

## Corporate Medical Policy

### Hematopoietic Stem-Cell Transplantation for Acute Myeloid Leukemia

<b>File Name:</b>	hematopoietic_stem-cell_transplant_for_acute_myeloid_leukemia
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#### Description of Procedure or Service

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Acute myeloid leukemia (AML) (also called acute nonlymphocytic leukemia) refers to a set of leukemias that arise from a myeloid precursor in the bone marrow. There is a high incidence of relapse, which has prompted research into a variety of post-remission strategies using either allogeneic or autologous hematopoietic stem-cell transplantation (HSCT). HSCT refers to a procedure in which hematopoietic stem cells are infused to restore bone marrow function in cancer patients who receive bone-marrow-toxic doses of cytotoxic drugs with or without whole-body radiation therapy.

#### **Hematopoietic Stem-Cell Transplantation**

Hematopoietic stem cells may be obtained from the transplant recipient (autologous HSCT) or from a donor (allogeneic HSCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates. Although cord blood is an allogeneic source, the stem cells in it are antigenically “naïve” and thus are associated with a lower incidence of rejection or graft-versus-host disease (GVHD). Cord blood is discussed in greater detail in the Cord Blood as a Source of Stem Cells medical policy.

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

#### **Conventional Preparative Conditioning for HSCT**

The conventional (“classical”) practice of allogeneic HSCT involves administration of cytotoxic agents (e.g., cyclophosphamide, busulfan) with or without total body irradiation at doses sufficient to destroy endogenous hematopoietic capability in the recipient. The beneficial treatment effect in this procedure is due to a combination of initial eradication of malignant cells and subsequent graft-versus-malignancy (GVM) effect that develops after engraftment of allogeneic stem cells within the patient’s bone marrow space. While the slower GVM effect is considered to be the potentially curative component, it may be overwhelmed by extant disease without the use of pretransplant conditioning. However, intense conditioning regimens are limited to patients who are sufficiently fit medically to tolerate substantial adverse effects that include pre-engraftment opportunistic infections secondary to loss of endogenous bone marrow function and organ damage and failure caused by the cytotoxic drugs. Furthermore, in any allogeneic HSCT, immune suppressant drugs are required to minimize graft rejection and GVHD, which also increases susceptibility of the patient to opportunistic infections.

The success of autologous HSCT is predicated on the ability of cytotoxic chemotherapy with or without radiation to eradicate cancerous cells from the blood and bone marrow. This permits subsequent

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engraftment and repopulation of bone marrow space with presumably normal hematopoietic stem cells obtained from the patient prior to undergoing bone marrow ablation. As a consequence, autologous HSCT is typically performed as consolidation therapy when the patient's disease is in complete remission. Patients who undergo autologous HSCT are susceptible to chemotherapy-related toxicities and opportunistic infections prior to engraftment, but not GVHD.

## **Reduced-Intensity Conditioning for Allogeneic HSCT**

Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses or less intense regimens of cytotoxic drugs or radiation than are used in conventional full-dose myeloablative conditioning treatments. The goal of RIC is to reduce disease burden, but also to minimize as much as possible associated treatment-related morbidity and non-relapse mortality (NRM) in the period during which the beneficial GVM effect of allogeneic transplantation develops. Although the definition of RIC remains arbitrary, with numerous versions employed, all seek to balance the competing effects of NRM and relapse due to residual disease. RIC regimens can be viewed as a continuum in effects, from nearly total myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allogeneic HSCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full-donor chimerism, which may be supplemented with donor lymphocyte infusions to eradicate residual malignant cells. For the purposes of this policy, the term "reduced-intensity conditioning" will refer to all conditioning regimens intended to be nonmyeloablative, as opposed to fully myeloablative (conventional) regimens.

## **Acute Myeloid Leukemia (AML)**

Acute myeloid leukemia (sometimes called "acute nonlymphocytic leukemia" [ANLL]) refers to a set of leukemias that arise from a myeloid precursor in the bone marrow. AML is characterized by proliferation of myeloblasts, coupled with low production of mature red blood cells, platelets, and often non-lymphocytic white blood cells (granulocytes, monocytes). Clinical signs and symptoms are associated with neutropenia, thrombocytopenia, and anemia. The incidence of AML increases with age, with a median of 67 years. About 13,000 new cases are diagnosed annually.

