



CIGNA MEDICAL COVERAGE POLICY

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Subject Stem-Cell Transplantation for Acute Myelogenous Leukemia

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Table of Contents

Coverage Policy	1
General Background	2
Coding/Billing Information	8
References	9
Policy History.....	16

Hyperlink to Related Coverage Policies

Donor Lymphocyte Infusion
Stem-Cell Transplantation for Myelodysplastic Syndrome
Transplant Donor Charges
Umbilical Cord Blood Banking

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Coverage Policy

CIGNA covers myeloablative allogeneic hematopoietic stem-cell transplantation (HSCT) from a human leukocyte antigen (HLA)-matched donor (i.e., at least five of six match of the HLA-A, HLA-B, and HLA-DRB1 antigens) as medically necessary for the treatment of an adult or child with acute myelogenous leukemia (AML) when ANY of the following criteria is met:

- first remission for a high-risk** individual
- second or subsequent remission
- failed induction
- no induction treatment and any of the following:
 - antecedent hematological disease
 - treatment-related secondary AML

CIGNA covers a second myeloablative allogeneic HSCT from an HLA-matched donor ((i.e., at least five of six match of the HLA-A, HLA-B, and HLA-DRB1 antigens) as medically necessary for the treatment of an adult or child with AML when BOTH of the following criteria are met:

- relapse of disease occurring more than six months after first allogeneic HSCT
- second or subsequent remission

CIGNA covers reduced-intensity or non-myeloablative allogeneic HSCT from a human leukocyte antigen (HLA)-matched donor (i.e., at least five of six match of the HLA-A, HLA-B, and HLA-DRB1 antigens) as

medically necessary for the treatment of an adult with AML when the criteria for an allogeneic HSCT are met but a myeloablative regimen is contraindicated because of age or comorbidity.

CIGNA covers autologous HSCT as medically necessary for the treatment of an adult or child with AML for whom allogeneic HSCT is not available or is not appropriate when EITHER of the following criteria is met:

- first remission for a high risk* individual
- second or subsequent remission

CIGNA does not cover EITHER of the following procedures for the treatment of AML because each is considered experimental, investigational or unproven:

- non-myeloablative allogeneic HSCT for a child with AML
- tandem HSCT

***High-risk includes ANY of the following:**

- requiring more than one cycle to achieve remission
- disease refractory to chemotherapy
- white blood cell (WBC) count > 100,000/ml³
- French-American-British (FAB) subtype M4 and M5
- chromosome translocations t(10;11), t(1;22), t(6;9), t(9;22)
- chromosomal abnormalities of chromosome 7 or 5, the long arm of chromosome 3, or 11q23
- trisomy 8
- antigen CD34 and/or P-glycoprotein (MDR1 gene product)
- internal tandem duplication mutations of the FLT3 gene
- history of CNS involvement
- systemic infection at diagnosis
- treatment-induced AML
- history of myelodysplastic syndrome

General Background

Acute myelogenous leukemia (AML), also known as acute granulocytic leukemia, acute myeloid leukemia and acute nonlymphocytic leukemia (ANLL), is a malignancy of the hematopoietic tissues of the bone marrow resulting from acquired genetic damage. In most cases, the cause of AML is unknown; however, several factors are thought to be associated with an increased risk of the disease including the use of chemotherapy for the treatment of other cancers (Leukemia & Lymphoma Society, 2008a). AML can occur at any age, but it primarily affects adults and infants (i.e., age less than one year). For adults, the probability of three-year overall survival (OS) is 25%; for children, three-year OS is 40%–58% (National Cancer Institute [NCI], 2010 [a]; [b]).

Two systems are commonly used to classify AML. The French-American-British (FAB) Cooperative Group classification is based on morphological-histochemical cell characteristics and identifies eight subtypes of AML, categorized as M0-M7. The newer, World Health Organization Classification System incorporates clinical, morphologic, immunophenotypic, cytogenetic and molecular markers that can be used to direct treatment.

