Policy Number	SUR703.029
Policy Effective Date	04/01/2025

Hematopoietic Cell Transplantation for Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)

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SUR703.002: Hematopoietic Cell Transplantation (HCT) or Additional Infusion Following Preparative Regimens (General Donor and Recipient Information)

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Coverage

Allogeneic hematopoietic cell transplantation **may be considered medically necessary** to treat chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) in individuals with markers of poor-risk disease (refer to "Staging and Prognosis of CLL/SLL" in Policy Guidelines section below).

Autologous hematopoietic cell transplantation **is considered experimental, investigational and/or unproven** to treat CLL or SLL.

Policy Guidelines

Staging and Prognosis of Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma:
Two scoring systems are used to determine stage and prognosis of individuals with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). As outlined in Table 1, the Rai

and Binet staging systems classify individuals into 3 risk groups with different prognoses and are used to make therapeutic decisions.

Table 1. Rai and Binet Classification for CLL or SLL

Rai Stage	Risk	Description	Median Survival, y	Binet Stage	Description	Median Survival, y
0	Low	Lymphocytosis	>10	A	<3 lymphoid areas, normal hemoglobin and platelets	>10
I	Int	Lymphocytosis + lymphadenopathy	7 to 9	B	≥3 lymphoid areas, normal hemoglobin and platelets	7
II	Int	Lymphocytosis + splenomegaly/ hepatomegaly ± lymphadenopathy	7 to 9			
III	High	Lymphocytosis + anemia ± lymphadenopathy, hepatomegaly, or splenomegaly	1.5 to 5	C	Any number of lymphoid areas, anemia, thrombocytopenia	5
IV	High	Lymphocytosis + thrombocytopenia ± anemia, splenomegaly or lymphadenopathy	1.5 to 5			

CLL: chronic lymphocytic leukemia; Int: Intermediate; SLL: small lymphocytic lymphoma; y: year(s).

Because prognoses of individuals vary within the different Rai and Binet classifications, other prognostic markers are used in conjunction with staging to determine clinical management.

The National Comprehensive Cancer Network guideline on CLL/SLL stated the following as unfavorable prognostic factors: DNA sequencing with mutated *TP53* or ≤2% immunoglobulin heavy-chain variable (*IGHV)* mutation; interphase cytogenetics with del17p or deletion of 11q (del11q); or complex karyotype (≥3 unrelated chromosome abnormalities in more than 1 cell on karyotype).

Description

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; in SLL, they are generally confined to lymph nodes. The Revised European-American/World Health Organization 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, but can undergo transformation to a more aggressive form of disease (e.g., Richter 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 treatment outcomes are comparable for both diseases. Both low- and intermediate-risk CLL and SLL demonstrate relatively good prognoses, with median survivals of 6 to 10 years; however, 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 disease history prompted an investigation of hematopoietic cell transplantation (HCT) as a possible curative regimen.

Hematopoietic Cell Transplantation

HCT 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 HCT) or from a donor (allogeneic HCT [allo-HCT]). These cells 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 “naive” 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 HCT. However, immunologic compatibility between donor and patient is critical for achieving a good outcome of allo-HCT. 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.

Conditioning for HCT

Conventional Conditioning for HCT

The conventional practice of allo-HCT 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 effect that develops after engraftment of allogeneic stem

cells within the patient's bone marrow space. The slower graft-versus-malignancy effect is considered the potentially curative component, but 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 events 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 allo-HCT, immunosuppressant drugs are required to minimize graft rejection and GVHD, which also increases the susceptibility of the patient to opportunistic infections.

The success of autologous HCT 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 before undergoing bone marrow ablation. As a consequence, autologous HCT is typically performed as consolidation therapy when the patient's disease is in complete remission. Patients who undergo autologous HCT are susceptible to chemotherapy-related toxicities and opportunistic infections before engraftment, but not GVHD.

