy # 00049

Original Effective Date: 01/28/2002

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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.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

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.*

Allogeneic Hematopoietic Cell Transplant

Based on review of available data, the Company may consider allogeneic hematopoietic cell transplantation (HCT) using a reduced-intensity conditioning regimen as a treatment of acute myeloid leukemia (AML) in individuals who are in complete marrow and extramedullary remission (complete remission [CR1] or beyond), and who for medical reasons would be unable to tolerate a myeloablative conditioning regimen (see Policy Guidelines section) to be **eligible for coverage**.**

Autologous Hematopoietic Cell Transplant

Based on review of available data, the Company may consider autologous hematopoietic cell transplantation (HCT) to treat acute myeloid leukemia (AML) in complete remission [CR1] or beyond, or relapsed AML, if responsive to intensified induction chemotherapy in individuals who are not candidates for allogeneic HCT to be **eligible for coverage**.**

When Services May Be 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.*

Allogeneic Hematopoietic Cell Transplant

Based on review of available data, the Company may consider allogeneic hematopoietic cell transplantation (HCT) using a myeloablative conditioning regimen to be **eligible for coverage**.**

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Patient Selection Criteria

Coverage eligibility will be considered for allogeneic HCT using a myeloablative conditioning regimen to treat:

- poor- to intermediate-risk AML in first complete remission (CR1) (see Policy Guidelines section for information on risk stratification); or
- AML that is refractory to standard induction chemotherapy but can be brought into complete remission (CR) with intensified induction chemotherapy; or
- AML that relapses following chemotherapy-induced CR1 but can be brought into second complete remission (CR2) or beyond with intensified induction chemotherapy; or
- AML in individuals who have relapsed following a prior autologous HCT but can be brought into CR with intensified induction chemotherapy and are medically able to tolerate the procedure.

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 and autologous hematopoietic cell transplantation (HCT) in individuals not meeting any of the above criteria to be **investigational**.*

Policy Guidelines

Primary refractory acute myeloid leukemia (AML) is defined as leukemia that does not achieve a complete remission after conventionally dosed (nonmarrow ablative) chemotherapy.

In the French-American-British criteria, the classification of AML is solely based on morphology as determined by the degree of differentiation along different cell lines and the extent of cell maturation.

Clinical features that predict poor outcomes of AML therapy include, but are not limited to, the following:

- Treatment-related AML (secondary to prior chemotherapy and/or radiotherapy for another malignancy)
- AML with antecedent hematologic disease (eg, myelodysplasia)
- Presence of circulating blasts at the time of diagnosis
- Difficulty in obtaining first complete remission with standard chemotherapy
- Leukemias with monocytoid differentiation (French-American-British classification M4 or M5).

The newer, currently preferred, World Health Organization classification of AML incorporates and interrelates morphology, cytogenetics, molecular genetics, and immunologic markers. It attempts to construct a classification that is universally applicable and prognostically valid. The World Health

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Organization system was adapted by National Comprehensive Cancer Network to estimate individual prognosis to guide management, as shown in Table PG1.