Factors that may be predictive of increased morbidity and mortality include central nervous system involvement with leukemia, systemic infection at diagnosis, elevated white blood count (i.e., >100,000 mm³), treatment-induced AML and history of myelodysplastic syndrome. Additionally, certain gene and cytogenetic abnormalities have been identified as high-risk for a poor prognosis with chemotherapy. These include internal tandem duplication of the FLT3 gene, deletions of the long arms or monosomies of chromosomes 5 or 7; translocations or inversions of chromosome 3, t(6;9), t(9;22) and abnormalities of chromosome 11q23, t(10;11) translocation, t(1;22)(p13;q13) translocation, trisomy 8, and certain antigens/glycoproteins.

Successful treatment of acute myelogenous leukemia (AML) is divided into two major phases: induction-to attain remission, and postremission consolidation/intensification-to maintain remission (National Cancer Institute [NCI], 2010a). Postremission therapy is always indicated in therapy that is planned with curative intent. Current approaches to postremission therapy include allogeneic or autologous hematopoietic stem-cell transplantation (HSCT) with high-dose chemotherapy or chemoradiation therapy (NCI, 2010a).

Stem-Cell Transplantation

Stem-cell transplantation refers to transplantation of hematopoietic stem cells (HSCs) from a donor into a patient. HSC transplantation (HSCT) can be either autologous (using the patient's own stem cells) or allogeneic (using stem cells from a donor).

Alternative Donor Sources: In allogeneic HSCT, it is preferable for donors to have a human leukocyte antigen (HLA) type that is identical to the recipient. Matching is performed on the basis of variability at three of more loci of the HLA gene (e.g., HLA-A, HLA-B, HLA-DRB1). As HLA variability increases, transplant-related morbidity and mortality, including graft rejection and graft-versus-host disease, also increase. Alternative donor sources including matched-unrelated and unmatched-related donors (e.g., haploidentical donors) are being evaluated for individuals with acute leukemia who do not have an HLA-identical donor. According to the NCI (2010a) the use of alternate donors results in substantial rates of treatment-related mortality, with disease-free survival (DFS) rates less than 35% (NCI, 2010a).

Regarding the safety and effectiveness of unmatched related or haploidentical donor allogeneic HSCT, recent modifications in chemotherapy protocols utilizing T-cell depletion, 'megadoses' of stem-cells, better antimicrobial therapy, and reduced intensity conditioning have significantly reduced early transplant-related mortality and graft-versus-host disease, and enabled robust and prompt engraftment. However, the primary problems related to delayed immune reconstitution causing post-transplant infectious complications and relapse remain, limiting the effectiveness of haploidentical transplantation (Peccatori, 2010; Koh, 2008). Randomized controlled clinical trials are needed to determine improved health outcomes compared with allogeneic HSCT using HLA-matched sibling donors. Although promising as a means of expanding the availability of allogeneic HSCT for individuals with AML who do not have an HLA-matched sibling donor, at this time the role of this therapy has not been established.

Myeloablative Allogeneic HSCT: Allogeneic HSCT results in the lowest incidence of leukemic relapse, which has led to the concept of a graft-versus-leukemia effect. DFS rates using allogeneic transplantation in first complete remission range from 45% to 60%. Although allogeneic HSCT provides the most potent anti-leukemia effect of any post remission therapy in AML as demonstrated by the lowest rates of relapse, use of allogeneic HSCT as post remission therapy results in transplant-related morbidity and mortality rates of 20%–40%, even with the use of an HLA-matched sibling donor (NCI, 2010a).

If an HLA-matched sibling donor is available allogeneic HSCT is the preferred therapy for most individuals up to age 60 years who present with intermediate-risk karyotypes or high-risk cytogenetics (NCI, 2010a). AML arising from myelodysplasia or secondary to previous cytotoxic chemotherapy also has a lower rate of remission than de novo AML and, according to the NCI data suggest that individuals with these subsets of leukemia may be treated with allogeneic transplantation if their overall performance status is adequate.

Individuals at high risk of relapse are unlikely to be cured with consolidation chemotherapy, and allogeneic HSCT allows the best chance for cure (NCI, 2010a; NCI, 2010b). No standard regimen exists for the treatment of relapsed AML, particularly in patients with first complete remission duration of less than one year (NCI, 2010a). A subset of relapsed patients treated aggressively may have extended disease-free survival; however, cures in patients following a relapse are thought to be more commonly achieved using HSCT (NCI, 2010a). Patients who are treated with allogeneic HSCT have a significantly better survival rate compared to patients who are treated with other therapies (Giles, 2005). Allogeneic HSCT with an HLA-matched donor in early first relapse or in second complete remission provides a DFS rate of approximately 30% (NCI, 2010a).

