Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 11/1/12**
(See policy history boxes for previous effective dates)

Title: BMT/Stem-Cell Transplantation for Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma – Autologous or Allogeneic

Description/Background

Hematopoietic Stem-Cell Transplantation
Hematopoietic stem-cell transplantation (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 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).

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 of 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 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 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 totally 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.

Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma

Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are neoplasms of hematopoietic origin characterized by the accumulation of lymphocytes with a mature, generally well-differentiated morphology. In CLL, these cells accumulate in blood, bone marrow, lymph nodes and spleen, while in SLL they are generally confined to lymph nodes. The Revised European-American/WHO Classification of Lymphoid Neoplasms considers B-cell CLL and SLL a single disease entity.

CLL and SLL share many common features and are often referred to as blood and tissue counterparts of each other, respectively. Both tend to present as asymptomatic enlargement of the lymph nodes, tend to be indolent in nature but can undergo transformation to a more aggressive form of disease (e.g., Richter's transformation). The median age at diagnosis of CLL is approximately 72 years, but it may present in younger individuals, often as poor-risk disease with significantly reduced life expectancy.

Treatment regimens used for CLL are generally the same as those used for SLL, and outcomes of treatment are comparable for the two diseases. Both low- and intermediate-risk CLL and SLL

demonstrate relatively good prognoses with median survivals of 6 to 10 years, while the median survival of high-risk CLL or SLL may only be 2 years. Although typically responsive to initial therapy, CLL and SLL are rarely cured by conventional therapy, and nearly all patients ultimately die of their disease. This natural history prompted investigation of hematopoietic stem-cell transplantation as a possible curative regimen.

Staging and Prognosis of CLL/SLL

Two scoring systems are used to determine stage and prognosis of patients with CLL/SLL. As outlined in the Table 1, the Rai and Binet staging systems classify patients into 3 risk groups with different prognoses, and are used to make therapeutic decisions.

Table 1. Rai and Binet Classification for CLL/SLL

Rai Stage	Risk	Description	Median Survival (yr)	Binet Stage	Description	Median Survival (yr)
0	Low	Lymphocytosis	> 10	A	3 or fewer lymphoid areas, normal hemoglobin and platelets	> 10
I	Intermediate	Lymphocytosis plus lymphadenopathy	7-9	B	3 or more lymphoid areas, normal hemoglobin and platelets	7
II	Intermediate	Lymphocytosis plus splenomegaly plus/minus lymphadenopathy	7-9			
III	High	Lymphocytosis plus anemia plus/minus lymphadenopathy or splenomegaly	1.5-5	C	Any number of lymphoid areas, anemia, thrombocytopenia	5
IV	High	Lymphocytosis plus thrombocytopenia plus/minus anemia, splenomegaly or lymphadenopathy	1.5-5			
Note: Lymphocytosis = lymphocytes > 15 x 10^9/L for 4 wks; anemia = hemoglobin < 110 g/L; thrombocytopenia = platelets < 100 x 10^9/L						

Because prognosis of patients varies within the different Rai and Binet classifications, other prognostic markers are used in conjunction with staging to determine clinical management. These are summarized in Table 2, according to availability in clinical centers.

Table 2. Markers of Poor Prognosis in CLL/SLL

Community Center	Specialized Center
Advanced Rai or Binet stage	IgVh wild type
Male sex	Expression of ZAP-70 protein
Atypical morphology or CLL/PLL	del 11q22-q23 (loss of ATM gene)
Peripheral lymphocyte doubling time < 12 months	del 17p13 (loss of p53) trisomy 12
$CD38^+$	Elevated serum CD23
Elevated beta2-microglobulin level	Elevated serum tumor necrosis factor-a
Diffuse marrow histology	Elevated serum thymidine kinase
Elevated serum lactate dehydrogenase level	
Fludarabine resistance	

Some patients for whom a conventional myeloablative allotransplant could be curative may be considered candidates for RIC allogeneic HSCT. These include those 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 who relapses following a conventional myeloablative allogeneic HSCT could undergo a second myeloablative procedure if a suitable donor is available and his or her 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.

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, with whom usually there 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.

Regulatory Status

The FDA must approve the chemotherapeutic agents and biologic response modifiers used during high-dose chemotherapy, and the devices used to process the stem cells

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Medical Policy Statement

The safety and effectiveness of *allogeneic* hematopoietic stem-cell transplantation have been established. It may be considered a useful therapeutic option for patients meeting patient selection criteria.