Reduced-Intensity Conditioning for Allo-HCT
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 nonrelapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. Although the definition of RIC remains arbitrary, with numerous versions employed, all seek to balance the competing effects of nonrelapse mortality and relapse due to residual disease. RIC regimens can be viewed as a continuum in effects, from near totally myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allo-HCT initially demonstrate donor cell engraftment and bone marrow-mixed chimerism. Most will subsequently convert to full-donor chimerism, which may be supplemented with donor lymphocyte infusions to eradicate residual malignant cells. For this medical policy, the term *reduced-intensity conditioning* will refer to all conditioning regimens intended to be nonmyeloablative, as opposed to fully myeloablative (conventional) regimens.

Regulatory Status
The U.S. Food and Drug Administration (FDA) regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research (CBER), under Code of Federal Regulation (CFR) title 21, parts 1270 and 1271. Hematopoietic cells are included in these regulations.

Rationale

Medical policies assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Allogeneic Hematopoietic Cell Transplantation

Clinical Context and Therapy Purpose

The purpose of allogeneic hematopoietic cell transplantation (HCT) in individuals who have chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) and markers of poor-risk disease is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals with CLL or SLL and markers of poor-risk disease.

Interventions

The therapy being considered is allogeneic HCT (allo-HCT).

Comparators

The following therapies are currently being used to treat CLL and SLL: chemotherapy and/or immunotherapy.

Outcomes

The general outcomes of interest are overall survival (OS), disease-specific survival, change in disease status, treatment-related mortality, and treatment-related morbidity.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Data compiled in review articles through 2012 suggested that myeloablative allo-HCT has curative potential for CLL or SLL. (1-4) Long-term disease control (33%-65% overall survival [OS] at 3-6 years) due to a low rate of late recurrences has been observed in all published series, regardless of donor source or conditioning regimen. (5) 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 allo-HCT to older or less fit patients who account for the larger proportion of this disease than younger patients, as outlined in two 2009 review articles. (5, 6) Six published nonrandomized studies involved a total of 328 patients with advanced CLL who underwent RIC allo-HCT using conditioning regimens that included fludarabine in various combinations including cyclophosphamide, busulfan, rituximab, alemtuzumab, and total body irradiation. (7-12) Most patients in these series were heavily pretreated, with a median of 3 to 5 courses of prior regimens. Among individual studies, 27% to 57% of patients had chemotherapy-refractory disease, genetic abnormalities including a 17p13 deletion, 11q22 deletion, 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 a human leukocyte antigen (HLA)-identical sibling. Reported nonrelapsing mortality (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 ranging from 1.7 to 5 years. OS rates ranged from 48% to 70% at follow-up that ranged from 2 to 5 years. Similar results were reported for progression-free survival (PFS), which was 34% to 58% at 2- to 5-year follow-up. Very similar results were reported from a phase 2 study published in 2010 of RIC allo-HCT in patients (n=90; median age, 53 years; range, 27-65) with poor-risk CLL, defined as having one of the following: refractoriness or early relapse (i.e., <12 months) after purine-analogue therapy; relapse after autologous HCT; or progressive disease in the presence of an unfavorable genetic marker (11q or 17p deletion, and/or unmutated immunoglobulin heavy-chain variable-region status and/or usage of the *VH3-21* gene). (13) With a median follow-up of 46 months, 4-year NRM, event-free survival (EFS), and OS were 23%, 42%, and 65%, respectively. EFS estimates were similar for all genetic subsets, including those with a 17p deletion.

Section Summary: Allogeneic HCT

For individuals who have CLL/SLL and markers of poor-risk disease who receive allo-HCT, the evidence includes single-arm prospective and registry-based studies. No RCTs evaluating allo-HCT in patients with CLL were identified. Data from nonrandomized studies found OS rates between 48% and 70% at 2 to 5 years and PFS rates of 34% to 58% at 2 to 5 years after allo-HCT for poor-risk CLL. Despite not being randomized, these studies suggest that allo-HCT can provide long-term disease control and OS in patients with poor-risk CLL and SLL.

