Clinical Policy: Nonmyeloablative Allogeneic Stem Cell Transplants

Reference Number: LA.CP.MP.141 Coding Implications
Date of Last Revision: 42/235/22 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.

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/ 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. Schwachkman-Diamond syndrome;
   c. Diamond-Blackfan ~~Diamond~~ syndrome;
   d. KCostmann syndrome;
   e. Fanconi anemia;
5. Paroxysmal nocturnal hemoglobinuria;
6. Chronic lymphocytic leukemias;
7. Chronic myelogenous leukemia;
8. Congenital immunodeficiency syndromes:
9. Hodgkin's lymphoma: primary refractory or relapsed, including those who have relapsed after an autologous bone marrow transplant;
10. 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;

11. Myelodysplastic syndromes;
12. Lysosomal storage disorders types IH/IS (Hurler/Hurler-Scheie), VI (maroteaux), VII (Sly);
13. Macrophage discords such as hemophagocytic lymphohistiocytosis (HLH);
14. Myeloproliferative neoplasms such as, but not limited to:
    a. Chronic myeloid leukemia;
    b. Juvenile myelomonocytic leukemia;
    c. Primary myelofibrosis;
    d. Essential thrombocytosis;

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) scan or echocardiogram with ejection fraction (EF) < 45%;
4. Pulmonary function, one of the following:
    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, one of the following:
    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. Infections with highly virulent and/or resistant microbes that are poorly controlled pre-transplant;
2. Inability to adhere to the regimen necessary to preserve the transplant, even with caregiver support;
3. Absence of an adequate or reliable social support system;
4. Active substance use or dependence including current tobacco use, vaping, marijuana use~~smoking~~, (unless prescribed by a licensed practitioner), or intravenous~~IV~~ drug use without convincing evidence of risk reduction behaviors, (unless urgent transplant timelines are present, in which case a commitment to reducing behaviors is acceptable) ~~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.
5.

II. It is the policy of Louisiana Healthcare Connections that current evidence does not support the use of nonmyeloablative/RIC allogeneic transplants ~~are experimental / investigational~~ 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.[7] 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.[21] 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.[1,22]

~~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 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.~~

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 2022~~0~~, 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.

CPT® Codes [SS1]	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
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, 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
38232	Bone marrow harvesting for transplantation; autologous
38240	Hematopoietic progenitor cell (HPC), allogeneic transplantation per donor
38241	Hematopoietic progenitor cell (HPC); autologous transplantation
38243	Hematopoietic progenitor cell (HPC); HPC boost

HCPCS Codes [SS2]	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

* All non-covered codes are reviewed for medical necessity for members under 21 years old

~~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, hematpoietic and related tissue~~
~~D46.0-D46.9~~	~~Myeloplastic syndromes~~
~~D56.0-D56.9~~	~~Thalassemia~~
~~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	Revision Date	Approval Date
Converted corporate to local policy.	08/15/2020	
Annual review completed. References Updated.	3/21	

Reviews, Revisions, and Approvals	Revision Date	Approval Date
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.	~~24~~/23	

References

1. American Cancer Society. Types of Stem Cell Transplants for Cancer Treatment. https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/stem-cell-transplant/types-of-transplants.html. Published March 20, 2020. Accessed December 21, 2022.
2. Angelucci E, Benz EJ. Hematopoietic cell transplantation for transfusion-dependent thalassemia. UpToDate. www.uptodate.com. Updated October 25, 2021. Accessed December 21, 2022.
3. 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
4. Brodsky RA. Paroxysmal nocturnal hemoglobinuria. *Blood*. 2014;124(18):2804 to 2811. doi:10.1182/blood-2014-02-522128
5. Brodsky RA. Treatment and prognosis of paroxysmal nocturnal hemoglobinuria. UpToDate. www.uptodate.com. Updated December 3, 2021. Accessed December 21, 2022.

