

Clinical Policy: Nonmyeloablative Allogeneic Stem Cell Transplants

Reference Number: LA.CP.MP.141

Date of Last Revision: 3/25

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Allogeneic hematopoietic stem cell transplants that do not destroy all of the hematopoietic cells in the bone marrow are termed reduced-intensity or nonmyeloablative conditioning regimens. Although there are no clear definitions, reduced-intensity conditioning (RIC) generally destroys more hematopoietic cells and is more toxic than nonmyeloablative conditioning, but less so than myeloablative conditioning. Both nonmyeloablative and RIC regimens are categorized as non-fully ablative regimens and are used interchangeably in this policy, unless otherwise noted. RIC/nonmyeloablative approaches can circumvent the need for high-dose conditioning regimens that are associated with organ toxicity and mortality depending on graft vs. tumor and immunosuppressive mechanisms.¹

Note:

- Please refer to LA.CP.MP.108 for requests for Allogeneic Hematopoietic Cell Transplants for Sickle Cell Anemia and β -Thalassemia.
- Please refer to LA.CP.MP.162 Tandem Transplant if request is for an allogeneic reduced conditioning transplant for multiple myeloma in a tandem transplant.

Policy/Criteria

- I. It is the policy of Louisiana Healthcare Connections that nonmyeloablative/reduced-intensity conditioning (RIC) allogeneic transplants are **medically necessary** for members/enrollees who meet all of the following criteria:
 - A. Candidate for allogeneic stem cell transplantation for any of the following diagnoses:
 1. Acute lymphoblastic leukemia;
 2. Acute myelogenous leukemia;
 3. Acquired bone marrow failure such as severe aplastic anemia;
 4. Familial bone marrow failure syndromes such as, but not limited to, one of the following:
 - a. Dyskeratosis congenita;
 - b. Shwachman-Diamond syndrome;
 - c. Diamond-Blackfan anemia;
 - d. Kostmann syndrome;
 - e. Fanconi anemia;
 5. Paroxysmal nocturnal hemoglobinuria;
 6. Chronic lymphocytic leukemias;
 7. Chronic myelogenous leukemia;
 8. Congenital immunodeficiency syndromes;
 9. Non-Hodgkin's lymphoma, any of the following:
 - a. Primary refractory or relapsed, including those who have relapsed after having an autologous bone marrow transplant (excluding diffuse large B-cell lymphoma);
 - b. Follicular lymphomas;

CLINICAL POLICY

Non-Myeloablative Allogeneic Stem Cell Transplants



- c. Mantle cell lymphoma;
 - d. Diffuse large B-cell lymphoma that is in remission following second-line therapy for relapsed or refractory disease;
 - 10. Myelodysplastic syndromes;
 - 11. Lysosomal storage disorders types IH/IS (Hurler/Hurler-Scheie), VI (maroteaux), VII (Sly);
 - 12. Macrophage disorders such as hemophagocytic lymphohistiocytosis (HLH);
 - 13. Myeloproliferative neoplasms such as, but not limited to:
 - a. Chronic myeloid leukemia;
 - b. Juvenile myelomonocytic leukemia;
 - c. Primary myelofibrosis;
 - d. Essential thrombocytosis;
 - e. Polycythemia vera;
 - B. Unsuitable for conventional high-dose myeloablative allografting because of untreatable significant dysfunction of another major organ system and/or severe comorbidities, including, but not limited to, any of the following:
 - 1. Bilirubin > 2 mg/dL;
 - 2. Hemostasis: international normalized ratio (INR) > 1.6 (unless on oral anticoagulants);
 - 3. Cardiac function: multigated acquisition (MUGA) scan or echocardiogram with ejection fraction (EF) $< 45\%$;
 - 4. Pulmonary function, one of the following:
 - a. Forced expiratory volume in 1 second (FEV1) $\leq 50\%$ of predicted value;
 - b. Diffusing capacity of the lung for carbon monoxide (DLCO) $\leq 60\%$ of predicted value;
 - 5. Performance scale index, one of the following:
 - a. Karnofsky or Lansky score $< 70\%$;
 - b. Eastern Cooperative Oncology Group (ECOG) performance score > 2 .
- II.** It is the policy of Louisiana Healthcare Connections that current evidence does not support the use of nonmyeloablative/RIC allogeneic transplants for any of the following indications:
- A. Solid tumors including, but not limited to:
 - 1. Brain tumors;
 - 2. Ovarian epithelia and mixed epithelial/germ cell cancers;
 - 3. Primitive neuroectodermal tumors (PNET), including medulloblastoma and ependymoma;
 - 4. Renal cell carcinoma;
 - 5. Testicular cancer;
 - 6. Wilms tumor;
 - 7. Ewing sarcoma;
 - 8. Melanoma;
 - 9. Osteosarcoma;
 - 10. Rhabdomyosarcoma;
 - 11. Retinoblastoma;
 - 12. Germ cell tumors;

