



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Stem-Cell Transplantation for Acute Lymphocytic/Lymphoblastic Leukemia

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INSTRUCTIONS FOR USE

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Coverage Policy

CIGNA covers myeloablative allogeneic hematopoietic stem-cell transplantation (HSCT) from a human leukocyte antigen (HLA)-matched donor (at least five of six HLA-match) as medically necessary for the treatment of acute lymphocytic/lymphoblastic leukemia (ALL) when ANY of the following criteria are met:

- failed induction therapy
- second or subsequent remission
- late marrow relapse with high tumor load as indicated by a peripheral blast count of 10,000/ μ L or more
- B-cell lineage ALL with marrow relapse while on treatment or within six months after termination of therapy
- T-cell lineage ALL with marrow relapse
- first remission for adults with poor prognosis**
- first remission for children with high risk of disease relapse***

CIGNA covers a second myeloablative allogeneic HSCT from an HLA-matched donor (at least five of six HLA-match) as medically necessary for the treatment of ALL when relapsed disease occurs more than six months after first allogeneic HSCT.

CIGNA covers autologous HSCT for the treatment of ALL as medically necessary in children who are ineligible for allogeneic HSCT when there is no active disease and EITHER of the following criteria is met:

- first remission with high risk of disease relapse***
- second or later remission

CIGNA does not cover ANY of the following procedures for the treatment of ALL because each is considered experimental, investigational or unproven (this list may not be all-inclusive):

- nonmyeloablative allogeneic HSCT (adults only)
- tandem (also known as sequential) transplants
- autologous transplants (adults only)

CIGNA does not cover HSCT for the treatment of ALL when ANY of the following conditions are present because it is considered not medically necessary (this list may not be all-inclusive):

- active central nervous system (CNS) involvement
- presence of any significant comorbid medical or psychiatric illness which would significantly compromise the clinical care and chances of survival
- advanced age (adults)

****Poor prognosis acute lymphocytic/lymphoblastic leukemia in adults includes ANY of the following:**

- longer than four weeks to achieve a complete remission
- age >35 years
- white blood cell count (WBC) greater than $30 \times 10^9 /L$ (30,000/ μ L) in B-cell lineage ALL
- WBC greater than $50 \times 10^9 /L$ (50,000/ μ L) in T-cell lineage ALL
- null cell phenotype
- extramedullary disease
- presence of chromosome abnormalities (e.g., t(9;22)(q34;q11) (the Philadelphia chromosome), t(4;11), t(8,14), t(2,8), (8,22), MLL gene (11q23) or t(1;19)
- elevated beta 2 microglobulin
- deletion of chromosome 7
- trisomy 8
- hypodiploidy

*****High-risk of disease relapse in children includes ANY of the following:**

- failure to achieve a complete remission (CR) within four weeks of induction therapy
- high minimal residual disease at end of remission induction
- relapse while on chemotherapy
- first CR lasting <24 months
- infancy (age younger than one year)
- age \geq 10 years
- white blood cell count (WBC) > 50,000/mcL
- extramedullary disease
- presence of chromosomal abnormalities (e.g., t(9;22)(q34;q11) (the Philadelphia chromosome), t(4;11), t(8,14), t(1,19), or MLL gene (11q23)
- hypodiploidy
- near-haploid ALL (i.e., 24 to 28 chromosomes)
- acute lymphocytic/lymphoblastic leukemia resulting from prior cancer therapy

General Background

Acute lymphocytic leukemia (ALL), also known as acute lymphoblastic leukemia and acute lymphoid leukemia, is a heterogeneous group of disorders and one of the most common forms of leukemia. Many cases of ALL can be categorized on the basis of a single characteristic cytogenetic abnormality that affects prognosis.

Abnormalities thought to be associated with unfavorable outcomes are the lack of cALLa, CD10 antigen, B-cell type ALL, CD7+, CD2, and CD5 immunotypes, near haploidy (i.e., 24–28 chromosomes per cell), hypodiploidy (i.e., <45 chromosomes per cell), >65 chromosomes per cell, and MLL gene rearrangements (11q23,). Other chromosomal abnormalities associated with poor prognoses include t(4;11), t(9;22, deletion of chromosome 7 or trisomy 8, and a variety of translocations including t(2;8), t(8;12), and t(8;22)(National Cancer Institute [NCI], 2010a, 2010b).

