Stem-Cell Transplantation for Acute Lymphocytic/Lymphoblastic Leukemia

Table of Contents

Coverage Policy .................................................. 1
Overview.............................................................. 2
General Background ........................................... 3
Coding/Billing Information ................................. 9
References .......................................................... 10

Related Coverage Resources

Donor Lymphocyte Infusion
Transplantation Donor Charges
Umbilical Cord Blood Banking

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Coverage Policy

Allogeneic hematopoietic stem-cell transplantation (HSCT) from an appropriately-matched human leukocyte antigen (HLA) donor is considered 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/μL 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***

A second allogeneic HSCT from an appropriately-matched HLA donor is considered medically necessary for the treatment of ALL when relapsed disease occurs more than six months after first allogeneic HSCT.

A tandem/sequential HSCT for the treatment of ALL is considered experimental, investigational or unproven.
HSCT for the treatment of ALL is considered not medically necessary when ANY of the following conditions are present:

- 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 in an adult

**Poor prognosis acute lymphocytic/lymphoblastic leukemia in an adult includes ANY of the following criteria:**

- longer than four weeks to achieve a complete remission
- age >35 years
- white blood cell count (WBC) greater than $30 \times 10^9 /L (30,000/\mu L)$ in B-cell lineage ALL
- WBC greater than $50 \times 10^9 /L (50,000/\mu L)$ 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), t(8,22), MLL gene (11q23) or t(1;19)
- complex karyotype (i.e., ≥5 chromosomal abnormalities)
- elevated beta 2 microglobulin
- deletion of chromosome 7
- trisomy 8
- hypodiploidy

***High-risk of disease relapse in a child includes ANY of the following criteria:**

- 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 ≥ 10 years
- white blood cell count (WBC) > 50,000/mcL
- extramedullary disease
- presence of chromosome 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

**Overview**

This Coverage Policy addresses hematopoietic stem-cell transplantation (HSCT) for the treatment of acute lymphocytic/lymphoblastic leukemia (ALL).

ALL is a fast growing type of leukemia in which there are too many immature white blood cells (i.e., lymphoblasts) in the blood and bone marrow.

HSCT involves taking hematopoietic stem cells that can regenerate all the blood cells normally produced in the bone marrow from the bone marrow or blood of a donor, and infusing them into a person with acute lymphocytic/lymphoblastic leukemia.
General Background

Acute lymphocytic leukemia (ALL), also known as acute lymphoblastic leukemia and acute lymphoid leukemia, is one of the most common forms of leukemia. ALL is an aggressive type of leukemia characterized by the presence of too many lymphoblasts or lymphocytes in the bone marrow and peripheral blood (National Cancer Institute [NCI], 2017).

Factors associated with unfavorable outcomes include 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, MLL gene rearrangements (11q23, ) and complex karoytpe (≥ 5 chromosomal abnormalities). Other chromosomal abnormalities associated with poor prognoses include t(4;11), t(9;22, deletion of chromosome 7 or trisomy 8, trisomy 21, and a variety of translocations including t(2;8), t(8;12), and t(8;22). Age younger than one year and ≥ 10 years, male sex, testicular involvement at diagnosis, higher white blood cell (WBC) counts (e.g., >50,000/µL), the presence of central nervous system (CNS) disease at diagnosis and the presence of minimal residual disease after therapy have also been shown to be negative prognostic factors for the outcome of children with high-risk ALL (NCI, 2017b; 2017b; Sramkova, 2007). In adults, elevated B2-microglobulin and advanced age are also associated with poor outcomes.

The rate at which the disease enters complete remission (CR) correlates to treatment and survival outcome. Induction chemotherapy is administered to produce a 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 WBC, including differential, hematocrit/hemoglobin levels, and platelet count. 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, 2017b). Hematopoietic stem-cell transplantation (HSCT) has been proposed as a treatment option for selected individuals with ALL.

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).