Relative contraindications:
The selection process for approved tissue transplants is designed to obtain the best result for each patient. Therefore, relative contraindications to HSCT may include, but are not limited to:

- Poor cardiac function: Ejection fraction should be greater than 45% with no overt symptoms of congestive heart failure.
- Poor pulmonary function: Pulmonary function tests must be greater than or equal to 50% of predicted value.
- Poor renal function: Renal creatinine clearance should be greater than 40 ml/min or creatinine must be less than or equal to 2mg/dl.
- Poor liver function: There should be no history of severe chronic liver disease
- Presence of HIV or an active form of hepatitis B, hepatitis C or human T-cell lymphotropic virus (HTLV-1).

Autologous hematopoietic stem-cell transplantation is considered experimental and investigational to treat chronic lymphocytic leukemia or small lymphocytic lymphoma.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

Inclusions:
For *allogeneic* hematopoietic stem-cell transplantation, the patient must have

- Chronic lymphocytic leukemia or small cell lymphocytic leukemia AND
- Markers of poor-risk disease (see Table 2).

Use of a myeloablative or reduced-intensity pretransplant conditioning regimen should be individualized based on factors that include patient age, the presence of comorbidities, and disease burden.

Relative contraindications:
The selection process for approved tissue transplants is designed to obtain the best result for each patient. Therefore, relative contraindications to HSCT may include, but are not limited to:

- Poor cardiac function: Ejection fraction should be greater than 45% with no overt symptoms of congestive heart failure.
- Poor pulmonary function: Pulmonary function tests must be greater than or equal to 50% of predicted value.
- Poor renal function: Renal creatinine clearance should be greater than 40 ml/min or creatinine must be less than or equal to 2mg/dl.
- Poor liver function: There should be no history of severe chronic liver disease
- Presence of HIV or an active form of hepatitis B, hepatitis C or human T-cell lymphotropic virus (HTLV-1).

Exclusions:
Autologous hematopoietic stem-cell transplantation

CPT / HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

38204	38205	38207	38208	38209	38210
38211	38212	38213	38214	38215	38220
38221	38230	38240	38242	S2140	S2142
S2150					

Other codes (investigational, not medically necessary, etc.):

38206	38232	38241

Rationale

This policy initially was based on two TEC Assessments, one from 1999 on autologous hematopoietic stem-cell transplantation (autologous HSCT) for chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) (1); the other from 2002 on allogeneic hematopoietic stem-cell transplantation (allogeneic HSCT) to treat CLL or SLL. (2) Both documents indicated that existing data were insufficient to permit scientific conclusions regarding the use of either procedure, limited by interstudy heterogeneity in patient's baseline characteristics, procedural differences, sample size, and short follow-up. A direct comparative analysis from the International Bone Marrow Transplant Registry (IBMTR) commissioned by TEC in 2002 to analyze allogeneic HSCT results was insufficient to permit scientific conclusions on the net health outcome of this procedure for relapsed or refractory CLL or SLL.

Literature searches conducted between 2002 and July 2008 found no randomized trials of hematopoietic SCT compared with conventional-dose therapy for CLL or SLL. Recent reviews discuss uncertainties with respect to the type of transplant (autologous vs. allogeneic), the intensity of pretransplant conditioning, the optimal timing of transplantation in the disease course, the baseline patient characteristics that best predict likelihood of clinical benefit from transplant, and the long-term risks of adverse outcomes. (3-8) The conclusions reached in these reviews suggest that while autologous HSCT may prolong survival in selected patients with CLL or SLL, for example, those with chemotherapy-sensitive malignancy who had a good response to front-line therapy and transplanted early in the course of disease, it has not yet been shown to be curative.