The pathogenesis of AML is unclear. It can be subdivided according to resemblance to different subtypes of normal myeloid precursors using the French-American-British (FAB) classification. This system classifies leukemias from M0–M7, based on morphology and cytochemical staining, with immunophenotypic data in some instances. The World Health Organization (WHO) subsequently incorporated clinical, immunophenotypic and a wide variety of cytogenetic abnormalities that occur in 50% to 60% of AML cases into a classification system that can be used to guide treatment according to prognostic risk categories. (see Policy Guidelines)

The WHO system recognizes 5 major subcategories of AML: 1) AML with recurrent genetic abnormalities; 2) AML with multilineage dysplasia; 3) therapy-related AML and myelodysplasia (MDS); 4) AML not otherwise categorized; and 5) acute leukemia of ambiguous lineage. AML with recurrent genetic abnormalities includes AML with t(8;21)(q22;q22), inv(16)(p13;q22) or t(16;16)(p13;q22), t(15;17)(q22;q12), or translocations or structural abnormalities involving 11q23. Younger patients may exhibit t(8;21) and inv(16) or t(16;16). AML patients with 11q23 translocations include two subgroups: AML in infants and therapy-related leukemia. Multilineage dysplasia AML must exhibit dysplasia in 50% or more of the cells of two lineages or more. It is associated with cytogenetic findings that include -7/del(7q), -5/del(5q), +8, +9, +11, del(11q), del(12p), -18, +19, del(20q)+21, and other translocations. AML not otherwise categorized includes disease that does not fulfill criteria for the other groups, and essentially reflects the morphologic and cytochemical features and maturation level criteria used in the FAB classification, except for the definition of AML as having a minimum 20% (as opposed to 30%) blasts in the marrow. AML of ambiguous lineage is diagnosed when blasts lack sufficient lineage-specific antigen expression to classify as myeloid or lymphoid.

Molecular studies have identified a number of genetic abnormalities that also can be used to guide prognosis and management of AML. Cytogenetically normal AML (CN-AML) is the largest defined

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subgroup of AML, comprising about 45% of all AML cases. Despite the absence of cytogenetic abnormalities, these cases often have genetic mutations that affect outcomes, of which six have been identified. The FLT3 gene that encodes FMS-like receptor tyrosine kinase (TK) 3, a growth factor active in hematopoiesis, is mutated in 33%–49% of CN-AML cases; among those, 28%–33% consist of internal tandem duplications (ITD), 5%–14% are missense mutations in exon 20 of the TK activation loop, and the rest are point mutations in the juxtamembrane domain. All FLT3 mutations result in a constitutively activated protein, and confer a poor prognosis. Several pharmaceutical agents that inhibit the FLT3 TK are under investigation.

Complete remission 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 in 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 postremission (consolidation) strategies, typically using high-dose chemotherapy with autologous HCT or high-dose or reduced-intensity chemotherapy with 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.

**\*\*\*Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

## Policy

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**BCBSNC will provide coverage for Hematopoietic Stem-cell Transplantation for Acute Myeloid Leukemia (AML) when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.**

**Some patients may be eligible for coverage under Clinical Trials. Refer to the policy on Clinical Trial Services.**

## Benefits Application

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This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

**Some health benefit plans may exclude benefits for transplantation.**

## When Hematopoietic Stem-Cell Transplantation for Acute Myeloid Leukemia is covered

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1. Allogeneic hematopoietic stem-cell transplantation (HSCT) using a myeloablative conditioning regimen may be considered medically necessary to treat:
  - a. Poor- to intermediate-risk AML in first complete remission (CR1); **or**
  - b. AML that is refractory to standard induction chemotherapy but can be brought into CR with intensified induction chemotherapy; **or**
  - c. AML that relapses following chemotherapy induced CR1 but can be brought into CR2 or beyond with intensified induction chemotherapy; **or**
  - d. AML in patients who have relapsed following a prior autologous HSCT, but can be brought into CR with intensified induction chemotherapy and are medically able to tolerate the procedure.
2. Allogeneic HSCT using a reduced-intensity conditioning regimen may be considered medically necessary as a treatment of AML in patients who are in complete marrow and extramedullary

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remission (CR1 or beyond), and who for medical reasons would be unable to tolerate a myeloablative conditioning regimen.

3. Autologous HSCT may be considered medically necessary to treat AML in CR1 or beyond, or relapsed AML if responsive to intensified induction chemotherapy.

## When Hematopoietic Stem-Cell Transplantation for Acute Myeloid Leukemia it is not covered

Hematopoietic stem-cell transplantation for acute myeloid leukemia is considered not medically necessary when the medical criteria listed above are not met.