The selection of an appropriately-matched allogeneic donor source is dependent on several variables including the availability of a human leukocyte antigen (HLA)-identical sibling donor, and stage of disease. It is preferable for donors to have an HLA type that is identical to the recipient due to the potential for increased complications such as graft rejection and graft-versus-host disease; however, only about one-third of individuals who might otherwise be eligible for allogeneic HSCT have an HLA-matched sibling donor. Especially for individuals with high-risk disease, additional appropriate donor sources may include HLA-matched unrelated and HLA partially-matched related donors.

A boost of hematopoietic progenitor or stem cells, also referred to as a hematopoietic stem-cell infusion (HSCI) may be used to facilitate more rapid hematopoietic recovery, graft loss, or loss of chimerism following HSCT. The cell product used for a boost may be a previously cryopreserved cell product that contains stem cells or may alternatively require the donor to undergo additional evaluation, mobilization, and harvest. A boost is not preceded by a preparative regimen, and may be required when additional conventional chemotherapy is given to treat relapse and reestablish remission after transplantation. Prolonged cytopenias and immunosuppression may result, requiring additional HSCI which is typically given days to weeks after reinduction chemotherapy (LeMaistre, 2013).

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

**Allogeneic Hematopoietic Stem-Cell Transplantation (HSCT)**

**Adults:** Although data are not robust, allogeneic HSCT may be an acceptable treatment option for who have an HLA appropriately-matched donor. Allogeneic HSCT is supported by professional society consensus in the form of published guidelines.

Several randomized controlled trials (RCTs) and case studies have demonstrated improved outcomes with the use of myeloablative conditioning and 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; Oyekunle, 2006). Although 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, 2017a; Cornelissen, 2009; Fielding, 2007, Thomas, 2004). A Cochrane systematic review and meta-analysis by Pidala (2011) of 14 eligible studies involving 3157 patients supports matched-sibling donor allogeneic HSCT as the optimal post-remission therapy in individuals with ALL aged 15 years or over. There was a statistically significant overall survival advantage in favor of the donor versus no donor group (p = 0.01), as well as significant improvement in disease-free survival in the donor group (p = 0.004). Those in the donor group had significant reduction in primary disease relapse (p= 0.0004) and significant increase in non-relapse mortality (p0.001).The authors note this therapy offers superior overall survival and disease-free survival, and significantly reduces the risk of disease relapse, but does impose an increased risk of non-relapse mortality.

The results of a prospective clinical trial by Goldstone (2008) suggest 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, 2017a).

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, hematopoietic stem-cell transplantation (HSCT) may be a consideration (NCI, 2017a; 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). Poorer outcome is also noted for adults who have shorter remission durations (e.g., <6 months) after the first allograft compared with 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, 2017a).
**Children:** Most patients with persistent leukemia at the end of the 4-week induction phase have a poor prognosis and may benefit from an allogeneic hematopoietic stem cell transplant (HSCT) once CR is achieved (NCI, 2017b). Those who undergo HSCT in remission have better outcomes (Klingebiel, 2005). 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.

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 leukemia (ALL) (Eckert, 2013; Schrauder, 2006; Balduzzi, 2005; Dalle, 2005; Sanders, 2005; Eapin, 2004). Children receiving human leukocyte antigen (HLA)-matched sibling allogeneic 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 (Gupta, 2013; Malempati, 2007; Ribera, 2007; Gaynon, 2006; Badell, 2005). In a meta-analysis by Gupta et al. (2013), data from 13 studies including 2962 patients, excluding Philadelphia chromosome-positive patients, showed a survival benefit for having a matched sibling donor for patients <35 years of age (p=0.0003) but not for those >35 years of age (p=0.9) because of the higher absolute risk of nonrelapse mortality for older patients. No differences were noted by risk group. There was a trend toward inferior survival for autograft versus chemotherapy (p=0.06). No beneficial effect of autografting was seen compared with chemotherapy.