Certain other characteristics are associated with poor prognosis. In children, younger age at diagnosis, higher white blood cell (WBC) counts (e.g., >50,000/ μ L), the presence of central nervous system (CNS) disease at diagnosis, and the presence of minimal residual disease after therapy has been shown to be negative prognostic factors for the outcome of children with high-risk ALL (NCI, 2010b; Sramkova, 2007). Gender may be also be an important factor; girls have a slightly better prognosis than boys, thought to be partially due to the occurrence of testicular relapse among boys, and an increased risk for bone marrow and CNS relapse. In adults, elevated B2-microglobulin and advanced age are associated with poor outcomes.

Induction chemotherapy is administered to produce a complete remission (CR) in the bone marrow, evidenced by a normocellular marrow with <5% blasts, no signs or symptoms of CNS leukemia or extramedullary infiltration, and normal complete white blood cell count, differential, hematocrit/hemoglobin levels, and platelet count. The rate at which the disease enters CR correlates to treatment and survival outcome. In children, therapy is tailored based on the risk of treatment failure; those children who have very good outcomes with modest therapy are spared more aggressive and toxic treatment (NCI, 2010b).

Stem Cell Transplantation

Stem-cell transplantation refers to transplantation of hematopoietic stem cells (HSCs) from a donor into an individual. HSCs are immature cells that can develop into any of the three types of blood cells (red cells, white cells or platelets). Hematopoietic stem-cell transplantation (HSCT) can be either autologous (using the person's own stem cells) or allogeneic (using stem cells from a donor).

Allogeneic HSCT

Adults: Several randomized controlled trials (RCTs) and case studies have demonstrated improved outcomes with the use of myeloablative allogeneic HSCT in subsets of adults with five-year overall survival (OS) rates of 28%–69% (Cornelissen, 2009; Tomblyn, 2009; Goldstone, 2008; Fielding, 2007; Vey, 2007; Gokbuget, 2006; Oyekunle, 2006; Camera, 2004). While allogeneic HSCT is generally associated with lower relapse rates and higher cure incidences than either autologous HSCT or chemotherapy this is partially offset by an increased treatment-related mortality rate due to graft-versus-host disease, veno-occlusive disease of the liver and interstitial pneumonitis (NCI, 2010a; Cornelissen, 2009; Fielding, 2007, Thomas, 2004).

The results of a prospective clinical trial by Goldstone (2008) suggests that a graft-versus-leukemia (GVL) effect may exist, and that the use of a sibling donor allogeneic HSCT as consolidation therapy provides the greatest chance for long term survival for standard risk adult ALL in first remission. This study also suggests that in the absence of a sibling donor, maintenance chemotherapy is preferable to autologous HSCT as postremission therapy (NCI, 2010a).

Patients who experience a relapse after remission can be expected to succumb within one year, even if a second complete remission is achieved. If there are appropriate available donors, HSCT may be a consideration (NCI, 2010a; Fielding, 2009). Allogeneic HSCT offers these patients the best chance for long-term disease-free survival (DFS); however, once these individuals are beyond second remission, the results of all allografting procedures worsen considerably, with only 10–15% of patients becoming long-term, disease-free survivors (Redaelli, 2005; Garcia-Manero and Thomas, 2001). A worse outcome is also noted in adults who have shorter remission durations (e.g., <6 months) after the first allograft than in those patients whose remission lasts longer than six months. Adults for whom a human leukocyte antigen (HLA) -matched donor is not available are excellent candidates for enrollment in clinical trials that are studying autologous transplantation, immunomodulation, and novel chemotherapeutic or biological agents (NCI, 2010a).

Children: For the two to four percent of children that fail to achieve remission with initial chemotherapy, further attempts at induction chemotherapy are often unsuccessful and prognosis is usually poor. Allogeneic hematopoietic stem-cell transplantation (HSCT) may be performed immediately after recovery from initial induction therapy and may be used as a substitute for multiple cycles of intensive post-remission chemotherapy. Those who undergo HSCT in remission have better outcomes (NCI, 2010b; Klingebiel, et al., 2005). Although variables exist, several studies have demonstrated improved outcomes with the use of myeloablative allogeneic HSCT compared with autologous HSCT or chemotherapy in selected infants and children with acute lymphoblastic/lymphocytic leukemia (ALL) (Schrauder, 2006; Balduzzi, 2005; Dalle, 2005; Sanders, 2005; Eapin, 2004). Children receiving human leukocyte antigen (HLA)-matched sibling HSCT in first complete remission (CR) have disease-free survival (DFS) rates of 70–80%, with low relapse rates of 0–10%, although some high-risk individuals (e.g., those with Philadelphia 1 positive [Ph1+] ALL) have lower survival rates of 50–65%. Other studies have demonstrated no significant differences in survival outcomes with allogeneic HSCT (Malempati, 2007; Ribera, 2007; Gaynon, 2006; Badell, 2005).