Literature Review

AML in Remission: Several randomized controlled trials, meta-analyses and retrospective reviews have demonstrated relapse-and disease-free survival benefit with the use of myeloablative allogeneic HSCT for individuals with in remission (Koreth, 2009; Gorin, 2008; Fagioli, 2008; Gassas, 2008; Cornelissson, 2007; Flynn, 2007; Bleakley, 2002). Koreth et al. (2009) reported results of a systematic review and meta-analysis of 24 trials

involving 6007 adults comparing myeloablative allogeneic hematopoietic stem-cell transplantation (HSCT) with non-allogeneic HSCT therapies. The data indicated statistically significant improved relapse-free (RFS) and overall survival (OS) with allogeneic HSCT for adults with poor- and intermediate risk acute myelogenous leukemia (AML) in first complete remission. No improvement was noted for individuals with good-risk disease.

Prospective trials of transplantation in children with AML suggest that 60% to 70% of children with human leukocyte antigen (HLA)-matched donors available who undergo allogeneic HSCT during their first remission experience long-term remissions. Prospective trials of allogeneic HSCT compared with chemotherapy and/or autologous HSCT have demonstrated a superior outcome for patients who were assigned to allogeneic transplantation based on availability of a related six-of-six or five-of-six HLA-matched donor (NCI, 2010b). In a systematic review and meta-analysis of studies involving HSCT for children with AML, Bleakley et al. (2002) compared outcomes for patients in first complete remission who were treated with allogeneic HSCT, autologous HSCT, or intensive chemotherapy. Results of the analysis showed that allogeneic HSCT reduced the risk of relapse and improved disease-free (DFS) and overall survival (OS) compared with intensive chemotherapy. The autologous HSCT studies were too heterogeneous to allow any generalized conclusions.

Refractory or Relapsed AML: Dvorak et al. (2008) retrospectively analyzed the results of 32 HSCTs (11 autologous, 21 allogeneic) performed for children with relapsed (n=29) or refractory (n=3) AML. Multiple donor types, conditioning regimens and graft-versus-host disease prophylaxis were utilized. Median times to relapse for the allogeneic and autologous groups were 13.5 and 15.3 months, respectively. All patients achieved morphologic complete remission prior to transplant. There were no significant differences between the OS for the allogeneic and autologous groups ($p=1.00$) or for event-free survival between the two groups ($p=.81$).

Relapse After Prior Allogeneic Transplant: A second myeloablative allogeneic HSCT has been proposed for individuals with AML who have undergone allogeneic HSCT and subsequently have disease relapse or progression. Hosing et al. (2005) evaluated outcomes from 72 patients with AML who were in disease relapse at the time of a second HSCT. Treatment-related mortality (TRM) was 36%. Patients who had relapsed or progressed more than one year after the first transplant had significantly better outcomes compared to patients who relapsed or progressed within one year. Patients with low leukemia burden (i.e., no peripheral blood blasts and $\leq 5\%$ bone marrow blasts) at the time of the second HSCT had a five-year overall survival rate of 25%, compared to those with a high disease burden who had a five-year survival rate of 12%.

Summary for Myeloablative Allogeneic HSCT: According to the NCI, myeloablative allogeneic HSCT provides the most potent anti-leukemic effect of any post-remission therapy. It is considered an acceptable therapy for the treatment of selected adults and children with AML.