6. National coverage determination: Stem cell transplants (110.23). Centers for Medicare and Medicaid Services Web site. http://www.cms.hhs.gov/mcd/search.asp. Published January 27, 2016. Accessed December 21, 2022.
7. Deeg HJ, Sandmaier BM. Determining eligibility for allogeneic hematopoietic cell transplantation. UpToDate. www.uptodate.com. Updated February 21, 2022. Accessed December 21, 2022.
8. 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 to 41. doi:10.1177/107327480301000104
9. Negrin RS. Treatment of high or very high risk myelodysplastic syndromes. UpToDate. www.uptodate.com. Updated July 28, 2020. Accessed December 21, 2022.
10. 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
11. 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
12. Moskowitz C, Alencar AJ. Hematopoietic cell transplantation in classic Hodgkin lymphoma. UpToDate. www.uptodate.com. Updated March 17, 2022. Accessed December 21, 2022.
13. 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
14. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: B-cell lymphomas. Version 5.2022. https://www.nccn.org/home. Published July 12, 2022. Accessed December 21, 2022.
15. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: Chronic lymphocytic leukemia/small lymphocytic lymphoma. Version 1.2023. https://www.nccn.org/home. Published August 30, 2022. Accessed December 21, 2022.
16. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: Chronic myeloid leukemia. Version 1.2023. https://www.nccn.org/home. Published August 5, 2022. Accessed December 21, 2022.
17. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: Hodgkin Lymphoma. Version 2.2023. https://www.nccn.org/home. Published November 8, 2022. Accessed December 21, 2022.
18. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: Multiple Myeloma. Version 3.2023. https://www.nccn.org/home. Published December 8, 2022. Accessed December 21, 2022.
19. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: Myelodysplastic syndromes. Version 1.2023. https://www.nccn.org/home. Published September 12, 2022. Accessed December 21, 2022.
20. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: Myeloproliferative Neoplasms. Version 3.2022. https://www.nccn.org/home. Published August 11, 2022. Accessed December 21, 2022.

21. Negrin RS. Early complications of hematopoietic cell transplantation. UpToDate. www.uptodate.com. Updated June 30, 2022. Accessed December 21, 2022.
22. Negrin RS. Preparative regimens for hematopoietic cell transplantation. UpToDate. www.uptodate.com. Updated February 4, 2022. Accessed December 21, 2022.
23. 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
24. 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
25. 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
26. 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
27. Sieff CA. Overview of hematopoietic stem cells. UpToDate. www.uptodate.com. Updated March 9, 2022. Accessed December 21, 2022.
28. Storb R, Sandmeier BM. Nonmyeloablative allogenic hematopoietic cell transplantation. *Haematologica*. 2016;101(5): 521 to 530. doi:10.3324/haematol.2015.132860
29. Tefferi A. Management of primary myelofibrosis. UpToDate. www.uptodate.com. Updated October 7, 2022. Accessed December 21, 2022.
30. 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
31. Rajkumar SV. Multiple myeloma: Use of allogeneic hematopoietic cell transplantation. UpToDate. www.uptodate.com. Updated March 28, 2022. Accessed December 21, 2022.
32. Mikhael J, Ismaila N, Cheung MC, et al. Treatment of Multiple Myeloma: ASCO and CCO Joint Clinical Practice Guideline [published correction appears in J Clinical Oncol. 2020 Jul 20;38(21):2469]. *J Clin Oncol*. 2019;37(14):1228 to 1263. Doi:10.1200/JCO.18.02096
33. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: Primary cutaneous lymphomas. Version 2.2022. https://www.nccn.org/home. Published June 8, 2022. Accessed December 22, 2022.
34. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: T-cell lymphomas. Version 2.2022. https://www.nccn.org/home. Published March 7, 2022. Accessed December 22, 2022.