Allogeneic HSCT may be the best therapy for individuals who relapse after a CR. HSCT may be considered for children with T-cell ALL and marrow relapse, patients with precursor B-cell ALL and marrow relapse occurring while on treatment or within six months of termination of therapy, and late marrow relapse with high tumor load as indicated by a peripheral blast count of 10,000/ μ L or more (NCI, 2010b). Overall DFS rates for individuals in second CR range from 40–60% (Steuber, 2003). For patients relapsing after an allogeneic HSCT for relapsed ALL, a second ablative allogeneic HSCT may be feasible in a subset of children. Among this group, approximately 10% to 30% may achieve long-term event-free survival. Prognosis is more favorable for children with longer duration of remission after the first HSCT and for those with complete remission at the time of second transplantation (NCI, 2009). Many patients may be unable to undergo a second HSCT due to failure to achieve remission, early toxic death or severe organ toxicity.

Based on the published peer-reviewed scientific literature allogeneic HSCT may be an effective treatment for selected children and adults with ALL.

Autologous HSCT

Although autologous HSCT results in a lower rate of treatment-related complications and mortality than with an allogeneic HSCT, the absence of the graft versus leukemia effect, potential leukemia cell contamination of the autologous marrow, and limited ability to eliminate minimal residual disease following the procedure raise barriers to the effectiveness of autologous HSCT. In most studies, autologous HSCT results are inferior to those for allogeneic HSCT.

Adults: No advantage in terms of DFS has been demonstrated for individuals receiving autologous HSCT compared with chemotherapy alone. Multiple clinical studies do not support the use of autologous HSCT in adults in relapse or with refractory ALL (Tavemier, 2007; Dhedrin, 2006; Hahn, 2006; Redaelli, 2005; Ribera, 2005; Thomas, 2004); however, it remains a focus of research interest. In the randomized multicenter study by Thomas et al. (2004), the use of autologous HSCT did not confer a significant benefit of autologous HSCT over chemotherapy alone for persons with high-risk ALL. In an intention-to-treat analysis, there was no significant difference in outcomes between persons with poor-prognosis disease who were treated with autologous HSCT compared with those who received standard-dose chemotherapy. The median DFS rates were 15.2 months and 11 months, respectively, with median overall survival (OS) rates of 28 months and 26.1 months, respectively, for those receiving HSCT compared with standard chemotherapy. There was a trend toward improved OS in patients who received autologous HSCT versus chemotherapy alone, with three-year OS rates of 44% versus 35%, respectively, and five-year OS rates of 32% and 21%, respectively.

Dhedrin et al. (2006) evaluated the results of autologous HSCT compared with chemotherapy by performing an individual data-based overview analysis of the Leucemies Aigues Lymphoblastique de'Adulte (LALA)-85, LALA-87, and LALA-94. Three-hundred forty-nine patients with ALL were eligible for randomization to chemotherapy or autologous HSCT. Using an intent-to-treat analysis, OS and DFS were not significantly different in the two treatment arms. The cumulative incidence of relapse was 78% versus 66%, respectively, for the chemotherapy and autologous HSCT arms. At 10 years, the estimated overall survival (OS) was 13% versus 20%, respectively, ($p=0.78$) for the chemotherapy and autologous hematopoietic stem-cell transplantation (HSCT) arms. Estimated disease-free survival (DFS) were 12% and 20%, respectively, ($p=0.10$) for the chemotherapy and autologous HSCT arms. Cumulative incidence of relapse at 10 years was 84% and 76%, respectively,

($p=0.08$) for the chemotherapy and autologous HSCT arms. This analysis failed to demonstrate the benefit of autologous HSCT over chemotherapy.

