

Clinical Policy: Nonmyeloablative Allogeneic Stem Cell Transplants

Reference Number: LA.CP.MP.141

Date of Last Revision: 3/21

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, while maintaining adequate response in certain cancers and blood disorders.

Note: Please refer to LA.MP. 108 for requests for Allogeneic Hematopoietic Cell Transplants for Sickle Cell Anemia and β -Thalassemia

Please refer to LA.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/RIC allogeneic transplants are medically necessary for members 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. Aplastic anemia;
 4. Paroxysmal nocturnal hemoglobinuria;
 5. Chronic lymphocytic leukemias;
 6. Chronic myelogenous leukemia;
 7. Congenital immunodeficiency syndromes: molecular remissions induced by Gleevec
 8. Hodgkin's lymphoma (formerly Hodgkin's disease): primary refractory or relapsed, including those who have relapsed having an autologous bone marrow transplant
 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;
 - 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. Myelofibrosis.

- 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 scan (MUGA) or echocardiogram with ejection fraction (EF) < 45%;
 4. Pulmonary function:
 - a. Forced expiratory volume in 1 second (FEV1) ≤ 50% of predicted value; or
 - b. Diffusing capacity of the lung for carbon monoxide (DLCO) ≤ 50% of predicted value;
 5. Performance scale index:
 - a. Karnofsky or Lansky score < 70%; or
 - b. Eastern Cooperative Oncology Group (ECOG) performance score ≤ 2;
- C.** Does not have ANY of the following absolute contraindications:
1. Chronic infection with highly virulent and/or resistant microbes that are poorly controlled pre-transplant;
 2. Current non-adherence to medical therapy or a history of repeated or prolonged episodes of non-adherence to medical therapy that are perceived to increase the risk of non-adherence after transplantation;
 3. Psychiatric or psychological condition associated with the inability to cooperate or comply with medical therapy;
 4. Absence of an adequate or reliable social support system;
 5. Substance abuse or dependence (including tobacco and alcohol) without convincing evidence of risk reduction behaviors, such as meaningful and/or long-term participation in therapy for substance abuse and/or dependence. Serial blood and urine testing may be used to verify abstinence from substances that are of concern.
- II.** It is the policy of Louisiana Healthcare Connections that nonmyeloablative/RIC allogeneic transplants are experimental / investigational for the following indications:
- A.** Astrocytomas and gliomas
 - B.** Beta thalassemia
 - C.** Breast cancer
 - D.** Dermatomyositis
 - E.** Ewing sarcoma
 - F.** Germ cell Tumors
 - G.** Idiopathic thrombocytopenic purpura
 - H.** Juvenile rheumatoid arthritis
 - I.** Lupus erythematosus
 - J.** Medulloblastoma
 - K.** Melanoma
 - L.** Multiple sclerosis
 - M.** Osteosarcoma
 - N.** Ovarian epithelia and mixed epithelia/germ cell cancers
 - O.** Polycythemia vera

- P. Polymyositis
- Q. Ovarian germ cell Tumors
- R. Primitive Neuroectodermal Tumors (PNET), including medulloblastoma and ependymoma
- S. Renal cell carcinoma
- T. Retinoblastoma
- U. Rhabdomyosarcoma
- V. Severe systemic rheumatoid arthritis, adult and juvenile
- W. Sarcoma
- X. Systemic lupus erythematosus
- Y. Systemic sclerosis
- Z. Testicular Cancer
- AA. Wilms tumor
- BB. Multiple myeloma (except in tandem transplant- refer to LA.MP. 162)
- CC. Neuroblastoma.

Background

Allogeneic stem cell transplant (AlloBMT) has been used as a treatment for cancer and diseases of the blood system for many years. For this treatment, stem cells are collected from either related or unrelated donors. 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 an allogeneic stem cell transplantation to rescue bone marrow and restore normal immune function. Major limitations of this technique are the associations with serious side effects and high mortality. All stem cell transplants (SCTs) preparative regimens have the potential for extensive toxicity. Loss of appetite and energy, alopecia, and nausea/vomiting are very frequent and add 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 bacterial and fungal infections. Any decrease in toxicity, without concomitant loss of efficacy, would be desirable.