## Policy Guidelines

Refer to the individual member's benefit booklet for prior review requirements.

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

In the French-American-British (FAB) 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 (e.g., myelodysplasia)
- Presence of circulating blasts at the time of diagnosis
- Difficulty in obtaining first complete remission with standard chemotherapy
- Leukemias with monocytoid differentiation (FAB classification M4 or M5)

The newer, currently preferred, World Health Organization (WHO) classification of AML incorporates and interrelates morphology, cytogenetics, molecular genetics, and immunologic markers in an attempt to construct a classification that is universally applicable and prognostically valid. The WHO system was adapted by the National Comprehensive Cancer Network (NCCN) to estimate individual patient prognosis to guide management.

### Risk Status of AML Based on Cytogenetic and Molecular Factors

Risk Status	Cytogenetic Factors	Molecular Abnormalities
Better	Inv(16), t(8;21), t(16;16)	Normal cytogenetics with isolated NPM1 mutation
Intermediate	Normal +8 only, t(9;11) only Other abnormalities not listed with better-risk and poor-risk cytogenetics	c-KIT mutation in patients with t(8;21) or inv(16)
Poor	Complex (3 or more abnormalities) -5, -7, 5q-, 7q-, +8, Inv3, t(3;3), t(6;9), t(9;22) Abnormalities of 11q23, excluding t(9;11)	Normal cytogenetics with isolated FLT3-ITD mutations

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

# Hematopoietic Stem-Cell Transplantation for Acute Myeloid Leukemia

Some patients for whom a conventional myeloablative allotransplant could be curative may be considered candidates for reduced-intensity conditioning (RIC), or non-myeloablative conditioning allogeneic HSCT. It is important to recognize that the myeloablative intensity of different conditioning regimens varies substantially and that the distinction between myeloablative regimens and RIC regimens has not been defined. In this setting, patient selection is critical, and variations exist in the criteria used by transplant centers in the United States and worldwide. In general, candidates for RIC or non-myeloablative conditioning regimen allogeneic HSCT include patients whose age (typically older than 60 years) or comorbidities (e.g., liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy, low Karnofsky Performance Status) preclude use of a standard myeloablative conditioning regimen. A patient whose disease relapses following a conventional myeloablative allogeneic HSCT could undergo a second myeloablative procedure if a suitable donor is available and the patient's medical status would permit it. However, this type of patient would likely undergo RIC prior to a second allogeneic HSCT if a complete remission could be re-induced with chemotherapy.

Autologous HSCT is used for consolidation treatment of intermediate- to poor-risk disease in complete remission, among patients for whom a suitable donor is not available. Better-risk AML often responds well to chemotherapy with prolonged remission if not cure.

The ideal allogeneic donors are HLA-identical siblings, matched at the HLA-A, -B, and DR loci (6 of 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, for which there usually is sharing of only 3 of the 6 major histocompatibility antigens. The majority of patients will have such a donor; however, the risk of GVHD and overall morbidity of the procedure may be severe, and experience with these donors is not as extensive as that with matched donors.

For individuals who have documented cytogenetic- or molecular-documented intermediate- or poor-risk AML in first complete remission (CR1) who receive allo-HSCT with myeloablative conditioning, the evidence includes randomized controlled trials (RCTs) and matched cohort studies. Relevant outcomes are overall survival (OS) and disease-specific survival (DSS). The evidence shows allogeneic HSCT in this setting improves OS and DSS rates compared with conventional chemotherapy. All RCTs employed natural randomization based on donor availability, and an intention-to-treat analysis. Although the compiled studies used different definitions of risk categories according to various cooperative groups (eg, SWOG, Medical Research Council, European Organisation for Research and Treatment of Cancer, Gruppo Italiano Malattie Ematologiche dell' Adulto), cytogenetic categories in those definitions are very similar to recent guidelines from the National Comprehensive Cancer Network (NCCN). Survival rates appear to be associated with presence of minimal residual disease and risk category. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have AML refractory to standard induction chemotherapy but which can be brought into first complete remission or beyond with intensified induction chemotherapy who receive allo-HSCT with myeloablative conditioning, the evidence includes retrospective data compiled from patients entered in phase 3 trials and registry data. Relevant outcomes are overall survival (OS) and disease-specific survival (DSS). The evidence would suggest allogeneic HSCT in this setting improves OS and DSS rates better than with 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 a meaningful improvement in the net health outcome.