Allogeneic HSCT may be the best therapy for individuals who relapse after a complete remission (CR) (NCI, 2017b). 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/μL or more (NCI, 2017b). 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, 2017b). However, many patients may be unable to undergo a second HSCT due to failure to achieve remission, early toxic death or severe organ toxicity.

**Non-Myeloablative Conditioning**

Non-myeloablative preparative regimens, also known as 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). Although data are not robust, retrospective case studies demonstrate overall survival (OS) rates of 29%–43% in selected populations (Abdul Wahid, 2014; Mohty, 2008; Guterriez, 2007; Hamaki, 2005; Massenkeil, 2005).

Abdul Wahid et al. (2014) performed a meta-analysis of 23 clinical trials reported between 1990 and 2013 involving 15,258 adult patients that compare survival outcomes after reduced intensity (RIC) HSCT versus conventional myeloablative chemotherapy (MAC) HSCT. Pooled estimate from all trials showed that the <2-year OS and >2-year OS rates were comparable between the two groups. The 2–6 year progression-free survival (PFS), nonrelapse mortality, acute graft-versus-host disease (GvHD) and chronic GvHD rates were reduced after RIC-HCT, but relapse rate was increased. Similar outcomes were observed regardless of disease type and status at transplantation. Data from this study suggest no OS benefit of myeloablative allogeneic HSCT over reduced intensity HSCT for this study cohort.

Massenkeil, et al. (2005) retrospectively compared a group of 25 adults with ALL or acute myelogenous leukemia after reduced-intensity conditioning (RIC) to a historical group of 50 matched controls who received high-dose conditioning. Onset of acute GvHD was notably delayed after RIC with a median of 83 days as compared to 26 days after myeloablative HSCT (p=0.001). TRM rates were not significant between groups (p=.029). Probability of DFS at three years was 43% and 49% for the RIC and high-dose conditioning groups, respectively (p=.218). OS at three years was 40% at a median of 13 months and 37%, median survival of 21
months, respectively, for those receiving RIC compared with high-dose conditioning \( (p=.930) \). Relapse rate for patients receiving RIC was 60% compared to 40% in patients receiving high-dose conditioning.

**Autologous HSCT**

Data are not robust regarding improved overall survival rates for the use of autologous HSCT compared with allogeneic HSCT. However, this therapy may result in improved disease-free survival (DFS) and may be an acceptable treatment option for selected individuals who are ineligible for allogeneic HSCT.

Although autologous HSCT results in a lower rate of treatment-related complications and mortality than 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. Published study results regarding improved outcomes are mixed, suggesting that autologous HSCT was either of similar effectiveness to, or less effective than chemotherapy alone (Goldstone, 2008; Tavemier, 2007; Dhedrin, 2006; Hahn, 2006; Redaelli, 2005; Ribera, 2005; Thomas, 2004). In the randomized multicenter study by Thomas et al. (2004), the use of autologous HSCT did not confer a significant benefit over chemotherapy without transplantation for persons with high-risk ALL. However, there was a trend toward improved overall survival (OS) in patients who received autologous HSCT with three-year OS rates of 44% versus 35%, respectively, and five-year OS rates of 32% and 21%, respectively. Data also suggest 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 in a number of studies (Ribera, 2006; Sandler, 2006; Badell, 2005).

**Tandem (Sequential) Transplantation**

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

**Professional Societies/Organizations**

**National Cancer Institute ([NCI], 2017a, 2017b):** Regarding treatment of adults and children with ALL the NCI notes the following:

**Adults:**

- Untreated adult ALL
  - standard remission induction therapy: If there are appropriate available donors and if the patient is younger than 55 years, bone marrow transplantation may be a consideration in the management of this disease.
- Adult ALL in remission
  - Autologous or allogeneic bone marrow transplant (BMT)
  - Results of clinical trials suggest that in the absence of a sibling donor, maintenance chemotherapy is preferable to autoBMT as postremission therapy.
- Recurrent ALL:
  - Standard treatment options for recurrent adult ALL may include reinduction chemotherapy followed by allogeneic bone marrow transplantation
  - An adult with recurrent ALL for whom an HLA-donor is not available is an excellent candidate for enrollment in clinical trials that are studying autologous transplantation for recurrent ALL.