Table PG1. Risk Status of Acute Myeloid Leukemia Based on Genetic Factors

Risk Category	Genetic Abnormality
Favorable	t(8;21)(q22;q22.1); <i>RUNX1-RUNX1T1</i> inv(16)(p13.1;q22) or t(16;16)(p13.1;q22); <i>CBFB-MYH11</i> Biallelic mutated <i>CEBPA</i> Mutated <i>NPM1</i> without <i>FLT3</i> -ITD or with <i>FLT3</i> -ITD ^{low}
Intermediate	Mutated <i>NPM1</i> and <i>FLT3</i> -ITD ^{high} Wild-type <i>NPM1</i> without <i>FLT3</i> -ITD or with <i>FLT3</i> -ITD ^{low} (without adverse-risk genetic lesions) t(9;11)(p21.3;q23.3); <i>MLLT3-KMT2A</i> Cytogenetic abnormalities not classified as favorable or adverse
Poor/Adverse	t(6;9)(p23;q34.1); <i>DEK-NUP214</i> t(v;11q23.3); <i>KMT2A</i> rearranged t(9;22)(q34.1;q11.2); <i>BCR-ABL1</i> inv(3)(q21.3;q26.2) or t(3;3)(q21.3;q26.2); <i>GATA2,MECOM(EV11)</i> -5 or del(5q); -7; -17/abn(17p) Complex karyotype, monosomal karyotype Wild-type <i>NPM1</i> and <i>FLT3</i> -ITD ^{high} Mutated <i>RUNX1</i> (if not co-occurring with favorable-risk AML subtypes) Mutated <i>ASXL1</i> (if not co-occurring with favorable-risk AML subtypes) Mutated <i>TP53</i>

AML: acute myeloid leukemia; ITD: internal tandem duplication.

The relative importance of cytogenetic and molecular abnormalities in determining prognosis and guiding therapy is under investigation.

The ideal allogeneic donors are human leukocyte antigen (HLA)-identical siblings, matched at the HLA-A, -B, and -DR (antigen-D related) loci (6 of 6). Related donors mismatched at 1 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 individual, for which there usually is sharing of only 3 of the 6 major histocompatibility antigens. Most individuals will have such a donor; however, the risk of graft-versus-host disease and overall morbidity of the procedure may be severe, and experience with these donors is not as extensive as that with matched donors.

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Background/Overview

Acute Myeloid Leukemia Treatment

Complete remission of acute myeloid leukemia (AML) can be achieved initially using induction therapy, consisting of conventional doses of combination chemotherapy. A complete response is achieved in 60% to 80% of adults younger than 60 years of age and 40% to 60% in patients older than 60 years of age. However, the high incidence of disease relapse has prompted research into a variety of post-remission (consolidation) strategies, typically using high-dose chemotherapy with autologous hematopoietic cell transplantation (HCT) or high-dose or reduced-intensity chemotherapy with allogeneic HCT (allo-HCT). The 2 treatments, autologous HCT and allo-HCT, represent 2 different strategies. The first, autologous HCT, is a “rescue,” but not a therapeutic procedure; the second, allo-HCT, is a “rescue” plus a therapeutic procedure.

Hematopoietic Cell Transplantation

Hematopoietic cell transplantation is a procedure in which hematopoietic stem cells are intravenously infused to restore bone marrow and immune function in patients with cancer 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). These cells 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 allo-HCT, immunologic compatibility between donor and patient is a critical factor for achieving a successful outcome. Compatibility is established by typing of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. Human leukocyte antigen 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 (GVHD), which increases susceptibility to opportunistic infections.

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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 GVHD.

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 (MAC) 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 nonrelapse mortality. The goal of RIC is to reduce disease burden and to minimize associated treatment-related morbidity and nonrelapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. Reduced-intensity conditioning regimens range from nearly 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 RIC will refer to all conditioning regimens intended to be nonmyeloablative.

A 2015 review in the *New England Journal of Medicine* summarized advances in the classification of AML, the genomics of AML and prognostic factors, and current and new treatments. The National Comprehensive Cancer Network guidelines provide updated information on genetic markers for risk stratification, and additional recent reviews summarize information on novel therapies for AML.⁷

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, parts 1270 and 1271. Hematopoietic stem cells are included in these regulations.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

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Description

Acute myeloid leukemia (AML) refers to leukemias that arise from a myeloid precursor in the bone marrow. There is a high incidence of relapse, which has prompted research into various post-remission strategies using either allogeneic (allo-) or autologous hematopoietic cell transplantation (HCT). Hematopoietic cell transplantation refers to a procedure that infuses hematopoietic stem cells to restore bone marrow function in individuals with cancer who receive bone marrow-toxic doses of drugs with or without whole-body radiotherapy.