For individuals who have AML that relapses after induction chemotherapy-induced first complete remission but which can be brought into second complete remission or beyond with intensified induction chemotherapy who receive allo-HSCT or auto-HSCT with myeloablative conditioning, 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 allogeneic HSCT in this setting improves OS better than conventional chemotherapy. Limitations of the evidence include the retrospective nature, lack of rigorous randomization, and pitfalls of

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registry data. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have documented cytogenetic or molecular intermediate-or poor-risk AML in the first complete remission or beyond who for medical reasons cannot tolerate a myeloablative conditioning regimen who receive all-HSCT with reduced-intensity conditioning (RIC), the evidence included 2 RCTs and other comparative and non-comparative studies. Relevant outcomes are OS, DSS, and treatment-related morbidity. The RCTs compared RIC with myeloablative conditioning (MAC) and reported similar rates in non-relapse mortality, relapse, and overall survival, though one of the trials was stopped early due to slow accrual of patients. Two retrospective comparative studies found no difference in overall survival or leukemia-free survival between the conditioning regimens. The evidence is sufficient to determine quantitatively that the technology results in a meaningful improvement in the net health outcome.

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

## **Billing/Coding/Physician Documentation Information**

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This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbssc.com](http://www.bcbssc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable Codes: 38205, 38206, 38230, 38232, 38240, 38241, 38242, 38243, S2150*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

## **Scientific Background and Reference Sources**

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BCBSA Medical Policy Reference Manual, 12/1/1999; 8.01.26

BCBSA Medical Policy Reference Manual, 8/18/2000; 8.01.26

Specialty Matched Consultant Advisory Panel - 11/2002

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 12/18/2002

Specialty Matched Consultant Advisory Panel - 11/2004

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 9/27/2005

Specialty Matched Consultant Advisory Panel - 3/2006

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 4/17/07

Specialty Matched Consultant Advisory Panel - 3/2008

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BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 5/14/09

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Acute myeloid leukemia. Retrieved 8/4/09 from [http://www.nccn.org/professionals/physician\\_gls/PDF/aml.pdf](http://www.nccn.org/professionals/physician_gls/PDF/aml.pdf)

Specialty Matched Consultant Advisory Panel – 5/2010

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 6/10/2010

Specialty Matched Consultant Advisory Panel – 4/2011

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 8/11/2011

Specialty Matched Consultant Advisory Panel – 4/2012

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 8/9/2012

Specialty Matched Consultant Advisory Panel – 4/2013

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 8/2013

Senior Medical Director – 9/2013

Specialty Matched Consultant Advisory Panel – 4/2014

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 8/14/2014

Specialty Matched Consultant Advisory Panel- 4/2015

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 8/13/2015

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 1/14/2016

Specialty Matched Consultant Advisory Panel- 4/2016

Specialty Matched Consultant Advisory Panel- 4/2017

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 7/13/2017

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 1/11/2018

Specialty Matched Consultant Advisory Panel-4/2018

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 1/17/2019

Specialty Matched Consultant Advisory Panel- 3/2019

BCBSA Medical Policy Reference Manual [Electronic]. 8.01.26, 1/16/2020

Specialty Matched Consultant Advisory Panel- 4/2020

Medical Director review 4/2020

## Policy Implementation/Update Information

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| 1/01 | Specialty Matched Consultant Advisory Group.   |
| 2/01 | Original Policy Issued.  |
| 2/03 | Specialty Matched Consultant Advisory Panel review 11/2002. No change in criteria. Codes 86812-86822 removed; codes 38231 and 86915 deleted and codes 38242, 38205 and 38206 added to the Billing/Coding section. System coding changes. |
| 1/04 | Benefits Application and Billing/Coding sections updated for consistency.  |