Autologous HCT

Clinical Context and Therapy Purpose

The purpose of autologous HCT in individuals who have CLL or SLL is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals with CLL or SLL.

Interventions

The therapy being considered is autologous HCT.

Comparators

The following therapies are currently being used to treat CLL and SLL: chemotherapy and/or immunotherapy.

Outcomes

The general outcomes of interest are OS, disease-specific survival, change in disease status, treatment-related mortality, and treatment-related morbidity.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Systematic Review

A 2015 systematic review of autologous HCT as first-line consolidation in CLL included a literature search through November 2014. (14) Four RCTs in adults were selected. Outcomes included OS, PFS, EFS, and harms (adverse events, treatment-related mortality, secondary malignancies). In these 4 trials, 301 patients were randomized to the autologous HCT arm and 299 to the control arm using first-line therapy without HCT as consolidation. Autologous HCT

did not result in a statistically significant improvement in OS (hazard ratio [HR], 0.91; 95% confidence interval [CI], 0.62 to 1.33) or in PFS (HR=0.70; 95% CI, 0.32 to 1.52). There was a statistically significant improvement in EFS favoring autologous HCT (HR=0.46; 95% CI, 0.26 to 0.83). A higher rate of secondary malignancy or treatment-related mortality was not associated with autologous HCT.

Randomized Controlled Trials

A phase 3 European Intergroup RCT (2011) addressed autologous HCT as second- or third-line treatment of CLL. (15) The trial compared autologous HCT (n=112) and postinduction observation (n=111) for consolidation in patients with CLL who achieved a complete response (CR; 59% of total) or very good partial response (VGPR; 27% of total) following fludarabine-containing induction therapy. Overall, patients' age ranged from 31 to 65 years, and they presented with Binet stage A progressive (14%), B (66%), and C (20%) disease. The population either did not have a 17p deletion or 17p deletion status was unknown. Median EFS (the primary outcome) was 51 months (range, 40-62 months) in the autograft group and 24 months (range, 17-32 months) in the observation group; 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 and 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 ($p=0.002$). OS probability at 5-year follow-up was 86% (95% CI, 77% to 94%) in the autograft arm and 84% (95% CI, 75% to 93%) in the observation arm ($p=0.77$), with no evidence of a plateau in the areas under the curve. There was no significant difference in NRM between groups (4% for autologous HCT vs. 0% for observation; $p=0.33$). Myelodysplastic syndrome (MDS) was observed at follow-up in 3 patients receiving an autograft and in 1 patient in the observational group.

In a subsequent 2014 report, authors of the European Intergroup RCT presented quality of life (QOL) findings from this trial. (16) Two secondary analyses were performed to investigate the impact of HCT and relapse on QOL. In the primary analysis, the authors demonstrated an adverse impact of HCT on QOL, which was largest at 4 months and continued throughout the first year after randomization. Further, a sustained adverse impact of relapse on QOL was observed, which worsened over time. Thus, despite better disease control by autologous HCT, the side effects turned the net effect toward inferior QOL in the first year and comparable QOL in the following 2 years after randomization.

Section Summary: Autologous HCT

For individuals who have CLL/SLL who receive autologous HCT, the evidence includes RCTs and a systematic review. A systematic review of RCTs did not find that autologous HCT as first-line consolidation therapy for CLL significantly improved OS or PFS compared with alternative treatments. An RCT evaluating autologous HCT as second- or third-line treatment of CLL did not find that HCT improved the net health outcome.

