Molina Clinical Policy
Donor Lymphocyte Infusion and Hematopoietic Stem Cell Boosts
Policy No. 210

Last Approval: 08/13/2025
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DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Donor Lymphocyte Infusion (DLI), donor leukocyte or buffy-coat infusion, is a form of adoptive immunotherapy performed after an allogeneic hematopoietic stem cell transplant (HSCT) to induce a graft-versus-leukemia or graft-versus-tumor response; which is a process where the donor lymphocytes recognize and kill the recipient's cancer cells without requiring the recipient to undergo additional high-dose chemotherapy. Lymphocytes from a donor's blood are given to a patient who has received a stem cell transplant from the same donor with the intent that the donor lymphocytes help treat relapsed, persistent, or refractory hematologic malignancy. DLI is not intended to solely augment donor chimerism or restore hematopoiesis due to the significantly higher risk of DLI inducing graft versus host disease (GVHD); therefore, DLI is used to enhance engraftment only in the setting of relapsed disease. Hematopoietic stem cell boost infusions are more appropriate as an isolated therapy for the sole goal of enhancing full donor chimerism and engraftment (Negrin 2025).

The main complications following DLI are the emergence of GVHD and myelosuppression. Approximately 60 – 70% of patients receiving DLI will develop GVHD, therefore DLI should be avoiding in patients with active acute or chronic GVHD, especially those with steroid resistant GVHD (Negrin 2025). DLI should also be avoided, when possible, in patients with graft failure, those who have host rather than donor chimerism, due to the risk of bone marrow hypoplasia. The ideal dose and timing of DLI is unknown and clinical practice varies. Patients who respond to DLI usually demonstrate a clinical response within two to three months; however, a full response may take one year or more. Reports have demonstrated durable responses lasting up to 20 years (Negrin 2025). DLI is used in most hematologic malignancies where allogeneic HSCT is performed, including chronic myeloid leukemia, acute myeloid leukemia, acute lymphoblastic leukemia, myelodysplastic syndromes, multiple myeloma, and Hodgkin's and non-Hodgkin's lymphoma (Negrin 2022).

Hematopoietic Stem Cell Boosts (HSCB), also known as hematopoietic progenitor cell boost, is an infusion of stem cells given to a patient following a full HSCT. The infusion is derived from cryopreserved stem cells from the original HSCT donor source, whether that be autologous or allogenic. The boost does not follow a complete conditioning regimen, as HSCT does; and is intended to restore hematopoiesis or augment poor graft function after HCST. HSCB infusions are administered to promote engraftment when poor graft function is detected. Monitoring chimerism, the percentage of donor derived cells in the transplant recipient, is an effective way to assess graft function. The degree to which a patient exhibits mixed chimerism can indicate poor graft function. Poor graft function is a severe complication of HSCT and defined as continued cytopenias and/or transfusion dependence. Administering a HSCB can help promote engraftment before full relapse or graft failure occurs, increasing the chance of a successful stem cell transplant and patient recovery.

COVERAGE POLICY

This policy does not address the administration of chimeric antigen receptor T cell (CAR T) therapy.

Donor Lymphocyte Infusion

Donor lymphocyte infusion may be **considered medically necessary** following a medically necessary *allogeneic* hematopoietic stem cell transplantation for a hematologic malignancy when ALL the following criteria are met:

1. Donor lymphocytes are collected from the original hematopoietic stem cell donor

2. Donor lymphocyte infusion intended for ONE of the following indications:
   a. Management of refractory, persistent, or relapsed hematologic malignancy
   b. To enhance conversion from mixed to full donor chimerism in the setting of confirmed relapsed disease
   c. A planned strategy to prevent relapsed hematologic malignancy in patients considered high risk for relapse

Limitations and Exclusions

The following are considered **experimental, investigational, and unproven** due to a lack of evidence:
1. DLI as a treatment for non-hematologic malignancies following a prior allogeneic hematopoietic stem cell transplantation
2. Genetic modification of donor lymphocytes