Autologous HSCT

A systematic review of autologous HSCT for CLL or SLL included 9 studies (total n=361, 292 of which were transplanted) identified from a search of MEDLINE databases from 1966 to September 2006. (9) Studies were included if they were full-publication English language reports of prospective randomized, non-randomized, or single-arm design. The analysis suggested that while autologous HSCT may achieve significant clinical response rates (74-100%) with relatively low treatment-related mortality (TRM) (0–9%), molecular remissions are typically short-lived, with subsequent relapse. Overall survival (OS) ranged from 68% at 3-years' follow-up to 58% at 6 years. Secondary myelodysplasia and myelodysplastic syndrome that may progress to frank acute myelogenous leukemia has been reported in 5-12% of patients in some studies of autologous HSCT, which suggests caution in considering this approach, especially given the indolent nature of CLL or SLL. The authors of the review concluded that in the absence of randomized, comparative studies, it is uncertain whether

autologous HSCT is superior to conventional chemotherapy (or current chemo-immunotherapy) combinations as first-line consolidation treatment in CLL or SLL patients, regardless of disease risk, or as salvage therapy in those with relapsed disease.

The conclusions of the systematic review of autologous HSCT outlined above are congruent with results of a Phase III randomized trial published in 2010 that compared autologous HSCT (n=112) or post-induction observation (n=111) for consolidation in patients with CLL who were in complete remission (CR; 59% of total) or very good partial remission (PR; 27% of total) following fludarabine-containing induction therapy. (10) Patient age ranged from 31-65 years, with Binet stage A progressive (14%), B (66%), and C (20%) disease. None were known to have 17p deletion; 45% were known to not carry 17p deletion, but that status was unknown in 54% of all patients. The primary outcome, median event-free survival (EFS), was 51 months (range: 40-62 months) in the autograft group, compared to 24 months (range: 17-32 months) in the observed group; the 5-year EFS was 42% and 24%, respectively (p<0.001). The relapse rate at 5-year follow-up was 54% in the autograft group versus 76% in the observational group (p<0.001); median time to relapse requiring therapy or to death (whichever came first) was 65 months (range: 59-71 months) and 40 months (range: 25-56 months), respectively (p=0.002). Overall survival probability at 5-year follow-up was 86% (95% confidence interval [CI]: 77-94%) in the autograft arm, versus 84% (95% CI: 75-93%) in the observation arm (p=0.77), with no evidence of a plateau in the curves. There was no significant difference in NRM between groups, 4% in the autologous HSCT group and 0% in the observation group (p=0.33). Myelodysplastic syndrome (MDS) was observed at follow-up in 3 patients receiving an autograft and in 1 patient in the observational group.

A subsequent prospective, randomized clinical trial assessed the efficacy of autologous HSCT in previously untreated CLL patients. (11) A total of 244 patients (181 males) of median age 56 years (range 31-66 years) had Binet stage B (n=185) or C (n=56) disease. Among enrollees, 237 started planned therapy, 6 of whom discontinued. All 231 patients underwent induction chemotherapy; 103 (45%) entered CR and were randomly allocated to autologous HSCT (n=52) or observation (n=53). The 3-year estimated OS rates were 98% (95% CI: 94%, 100%) in the observation arm, and 96% (95% CI: 90%, 100%) in the HSCT arm (p=0.73). The estimated HR for death was 1.2 (95% CI: 0.3, 3.8) in the HSCT arm relative to the observation arm (p=0.82). During the 36 months after randomization, HSCT was associated, on average, with an extra 9 months without clinical symptoms or blood signs of CLL progression (32 ± 1 month) compared with observation (23 ± 2 months). An editorial that accompanied this report suggests using autologous HSCT in this setting may prolong time to progression compared with observation, but that because OS is not improved, autologous HSCT remains investigational for CLL/SLL patients. (12, 13)

Allogeneic HSCT

Given that autologous HSCT based on myeloablative conditioning regimens has not been demonstrated to be a curative treatment of CLL/SLL, alternative modalities have been sought. Allogeneic HSCT has been under investigation for the past 2 decades based on a potent graft-versus-leukemia (GVL) effect expressed as a permanently active cellular immune therapy in the recipient, independent of chemotherapy-related cytotoxicity. As indicated in the Description section of this policy, allogeneic HSCT may include use of myeloablative or reduced-intensity pretransplant conditioning regimens.

Data compiled in numerous review articles suggest that myeloablative allogeneic HSCT has curative potential for CLL or SLL. (6-8) Long-term disease control (33-65% OS at 3 to 6 years)

due to a low rate of late recurrences has been observed in all published series, regardless of donor source or conditioning regimen. (14) However, high rates (24-47%) of treatment-related mortality (TRM) discourage this approach in early or lower-risk disease, particularly among older patients whose health status typically precludes the use of myeloablative conditioning.