Non-Myeloablative Allogeneic HSCT: Myeloablative allogeneic HSCT has resulted in unacceptable TRM for many patients, both due to the toxicity of the myeloablative regimen used as conditioning and the high incidence and severity of graft-versus host disease (GVHD) (Baron, 2007; Aoudjhane, 2005). However, relapse rates are higher with non-myeloablative therapy. Grigg et al. (2007) reported the results of a prospective multicenter trial involving 34 patients with AML with intermediate- or poor-risk cytogenetics in first complete remission (CR1) who had previous sibling allografts with reduced-intensity conditioning. Relapse rates at six months, one year and two years were 21%, 34% and 37%, respectively. Two-year survival rates range from 48% to 79% (Baron, 2007). In general, children have less toxicity and better outcomes after conventional allogeneic hematopoietic stem-cell transplantation (HSCT) than adults. Data are limited regarding the effectiveness of non-myeloablative HSCT in this population. The use of this treatment modality for pediatric patients with AML should be evaluated in prospective trials and used only in the context of clinical studies.

Literature Review

AML in Remission: Aoudjhane et al. (2005) compared the results of 722 patients with de novo AML or myelodysplastic syndrome who received a myeloablative allogeneic HSCT (n=407) or reduced intensity conditioning allogeneic HSCT (n=315). In a multivariate analysis, the risk of mortality was statistically significantly higher for patients receiving myeloablative conditioning compared with reduced-intensity conditioning. In comparison with myeloablative conditioning, reduced-intensity allogeneic HSCT was associated with more relapses but less transplant toxicity.

Martino et al. (2007) compared the results of patients with poor-risk acute myelogenous leukemia (AML) in first complete remission (CR1) or myelodysplastic syndrome treated with high-dose allogeneic hematopoietic stem-

cell transplantation (HSCT) (<50 years; n=35) or reduced-intensity conditioning followed by allogeneic HSCT (≥ 50 years; n=39). The type of transplant had no impact on any outcomes four years post-transplantation. The four-year non-relapse mortality was 19% and 20% for the high-dose and reduced-intensity conditioning group, respectively ($p=0.8$). Relapse and survival were equivalent in each group. The authors noted that this study was not powered to identify the impact of the type of conditioning on other outcomes.

Herr et al. (2007) conducted a retrospective review of registry data to compare the outcomes of 361 patients with de novo AML who received nonmyeloablative allogeneic HSCT with the results of 1369 patients who received high-dose chemotherapy and autologous HSCT. Unadjusted two-year nonrelapse mortality was 15% and 10% for the allogeneic and autologous groups, respectively ($p=0.01$). After adjustment for patient-, disease-, and transplant-related variables, multivariate analysis demonstrated a significant difference with less relapse in the allogeneic group compared to the autologous group ($p=0.013$). Results demonstrate superior outcomes after nonmyeloablative allogeneic HSCT compared with autologous HSCT.

Relapsed AML: Oran et al. (2007) reported the long-term results of 112 patients with AML or high-risk myelodysplastic syndrome who were treated with a reduced-intensity allogeneic HSCT. Complete remission (CR) was attained in 87% of the patients by day +30. Disease progression occurred in 29% of patients who achieved a CR after transplantation at a median of 4.2 months; all but three patients relapsed within a year after transplantation. The two-year overall survival (OS) for the entire cohort was 44%. Estimates of two-year OS were 66% for those in CR, 40% for patients not in CR but without circulating blasts, and 23% for those with active disease and circulating blasts.

Alyea et al. (2006) retrospectively analyzed the results of 136 patients with advanced AML and myelodysplastic syndrome undergoing allogeneic HSCT to determine the impact of conditioning regimen intensity on outcome. Thirty-nine patients with AML received nonmyeloablative conditioning (NST) (n=23) and 97 patients received a myeloablative regimen (n=59). Treatment-related mortality (TRM) for the nonmyeloablative conditioning (NST) group was 26% compared to 33% for the group receiving myeloablative HSCT. Cox regression analysis demonstrated that no factors, including the intensity of conditioning regimen, influenced either overall- or progression-free survival.

Summary for Non-Myeloablative Allogeneic HSCT: Non-myeloablative or reduced-intensity conditioning permits the use of allogeneic HSCT for certain subsets of adult patients with AML (e.g., > 50 years, adults who may be unable to tolerate the toxic effects of myeloablative chemotherapy prior to allogeneic HSCT) and it is considered an acceptable treatment option. Data are limited regarding the role of non-myeloablative allogeneic HSCT for the treatment of children with AML.