Hematopoietic Stem Cell Boost

Hematopoietic Stem Cell Boost may be **considered medically necessary** when ALL the following criteria are met:

1. Infusion follows ONE of the following treatments:
   a. A medically necessary hematopoietic stem cell transplantation (HSCT)
   b. CAR T therapy

2. Hematopoietic stem cell boost infusion is intended for ONE of the following indications:
   a. Promotion of engraftment following HSCT
   b. Enhancement of chimerism when studies reveal < 100% donor cells following HSCT
   c. Treatment of persistent cytopenias following CAR T therapy

3. Hematopoietic stem cell infusion is derived from the original hematopoietic stem cell donor, if following allogenic HSCT

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Hematopoietic Stem Cell Boost (HSCB) Infusions

Systematic Reviews and Meta-Analyses

Shahzad et al. (2021) conducted a systematic review and meta-analysis focusing on outcomes in adult patients who received CD34+ selected HSCB infusion for poor graft function after an allogenic hematopoietic stem cell transplant (HSCT). The primary outcomes assessed were overall response rate (ORR) and rates of complete response (CR), partial response (PR), acute versus host disease (GVHD), and overall survival (OS). Ultimately seven studies were evaluated for the review, for a total of 209 patients. The median time from allogenic HSCT to HSCB was 138 days (range, 113 to 450 days). The estimated pooled CR was 72% (95% CI, 63% to 79%; I2 = 26%; P = .23; n = 209) and pooled ORR was 80% (95% CI, 74% to 85%; I2 = 0%; P= .66; n = 209). A pooled PR was 13% (95% CI, 7% to 24%; I2 = 41%; P= .24; n = 171) based on available data from 5 of the 7 studies. After a median follow-up of 42 months (range, 30 to 77 months), the actuarial survival rate was 54% (95% CI, 47% to 61%; I2 = 0%; P = .62; n = 207) and OS ranged from 80% at 1 year to 40% at 9 years. Acute GVHD was reported in 33 patients post HSCB, with a pooled rate of 17% (95% CI, 13% to 23%; I2 = 0%; P= .43; n = 209). Overall, the systematic review results are favorable for patients receiving HSCB post allogenic HSCT in the setting of poor graft function. The limitations of this review were

6 of 7 studies being retrospective, small samples size, and heterogeneity across the studies. The authors concluded that prospective clinical trials are needed to confirm the efficacy of HSCB for poor graft function.

Non-Randomized Studies, Retrospective Reviews, and Other Evidence

Huang et al. (2025) conducted a single institution retrospective cohort review of adult patients who received a CD34+ selected HSCB infusion post- allogeneic HSCT. The patients were selected to receive an HSCB infusion due to poor graft function post- allogenic HSCT with the primary objective of achieving an appropriate hematologic response. CR was defined as absolute neutrophil count above 2500 /µL, hemoglobin above 8.0 g/dL without transfusions, and platelet count sustained above 150,000 /µL. Partial response was defined as meeting some but not all the CR criteria. Seventy-nine patients received HSCB for poor graft function with a median time between HSCT and HSCB being 105 days [61-164]. Seventy-two of the original 79 were available for evaluation. Of the 72 patients evaluated, the overall response rate was 75% (31% CR, 44% PR). The median response time was 13 days for neutrophiles [7-24], 37 days for hemoglobin [15-63], and 25 days for platelets [14-52]. Secondary outcomes measured transfusion dependence, of which 46% and 62% of patients were transfusion independent of red blood cells at 30 and 60 days after HSCB, respectively, while 58% and 63% were transfusion independent of platelets. Ten patients (14%) died from disease relapse and the median OS was 12 months. The authors concluded that HSCB infusions without a pre-treatment conditioning regimen is an effective treatment for poor graft function post- allogenic HSCT.