Summary of Evidence

For individuals who have cytogenetic or molecular intermediate- or poor-risk acute myeloid leukemia (AML) in first complete remission (CR1) who receive allogeneic (allo-) hematopoietic cell transplant (HCT) with myeloablative conditioning (MAC), the evidence includes systematic reviews, randomized controlled trials (RCTs), and matched cohort studies. Relevant outcomes are overall survival (OS) and disease-specific survival (DSS). The majority of the evidence has revealed that allo-HCT is better at improving OS and DSS rates in patients with AML in CR1 than conventional chemotherapy. One RCT found no difference in OS between allo-HCT and high-dose cytarabine, although the study had many limitations. All trials employed natural randomization based on donor availability and intention-to-treat analysis. Survival rates appear to be associated with the presence of minimal residual disease and risk category. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have AML refractory to standard induction chemotherapy who receive allo-HCT with MAC, the evidence includes retrospective data compiled from patients entered in phase 3 trials and registry data. Relevant outcomes are OS and DSS. The evidence would suggest that allo-HCT improves OS and DSS rates in patients who are refractory to induction chemotherapy better than conventional chemotherapy. While there are some limitations to the evidence, which include its retrospective nature, lack of rigorous randomization, and general pitfalls of registry data, these results may provide a clinically meaningful benefit for patients who do not have other treatment options. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have AML who relapsed after standard induction chemotherapy-induced CR1 who receive allo-HCT or autologous HCT with MAC, the evidence includes retrospective data compiled from patients entered in phase 3 trials and registry data. Relevant outcomes are OS and DSS. The evidence has shown that allo-HCT improves OS rates in patients with relapsed AML better than conventional chemotherapy. Limitations of the evidence include its retrospective nature, lack of rigorous randomization, and pitfalls of registry data. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have cytogenetic or molecular intermediate- or poor-risk AML in CR1 and for medical reasons cannot tolerate MAC who receive allo-HCT with reduced-intensity conditioning (RIC), the evidence includes 2 RCTs, 3 meta-analyses, and other comparative and noncomparative studies. Relevant outcomes are OS, DSS, and treatment-related morbidity. The RCTs compared RIC with MAC and reported similar rates in nonrelapse mortality, relapse, and OS, though 1 of the trials

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was stopped prematurely due to slow accrual of patients. Two retrospective comparative studies found no difference in OS or leukemia-free survival between the conditioning regimens. It appears unlikely that additional comparative evidence will be generated. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have AML in CR1 or beyond without a suitable allo-HCT donor who receive autologous HCT, the evidence includes prospective cohort studies in which patients with an available sibling donor were offered allo-HCT (biologic randomization) with random assignment of all others to autologous HCT or chemotherapy (or no further treatment); and randomized trials comparing autologous HCT with chemotherapy in all patients. Relevant outcomes are OS and DSS. Compared with chemotherapy, patients undergoing autologous HCT experienced reduced relapse and improved disease-free survival (DFS) rates. The OS did not differ between the groups. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information’ if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Society for Transplantation and Cellular Therapy

In 2020, the American Society for Transplantation and Cellular Therapy published expert panel recommendations on the role of hematopoietic cell transplant (HCT) in newly-diagnosed adult acute myeloid leukemia (AML). Recommendations were generated based on findings from a systematic review and graded based on prespecified criteria. Expert panel recommendations regarding allogeneic HCT (allo-HCT) and autologous HCT and the grades of the recommendations are as follows:

- Patients with unfavorable-risk in first remission (CR1) should undergo allo-HCT. (Grade A)
- Patients with intermediate-risk in CR1 should undergo allo-HCT. (Grade B)
- Patients with favorable-risk in CR1 should not undergo allo-HCT. (Grade C)
- The role of secondary mutational abnormalities in selecting a patient for allo-HCT is unclear. (Grade N/A [not applicable])
- The presence of measurable residual disease at the end of induction therapy should be considered an indication to offer allo-HCT. (Grade C)
- The role of allo-HCT is unclear in patients with induction failure. (Grade N/A)
- Patients with secondary acute myeloid leukemia in CR1 should undergo allo-HCT. (Grade D)
- Patients with therapy-related acute myeloid leukemia in CR1 should undergo allo-HCT. (Grade D)
- Patients ≥ 60 years in CR1 should undergo allo-HCT. (Grade B)