The development of reduced-intensity conditioning (RIC) regimens has extended the use of allogeneic HSCT to older or less fit patients who account for the larger proportion of this disease than younger patients, as outlined in several recent review articles. (7, 14, 15) Six published nonrandomized studies involved a total of 328 patients with advanced CLL who underwent RIC allogeneic HSCT using conditioning regimens that included fludarabine in various combinations that included cyclophosphamide, busulfan, rituximab, alemtuzumab, and total-body irradiation. (16-21) The majority of patients in these series were heavily pretreated, with a median 3-5 courses of prior regimens. Among individual studies, 27-57% of patients had chemotherapy-refractory disease, genetic abnormalities including del 17p13, del 11q22, and VH unmutated, or a combination of those characteristics. A substantial proportion in each study (18-67%) received stem cells from a donor other than an HLA-identical sibling. Reported NRM, associated primarily with graft-versus-host disease (GVHD) and its complications, ranged from 2% at 100 days to 26% overall at median follow-up that ranged from 1.7 years to 5 years. Overall survival rates ranged from 48-70% at follow-up that ranged from 2-5 years. Similar results were reported for progression-free survival (PFS), 34-58% at 2-5 year follow-up. Very similar results were reported from a Phase II study published in 2010 of RIC allogeneic HSCT in patients (n=90; median age 53 years, range: 27-65 years) with poor-risk CLL, defined as having 1 of the following: refractoriness or early relapse (i.e., less than 12 months) after purine-analog therapy; relapse after autologous HSCT; or, progressive disease in the presence of an unfavorable genetic marker (11q or 17p deletion, and/or unmutated IgVh status and/or usage of the VH3-21 gene). (22) With a median follow-up of 46 months, 4-year NRM, EFS and OS were 23%, 42%, and 65%, respectively. EFS was similar for all genetic subsets, including those with a 17p deletion mutation.

Summary

A substantial body of evidence from single-arm prospective and registry-based studies suggests allogeneic HSCT can provide long-term disease control and overall survival in patients with poor-risk CLL/SLL and otherwise dismal prognosis. This conclusion is supported by clinical input from transplant specialists as noted below. Until recently, it has been unclear what patient- and disease-specific characteristics can be used to select patients who could benefit from allogeneic HSCT compared to those for whom less-intense or no therapy may be indicated. This question has been addressed by investigations of cytogenetic and molecular abnormalities that can be associated with differential response to various therapies. (23) Some of these are outlined in Table 2 in the Policy Guidelines section above.

Autologous HSCT is feasible in younger patients but is not curative, particularly in those with poor-risk CLL. None of the single-arm or registry studies of autologous HSCT published to date has shown a plateau in overall survival (OS) at 4 to 6 years post-transplant. It may result in prolongation of overall survival, compared with conventional therapy, but this must be considered in the context of improved outcomes using conventional chemoimmunotherapy.

Clinical Guidelines

European Group for Blood and Marrow Transplantation (EBMT)

In June 2005, the EBMT convened a consensus panel to identify situations in which allogeneic HSCT is indicated for patients with CLL. (24) Information for this evidence-based consensus

was based on a MEDLINE search, meeting abstracts, and unpublished investigator-derived data. The panel considered 4 key issues:

- Does graft-versus-leukemia (GVL) activity in CLL exist?
- If yes, is it effective in high-risk CLL?
- What is the success rate of allogeneic HSCT in CLL?
- Which prognostic risk level justifies allogeneic HSCT?

The EBMT panel concluded that there is sound evidence that GVL activity is effective and represents the main contributor to durable disease control after allogeneic HSCT, even in poor-risk patients. It further concluded that long-term disease-free survival and possibly cure may be achieved in 33-67% of patients who undergo allogeneic HSCT for poor-risk CLL. While allogeneic HSCT for CLL is a procedure with evidence-based efficacy for poor-risk CLL, evidence is not sufficient to identify a generally superior conditioning regimen. The optimum choice of conditioning regimens may vary: in the presence of older age, comorbidity and sensitive disease; RIC regimens might be appropriate, whereas myeloablative regimens might be preferable in younger patients with good performance status but poorly controlled disease. The EBMT statement further suggests that these cases be discussed with a transplant center as early as possible to avoid extensive cytotoxic pretreatment or disease transformation. Furthermore, because the optimum transplant strategy may vary according to the clinical situation, it should be defined whenever possible in approved prospective clinical protocols.