Fraint et al. (2024) conducted a retrospective cohort analysis of all pediatric patients who received a CD34+ HSCB infusion post-allogenic HSCT due to poor graft function, which was defined as a decline in ANC prompting use of G-CSF support, need for PRBC transfusion to maintain HB ≥ 7 g/dL, or in the case of primary thrombocytopenia defined as failure to achieve a platelet count ≥ 50,000 by day +60, or secondary thrombocytopenia defined as platelet count ≤ 50,000 occurring after recovery (≥100,000) and persisting for more than 30 days. CR was defined as achievement of an ANC ≥ 500×10^6/L without need for G-CSF support and Hemoglobin ≥ 7 g/dL and platelet count ≥ 50×10^9/L without transfusion support by 60 days after HSCB. Durable CR was defined as having achieved CR and remaining so at time of last follow-up. Fourteen patients received a HSCB infusion post-allogenic HSCT, seven for underlying malignant disease and seven for underlying non-malignant disease. The median time between HSCT and HSCB was 148 days (range: 50–431 days). The probability of CR at 60 days was 79% (95% CI 57–100%). Despite achieving CR, 1 patient died from the subsequent development of autoimmune hemolytic anemia, and another died from acute GVHD post-HSCB. Bone marrow biopsies were performed in 11 of 14 patients prior to HSCB and were notably hypocellular with a median of 10% cellularity (range: <5% – 70%), with a median donor bone marrow chimerism of 100% (range: 86–100%), and a median donor T cell chimerism of 87% (range: 0–100%). The overall survival following HSCB at both 2 and 5 years was 78% (95% CI: 56–100%).

Varga et al. (2024) conducted a retrospective cohort analysis on 42 patients with multiple myeloma who received a CD34+ HSCB infusion due to persistent cytopenias post- BCMA directed CAR T therapy. Thirteen patients had ISS stage III disease, 54.8% had extramedullary disease and 35.7% had high risk cytogenetics. Twenty-six patients received ide-cel, and 16 patients received cilta-cel. Forty patients (95.2%) developed cytokine release syndrome (95% grade ½). All but one patient required G-CSF support, and 23 patients (53.5%) received a thrombopoietin agonist. The median time to receiving a CD34+ HSCB infusion was 53 days (range 24-871) after CAR T infusion. All patients achieved cell count recovery after a median of 22.5 days (range 9-93) following CD34+ HSCB. In total, 82.9% achieved a >VGPR, 12.2% achieved a PR, one patient attained minimal response, and one patient had disease progression. Twenty-one patients (50%) developed an infection, and 13 patients died (8 from myeloma, 2 from CAR-T-related complications, 2 from infection, 1 from an unrelated cause). The median follow-up period was 13 months (range 1-27), with a 12-mo OS for ide-cel of 67.3% (95% CI: 48.7%-86%) and 76.2% (95% CI: 52.5%-99.8%) for cilta-cel.

Davis et al. (2023) conducted a retrospective cohort analysis of 19 patients who received a CD34+ HSCB infusion due to persistent cytopenias post- BCMA directed CAR T therapy for the treatment of relapsed refractory multiple myeloma. As this was a multicenter analysis, the indications and timing for an HSCB infusion varied between physicians and institutions. HSCB infusions were given at a median of 53 days (range 24-126) after CAR T-cell therapy. Of the 19 patients who received an HSCB infusion, 18 (95%) patients successfully recovered hematopoiesis with 1 patient dying of CAR T related hemophagocytic lymphohistiocytosis before engraftment. The median days to engraftment were 14 (range 9-39) for neutrophils, 17 (range 12-39) for platelets, and 23 (range 6-34) for hemoglobin. At a median follow-up of 186 days (range 7-531), 7 (37%) patients had myeloma relapse, and 4 (21%) had died of progression of disease. Zero patients experienced infusion reactions or GVHD. The authors concluded that HSCB infusions can be effectively and safely used to promote hematopoietic recovery post- CAR T therapy.