Children: Autologous HSCT is rarely a treatment option because of the presence of leukemic cells in the blood and marrow; however, it may be an acceptable treatment option for selected children who do not have a human leukocyte antigen (HLA)-identical donor or who are unable to tolerate high-dose therapy. Although some studies demonstrate inferior outcomes with autologous HSCT compared with those achieved with allogeneic HSCT, this therapy may result in improved DFS in selected children with high-risk acute lymphocytic/lymphoblastic leukemia (ALL) who have experienced complete remission (CR) and for those with high risk of relapse (Ribera, 2006; Sandler, 2006; Badell, 2005).

There are limited data regarding the use of autologous HSCT for children in relapse or with refractory ALL. The major limitations are drug resistance in the leukemia cell clones, lack of significant graft-versus-leukemia (GVL) effect, and difficulty associated with collecting uncontaminated stem cells. The lack of a graft-versus-leukemia reaction results in a higher incidence of disease relapse with autologous HSCT than occurs with allogeneic HSCT. Contamination of autografts by malignant cells may account for the difference.

The published peer-reviewed scientific literature does not demonstrate the effectiveness of autologous HSCT over allogeneic HSCT or standard-dose chemotherapy for the treatment of adults with ALL. Although data are not robust, autologous HSCT is an acceptable treatment option for selected children who are ineligible for allogeneic HSCT.

Non-Myeloablative Stem-Cell Transplant: Non-myeloablative preparative regimens (i.e., mini-transplants) are designed to reduce regimen-related toxicities and allow allogeneic HSCT in persons who are older, have comorbid conditions or have toxicities from previous treatment (Maloney, et al., 2002). Randomized controlled trial data are limited regarding the effectiveness of this therapy in adults and children with ALL. Retrospective case studies demonstrate OS rates of 29%–43%, with relapse rates up to 60%. Treatment-related mortality rates range from 21–27% (Mohty, 2008; Guterriez, 2007; Hamaki, 2005; Massenkeil, 2005).

On behalf of the European group for Blood and Marrow Transplantation, Mohty et al. (2008) published results of a retrospective review of adults with acute ALL who underwent reduced-intensity conditioning allogeneic HSCT. Two-year OS and leukemia-free survival (LFS) for the total population were 31% and 21%, respectively, with a relapse incidence of 51% and non-relapse mortality of 28%. Overall survival (OS), leukemia-free survival, and non-relapse mortality were significantly better in patients transplanted in first complete remission (CR) than in second or third CR ($p<0.003$, $p<0.002$, $p<0.01$, respectively).

Guterriez et al. (2007) prospectively evaluated the therapeutic value of non-myeloablative conditioning with allogeneic hematopoietic stem-cell transplantation (HSCT) in 43 adults with B-lineage acute lymphocytic/lymphoblastic leukemia (ALL) in second CR. Sixty-five percent of the patients had a leukemia relapse after the treatment. The OS was 31%; median survival was 235 days, and treatment-related mortality (TRM) was 21%.

Massenkeil, et al. (2005) retrospectively compared a group of 25 adults with acute lymphocytic/lymphoblastic leukemia (ALL) or acute myelogenous leukemia after reduced-intensity conditioning (RIC) to a historical group of 50 matched controls who received high-dose conditioning. Probability of disease-free survival (DFS) at three years was 43% and 49% for the RIC and high-dose conditioning groups, respectively. OS was 40% and 37%, respectively, for those receiving RIC compared with high-dose conditioning. Relapse rate for patients receiving RIC was 60% compared to patients receiving high-dose conditioning.

These results are supported by a prospective trial of RIC allogeneic HSCT in 33 adults with ALL who were not eligible for conventional myeloablative chemotherapy (Hamaki, et al., 2005). The patient population was heterogeneous for disease status and risk classification. Treatment-related mortality (TRM) was 27% and two-year OS was 29.7%. The one-year progression-free survival rate was 30.6% for those who underwent HSCT in first or second CR and 28.6% in patients who underwent HSCT in relapse or induction failure.

Although results are promising, these studies are limited by uncontrolled study design, small sample size, heterogeneity of study population, and short follow-up. Although it remains a topic of research interest the role of non-myeloablative HSCT for the treatment of ALL has not yet been established.