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- 2/04 Individual CPT codes listed for CPT code ranges, 38240-38242 under Billing/Coding section.
- 7/29/04 HCPCS code S2150 added to Billing/Coding section.
- 12/9/04 Specialty Matched Consultant Advisory Panel review 11/29/2004. No changes to criteria. Revised Description of Procedure or Service section. Added policy number to Policy Key Words section. "Hematopoietic" and "Opportunistic" added to Definitions. References added.
- 4/10/06 Specialty Matched Consultant Advisory Panel review 3/15/2006. No changes to policy. References added.
- 6/2/08 Specialty Matched Consultant Advisory Panel review 3/17/08. Added reference to the Clinical Trials policy to the "Policy" section. Changed wording in the "When Covered" section #2.e. from "such as" to "including but not limited to". References added.
- 9/14/09 Reviewed with Senior Medical Director 8/26/09. Policy named changed from "Bone Marrow Transplant for Acute Myelogenous Leukemia" to "Hematopoietic Stem-Cell Transplant for Acute Myelogenous Leukemia". Description revised. Removed reference to "Bone Marrow Transplant, high dose chemotherapy and stem cell support" and inserted "hematopoietic stem-cell transplantation" in the "Policy" section. Completely revised the "When Covered" section to indicate; "1. Allogeneic hematopoietic stem-cell transplantation (HSCT) using a myeloablative conditioning regimen may be considered medically necessary to treat: a) Poor- to intermediate-risk AML in remission, or b) AML that is refractory to, or relapses following standard induction chemotherapy, or c) AML in patients who have relapsed following a prior autologous HSCT and are medically able to tolerate the procedure. 2. Allogeneic HSCT using a reduced-intensity conditioning regimen may be considered medically necessary as a treatment of AML in patients who are in complete marrow and extramedullary remission, and who for medical reasons would be unable to tolerate a myeloablative conditioning regimen. 3. Autologous HSCT may be considered medically necessary to treat AML in first or second remission or relapsed AML if responsive to intensified induction chemotherapy." Updated "Policy Guidelines" section. References added. (btw)
- 6/22/10 Policy Number(s) removed. (amw)
- 7/6/10 Specialty Matched Consultant Advisory Panel review 5/24/2010. Changed the title from "Myelogenous to "Myeloid". Removed the following statement; Services for or related to the search for a donor is not covered." From the "Benefits Application" section. No changes to policy statement. References added. (btw)
- 5/24/11 Specialty Matched Consultant Advisory Panel review 4/27/11. No change to policy intent. Added the Risk Status of AML Based on Cytogenetic and Molecular Factors table to the "Policy Guidelines" section. Removed the following statements from the "Policy Guidelines" section; "While some high dose chemotherapy (HDC) protocols can be administered on an outpatient basis, typically the patient is hospitalized for management of the marrow ablative complications of the therapy." and "All patients receiving whole body radiotherapy, typically those receiving an allogeneic transplant (from donor to patient), will require prolonged hospitalization." References added. (btw)
- 2/21/12 New 2012 CPT code 38232 added to Billing/Coding section. (btw)
- 5/15/12 Specialty Matched Consultant Advisory Panel review 4/18/2012. Changed the "When Not Covered" section from "investigational" to "Hematopoietic stem-cell transplantation for acute myeloid leukemia is considered not medically necessary when the medical criteria listed above are not met." Policy Guidelines updated. Reference added. (btw)

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- 10/30/12 Reference added. (btw)
- 1/15/13 Added new CPT code, 38243, to Billing/Coding section. (btw)
- 4/30/13 Specialty Matched Consultant Advisory Panel review 4/17/2013. Policy Guidelines updated. No change to policy intent. (btw)
- 10/15/13 Description updated. No change to policy intent. Senior Medical Director review 9/14/2013. Reference added. (btw)
- 5/13/14 Specialty Matched Consultant Advisory Panel review 4/29/2014. No change to policy. (btw)
- 11/11/14 Reference added. (lpr)
- 5/26/15 Specialty Matched Consultant Advisory Panel review 4/29/2015. No change to policy. (lpr)
- 10/30/15 Updated Policy Guidelines section. Updated “When Covered” section statements for clarification. Created new bullet d. with division of bullet c. No change to policy intent. Reference added. (lpr).
- 5/31/16 Updated Description section. Reference added. Specialty Matched Consultant Advisory Panel review 4/27/2016. No change to policy statement. (lpr)
- 5/26/17 Specialty Matched Consultant Advisory Panel review 4/26/2017. No change to policy statement. (lpr)
- 8/11/17 Updated Policy Guidelines section. Reference added. No change to policy intent. (lpr)
- 5/11/18 Specialty Matched Consultant Advisory Panel review 4/25/2018. Reference added. No change to policy statement. (lpr)
- 4/16/19 Specialty Matched Consultant Advisory Panel review 3/20/2019. Reference added. No change to policy statement. (lpr)
- 5/26/20 Specialty Matched Consultant Advisory Panel review 4/15/2020. Reference added. No change to policy statement. (lpr)

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