Mullanfiroze et al. (2022) conducted a retrospective cohort analysis on 99 pediatric and adult patients with relapse/refractory B-acute lymphoblastic leukemia who received CAR T-cell therapy. Forty-seven patients did not undergo allogenic HSCT prior to CAR T therapy, and 23 (48.9%) of 47 developed grade 3 to 4 cytopenia. This is statistically similar to the 52 patients who underwent allogenic HSCT prior to CAR T therapy, 23 (44.2%) of the 52 patients developed grade 3 to 4 cytopenia. Of those 23 pre-treated HSCT patients who developed cytopenia, 7 (30.4%) were treated with a CD34+ HSCB infusion derived from the original donor. Four of the 7 patients had significant infections prior to the HSCB infusion. The median time to HSCB infusion was 2.6 months (range, 1.9-16.5 months). The indications for HSCB were red cell and/or platelet transfusion and/or G-CSF dependence due to grade ≥3 CTCAE anemia, thrombocytopenia, and/or neutropenia (bicytopenia, n = 1; pancytopenia, n = 6), with or without infections beyond 1 month after CAR T-cell therapy. Zero patients developed acute or chronic graft versus host disease, and one developed grade 2 cytokine release syndrome. One patient died on day 24 post HSCB infusion due to disseminated mucormycosis related hemorrhage, and one patient relapsed on day 38 post HSCB. Of the remaining 5 patients, 1 had transient recovery of bicytopenia followed by recurrence of cytopenias until demise. The remaining four patients recovered neutrophils >1 × 109/L without G-CSF by a median day 42 (range, 11-192 days), were blood transfusion independent by a median day 33 (range, 4-106 days), and platelet transfusion independent by a median day 33 (range, 7-73 days). At the median follow-up of 9 months post HSCB, 3 of 7 patients had a B-ALL relapse, 2 of 7 died of infectious complications related to prolonged cytopenia, and 2 of 7 are alive in CR and with complete hematological recovery at last follow-up. Despite the small sample size, the authors recommend $CD34^+$ HSCB in patients who have a severely hypocellular bone marrow and demonstrate transfusion dependence and/or severe neutropenia persisting at 3 months after CAR T-cell therapy.

Donor Lymphocyte Infusions

There are no randomized controlled trials comparing DLI to other methods of treatment for relapse, refractory or persistent disease following allogeneic transplantation for hematological diseases. The literature consists of retrospective reviews and prospective studies and is varied for reporting methods of cell collection, timing of infusion, cell dose infused, and cell subtype used. Many studies report disease-specific outcomes. Research continues for genetic modification of donor lymphocytes; however, the literature is insufficient to determine long-term benefits on health outcomes when used in the treatment of hematological malignancies.

Non-Randomized Studies, Retrospective Reviews, and Other Evidence

Yang et al. (2024) completed a multicenter retrospective study to determine “the superiority of prophylactic modified DLI and preemptive modified DLI in patients with high-risk relapse features [with] acute leukemia.” High-risk features were defined as 1) failure to achieve complete remission following two cycles of induction chemotherapy, 2) advanced disease at transplantation, 3) minimal residual disease positive at transplantation, and 4) acute leukemia with unfavorable genetic abnormalities according to National Comprehensive Cancer Network guidelines. Patients included in the study had already undergone myeloablative conditioning and allogeneic HSCT before receiving DLI. Peripheral blood stem cells and/or bone marrow cells obtained for DLI were infused without ex vivo T cell depletion. All patients received cyclosporin A, methotrexate, and low-dose mycophenolate mofetil for GVHD prophylaxis. Patients receiving prophylactic DLI received DLI “three months after HSCT for patients with high-risk acute leukemia in continuous complete remission with undetectable minimal residual disease and complete chimeric if they had no history of acute GVHD greater than grade II.” Patients receiving preemptive DLI “stopped immunosuppressive drugs and received [DLI] immediately after [minimal residual disease] turning positive with morphology remission.” A total of 271 patients were included in data analysis with 95 in the prophylactic DLI cohort and 176 in the preemptive DLI cohort. Results showed a higher progression-free survival (63.4% vs. 53.0%, p=0.026) and overall survival (OS) (65.2% vs. 57.0%, p=0.14) for the prophylactic DLI cohort. The prophylactic DLI cohort also had a lower cumulative incidence of relapse compared to the preemptive DLI cohort (25.3% vs. 36.7%, p=0.02). Both cohorts had comparable cumulative rates of grade III-IV acute and chronic GVHD and non-relapse mortality. Overall results demonstrated reduced post-transplant relapse and improved long-term survival for “early scheduled prophylactic DLI rather than preemptive DLI after detectable minimal residual disease” in high-risk patients with acute leukemia.