13. Neuroblastoma;
14. Multiple myeloma (except in tandem transplant- refer to CP.MP.162);
- B. Autoimmune disorders including, but not limited to:
 1. Multiple sclerosis;
 2. Rheumatoid arthritis;
 3. Juvenile idiopathic arthritis;
 4. Systemic lupus erythematosus;
 5. Systemic sclerosis;
 6. Dermatomyositis;
 7. Polymyositis;
 8. Scleroderma;
- C. Hemoglobinopathies including, but not limited to:
 1. Thalassemias;
 2. Sickle cell anemia.

Background

Allogeneic hematopoietic cell transplantation (HCT) has been used as a treatment for cancer and diseases of the blood system for decades. For this treatment, stem cells are collected from either related or unrelated donors.¹ During the conditioning phase, high doses of chemotherapy (HDC), with or without radiation therapy, are used to eradicate the disease, and this is followed by infusion of stem cells to rescue bone marrow and restore normal immune function. Major limitations of this technique include the increased risk of high morbidity and mortality related to increased age, relapsed or refractory disease or disease with an elevated risk of relapse following HCT, a history of aggressive chemotherapy, and comorbidities.² All stem cell transplants (SCTs) preparative regimens have the potential for extensive toxicity. Loss of appetite and energy, alopecia, and nausea/vomiting occur frequently and contribute to poor physical and emotional tolerance of the transplant procedure. In addition, mucositis, diarrhea, and transient pancytopenia are inevitable side effects of most preparative regimens, and these complications are synergistic in dramatically increasing the risk of infections during and post-transplant.³ Any decrease in toxicity, without concomitant loss of efficacy, would be desirable.

Myeloablative means that the treatment kills (ablates) the stem cells in the bone marrow; the cells that produce new blood cells. Several less intense conditioning regimens have been developed and rely more on immuno-suppression than cytotoxic effects to permit engraftment of donor cells. These regimens are collectively termed nonmyeloablative. Studies have shown that donor allogeneic stem cells can engraft in recipients using less-intensive conditioning regimens that are sufficiently immunosuppressive to permit graft-host tolerance. This manifests as a stable mixed donor-host hematopoietic chimerism, a term which means coexistence of donor and recipient cells. Nonmyeloablative allogeneic transplants, also referred to as “mini-transplant” or “transplant lite”, are thought to be potentially as effective as conventional HDC followed by an allogeneic stem cell transplantation, but with decreased morbidity and mortality related to the less intense, nonmyeloablative chemotherapy conditioning regimen.^{1,4}

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted

CLINICAL POLICY

Non-Myeloablative Allogeneic Stem Cell Transplants



2024, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage and may not support medical necessity. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

NOTE: Coverage is subject to each requested code's inclusion on the corresponding LDH fee schedule. Non-covered codes are denoted (*) and are reviewed for Medical Necessity for members under 21 years of age on a per case basis.