Autologous HSCT: Several studies have demonstrated no benefit in overall survival (OS) with the use of autologous HSCT compared with standard postremission chemotherapy in CR1; however, disease-free survival (DFS) rates of 35%–50% have been noted. According to the National Cancer Institute (NCI), autologous HSCT is a reasonable treatment option for patients in second complete remission, offering DFS that may be comparable to autografting in CR1 (2010a). TRM ranges from 10% to 20%.

Literature Review

Acute Myelogenous Leukemia (AML) in Remission: Thomas et al. (2007) reported the results of a prospective study including 757 patients with de novo previously untreated AML or secondary AML. Ultimately, 35 patients received autologous HSCT after consolidation with high-dose chemotherapy HSCT. Three-year DFS and OS rates were 28% and 39%, respectively, for the transplanted patients. The three-year relapse incidence was 57%.

Ravindranath et al. (2005) performed a retrospective review of the results of a total of 1823 children with AML enrolled in four consecutive Pediatric Oncology Group (POG) clinical trials. Of these, POG 8821 compared the efficacy of autologous HSCT with that of intensive consolidation chemotherapy. Intent-to-treat analysis revealed similar five-year event-free survival (EFS) estimates for the autologous HSCT (36%) and intensive chemotherapy (35%) groups. There was a high rate of treatment-related mortality in the autologous HSCT group.

Two meta-analyses evaluated the outcomes of autologous hematopoietic stem-cell transplantation (HSCT) versus chemotherapy in six studies of adult patients with acute myelogenous leukemia (AML) in first complete

remission (CR1). Patients receiving autologous HSCT had better event-free survival (EFS) in both studies; however, there was no difference in overall survival (OS). The studies did not address the effect in the high-risk population (Levi, et al., 2004; Nathan, et al., 2004).

Relapsed AML: Thomas et al. (2005) retrospectively reviewed the outcomes of 262 patients with relapsing and refractory leukemia achieving complete remission (CR). Transplantation was one of three favorable prognostic factors correlated with EFS: Three-year EFS rates were 68% versus 23% for autologous and allogeneic HSCT, respectively. Three-year probabilities of transplant-related mortality (TRM) were 11% and 47%, respectively, for autologous and allogeneic HSCT, respectively. In multivariate analysis, outcomes with autologous HSCT were significantly better than with allogeneic HSCT ($p < 0.01$) or chemotherapy ($p = 0.001$). Outcomes from allogeneic HSCT were not significantly different than chemotherapy.

Summary for Autologous HSCT: Overall, autologous HSCT appears inferior to allogeneic HSCT for the treatment of adults and children with AML, but may provide benefit to high-risk patients who have limited options because they lack a matched donor or cannot tolerate the conditioning therapy required for allogeneic HSCT. According to the NCI (2010a), autologous HSCT may be an acceptable treatment option for individuals in second complete remission.

Tandem (Sequential) Transplantation: There are scarce data in the published peer-reviewed medical literature to support the safety and effectiveness of tandem (also known as sequential) transplants for the treatment of AML. At this time the role of this therapy has not been established.

Contraindications

The presence of any significant co-morbid conditions that would significantly compromise clinical care and chances of survival is a contraindication to transplant. Greater age is associated with a higher incidence of post-transplantation complications; therefore, many centers restrict myeloablative allogeneic transplantation to patients age 55 or younger. Relative contraindications to HSCT include, but are not limited to:

- poor cardiac function (ejection fraction < 45%)
- poor liver function (bilirubin > 2.0mg/dl and transaminases greater than two times normal), unless related to AML
- poor renal function (creatinine clearance < 50ml/min)
- poor pulmonary function [diffusion capacity (DLCO) < 60% of predicted]
- active central nervous system involvement
- a pattern of demonstrated patient noncompliance which would place a transplant at serious risk of failure
- presence of human immunodeficiency virus OR an active form of any ONE of the following:
 - hepatitis B virus (HBV)
 - hepatitis C virus (HCV)
 - human T-cell lymphotropic virus (HTLV)-1
 - Karnofsky rating <60% and/or Eastern Cooperative Oncology Group (ECOG) performance status >2

Professional Societies/Organizations

National Cancer Institute (NCI): Regarding HSCT for adults with AML the NCI (2010a) notes:

- Adults with untreated AML may be treated primarily with allogeneic bone marrow transplantation if their overall performance status is adequate
- Current approaches to postremission therapy include high-dose chemotherapy or chemoradiation therapy with autologous bone marrow rescue, and high-dose marrow-ablative therapy with allogeneic bone marrow rescue.
- Allogeneic HSCT can salvage some patients whose disease fails to go into remission with intensive chemotherapy (i.e., primary refractory leukemia).
- Autologous bone marrow transplantation is an option for patients in second complete remission.