Rashidi et al. (2023) completed a multicenter phase 2 clinical trial to determine the efficacy of a 10-day decitabine and ruxolitinib in reducing the toxicity and improving the efficacy of dose-escalated DLI in patients with relapsed acute myeloid leukemia and myelodysplastic syndromes. The primary outcome measured was OS at 6 months. Secondary outcomes included the cumulative incidence of grade II-IV acute GVHD at 6 months and the rate of nonrelapse mortality and progression free survival at 1 year. The trial was terminated early due to the observable futility of the treatment. A total of 14 patients were included in the data analysis. Results from the available data showed a 6-month

OS of 36%, a 6-month cumulative incidence of grade II-IV acute GVHD of 57%, a 1-year progression free survival of 7%, and a 1-year nonrelapse mortality of 14%.

Ros-Soto et al. (2022) completed a retrospective study to determine patient and donor factors affecting achievement of full donor chimerism (defined as ≥ 95% cells of donor origin) and disease remission along with observed complications following DLI. A total of 100 patients with either 1) acute myelogenous leukemia, 2) acute lymphoblastic leukemia, 3) myelodysplastic syndrome, 4) Hodgkin's and non-Hodgkin's lymphomas, 5) multiple myeloma, or 6) myeloproliferative neoplasms were included in the study. Indications for DLI included T-cell mixed chimerism (present in 61 patients) and relapsed disease (present in 39 patients) with both indications also serving as study cohorts for analysis. All patients included in the study received reduced intensity conditioning and 93% of patients received T-cell depletion with Alemtuzumab. DLI was administered based on institutional-specific protocols. Chimerism was "assessed at days 30 and 100 after transplantation and then repeated every 3 months until 3 years after transplantation." Repeat samples were obtained monthly if full donor chimerism was not achieved. Results were based on a median follow-up period of 36 months (range 1.4-160.1 months). Forty patients (65.6%) with mixed chimerism attained full donor chimerism. Fifteen out of 61 patients (24.6%) experienced disease relapse following initial DLI. OS, relapse following DLI, and disease-free survival (DFS) at 1-*year post-transplant was 85%, 14.8%, and 77% for the mixed chimerism cohort and 54%, 12.8%, and 44% for the relapse cohort. OS, relapse following DLI, and DFS at 2 years post-transplant was 74%, 16.4%, and 69% for the mixed chimerism cohort and 44%, 17.9%, and 33% for the relapse cohort. OS, relapse following DLI, and DFS at 5 years post-transplant was 65%, 24.9%, and 57% for the mixed chimerism cohort and 24%, 21.3%, and 21% for the relapse cohort. Twenty-nine patients developed acute GVHD (8 grade I, 12 grade II, 6 grade III, 3 grade IV) with a cumulative incidence of 23% at day 100. The incidence of acute GVHD was noted to be higher in patients whose donors were ≥ 30 years of age. Twenty-four patients developed chronic GVHD (9 mild, 12 moderate, 3 severe) with a cumulative incidence of 22% at 1 year. Graft failure occurred in 2 patients; however, both patients remained alive at the time of censoring. GVHD-free/relapse-free survival was reported on the mixed chimerism cohort at 1-year post-transplant and was noted to be 71%. Factors associated with improved overall survival, disease control, and GVHD-free/relapse-free survival during multivariate analysis included patients achieving and remaining in full donor chimerism and patients whose donors were < 30 years of age.