Summary of Evidence

For individuals who have chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) and markers of poor-risk disease who receive allogeneic hematopoietic cell transplantation (allo-HCT), the evidence includes single-arm prospective and registry-based studies. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related mortality and morbidity. Data have suggested that allo-HCT can provide long-term disease control and overall survival in patients with poor-risk CLL/SLL. High rates of treatment-related morbidity discourage this approach in lower risk disease, particularly among older patients whose health status typically precludes the use of myeloablative conditioning. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have CLL/SLL who receive autologous HCT, the evidence includes randomized controlled trials (RCTs) and a systematic review. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related mortality and morbidity. Autologous HCT is feasible in younger patients but is not curative, particularly in those with poor-risk CLL. Studies of autologous HCT published to date have not shown improvement in overall survival in patients with CLL/SLL, and results must be considered in the context of improved outcomes with the use of newer chemoimmunotherapy agents. Furthermore, evidence from the European Intergroup RCT has suggested quality of life issues are important in selecting patients for autologous HCT and may dictate the management course for patients who are otherwise candidates for this approach. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

American Society for Blood and Marrow Transplantation (ASBMT)

In 2015, the ASBMT published guidelines on indications for allo-HCT and autologous HCT for CLL. (17) Recommendations described the current consensus on use of HCT in and out of the clinical trial setting. Treatment recommendations are shown in Table 2.

Table 2. 2015 Recommendations for Allogeneic and Autologous HCT for CLL

Adult Indications	Allogeneic HCT	Autologous HCT
High risk, first or greater remission	C	N
T-cell, prolymphocytic leukemia	R	R
B-cell, prolymphocytic leukemia	R	R
Transformation to high-grade lymphoma	C	C

C: standard of care, clinical evidence available; CLL: chronic lymphocytic leukemia; HCT: hematopoietic cell transplantation; N: Not generally recommended; R: standard of care, rare indication.

In 2016, the Society published clinical practice recommendations with additional detail on allo-HCT for CLL. (18) Recommendations are shown in Table 3.

Table 3. 2016 Recommendations for Allogeneic HCT for CLL

Indications	Allogeneic HCT
High Risk CLL	• Not recommended in the first-line consolidation setting.

	• Not recommended for patients who relapse after first-line therapy and demonstrate sensitive disease after second line therapy (not BCR inhibitors). • Recommended for patients who relapse after first-line therapy, have refractory disease after second-line therapy (not BCR inhibitors) and show an objective response to BCR inhibitors or to a clinical trial. • Recommended for patients who relapse after first-line therapy, have refractory disease after second-line therapy (including BCR inhibitors but not BCL-2 inhibitors) and show an objective response to BCL-2 inhibitors or to a clinical trial. • Recommended when there is a lack of response or there is progression after BCL-2 inhibitors.
Richer Transformation	Recommended after achieving an objective response to anthracycline-based chemotherapy.
Purine Analogue Relapsed and/or Refractory Disease	Not recommended.

BCR: B-cell receptor; BCL-2: B-cell lymphoma 2; CLL: chronic lymphocytic leukemia; HCT: hematopoietic cell transplantation.

American Society for Transplantation and Cellular Therapy (ASTCT)

In 2020, the ASTCT published guidelines on indications for HCT and immune effector cell therapy. (19) Recommendations for CLL are shown in Table 4.

Table 4. 2020 Recommendations for Allogeneic HCT for CLL

Adult Indications	Allogeneic HCT	Autologous HCT
High-risk, first or greater remission	S	N
T cell, prolymphocytic leukemia	S	R
B cell, prolymphocytic leukemia	R	R
Transformation to high-grade lymphoma	C	S

C: standard of care, clinical evidence available; Cll: chronic lymphocytic leukemia; HCT: hematopoietic cell transplantation; N: not generally recommended; R: standard of care, rare indication; S: standard of care

National Comprehensive Cancer Network (NCCN) Guidelines

Current NCCN guidelines (v.3.2024) for CLL and SLL state the following regarding HCT: (20)

- "Allogeneic HCT can be considered for relapsed/refractory disease after prior therapy with Bruton's tyrosine kinase inhibitors (BTKi)- and venetoclax-based regimens in patients without significant comorbidities."
- "Long-term results from several prospective studies showed that allogeneic HCT can provide long-term disease control and also overcome the poor prognosis associated with del(17p) and TP53 mutations. Available data suggest that CK (≥5 abnormalities) is associated with

inferior overall survival [OS] and event-free survival [EFS] following allogeneic HCT with reduced-intensity conditioning in patients with high-risk interphase cytogenetics."