CPT® Codes	Description
38204	Management of recipient hematopoietic progenitor cell donor search and cell acquisition
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing, per donor
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; allogeneic
38240	Hematopoietic progenitor cell (HPC), allogeneic transplantation per donor

HCPCS Codes	Description
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 posttransplant care in the global definition

Reviews, Revisions, and Approvals	Review Date	Approval Date	Effective Date
Converted corporate to local policy.	8/15/20		
Annual review completed. References Updated	3/21		
Annual review. Rephrased criteria I.A.3. from “aplastic anemia” to “acquired bone marrow failure such as severe aplastic anemia.” Added new indication I.A.4., “Familial bone marrow syndromes such as....” Removed “molecular remissions induced by Gleevec” from I.A.8.” Added criteria points 13. and 14. to criteria I.A. “Experimental/investigational” verbiage in criteria II. replaced with descriptive language. Sorted list of non-supported indications in criteria II. into 3 subcategories, solid tumors, autoimmune disorders and hemoglobinopathies. In criteria I.C., combined and rephrased contraindications 2. and 3. and updated verbiage regarding substance abuse and dependence in 4. Minor rewording in description and background with no impact on criteria. Removed ICD-10 codes D57.00-D57.819 for sickle-cell disorders from ICD-10 table of codes to support coverage. References reviewed and updated. Changed “review date” in the header to “date of last revision” and “date” in the revision log header to “revision date.” Reviewed by specialist. Added and may not support medical necessity	5/22	8/13/22	
Annual review completed. Criteria I.C.4. updated to exclude marijuana use when prescribed by a licensed practitioner and include required commitment to reducing substance use behaviors if urgent transplant timelines are present. Background updated; minor rewording with no clinical significance. Added CPT codes 38206, 38232, 38241, and 38243. ICD-10 diagnosis code table removed. References reviewed and updated.	4/23	7/21/23	
Annual review. Removed Hodgkin’s lymphoma from Criteria I.A.9. per updated National Comprehensive Cancer Network (NCCN) recommendations. Added Criteria I.A.13.e. to include polycythemia vera. Updated Criteria I.B.4.b. from diffusing capacity of the lung for carbon monoxide (DLCO) ≤ 50% of predicted value to DLCO ≤ 60% of predicted value. Removed absolute contraindications in Criteria I.C. References reviewed and updated. Reviewed by internal specialist and reviewed by external specialist.	3/24	5/22/24	6/21/24
Annual review. Updated verbiage for macrophage disorders in Criteria I.A.12. for clarity. References reviewed and updated. Reviewed by internal specialist.	03/25	5/20/25	6/19/25

References

1. American Cancer Society. Types of Stem Cell and Bone Marrow. <https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/stem-cell-transplant/types-of-transplants.html>. Published May 04, 2023. Accessed December 19, 2024.