Merker et al. (2019) completed a retrospective study to compare the administration of DLI and cytokine-induced killer cell therapy "for the treatment of relapsing hematologic malignancies after allogeneic HSCT." A total of 91 patients were included in the study, with 55 included in the DLI cohort and 36 included in the cytokine-induced killer cell therapy cohort. Included patients were diagnosed with either 1) acute myelogenous leukemia, 2) chronic myelogenous leukemia, 3) acute lymphoblastic leukemia, 4) biphenotypic leukemia, or 5) T cell non-Hodgkin's lymphoma. Chimerism and minimal residual disease in peripheral blood and bone marrow samples were assessed at days 30, 60, and 90 following transplantation and then at months 6, 12, and 18 following transplantation. Mixed chimerism was defined as "1% autologous cells in 2 consecutive samples and patients with > 1% of autologous cells in a single sample post-transplantation." Chimerism monitoring was completed using peripheral blood testing weekly, and minimal residual disease testing was done monthly using bone marrow samples. Pre-emptive cellular immunotherapy (DLI or cytokine-induced killer cell therapy) was offered to patients with detectable minimal residual disease, mixed chimerism, and/or overt hematologic relapse with a maximum of grade I acute GVHD. Prophylactic treatment was provided to patients with refractory disease at the time of HSCT. DLI and cytokine-induced killer cell therapy was stopped if minimal residual disease cleared or mixed chimerism converted to full donor chimerism. Of the patients receiving DLI, 36 had molecular hematologic relapse, 10 had overt hematologic relapse, and 9 had active disease at the time of transplantation. Of the patients receiving cytokine-induced killer cell therapy, 17 had molecular relapse following transplantation, 11 had refractory disease, and 8 experienced hematologic relapses. Results were based on a median follow-up period of 27.9 months (range 0.9-149.2 months). Approximately 29% of patients receiving DLI achieved complete remission compared to 53% of patients receiving cytokine-induced killer cell therapy. Relapse occurred in approximately 71% of patients receiving DLI compared to 47% of patients receiving cytokine-induced killer cell therapy. All patients with overt hematologic relapse in both groups died. The 6-month OS was 57% for those in the DLI cohort compared to 77% for those in the cytokine-induced killer cell therapy cohort. The 6-month relapse rates were 55% for the DLI cohort and 22% for the cytokine-induced killer cell therapy cohort. Acute GVHD occurred in 19 (35%) of patients in the DLI cohort compared to 9 (25%) of patients in the cytokine-induced killer cell therapy cohort. The majority of patients (n=12) in the DLI cohort developed grade I acute GVHD compared to the majority of patients (n=5) in the cytokine-induced killer cell therapy cohort developing grade II acute GVHD. Researchers noted that patients in the cytokine-induced killer cell therapy cohort had a much more "unfavorable situation at the time of HSCT" compared to those in the DLI cohort, yet those in the cytokine-induced killer cell therapy cohort had better overall outcomes, suggesting that cytokine-induced

killer cell therapy was superior to DLI.

Bejanyan et al. (2015) reported outcomes of 1788 acute myelogenous leukemia patients who relapsed after allogeneic HSCT in complete remission 1 or complete remission 2, among whom 1231 (69%) received subsequent intensive therapy that included DLI. Of 1231 patients who received treatment, 660 (54%) received chemotherapy alone, 202 (16%) received DLI with or without chemotherapy, and 369 (30%) received a second allogeneic HSCT with or without additional chemotherapy or DLI. Among all patients who received DLI, 87 (33%) survived more than 1 year after relapse. The median survival was 7 months with a range of 1 to 177 months. Cell based therapy (DLI or second HSCT) resulted in significantly better post relapse OS compared with those who received chemotherapy alone. Results are consistent with other reports of DLI in patients who relapse after allogeneic HSCT for acute myelogenous leukemia.