- For adults with AML arising from myelodysplasia or secondary to previous cytotoxic chemotherapy may be treated primarily with allogeneic bone marrow transplantation if their overall performance status is adequate.

In children with acute myelogenous leukemia (AML) the National Cancer Institute (NCI, 2010b) notes:

- Matched family-donor hematopoietic stem-cell transplantation (HSCT) is an option only after first relapse and the achievement of a second complete remission.
- There is evidence suggesting an advantage for allogeneic HSCT in patients in complete remission with intermediate-risk characteristics
- For recurrent AML consolidation chemotherapy followed by HSCT is the treatment of choice.

The National Comprehensive Cancer Network™ (NCCN™): The NCCN publishes guidelines for the treatment of adults only. Clinical Practice Guidelines in Oncology for AML (2010) suggest that age 60 is considered a therapeutic divergence point for induction therapy recommendations. The Guidelines note

- “Allogeneic sibling HSCT or human leukocyte antigen (HLA)-matched unrelated donors or clinical trial may be given as consolidation therapy for patients with poor-risk cytogenetics or molecular abnormalities.
- If relapse is detected when the tumor burden is low and the patient has a previously identified sibling or unrelated donor, allogeneic HSCT can be considered.
- Salvage chemotherapy followed by matched sibling or alternate donor HSCT should be considered only if the patient has achieved remission or in the context of a clinical trial.

For adults ≥60 years old:

- For older patients (> 60 years) with AML, the panel recommends using patient performance status, in addition to adverse features (such as unfavorable cytogenetics and therapy related AML or prior myelodysplastic syndrome and comorbid conditions) to select treatment rather than using their chronological age alone.
- The role of myeloablative allogeneic HSCT is limited due to significant comorbidities, but there has been ongoing interest in reduced intensity allogeneic HSCT as consolidation therapy.
- Reduced intensity allogeneic HSCT is considered an additional option for patients 60 years and older for the following indications: (1) as a post-remission therapy for those achieving a complete response to induction therapy (2) for treatment of induction failure only in patients with low volume disease

For adults <60 years of age:

- Transplantation without induction may be considered for those with antecedent myelodysplasia or treatment-related leukemia who have an available sibling donor and who have relatively low percentage marrow involvement.
- Choices for post-remission consolidation therapy include autologous HSCT and allogeneic HSCT from sibling or unrelated donors.
- Allogeneic HSCT may be considered as primary therapy following salvage chemotherapy for persons <60 years who experience an early relapse after induction therapy
- Individuals who experience relapse after a long remission may be candidates for allogeneic HSCT if remission is achieved.
- Transplant based options (either matched sibling or alternate donor HSCT or one to two cycles of dose intensive cytarabine followed by autologous stem cell transplantation) afforded a lesser risk of relapse and a somewhat higher disease free survival as consolidation for most patients with intermediate risk cytogenetics.”

American Society for Blood and Marrow Transplantation (ASBMT): The ASBMT (2007) published a position statement regarding treatment guidelines for children with AML which notes:

- Autologous stem-cell transplant (SCT) and chemotherapy in the first complete remission (CR1) are equivalent in outcomes. The lack of data on quality of life, secondary malignancies, and other late effects of treatment prevent a recommendation of one treatment over the other.
- Allogeneic hematopoietic stem-cell transplantation (HSCT) is recommended in CR1.
- In allogeneic SCT versus chemotherapy in the CR2, the expert panel acknowledged a lack of evidence comparing matched related allogeneic donors (MRD) versus chemotherapy. The panel recommends the use of any suitable MRD if one is available. Use of a matched unrelated donor (MUD) or other alternative donor SCT is recommended in the context of a clinical trial.
- In CR2, the consensus recommends using any suitable MRD or MUD over autologous SCT
- MRD allogeneic SCT is preferred in the first or second CR.

