Molina Clinical Policy
Haploidentical Allogeneic Hematopoietic Cell Transplantation in Blood Cancers: Policy No. 362

Last Approval: 4/13/2022
Next Review Due By: April 2023

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

Allogeneic hematopoietic cell transplantation (HCT) may cure a broad variety of malignant and non-malignant hematologic disorders. The hematopoietic stem cells required are typically obtained from a related or unrelated donor's bone marrow or peripheral blood. For best outcomes, the stem cell donor is a human leukocyte antigen (HLA)-matched sibling. Potential donors include biological parents; biological children; full or half siblings; and even extended family donors such as aunts, uncles, nieces, nephews, cousins, or grandchildren. There is a 25 percent chance that a sibling will match the patient in developing nations. When there is not an HLA-matched sibling, alternative sources of donor grafts may be used including, but not limited to suitably HLA-matched adult unrelated donors, umbilical cord blood stem cells, and partially HLA-mismatched, or HLA-haploidentical, related donors. Challenges of an HLA-haploidentical HCT include the intense bi-directional alloreactivity leading to high incidences of graft rejection and graft-versus-host disease (GVHD). Due to advances in graft engineering and pharmacologic prophylaxis of GVHD, risks are reduced of graft failure and GVHD. (Fuchs & Luznik, 2021).

COVERAGE POLICY

All transplants require prior authorization from the Corporate Transplant Department. Solid organ transplant requests will be reviewed by the Corporate Senior Medical Director or qualified clinical designee. All other transplants will be reviewed by the Corporate Senior Medical Director or covering Medical Director. If the criteria are met using appropriate NCD and/or LCD guidelines, State regulations, and/or MCP policies the Corporate Senior Medical Director's designee can approve the requested transplant.

Office visits with participating Providers do NOT require prior authorization. Providers should see the Member in office visits as soon as possible and without delay. Failure to see the Member in office visits may be considered a serious quality of care concern.

Haploidentical Allogeneic Hematopoietic Cell Transplantation Criteria (AMR, 2020)

Haploidentical allogeneic hematopoietic cell transplantation **may be considered a medically necessary** option when there are no matched sibling or unrelated donors for the following blood cancers:*

1. Acute Myelogenous Leukemia (AML); **OR**
2. Aplastic Anemia and other Bone Marrow Failure Disorders; **OR**
3. Hodgkin's Lymphoma

HLA-haploidentical donor selection criteria incudes **ALL** of the following:

1. Donor must be medically, socially, and psychologically fit to donate; **AND**
2. Donor age <40 years preferred over donor age ≥40 years; **AND**

3. No major ABO incompatibility between donor and recipient; major ABO incompatibilities include:
   a. Recipient blood type O: Donor type A, B, or AB; **OR**
   b. Recipient blood type A: Donor blood type B or AB; **OR**
   c. Recipient blood type B: Donor blood type A or AB; **OR**
   d. Recipient blood type AB: No major ABO incompatibilities

AND

4. Matched CMV IgG serologic status between donor and recipient include:
   a. For a recipient who is CMV IgG negative, use a CMV IgG negative donor; **OR**
   b. For a recipient who is CMV IgG positive, use a CMV IgG positive donor

AND

5. Use an ABO compatible donor over a minor ABO incompatible donor (ABO compatible transplants are O→O, A→A, B→B, or AB→AB).

*Note: Please see the specific MCP for clinical criteria for each of the above diagnoses

For Members with Significant or Daily Marijuana Use

1. Documentation of compliance with a physician prescribed and managed program of abstinence, and a reasonable expectation that the Member will be abstinent from marijuana use during the transplant and immediate post-transplant time period. Daily marijuana use is an absolute contraindication for both transplant and pre-transplant evaluation unless there is a state mandate applicable for medical marijuana use and transplants, and there is documentation of Member compliance with a physician prescribed plan of care for prescribed marijuana use.
2. If the Member's marijuana use is in compliance with a formal, State-based program for managed medical marijuana, the request should include:
   - Documentation of the Plan of Care for medical marijuana (including the medical decision making that supports the use of medical marijuana); **AND**
   - Transplant Provider agreement with the Plan of Care (including agreement to be accountable for managing the Member's use of medical marijuana).

Limitations and Exclusions

Absolute contraindications to the use of a specific HLA-haploidentical donor include:

1. Donor is medically or psychologically unfit; **AND**
2. Recipient has anti-donor HLA antibodies of sufficient strength to result in a positive crossmatch result by flow cytometry or by complement-dependent cytotoxicity assay; **AND**

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

At the current time, there are no published randomized controlled trials of haploidentical HCT that compare either umbilical cord blood HCT or mismatched unrelated donor HCT. For patients with acute leukemia in complete remission or with lymphoma, the United States Blood and Marrow Transplant Clinical Trials Network conducted a phase III, randomized trial of reduced intensity conditioning and transplantation of either double unrelated donor umbilical cord

blood or HLA-haploidentical bone marrow (BMT CTN 1101; NCT01597778). The results of this trial have not yet been published. Data regarding outcomes are mostly from retrospective analyses and large multi-institutional studies comparing post-transplant graft vs. host disease (GVHD), transplant related mortality, disease-free survival, or relapse. For peer-reviewed studies used in the development and update of this policy, please see the *Reference* section.