National and Specialty Organizations

The **National Comprehensive Cancer Network (NCCN)** published *Clinical Practice Guidelines in Oncology* for the following topics:

- *Acute Lymphoblastic Leukemia (*[1]2024) – DLI may be considered for patients with relapsed disease following allogeneic HSCT.
- *Pediatric Acute Lymphoblastic Leukemia* ([2]2024) – DLI is **not** recommended as a treatment for advanced acute lymphoblastic leukemia in pediatric patients due to significant risk of GVHD.
- *Acute Myeloid Leukemia* ([3]2024) – No official recommendation for DLI, although the NCCN references a study suggesting DLI "may be a treatment option for therapy in patients who have acute myeloid leukemia that relapses after allogeneic HSCT."
- *Chronic Myelogenous Leukemia* ([4]2024) – A tyrosine kinase inhibitor may be considered with or without DLI as an additional treatment option if there is a positive quantitative RT-PCR test following allogeneic HSCT. DLI may encourage "durable molecular remissions in the majority of patients with relapsed chronic myelogenous leukemia following allogeneic HSCT." Studies show higher efficacy in the chronic phase compared to the advanced phase of relapse.
- *Multiple Myeloma* ([5]2024) – DLI may stimulate a graft-versus-myeloma effect which may benefit patients whose disease does not respond to (or relapses) following allogeneic HSCT.
- *Myelodysplastic Syndromes* ([6]2024) – DLI or a second allogeneic HSCT may be considered "for appropriate patients who had a prolonged remission after [initial allogeneic HSCT]" or if there is no response following the initial allogeneic HSCT.
- *T-Cell Lymphomas* ([7]2024) – No official recommendation for DLI, but the NCCN references a study showing induction of "long-term remissions in a few patients with [progressive disease] or disease relapse after allogeneic HSCT."

SUPPLEMENTAL INFORMATON

Acronym	Definition
HSCT	Hematopoietic Stem Cell Transplantation
HSCB	Hematopoietic Stem Cell Boost
CAR T	Chimeric Antigen Receptor T-cell
ORR	Overall Response Rate
OS	Overall Survival
PR	Partial Response
VGPR	Very Good Partial Response
CR	Complete Response
G-CSF	Granulocyte – Colony Stimulating Factor
PRBC	Packed Red Blood Cell
DLI	Donor Lymphocyte Infusion

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
38242	Allogeneic lymphocyte infusions
38243	Hematopoietic progenitor cell (HPC); HPC boost

HCPCS (Healthcare Common Procedure Coding System)

Code	Description
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 posttransplant care in the global definition

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APPROVAL HISTORY

08/13/2025	Title updated: Donor Lymphocyte Infusion and Hematopoietic Stem Cell Boosts. Removed criteria for augmentation of chimerism from DLI criteria. Added coverage criteria for hematopoietic stem cell boost infusions. IRO Peer Reviewed on July 10, 2025, by a practicing physician board certified in Medical Oncology and Hematology.
02/12/2025	Policy reviewed. No changes to coverage criteria.
02/14/2024	Policy reviewed, no changes to criteria. Updated Overview, Summary of Medical Evidence, and References. IRO Peer Review on January 22, 2024, by a practicing, board-certified physician with a specialty in Hematology.
02/08/2023	Policy reviewed, no changes to criteria.
02/09/2022	Policy reviewed; no changes made to coverage section; updated Summary of Medical Evidence and Reference sections.
02/09/2021	Policy reviewed, no changes.
06/17/2020	Policy reviewed, no changes.
06/19/2019	Policy reviewed, no changes.
07/10/2018	Policy reviewed, no changes.
09/19/2017	Policy reviewed, no changes.
09/15/2016	Policy reviewed, no changes.
12/16/2015	Policy reviewed, no changes.
11/11/2014	New policy.

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