~~1. American Cancer Society. Types of Stem Cell Transplants for Cancer Treatment. https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/stem-cell-transplant/types-of-transplants.html. Published March 20, 2020. Accessed January 12, 2022.~~
~~2. Angelucci E, Benz EJ. Hematopoietic cell transplantation for transfusion-dependent thalassemia. UpToDate. www.uptodate.com. Published October 25, 2021. Accessed January 12, 2022.~~

3. 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. doi:10.1038/sj.bmt.1702385
4. Brodsky RA. Paroxysmal nocturnal hemoglobinuria. *Blood*. 2014;124(18):2804-2811. doi:10.1182/blood-2014-02-522128
5. Brodsky RA. Treatment and prognosis of paroxysmal nocturnal hemoglobinuria. UpToDate. www.uptodate.com. Published December 3, 2021. Accessed January 13, 2022.
6. National coverage determination: Stem cell transplants (110.23). Centers for Medicare and Medicaid Services Web site. http://www.cms.hhs.gov/mcd/search.asp. Published January 27, 2016. Accessed January 13, 2022.
7. Deeg HJ, Sandmaier BM. Determining eligibility for allogeneic hematopoietic cell transplantation. UpToDate. www.uptodate.com. Published February 27, 2020. Accessed January 13, 2022.
8. 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. doi:10.1177/107327480301000104
9. Estey EH, Schrier SL, Negrin RS. Treatment of high or very high risk myelodysplastic syndromes. UpToDate. www.uptodate.com. Published July 28, 2020. Accessed January 13, 2022.
10. 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):5264-5270. doi:10.1182/blood-2009-07-234880
11. 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):336-343. doi:10.1111/ejh.12922
12. Moskowitz C, Alencar AJ. Hematopoietic cell transplantation in classic Hodgkin lymphoma. UpToDate. www.uptodate.com. Published August 30, 2021. Accessed January 13, 2022.
13. 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):724-729. doi:10.1016/j.bbmt.2014.02.001
14. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: B-cell lymphomas. Version 5.2021. https://www.nccn.org/home. Published September 22, 2021. Accessed January 14, 2022.
15. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: Chronic lymphocytic leukemia/small lymphocytic lymphoma. Version 1.2022. https://www.nccn.org/home. Accessed January 14, 2022.
16. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: Chronic myeloid leukemia. Version 2.2022. https://www.nccn.org/home. Published November 15, 2021. Accessed January 14, 2022.
17. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: Hodgkin Lymphoma. Version 1.2022. https://www.nccn.org/home. Published November 19, 2021. Accessed January 18, 2022.

18. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: Multiple Myeloma. Version 4.2022. https://www.nccn.org/home. Published December 14, 2021. Accessed January 18, 2022.
19. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: Myelodysplastic syndromes. Version 3.2022. https://www.nccn.org/home. Published January 13, 2022. Accessed January 18, 2022.
20. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines on Oncology: Myeloproliferative Neoplasms. Version 2.2021. https://www.nccn.org/home. Published August 18, 2021. Accessed January 18, 2022.
21. 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.e30. doi:10.1016/j.bbmt.2010.07.008
22. 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):1435-1439. doi:10.1016/j.bbmt.2014.05.012
23. 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):83-89. doi:10.1016/j.exphem.2013.07.003
24. 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):76-82. doi:10.1111/j.1365-2141.2011.08582.x
25. Sieff CA. Overview of hematopoietic stem cells. UpToDate. www.uptodate.com. Published September 15, 2021. Accessed January 13, 2022.
26. Storb R, Sandmeier BM. Nonmyeloablative allogenic hematopoietic cell transplantation. *Haematologica*. 2016;101(5): 521–530. doi:10.3324/haematol.2015.132860
27. Tefferi A. Management of primary myelofibrosis. UpToDate. www.uptodate.com. Accessed December 6, 2021. Accessed January 13, 2022.
28. 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):125-128. doi:10.1159/000357108
29. Rajkumar SV. Multiple myeloma: Use of allogeneic hematopoietic cell transplantation. UpToDate. www.uptodate.com. Published April 8, 2020. Accessed January 13, 2022.
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 Clincal Oncol. 2020 Jul 20;38(21):2469]. *J Clin Oncol*. 2019;37(14):1228-1263. Doi:10.1200/JCO.18.02096
31. Stephen J. Forman SJ, Negrin RS, Antin JH, Appelbaum FR. Thomas' Hematopoietic Stem Cell Transplantation. 5th Edition. John Wiley & Sons, Ltd. 2016.

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 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.