**Children:**

- Newly diagnosed ALL
  - Most patients with persistent leukemia at the end of the 4-week induction phase have a poor prognosis and may benefit from an allogeneic hematopoietic stem cell transplant (HSCT) once CR is achieved.
- Post-induction treatment, very-high risk ALL
  - On some clinical trials, very high-risk patients have been considered candidates for allogeneic hematopoietic stem cell transplantation (HSCT) in first complete remission (CR); however, there
are limited data regarding the outcome of this population. Controversy exists regarding which subpopulations could potentially benefit from HSCT.

- For infants with MLL translocations, the role of allogeneic stem cell transplant (SCT) during first remission remains controversial.
- Given the relatively favorable outcome that can be obtained in these patients with chemotherapy regimens used for pediatric ALL, there is no role for the routine use of allogeneic SCT in first remission for adolescents and young adults with ALL.

• Postreinduction therapy, second complete remission
  - Early-relapsing precursor B-cell ALL
    - For precursor B-cell 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 higher leukemia-free survival than a chemotherapy approach

• T-cell ALL
  - For patients with T-cell ALL who achieved remission after bone marrow relapse, outcomes with postreinduction chemotherapy alone have generally been poor,[5] and these patients are usually treated with allogeneic HSCT in second CR, regardless of time to relapse.

• Relapsed ALL
  - Relapse after allogeneic HSCT: a second ablative allogeneic HSCT may be feasible. However, many patients will be unable to undergo a second HSCT procedure because of failure to achieve remission, early toxic death, or severe organ toxicity related to salvage chemotherapy.

• Isolated CNS relapse
  - Standard treatment options for childhood ALL that has recurred in the CNS includes HSCT. The use of transplantation to treat isolated CNS relapse occurring less than 18 months from diagnosis, especially T-cell CNS relapse, requires further study.
  - Reduced-intensity approaches can also cure a percentage of patients when used as a second allogeneic transplant approach, but only if patients achieve a CR confirmed by flow cytometry.
  - Donor leukocyte infusion has limited benefit for patients with ALL who relapse after allogeneic HSCT.

National Comprehensive Cancer Network™ ([NCCN Guidelines™], 2017): Guidelines for acute lymphoblastic leukemia note that allogeneic HSCT may be appropriate for the following individuals:

Philadelphia (Ph) chromosome positive ALL:

- In adolescents and young adults ([AYA], 15-39 years) and adults, optimal timing of HSCT is not clear. For fit patients, additional therapy may be considered to eliminate minimal residual disease prior to transplant.
- For AYA in complete response, allogeneic HSCT is a treatment option if a donor is available.
- For AYA or adults (< 65 years) with relapsed/refractory ALL with less than CR, HSCT is one of several treatment options.
- For patients ≥65 years, or with substantial comorbidities allogeneic HSCT may be considered based on performance status, comorbidities and availability of appropriate transplant donor.
- For appropriate fit older adults (≥ 65 years) with PH + ALL who achieve remission, consideration of autologous HSCT or reduced –intensity allogeneic HSCT may be appropriate.

Ph-chromosome negative ALL:

- In AYA and adults, optimal timing of HSCT is not clear. For fit patients, additional therapy may be considered to eliminate minimal residual disease prior to transplant.
- In AYA and relatively fit adults (e.g., age ≥40 years but <65 or with no substantial comorbidities) achieving a CR following initial induction therapy if a matched donor is available particularly in patients with residual disease as assessed by Minimal Residual Disease (MRD) assays, or those with higher-risk cytogenetics (i.e., hypodiploidy, complex karyotype, MLL rearrangements), allogeneic HSCT may be considered. The benefit of allogeneic HSCT in the setting of MRD positive remission is currently unclear.
• In AYA experiencing less than a complete remission after initial induction therapy (i.e., primary refractory disease) may be considered for an allogeneic HSCT if a donor is available
• In AYA and adults with relapsed/refractory disease following an initial CR, allogeneic HSCT may be considered.
• For patients ≥65 years, or with substantial comorbidities allogeneic HSCT may be considered based on performance status, comorbidities and availability of appropriate transplant donor