2. Deeg HJ, Sandmaier BM. Allogeneic hematopoietic cell transplantation: Indications, eligibility, and prognosis. UpToDate. www.uptodate.com. Updated August 26, 2024. Accessed December 19, 2024.
3. Negrin RS. Early complications of hematopoietic cell transplantation. UpToDate. www.uptodate.com. Updated September 25, 2024. Accessed December 23, 2024.
4. Negrin RS. Preparative regimens for hematopoietic cell transplantation. UpToDate. www.uptodate.com. Updated September 11, 2023. Accessed December 23, 2024.
5. Brodsky RA. Paroxysmal nocturnal hemoglobinuria: Treatment and prognosis. UpToDate. www.uptodate.com. Updated November 06, 2024. Accessed December 23, 2024.
6. National coverage determination: Stem cell transplantation (formerly 110.8.1) (110.23). Centers for Medicare and Medicaid Services Web site. <http://www.cms.hhs.gov/mcd/search.asp>. Published March 06, 2024. Accessed December 23, 2024.
7. Angelucci E, Benz EJ. Hematopoietic stem cell transplantation and other curative therapies for transfusion-dependent thalassemia. UpToDate. www.uptodate.com. Updated December 03, 2024. Accessed December 23, 2024.
8. Negrin RS, Platzbecker U. Myelodysplastic syndromes/neoplasms (MDS): Treatment of higher-risk MDS. UpToDate. www.uptodate.com. Updated July 19, 2024. Accessed December 23, 2024.
9. Kröger N, Holler E, Kobbe G, et al. Allogeneic stem cell transplantation after reduced-intensity conditioning in patients with myelofibrosis: a prospective, multicenter study of the Chronic Leukemia Working Party of the European Group for Blood and Marrow Transplantation. *Blood*. 2009;114(26):5264 to 5270. doi:10.1182/blood-2009-07-234880
10. Lee SE, Park SS, Jeon YW, et al. Outcomes of allogeneic stem cell transplantation in patients with paroxysmal nocturnal hemoglobinuria with or without aplastic anemia. *Eur J Haematol*. 2017;99(4):336 to 343. doi:10.1111/ejh.12922
11. Moskowitz C, Alencar AJ. Hematopoietic cell transplantation in classic Hodgkin lymphoma. UpToDate. www.uptodate.com. Updated March 17, 2022. Accessed December 23, 2024.
12. Castagna L, Crocchiolo R, Furst S, et al. Bone marrow compared with peripheral blood stem cells for haploidentical transplantation with a nonmyeloablative conditioning regimen and post-transplantation cyclophosphamide. *Biol Blood Marrow Transplant*. 2014;20(5):724 to 729. doi:10.1016/j.bbmt.2014.02.001
13. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: B-cell lymphomas. Version 1.2025. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Published December 20, 2024. Accessed December 23, 2024.
14. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Chronic lymphocytic leukemia/small lymphocytic lymphoma. Version 1.2025. https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Published October 02, 2024. Accessed December 23, 2024.
15. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Chronic myeloid leukemia. Version 3.2025. https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf. Published November 27, 2024. Accessed December 23, 2024.
16. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hodgkin Lymphoma. Version 4.2024. https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. Published October 22, 2024. Accessed December 20, 2024.
17. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma. Version 1.2025.