In 2008 the ASBMT published a position statement regarding the role of cytotoxic therapy with HSCT for acute myelogenous leukemia (AML) in adults which notes:

- There is no significant advantage of autologous stem cell transplant (SCT) over chemotherapy.
- There is a survival advantage for allogeneic SCT versus chemotherapy for patients under age 55 with high risk cytogenetics.
- There is insufficient evidence to routinely recommend allogeneic HSCT for patients with intermediate cytogenetics, although this is a reasonable strategy.
- There is insufficient data to make a recommendation for the use of myeloablative regimens for patients over age 55.
- There is insufficient data to make a recommendation for reduced intensity conditioning (RIC) allogeneic SCT versus chemotherapy.
- For patients in second complete remission, allogeneic SCT is recommended if there is an available donor; otherwise an autologous SCT is recommended.
- There are insufficient data to make a recommendation for tandem versus single autologous SCT.
- Allogeneic SCT with a matched related donor is recommended if available; a matched unrelated donor SCT using reduced intensity conditioning may provide equivalent outcomes.

National Institute of Health Research/Health Technology Assessment Programme: Ashfaq et al. (2010) published a technology assessment of the clinical effectiveness and cost-effectiveness of stem-cell transplantation in the treatment of acute leukemia. The authors concluded “Bearing in mind the limitations, the existing evidence suggests that sibling donor allogeneic stem cell transplantation may be more effective than chemotherapy in adult AML (except in good-risk patients) in first complete remission (CR1), childhood AML in CR1, and adult acute lymphocytic leukemia in CR1. Autologous stem-cell transplantation is equal to or less effective than chemotherapy.”

National Marrow Donor Program (NMDP)/ASBMT: In development with the ASBMT, the NMDP (2009) lists the following as recommended timing for transplant consultation for acute myelogenous leukemia (AML): high-risk AML, including antecedent hematological disease (e.g., myelodysplasia), treatment-related leukemia, and induction failure; first complete remission (CR1) with poor-risk cytogenetics or molecular markers, and second complete remission (CR2) and beyond.

Summary

Evidence in the published peer-reviewed scientific literature supports the safety and effectiveness of myeloablative allogeneic and autologous hematopoietic stem-cell transplantation (HSCT) in carefully selected individuals with acute myelogenous leukemia (AML). Non-myeloablative allogeneic HSCT is an acceptable treatment option for selected adults with AML; however, the role of this therapy for the treatment of children has not been established for this indication. At present, the role of tandem (sequential) transplantation has not been established for the treatment of individuals with AML.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

CPT®* Codes	Description
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing
38210	Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-cell depletion
38211	Transplant preparation of hematopoietic progenitor cells; tumor cell depletion
38212	Transplant preparation of hematopoietic progenitor cells; red blood cell removal
38213	Transplant preparation of hematopoietic progenitor cells; platelet depletion
38214	Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion
38215	Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear, or buffy coat layer
38230	Bone marrow harvesting for transplantation
38240	Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic
38241	Bone marrow or blood-derived peripheral stem cell transplantation; autologous
38242	Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic donor lymphocyte infusions

HCPCS Codes	Description
S2140	Cord blood harvesting for transplantation, allogeneic
S2142	Cord blood derived stem-cell transplantation, allogeneic
S2150	Bone marrow or blood-derived stem cells (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications; including pheresis and cell preparation/storage; marrow ablative therapy; drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days of pre-and post-transplant care in the global definition

ICD-9-CM Diagnosis Codes	Description
205.00 – 205.02	Acute myeloid leukemia, acute

*Current Procedural Terminology (CPT®) © 2010 American Medical Association: Chicago, IL.

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	5/15/2008	0164	Stem-Cell Transplant for Acute Myelogenous Leukemia
Great-West Healthcare	6/21/2007	05.292.02	Bone Marrow Transplantation (BMT) for Acute Myelogenous Leukemia (AML) and Acute Promyelocytic Leukemia (APL)

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