Myeloablative means that the treatment kills (ablates) the myeloid stem cells in the bone marrow, the cells that produce new blood cells. Several less intense conditioning regimens have been developed recently 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. Once chimerism has developed, a further infusion of donor leukocytes may be given to eradicate malignant cells by inducing a graft vs. tumor effect. 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. Consequently, for patients with malignancies that are eligible for conventional HDC/AlloBMT, conditioning with milder, nonmyeloablative regimens represents a variation of an established procedure.

Coding Implications

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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 deletion within harvest. T-cell depletion
38211	Transplant preparation of hematopoietic progenitor cells; tumor 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 peripheral 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-10-CM Diagnosis Codes that Support Coverage Criteria

ICD-10-CM Code	Description
C74.00-C74.92	Malignant neoplasm of adrenal gland
C81.00-C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue
D46.0-D46.9	Myeloplastic syndromes
D56.0-D56.9	Thalassemia
D57.00-D57.819	Sickle-cell disorders
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]
D61.01-D61.09	Constitutional aplastic anemia
D75.81	Myelofibrosis
Z51.11	Encounter for antineoplastic chemotherapy
Z94.84	Stem cells transplant status

Reviews, Revisions, and Approvals	Review Date	Approval Date
Converted corporate to local policy.	08/15/2020	
Annual review completed. References Updated.	3/21	

References

1. American Cancer Society. Types of Stem Cell Transplants for Cancer Treatment. Revised May 11, 2016. Accessed 1/25/21.
2. American Society for Blood and Bone Marrow Transplantation. Policy Statements, Guidelines and Reviews. Available at: <http://asbmt.org/practice-resources/policy-statements> Accessed 1/25/21
3. Angelucci E, Benz EA. Hematopoietic cell transplantation for transfusion-dependent thalassemia. In: UpToDate. Negrin RS (Ed) UpToDate, Waltham MA. Accessed Jan 22, 2021
4. Bacigalupo A. Hematopoietic stem cell transplants after reduced intensity conditioning regimen (RI-HSCT): Report of a workshop of the European group for Blood and Marrow Transplantation (EBMT). Bone Marrow Transplant. 2000;25(8):803-805.
5. BlueCross BlueShield Association (BCBSA), Technology Evaluation Center (TEC). Nonmyeloablative allogeneic stem-cell transplantation for malignancy. TEC Assessment Program. Chicago, IL: BCBSA; May 2001;16(3).
6. Brodsky RA. Paroxysmal nocturnal hemoglobinuria. Blood. 2014;124(18):2804. Epub 2014 Sep 18.
7. Brodsky RA. Treatment and prognosis of paroxysmal nocturnal hemoglobinuria. In: UpToDate, Larson RA (Ed), UpToDate, Waltham MA. Accessed Jan 22, 2021.
8. Centers for Medicare and Medicaid Services. National Coverage Determination for Stem Cell Transplantation. NCD #110.23. Effective January 27, 2016.
9. Deeg HJ, Sandmaier BM. Determining eligibility for allogeneic hematopoietic cell transplantation. In: UpToDate. Chao NJ, UpToDate, Waltham, MA. Accessed Jan 22, 2021.
10. Djulbegovic B, Seidenfeld J, Bonnell C, Kumar A. Nonmyeloablative allogeneic stem-cell transplantation for hematologic malignancies: A systematic review. Cancer Control. 2003;10(1):17-41. Mini-Transplants (Nonmyeloablative Allogeneic Stem Cell Transplants) Aug 3.