American Society for Blood and Marrow Transplantation (ASBMT): On behalf of the ASBMT, Majhail et al. (2015) published a guideline document titled “Indications for Autologous and Allogeneic Hematopoietic Cell Transplantation: Guidelines from the American Society for Blood and Marrow Transplantation”. The ASBMT notes that for individuals <18 years, allogeneic HSCT is standard of care for the treatment of ALL with high risk characteristics for individuals in CR1 and CR2. Although large clinical trials and observational studies are not available, allogeneic HSCT has been shown to be effective in CR3 and beyond, and for those not in remission. Allogeneic HSCT is not generally recommended for use in individuals with standard risk disease in CR1. Autologous HSCT is not generally recommended for treatment of ALL.

For individuals ≥18 years the ASBMT notes that allogeneic HSCT is standard of care for the treatment of ALL in individuals with standard or high risk disease in CR1 and CR2. Although large clinical trials and observational studies are not available, allogeneic HSCT has been shown to be effective in CR3 and beyond, and for those not in remission. Autologous HSCT is not generally recommended for treatment of ALL in CR1 with high-risk characteristics, CR3 and beyond and individuals who are not in remission. Although large clinical trials and observational studies are not available, autologous HSCT has been shown to be effective for individuals in CR2 and for ALL with standard risk characteristics.

The National Marrow Donor Program ([NMDP]): The NMDP (1996-2017) notes the following regarding treatment of adults with ALL:

• Patients transplanted in earlier disease stage have better outcomes than patients with advanced disease
• Allogeneic hematopoietic cell transplantation (HCT) is superior to autologous transplantation or chemotherapy for patients with ALL in first complete remission (CR1). The survival advantage is of greater statistical significance for patients with standard-risk ALL than for patients with high-risk ALL
• In the absence of an HLA-matched donor, consider cord blood transplant or autologous HCT for adult ALL in CR1
• HLA-matched related and unrelated donor allogeneic HCT produces similar survival outcomes
• Reduced-intensity HCT using HLA-matched unrelated and unrelated donors is feasible and effective in older patients with B-cell acute lymphoblastic leukemia in CR1

Regarding treatment of children with ALL, the following is noted:

• Allogeneic HCT is recommended for pediatric ALL patients who experience primary induction failure, but subsequently achieve a first complete remission (CR1)
• Allogeneic HCT and intensive chemotherapy with imatinib have equivalent early outcomes for Ph+ ALL in CR1
• HLA-matched related and unrelated donors provide equivalent outcomes

The NMDP recommends that adults with ALL be referred for consultation for HSCT early after initial diagnosis including those in first complete remission, primary induction failure or relapse, presence of minimal residual disease after initial or subsequent therapy, and second complete remission and beyond, if not previously evaluated.

The NMDP also recommends children with ALL be referred for consultation for HSCT early after initial diagnosis all patients in first complete remission, primary induction failure or relapse, presence of minimal residual disease after initial or subsequent therapy, first relapse, CR2 and beyond, if not previously evaluated.
The American Board of Internal Medicine’s (ABIM) Foundation Choosing Wisely® Initiative (2014): No relevant statements.

Use Outside of the US: No relevant information.

### Coding/Billing Information

**Note:**
1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

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<thead>
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<th>CPT® Codes</th>
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<td>Cord blood derived stem-cell transplantation, allogeneic</td>
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<td>S2150</td>
<td>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</td>
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References


disease tests provide an independent predictor of clinical outcome in adult acute lymphoblastic

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