National Cancer Institute (NCI) Working Group on CLL

In 1988 and 1996, a National Cancer Institute Working Group (NCI-WG) on CLL published guidelines for the design and conduct of clinical trials to facilitate comparisons between treatments and establish definitions that could be used in scientific studies on the biology of this disease. The U.S. Food and Drug Administration (FDA) also adopted these guidelines in their evaluation and approval of new agents. An updated version of the NCI-WG guidelines has been published that provides management recommendations based on new prognostic markers, diagnostic parameters and treatment options. (25)

National Comprehensive Cancer Network (NCCN) Guidelines

Current NCCN Guidelines for non-Hodgkin's lymphoma do not include autologous HSCT as a therapeutic option in CLL or SLL. (26) NCCN indicates that allogeneic HSCT (conditioning regimen unspecified) may be considered, preferably in a clinical trial, for patients younger than age 70 years with high-risk disease (Rai high risk, or del17p) or as salvage treatment in those with progressive or relapsed disease.

Physician Specialty Society and Academic Medical Center Input

In response to requests, input was received from 1 specialty medical center reviewer, 1 academic medical center reviewer, and 2 Blue Distinction Center reviewers while this policy was under review. While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted. Three of 4 reviewers agree that allogeneic HSCT was of value in patients who have poor-risk CLL (see Policy Guidelines) and that this procedure should be medically necessary in this setting. However, the reviewers indicate that the specific approach (e.g., RIC versus myeloablative conditioning) should be individualized based upon criteria such as age and health status. All reviewers concur with the policy statement that autologous HSCT is experimental and investigational.

National Cancer Institute (NCI) Clinical Trials Database (PDQ®)
In December 2011, the NCI Clinical Trials Database indicated 7 Phase II/III trials that focused on a variety of hematopoietic SCT approaches for treatment of CLL or SLL, primarily relapsed or refractory disease, second-line therapy or more, available online at: http://www.cancer.gov/search/ResultsClinicalTrials.aspx?protocolsearchid=7157492 .

Government Regulations

National:

There is a National Coverage Determination for allogeneic SCT, which is covered under Medicare for the treatment of leukemia, leukemia in remission or aplastic anemia when it is reasonable and necessary.

Nationally Non-Covered Indications
Insufficient data exist to establish definite conclusions regarding the efficacy of AuSCT (autologous stem cell transplant) for the following conditions:

- Acute leukemia not in remission;
- Chronic granulocytic leukemia;
- Solid tumors (other than neuroblastoma);
- Up to October 1, 2000, multiple myeloma;
- Tandem transplantation (multiple rounds of AuSCT) for patients with multiple myeloma;
- Effective October 1, 2000, non primary AL amyloidosis; and,
- Effective October 1, 2000, thru March 14, 2005, primary AL amyloidosis for Medicare beneficiaries age 64 or older.

In these cases, AuSCT is not considered reasonable and necessary within the meaning of §l862(a)(1)(A) of the Act and is not covered under Medicare.

The following uses of **allogeneic** (HSCT) bone marrow transplantation are covered under Medicare:

- Effective for services performed on or after August 1, 1978, for the treatment of leukemia, leukemia in remission, or aplastic anemia when it is reasonable and necessary; and
- Effective for services performed on or after June 3, 1985, for the treatment of severe combined immunodeficiency disease (SCID), and for the treatment of Wiskott-Aldrich syndrome.
- Effective for services performed on or after August 4, 2010, for the treatment of Myelodysplastic Syndromes (MDS) pursuant to Coverage with Evidence Development (CED) in the context of a Medicare-approved, prospective clinical study.

Local:

No LCD on this topic.

Michigan Department of Community Health:

All bone marrow transplant charges are reimbursed at the hospital's cost to charge ratio. Coverage requires preauthorization.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

Refer to other Bone Marrow Transplant (BMT) policies.

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 6/7/12, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
11/1/12	7/30/12	7/30/12	Joint policy established

Next Review Date: 3rd Qtr, 2013

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: BMT/STEM-CELL TRANSPLANTATION FOR CHRONIC LYMPHOCYTIC LEUKEMIA AND SMALL LYMPHOCYTIC LYMPHOMA – AUTOLOGOUS OR ALLOGENEIC

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria apply.
BCNA (Medicare Advantage)	Covered; criteria apply
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.
BlueCaid	Covered; criteria apply.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.