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- Autologous HCT is a good alternative to chemotherapy consolidation in patients who are not eligible for allo-HCT. (Grade B)
- Myeloablative conditioning should be the preferred type of conditioning in patients who are fit for myeloablative conditioning, but reduced-intensity conditioning is an acceptable alternative in unfit patients. (Grade D)

In 2015, the American Society for Transplantation and Cellular Therapy (formerly The American Society for Blood and Marrow Transplantation) published guidelines on indications for autologous HCT and allo-HCT. An updated guideline was published in 2020. Table 1 summarizes recommendations for HCT in AML from the most recent guideline iteration.

Table 1. Recommendations for the Use of Hematopoietic Cell Transplantation to Treat Acute Myeloid Leukemia

Indication	Allo-HCT ^a	Autologous HCT ^a
<i>AML, age <18 years</i>		
First CR, low risk	N	N
First CR, intermediate risk	C	N
First CR, high risk	S	N
Second or greater CR	S	N
Not in remission	S	N
<i>AML, age ≥18 years</i>		
First CR, low risk	N	C
First CR, intermediate risk	S	C
First CR, high risk	S	N
Second CR	S	C
Third or greater CR	S	N
Not in remission	S	N

^a Recommendations were classified as follows: S, standard of care (well-defined and generally supported by evidence in the form of high quality clinical trials and/or observational studies); C, standard of care, clinical evidence available (large clinical trials are not available; however, sufficiently large cohort studies have shown efficacy with acceptable risk of morbidity and mortality); N, not generally recommended
allo-HCT: allogeneic hematopoietic cell transplantation; AML: acute myeloid leukemia; CR: complete remission ; HCT: hematopoietic cell transplantation

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In 2022, the American Society of Transplantation and Cellular Therapy published guidance on the role of HCT in pediatric AML and myelodysplastic syndrome. The guidelines state that HCT is recommended for patients in CR1 with unfavorable mutations/cytomolecular abnormalities but not for patients with favorable-risk lesions. HCT should also be considered for patients with primary induction failure, refractory disease after 2 to 3 cycles of chemotherapy, and relapse.

National Comprehensive Cancer Network

The National Comprehensive Cancer Network clinical guidelines (v. 3.2026) for AML state that allo-HCT is recommended for patients aged <60 years after standard-dose cytarabine induction with induction failure or significant residual disease without a hypocellular marrow. It is also recommended after high-dose cytarabine induction with induction failure, or as post-remission therapy in those with intermediate-risk or poor-risk cytogenetics. Allo-HCT is identified as a "reasonable option" for patients aged ≥60 years after standard-dose cytarabine induction with residual disease or induction failure or following complete response (preferably in a clinical trial). In addition, allo-HCT is recommended for relapsed or refractory disease. Autologous HCT is recommended as another option in patients with AML after standard induction chemotherapy-induced first complete remission, although allo-HCT is preferred.

In patients with acute promyelocytic leukemia, a subtype of AML, patients who achieve a molecular remission after second-line therapy should be considered for autologous HCT if they do not have contraindications to high-dose therapy. Allogeneic HCT should be reserved for patients who have persistent disease despite therapy for relapsed disease.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

The Centers for Medicare & Medicaid Services have the following national coverage determination on the use of cell transplantation for AML:

- Allogeneic: "...for the treatment of leukemia, leukemia in remission..."
- Autologous: "Acute leukemia in remission who have a high probability of relapse and who have no human leukocyte antigens (HLA)-matched."