Tandem (Sequential) Transplants

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 ALL. At this time the role of this therapy has not yet 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. Absolute contraindications to transplantation include active central nervous system (CNS) involvement and the presence of any significant co-morbid medical or psychiatric illness which would significantly compromise the clinical care and chances of survival. Additionally, advanced age in adults is associated with a higher incidence of on the higher prevalence of unfavorable cytogenetics and an increased frequency of medical conditions that affect the ability to tolerate intensive treatment. 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

The National Cancer Institute ([NCI], 2010a, 2010b)

Adult ALL in Remission: The NCI (2010a) notes “Current approaches to postremission therapy for adult ALL include short-term, relatively intensive chemotherapy followed by longer-term therapy at lower doses (maintenance), high-dose marrow-ablative chemotherapy or chemoradiation therapy with allogeneic stem cell rescue (alloBMT), and high-dose therapy with autologous stem cell rescue.” Results of the International ALL trial ECOG 2993 “suggest that in the absence of a sibling donor, maintenance chemotherapy is preferable to autoBMT as postremission therapy.”

In PH1-positive adult ALL, the NCI notes, “If a suitable donor is available, allogeneic bone marrow transplantation should be considered because remissions are generally short with conventional ALL chemotherapy clinical trials.”

Newly Diagnosed Childhood ALL: The NCI (2010b) notes “Patients with persistent leukemia at the end of the four week induction phase have a poor prognosis and may benefit from an allogeneic stem cell transplant once complete remission is achieved. The NCI also notes “Results of a Children’s Oncology Group study suggest that the presence of the Philadelphia chromosome should no longer be considered an absolute indication for transplantation in first remission.”

Recurrent ALL: The NCI (2010a) notes that “Patients with acute lymphoblastic leukemia (ALL) who experience a relapse following chemotherapy and maintenance therapy are unlikely to be cured by further chemotherapy alone. These patients should be considered for reinduction chemotherapy followed by allogeneic bone marrow transplantation. Patients for whom an HLA-matched donor is not available are excellent candidates for enrollment in clinical trials that are studying autologous transplantation, immunomodulation, and novel chemotherapeutic or biological agents.”

The NCI (2010b) notes that “Post second remission (CR2) therapy for patients who experience a bone marrow relapse while on therapy or within 6 months of discontinuing therapy generally includes HSCT.” “For B-precursor patients with an early marrow relapse, allogeneic transplant from a human leukocyte antigen (HLA)-identical sibling or matched unrelated donor that is performed in second remission has been reported in most studies to result in longer leukemia-free survival when compared with a chemotherapy approach. For B-precursor patients with a late marrow relapse, a primary chemotherapy approach after achievement of CR2 has resulted in survival rates of approximately 50%, and it is not clear whether allogeneic transplantation is associated with superior cure rate.” The NCI also notes “For patients with T-cell acute lymphoblastic leukemia and marrow relapse, outcomes with chemotherapy alone have generally been poor, and these patients are usually treated with allogeneic SCT in CR2, regardless of time to relapse. For patients relapsing after an allogeneic HSCT for relapsed ALL, a second ablative allogeneic HSCT may be feasible. Reduced intensity approaches can also cure a percentage of patients when used as a second allogeneic transplant approach, but only if patients achieve a complete remission confirmed by flow cytometry”

The American Society for Blood and Marrow Transplantation (ASBMT): The ASBMT published guidelines on the role of cytotoxic therapy with HSCT for the treatment of ALL in adults (Hahn, 2006). These guidelines include the following recommendations:

- In first complete remission (CR1), stem-cell transplantation (SCT) yields outcomes similar to chemotherapy and is not recommended as first-choice therapy. For high-risk patients, there are no direct comparisons but some data suggest an advantage for SCT.
- In second complete remission (CR2), SCT is recommended over chemotherapy, as a sizeable fraction of patients achieve extended leukemia-free survival compared to chemotherapy alone.
- Autologous purged SCT and autologous unpurged SCT produce leukemia-free survival comparable to chemotherapy.
- Although there are no direct comparisons, there appears to be a survival advantage for related allogeneic SCT compared to chemotherapy in Ph+ adult ALL patients in CR1 or subsequent remissions. Unrelated allogeneic SCT produces extended leukemia-free survival in some patients.
- Although there are no direct comparisons, there is a possible benefit of unrelated allogeneic SCT over chemotherapy in Ph+ adult ALL patients. Higher treatment-related mortality, however, may compromise the potential anti-tumor advantage of unrelated allogeneic SCT.
- There are not enough data evaluating non-myeloablative conditioning regimens to determine the effect on treatment-related mortality and leukemia-free survival. No recommendation can be made.
- A preponderance of evidence supports a recommendation of allogeneic over autologous SCT. There is insufficient evidence, however, to determine if this effect is more apparent in specific risk subgroups, including Ph+ adult ALL.