The **National Comprehensive Cancer Network (NCCN) (2021)** published *Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia.* The guidelines note that haploididentical transplantation may be considered a treatment option if no appropriated matched sibling donor is found and the patient is a candidate for HCT. (Category 2A recommendation).

The **NCCN** also published *Clinical Practice Guidelines in Oncology: Hematopoietic Cell Transplantation* (Saad et al., 2020) focus on the management of adult patients with malignant disease. Pretransplant recipient evaluation and management of acute and chronic GVHD are also reviewed.

SUPPLEMENTAL INFORMATION

None.

CODING & BILLING INFORMATION

CPT Codes

CPT	Description
38205	Blood-derived hematopoietic cell harvesting for transplantation, per collection; allogeneic
38230	Bone marrow harvesting for transplantation
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor

HCPCS Codes – N/A

ICD-10 Codes – N/A

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

4/13/2022	Policy reviewed; included marijuana use under absolute contraindications; updated Summary of Medical Evidence and Reference sections.
4/5/2021	Policy reviewed, no changes to criteria, updated references.
4/23/2020	New policy.

REFERENCES

Government Agencies

1. Centers for Medicare and Medicaid Services (CMS). Medicare coverage database. Available from CMS. Accessed February 16, 2022.
2. ClinicalTrials.gov. Double cord versus haploidentical (BMT CTN 1101). Available from ClinicalTrials. Published May 14, 2012. Updated December 1, 2021. Accessed February 16, 2022.

Evidence Based Reviews and Publications

1. Fuchs EJ, Luznik L. HLA-haploidentical hematopoietic cell transplantation. http://www.uptodate.com. Updated July 16, 2021. Accessed February 16, 2022. Registration and login required.
2. AMR Peer Review. Policy reviewed on February 25, 2020 by an Advanced Medical Reviews (AMR) practicing, board-certified physician(s) in the areas of Oncology and Hematology.

Peer Reviewed Publications

1. Ahmed S, Kanakry JA, et al. Lower graft-versus-host disease and relapse risk in post-transplant cyclophosphamide-based haploidentical versus matched sibling donor reduced-intensity conditioning transplant for Hodgkin lymphoma. Biol Blood Marrow Transplant. 2019 Sep;25(9):1859-1868. doi: 10.1016/j.bbmt.2019.05.025. Accessed February 16, 2022.
2. Bashey A, Zhang X, Sizemore CA, Manion K, Brown S, Holland HK, et al. T-cell-replete HLA-haploidentical hematopoietic transplantation for hematologic malignancies using post-transplantation cyclophosphamide results in outcomes equivalent to those of contemporaneous HLA-matched related and unrelated donor transplantation. J Clin Oncol. 2013 Apr 1;31(10):1310-6. doi: 10.1200/JCO.2012.44.3523. Accessed February 16, 2022.
3. Bazarbachi A, Labopin M, Angelucci E, Gülbas Z, Ozdogu H, Arat M, et al. Haploidentical transplant with post-transplant cyclophosphamide for T-cell acute lymphoblastic leukemia: A report from the European Society for Blood and Marrow Transplantation (EBMT) Acute Leukemia Working Party. Biol Blood Marrow Transplant. 2020 May;26(5):936-942. doi: 10.1016/j.bbmt.2020.01.003. Accessed February 16, 2022.
4. Bazarbachi A, Boumendil A, Finel H, Castagna L, Dominietto A, Blaise D, et al. Influence of donor type, stem cell source and conditioning on outcomes after haploidentical transplant for lymphoma - a LWP-EBMT study. Br J Haematol. 2020 Mar;188(5):745-756. doi: 10.1111/bjh.16182. Accessed February 16, 2022.
5. Bonini C, Peccatori J, Stanghellini MTL, Vago L, Bondanza A, Cieri N, et al. Haploidentical HSCT: A 15-year experience at San Raffaele. Bone Marrow Transplant. 2015 Jun;50 Suppl 2:S67-71. doi: 10.1038/bmt.2015.99. Accessed February 16, 2022.
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7. Burroughs LM, O'Donnell PV, Sandmaier BM, Storer BE, Luznik L, Symons HJ, et al. Comparison of outcomes of HLA-matched related, unrelated, or HLA-haploidentical related hematopoietic cell transplantation following nonmyeloablative conditioning for relapsed or refractory Hodgkin lymphoma. Biol Blood Marrow Transplant. 2008 Nov;14(11):1279-87. doi: 10.1016/j.bbmt.2008.08.014. Accessed February 16, 2022.
8. Chen D, Zhou D, Guo D, Xu P, Chen B. Comparison of outcomes in hematological malignancies treated with haploidentical or HLA-identical sibling hematopoietic stem cell transplantation following myeloablative conditioning: A meta-analysis. PLoS One. 2018 Jan 30;13(1):e0191955. Accessed February 16, 2022.
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National and Specialty Organizations

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APPENDIX

Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*