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
<i>Ongoing</i>			
NCT06643195	Immediate Allogeneic Hematopoietic Stem Cell Transplantation Versus Re-treatment for Patients	358	Sep 2027

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	With High-Risk Acute Myeloid Leukemia: a Randomised, Open-label, Phase 2 Clinical Trial.		
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NCT: national clinical trial.

^a Denotes industry-sponsored or cosponsored trial.

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Policy History

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12/06/2001	Medical Policy Committee review
01/28/2002	Managed Care Advisory Council approval
06/24/2002	Format revision. Coverage eligibility unchanged.
03/31/2004	Medical Director review
04/20/2004	Medical Policy Committee review. Format revision.
04/26/2004	Managed Care Advisory Council approval
04/05/2005	Medical Director review
04/19/2005	Medical Policy Committee review. Format revision. Coverage eligibility unchanged. Rationale/source revised.
05/23/2005	Managed Care Advisory Council approval
07/07/2006	Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
08/02/2006	Medical Director Review
08/09/2006	Medical Policy Committee approval, format revisions, addition of FDA/other governmental regulations, references updates. Coverage eligibility unchanged.
07/11/2007	Medical Director review

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07/18/2007	Medical Policy Committee approval. Coverage eligibility unchanged.
07/02/2008	Medical Director review
07/16/2008	Medical Policy Committee approval. Coverage eligibility unchanged. Rationale updated. "High-Dose Chemotherapy" removed from policy title.
07/02/2009	Medical Director review
07/22/2009	Medical Policy Committee approval. Extensive revision of coverage section. Updated background/overview, rationale and references.
07/01/2010	Medical Policy Committee approval
07/21/2010	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/04/2011	Medical Policy Committee review
08/17/2011	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/02/2012	Medical Policy Committee review
08/15/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/01/2013	Medical Policy Committee review
08/21/2013	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/04/2014	Medical Policy Committee review
09/17/2014	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 statements clarified with new language.
11/03/2016	Medical Policy Committee review
11/16/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
11/02/2017	Medical Policy Committee review
11/15/2017	Medical Policy Implementation Committee approval. Removed "stem" from the policy title, coverage statements and text. Added the phrase 'but can be brought into CR with intensified induction chemotherapy to the last criteria bullet for HCT using a myeloablative conditioning regimen. Added Policy Guidelines section.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/04/2019	Medical Policy Committee review
04/24/2019	Medical Policy Implementation Committee approval. Added (CR1 or beyond) as clarification for allogeneic hematopoietic tic cell transplant patients in complete marrow and extramedullary remission. Policy statement regarding medical necessity for auto-HCT changed to clarify that it applies to patients that are not

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	candidates for allo-HCT. Investigational statement added for patients not meeting allogeneic MN criteria.
04/02/2020	Medical Policy Committee review
04/08/2020	Medical Policy Implementation Committee approval. Revised investigational statement for the use of allogeneic and autologous hematopoietic cell transplant (HCT) for all other indications by adding “for acute myeloid leukemia” to be specific to this policy content.
04/01/2021	Medical Policy Committee review
04/14/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/07/2022	Medical Policy Committee review
04/13/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
	Coding update
04/06/2023	Medical Policy Committee review
04/12/2023	Medical Policy Implementation Committee approval. Replaced “patients” with “individuals” in the coverage section. Coverage eligibility unchanged.
04/04/2024	Medical Policy Committee review
04/10/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/03/2025	Medical Policy Committee review
04/09/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/02/2026	Medical Policy Committee review
04/10/2026	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 04/2027

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)†, copyright 2025 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.

The responsibility for the content of Louisiana Blue Medical Policy Coverage Guidelines is with Louisiana Blue and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Louisiana Blue Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Louisiana Blue Medical

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Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

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, 38232, 38240, 38241, 38243 Delete code effective 05/01/2026: 38242
HCPSC	S2140, S2142, S2150 Delete code effective 05/01/2025: S2152
ICD-10 Diagnosis	All related diagnoses

*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 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

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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.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan’s authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan’s pharmacy benefit.