- In patients with histologic transformation (Richter's) and progression, allogeneic HCT can be considered for certain patients with disease responding to initial chemotherapy. In addition, "autologous HCT may also be appropriate for patients with disease responding to initial therapy but who are not candidates for allogeneic HCT due to age, comorbidities, or lack of a suitable donor."

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov in November 2023 did not identify any ongoing or unpublished trials that would likely influence this policy.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	36511, 38204, 38205, 38206, 38207, 38208, 38209, 38210, 38211, 38212, 38213, 38214, 38215, 38220, 38221, 38222, 38230, 38232, 38240, 38241, 38242, 38243, 81265, 81266, 81267, 81268, 81370, 81371, 81372, 81373, 81374, 81375, 81376, 81377, 81378, 81379, 81380, 81381, 81382, 81383, 86805, 86806, 86807, 86808, 86812, 86813, 86816, 86817, 86821, 86822, 86825, 86826, 86828, 86829, 86830, 86831, 86832, 86833, 86834, 86835, 86849, 86950, 86985, 88240, 88241
HCPCS Codes	S2140, S2142, S2150

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
04/01/2025	Reviewed. No changes.
09/15/2024	Document updated with literature review. Minor editorial refinements made to Coverage; intent unchanged. Added/updated references 18-20.
01/01/2024	Reviewed. No changes.
03/01/2023	Document updated with literature review. The following changes/additions were made to Coverage related to staging and prognosis of chronic lymphocytic leukemia or small lymphocytic lymphoma: 1) RAI stage II and III description, and 2) National Comprehensive Cancer Network information on unfavorable prognostic factors. Added/updated the following reference(s): 19.
06/15/2021	Reviewed. No changes.

04/01/2020	Document updated with literature review. Coverage unchanged. The following reference was updated: 24. Title changed from: Hematopoietic Stem-Cell Transplantation for Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL).
04/15/2018	Reviewed. No changes.
06/01/2017	Document updated with literature review. Coverage unchanged.
05/15/2016	Reviewed. No changes.
05/01/2015	Document updated with literature review. The following was changed: Rai Staging System, Binet Classification System and Markers of Poor Prognosis moved from Description to Coverage Sections. Coverage unchanged. Title changed from Stem-Cell Transplant for Treatment of Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL).
02/01/2013	Document updated with literature review. The following was added as clarification to the medically necessary coverage: "markers of poor-risk disease." Description and Rationale significantly revised.
04/01/2010	New medical document originating from: SUR703.017, Peripheral/Bone Marrow Stem-cell Transplantation (PSCT/BMT) for Non-Malignancies; SUR703.018, Peripheral/Bone Marrow Stem-cell Transplantation (PSCT/BMT) for Malignancies; SUR703.022, Cord Blood as a Source of Stem-cells (CBSC); SUR703.023, Donor Leukocyte Infusion (DLI); **and** SUR703.024, Tandem/Triple High-Dose Chemoradiotherapy with Stem-cell Support for Malignancies. Stem-cell transplant continues to be medically necessary when stated criteria are met. [NOTE: A link to the medical policies with the following titles can be found at the end of the medical policy SUR703.002, Stem-Cell Reinfusion or Transplantation Following Chemotherapy (General Donor and Recipient Information): • Peripheral/Bone Marrow Stem-cell Transplantation (PSCT/BMT) for Non-Malignancies; • Peripheral/Bone Marrow Stem-cell Transplantation (PSCT/BMT) for Malignancies; • Cord Blood as a Source of Stem-cells; • Donor Leukocyte Infusion (DLI); and • Tandem/Triple High-Dose Chemoradiotherapy with Stem-cell Support for Malignancies.