The ASBMT (2006) also published guidelines on the role of cytotoxic therapy with HSCT for the treatment of ALL in children. These guidelines include the following recommendations:

- In first complete remission, matched related allogeneic SCT demonstrated benefit in very high-risk Ph+ pediatric ALL patients and is recommended over chemotherapy in this patient population.
- Matched related allogeneic SCT in second or subsequent remission has resulted in long-term survival that may be equivalent to or better than chemotherapy alone (especially for patients with a short first complete remission). There is insufficient evidence to support a recommendation for unrelated allogeneic transplant versus chemotherapy in this patient population. However, the precise role of related or unrelated allogeneic SCT in this setting requires further studies.

- Some pediatric acute lymphocytic/lymphoblastic leukemia (ALL) patients with late relapses achieve extended leukemia-free survival (LFS) with autologous purged stem-cell transplantation (SCT); however, the evidence is insufficient to determine that this is better than chemotherapy alone. For those with an early relapse, the outcomes with autologous purged SCT are less promising.
- There are insufficient data available on the use of autologous unpurged SCT in the treatment of pediatric ALL; however, this is not recommended as a priority area of research
- Outcomes comparing related vs. unrelated donor allogeneic SCT have not been adequately studied, especially in patients who have had high-resolution typing, and no recommendation can be made at this time
- Outcomes of autologous vs. allogeneic SCT have not been adequately studied and no recommendation can be made at this time.

The National Marrow Donor Program ([NMDP], 2009): The NMDP recommends that adults with high-risk ALL be referred for consultation for HSCT when the following characteristics are present: first complete remission (CR) up to age 35, high-risk over age 35 including: poor-risk cytogenetics (e.g., Philadelphia chromosome, 11q23 rearrangements), high white blood cell (>30,000–50,000) at diagnosis, central nervous system (CNS) or testicular leukemia, no complete remission (CR) within four weeks of initial treatment, induction failure, second CR and beyond.

The NMDP also recommends that children with high-risk ALL be referred for consultation for HSCT when one of the following characteristics is present: induction failure, Philadelphia chromosome positive, WBC >100,000 at diagnosis, 11q23 rearrangement, mature B-cell phenotype (Burkitt’s lymphoma), infant age at diagnosis, first CR duration <18 months, third CR and beyond.

Summary

The published peer-reviewed scientific literature supports the safety and effectiveness of myeloablative allogeneic hematopoietic stem-cell transplant (HSCT) from a human leukocyte antigen (HLA)-matched donor (at least five of six HLA-match) for the treatment of acute lymphocytic/lymphoblastic leukemia (ALL) in selected individuals.

Evidence in published peer-reviewed scientific literature supports the effectiveness of autologous HSCT in selected children with ALL who are ineligible for allogeneic HSCT; however, there is insufficient evidence to support the effectiveness of this therapy for adults.

There is insufficient evidence in the published peer-reviewed scientific literature to support the safety and effectiveness of non-myeloablative allogeneic or tandem HSCT for the treatment of ALL. The role of these therapies has not yet been established.

The published peer-reviewed scientific literature does not support the effectiveness of HSCT for the treatment of adults or children with ALL who have active central nervous system (CNS) involvement, in the presence of any significant co-morbid illness that would significantly compromise the patient’s clinical care and chances of survival, or advanced age.

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
204.00	Acute lymphoid leukemia without mention of remission
204.01	Acute lymphoid leukemia in remission

*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	10/15/2007	0163	Stem-Cell Transplant for Acute Lymphocytic/Lymphoblastic Leukemia: Adult
	9/15/2008	0165	Stem-Cell Transplant for Acute Lymphocytic/Lymphoblastic Leukemia: Pediatric
Great-West Healthcare	6/21/2007	05.293.02	Bone Marrow Transplantation (BMT) for Adult Acute Lymphocytic Leukemia (ALL)

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Connecticut General Life Insurance Company has acquired the business of Great-West Healthcare from Great-West Life & Annuity Insurance Company (GWLA). Certain products continue to be provided by GWLA (Life, Accident and Disability, and Excess Loss). GWLA is not licensed to do business in New York. In New York, these products are sold by GWLA’s subsidiary, First Great-West Life & Annuity Insurance Company, White Plains, N.Y.