- https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Published September 17, 2024. Accessed December 11, 2024.
18. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic syndromes. Version 1.2025.
https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Published November 15, 2024. Accessed December 19, 2024.
 19. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 2.2024.
https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Published August 08, 2024. Accessed December 20, 2024.
 20. Gagelmann N, Kröger N. Dose intensity for conditioning in allogeneic hematopoietic cell transplantation: can we recommend "when and for whom" in 2021?. *Haematologica*. 2021;106(7):1794 to 1804. Published 2021 Jul 1. doi:10.3324/haematol.2020.268839
 21. Brodsky RA. Paroxysmal nocturnal hemoglobinuria. *Blood*. 2014;124(18):2804 to 2811. doi:10.1182/blood-2014-02-522128
 22. Oliansky DM, Czuczman M, Fisher RI, et al. The role of cytotoxic therapy with hematopoietic stem cell transplantation in the treatment of diffuse large B cell lymphoma: update of the 2001 evidence-based review. *Biol Blood Marrow Transplant*. 2011;17(1):20 to 47.e30. doi:10.1016/j.bbmt.2010.07.008
 23. Pantin J, Tian X, Geller N, et al. Long-term outcome of fludarabine-based reduced-intensity allogeneic hematopoietic cell transplantation for debilitating paroxysmal nocturnal hemoglobinuria. *Biol Blood Marrow Transplant*. 2014;20(9):1435 to 1439. doi:10.1016/j.bbmt.2014.05.012
 24. Pophali PA, Klotz JK, Ito S, et al. Male survivors of allogeneic hematopoietic stem cell transplantation have a long term persisting risk of cardiovascular events. *Exp Hematol*. 2014;42(2):83 to 89. doi:10.1016/j.exphem.2013.07.003
 25. Samuelson S, Sandmaier BM, Heslop HE, et al. Allogeneic haematopoietic cell transplantation for myelofibrosis in 30 patients 60 through 78 years of age. *Br J Haematol*. 2011;153(1):76 to 82. doi:10.1111/j.1365-2141.2011.08582.x
 26. Sieff CA. Overview of hematopoietic stem cells. UpToDate. www.uptodate.com. Updated April 11, 2024. Accessed November 25, 2024.
 27. Storb R, Sandmaier BM. Nonmyeloablative allogeneic hematopoietic cell transplantation. *Haematologica*. 2016;101(5): 521 to 530. doi:10.3324/haematol.2015.132860
 28. Tefferi A. Myelofibrosis (MF): Management of primary MF and secondary MF. UpToDate. www.uptodate.com. Updated December 19, 2023. Accessed December 19, 2024.
 29. Velázquez-Sánchez-de-Cima S, Zamora-Ortiz G, Hernández-Reyes J, et al. Oral versus intravenous fludarabine as part of a reduced-intensity conditioning for allogeneic stem cell transplantation. *Acta Haematol*. 2014;132(1):125 to 128. doi:10.1159/000357108
 30. Mikhael J, Ismaila N, Cheung MC, et al. Treatment of Multiple Myeloma: ASCO and CCO Joint Clinical Practice Guideline [published correction appears in J Clin Oncol. 2020 Jul 20;38(21):2469]. *J Clin Oncol*. 2019;37(14):1228 to 1263. doi:10.1200/JCO.18.02096
 31. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Primary cutaneous lymphomas. Version 1.2025.
https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Published November 11, 2024. Accessed December 23, 2024.
 32. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: T-cell lymphomas. Version 1.2025. https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Published November 11, 2024. Accessed December 23, 2024.
 33. Rogers ZR, Myers KC. Shwachman-Diamond syndrome. UpToDate. www.uptodate.com.

CLINICAL POLICY

Non-Myeloablative Allogeneic Stem Cell Transplants



Updated August 12, 2022. Accessed December 23, 2024.

34. Khan S, Myers KC. Hematopoietic cell transplantation (HCT) for inherited bone marrow failure syndromes (IBMFS). UpToDate. www.uptodate.com. Updated April 12, 2024. Accessed December 23, 2024.
35. Chien JW, Sullivan KM. Carbon monoxide diffusion capacity: how low can you go for hematopoietic cell transplantation eligibility?. *Biol Blood Marrow Transplant*. 2009;15(4):447 to 453. doi:10.1016/j.bbmt.2008.12.509
36. Lussana F, Rambaldi A, Finazzi MC, et al. Allogeneic hematopoietic stem cell transplantation in patients with polycythemia vera or essential thrombocythemia transformed to myelofibrosis or acute myeloid leukemia: a report from the MPN Subcommittee of the Chronic Malignancies Working Party of the European Group for Blood and Marrow Transplantation. *Haematologica*. 2014;99(5):916-921. doi:10.3324/haematol.2013.094284

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended to recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or

CLINICAL POLICY
Non-Myeloablative Allogeneic Stem Cell Transplants
employees of LHCC.



This clinical policy is the property of LHCC. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members/enrollees and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members/enrollees and their representatives agree to be bound by such terms and conditions by providing services to members/enrollees and/or submitting claims for payment for such services.

©2023 Louisiana Healthcare Connections. All rights reserved. All materials are exclusively owned by Louisiana Healthcare Connections and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Louisiana Healthcare Connections. You may not alter or remove any trademark, copyright or other notice contained herein. Louisiana Healthcare Connections is a registered trademark exclusively owned by Louisiana Healthcare Connections.