11. Estey EH, Schrier SL, Negrin RS. Treatment of high or very high risk myelodysplastic syndromes. In: UpToDate. Larson RA (Ed). UpToDate, Waltham MA. Accessed Jan 25, 2021.
12. Hayes Search & Summary. Autologous Stem Cell Transplant Followed by Nonmyeloablative Allogeneic Stem Cell Transplant for the Treatment of Multiple Myeloma. Archived Nov 5, 2013.
13. Hayes. Medical Technology Directory. Nonmyeloablative Transplantation for Hematological Malignancies. September 10, 2010. Archived May 28, 2011.
14. Hayes. Health Technology Brief. Autologous Stem Cell Transplantation Followed by Nonmyeloablative Allogeneic Stem Cell Transplantation for Treatment of Multiple Myeloma. Oct 23, 2012. Archived November 25, 2013.
15. Hayes. Search & Summary. Allogeneic Stem Cell Transplant for Treatment of Chronic Myelogenous Leukemia. May 22, 2014. Archived June 22, 2015.
16. Hayes. Medical Technology Directory. Comparative Effectiveness Review of Influence of Pretransplant Treatment and Conditioning Strategies on Allogeneic Stem Cell Transplant Effectiveness for Treatment of Chronic Myelogenous Leukemia. June 2, 2016. Accessed Jan, 25, 2021.
17. Khan S. Hematopoietic cell transplantation for Diamond-Blackfan anemia and the myelodysplastic syndromes in children and adolescents. In:UpToDate. Mahoney DH, Negrin RS (Eds) UpToDate, Waltham, MA Accessed Jan 25, 2021 .
18. Khan S, Rodgers GF. Hematopoietic stem cell transplantation in sickle cell disease. In: UpToDate. Mahoney DH, Chao NJ (Eds) UpToDate, Waltham, MA. Accessed Jan 25, 2021.
19. Kroger 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. Epub 2009 Oct 7.
20. 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 Oct;99(4):336-343. doi: 10.1111/ejh.12922. Epub 2017 Jul 25.
21. Moskowitz. Hematopoietic cell transplantation in classic Hodgkin lymphoma. Accessed Feb 18, 2019.
22. Muthu V. Nonmyeloablative bone marrow and peripheral stem cell transplantation. *STEER*. 2001;1(1):1-12.
23. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology. B-cell lymphomas. Version 1.2020. Accessed Jan 25, 2021.
24. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology. Chronic lymphocytic leukemia/small lymphocytic lymphoma. Version 4.2020. Accessed Jan 25, 2021.
25. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology. Chronic myeloid leukemia. Version 2.2020. Accessed Jan 25, 2021.
26. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology. Hodgkin Lymphoma. Version 2.2019. Accessed Jan 25, 2021.
27. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology. Multiple Myeloma. Version 2.2020. Accessed Jan 25,2021.
28. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology. Myelodysplastic syndromes. Version 1.2020. Accessed Jan 20.

29. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology. Myeloproliferative Neoplasms. Version 3.2019. Accessed Jan 25, 2021.
30. 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):20-47.
31. 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. Epub 2014 May 17
32. 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 Feb;42(2):83-9. doi: 0.1016/j.exphem.2013.07.003. Epub 2013 Oct 17.
33. Samuelson S, Sandmaier BM, Heslop HE, et al. Allogeneic haematopoietic cell transplantation for myelofibrosis in 30 patients 60-78 years of age. *Br J Haematol.* 2011;153(1):76. Epub 2011 Feb 17.
34. Sieff CA. Overview of hematopoietic stem cells. In: UpToDate. Negrin RS (Ed). UpToDate, Waltham, MA. Accessed Jan 25, 2021.
35. Storb R, Sandmeier BM. Nonmyeloablative allogeneic hematopoietic cell transplantation. *Haematologica.* 2016 May; 101(5): 521–530. doi: 10.3324/haematol.2015.132860
36. Tefferi A. Management of primary myelofibrosis. In: UpToDate. Larsen RA (Ed), UpToDate, Waltham, MA. Accessed Jan 25, 2021 .
37. Velazquez-Sanchez-de-Cima S, Zamora-Ortiz G, Hernandez-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):125-128.
38. Rajkumar SV. Multiple myeloma: Use of allogeneic hematopoietic cell transplantation. In: UpToDate. Kyle RA (Ed) UpToDate. Accessed Jan 25, 2021.
39. Mikhael J, Ismaila N, Cheung MC, et al. Treatment of Multiple Myeloma: ASCO and CCO Joint Clinical Practice Guideline. *J Clin Oncol.* 2019 May 10;37(14):1228-1263. doi: 10.1200/JCO.18.02096. Epub 2019 Apr 1. Accessed 2/5/20:
<https://ascopubs.org/doi/10.1200/JCO.18.02096>

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.

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