

Subject: Haploidentical Allogeneic Hematopoietic Cell Transplantation in Blood Cancers		Original Effective Date: 4/23/20
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DISCLAIMER

This Molina clinical policy is intended to facilitate the Utilization Management process. 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 (i.e., 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 Molina clinical policy document and provide the directive for all Medicare members.¹

DESCRIPTION OF PROCEDURE/SERVICE/PHARMACEUTICAL²²

Allogeneic hematopoietic cell transplantation (HCT) is a potentially curative therapy for a wide variety of malignant and non-malignant hematologic disorders. The hematopoietic stem cells required for this procedure are usually obtained from the bone marrow or peripheral blood of a related or unrelated donor. Historically, the best results of allogeneic HCT have been obtained when the stem cell donor is a human leukocyte antigen (HLA)-matched sibling. Given the small family sizes

in developed nations and the 25 percent likelihood that any sibling is fully HLA-matched to the patient, an HLA-matched sibling can be found for only approximately 30 percent of patients. For patients who lack an HLA-matched sibling, alternative sources of donor grafts include suitably HLA-matched adult unrelated donors, umbilical cord blood stem cells, and partially HLA-mismatched, or HLA-haploidentical, related donors.

The major challenge of HLA-haploidentical HCT is intense bi-directional alloreactivity leading to high incidences of graft rejection and graft-versus-host disease (GVHD). Advances in graft engineering and in pharmacologic prophylaxis of GVHD have reduced the risks of graft failure and GVHD after HLA-haploidentical HCT, and have made this stem cell source a viable alternative for patients lacking an HLA-matched sibling.

Definitions: An HLA-haploidentical donor is one who shares, by common inheritance, exactly one HLA haplotype with the recipient and is mismatched for a variable number of HLA genes, ranging from zero to six, on the unshared haplotype. Potential HLA-haploidentical donors include biological parents; biological children; full or half siblings; and even extended family donors such as aunts, uncles, nieces, nephews, cousins, or grandchildren.

RECOMMENDATION CLINICAL CRITERIA

1. 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*: [ALL]
 - ☐ Acute Myelogenous Leukemia (AML); or
 - ☐ Aplastic Anemia and other Bone Marrow Failure Disorders; or
 - ☐ Hodgkin's Lymphoma
2. HLA-haploidentical donor selection criteria includes all of the following: ²²
 - ☐ Donor must be medically, socially, and psychologically fit to donate
 - ☐ Donor age <40 years preferred over donor age ≥40 years
 - ☐ No major ABO incompatibility between donor and recipient. Major ABO incompatibilities include:
 - Recipient blood type O: Donor type A, B, or AB
 - Recipient blood type A: Donor blood type B or AB
 - Recipient blood type B: Donor blood type A or AB
 - Recipient blood type AB: No major ABO incompatibilities
 - ☐ Matched CMV IgG serologic status between donor and recipient include:
 - For a recipient who is CMV IgG negative, use a CMV IgG negative donor
 - For a recipient who is CMV IgG positive, use a CMV IgG positive donor
 - ☐ 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**

LIMITATIONS ²²

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

- ☐ Donor is medically or psychologically unfit; or
- ☐ 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.

SUMMARY OF MEDICAL EVIDENCE²⁻²⁷

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).² 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.

PROFESSIONAL SOCIETY GUIDELINES

The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology for Acute Myeloid Leukemia mention that haploidentical 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)²⁸

CODING INFORMATION: THE CODES LISTED IN THIS POLICY ARE FOR REFERENCE PURPOSES ONLY. LISTING OF A SERVICE OR DEVICE CODE IN THIS POLICY DOES NOT IMPLY THAT THE SERVICE DESCRIBED BY THIS CODE IS COVERED OR NON-COVERED. COVERAGE IS DETERMINED BY THE BENEFIT DOCUMENT. THIS LIST OF CODES MAY NOT BE ALL INCLUSIVE.

CPT	Description
	N/A There are no specific codes for haploidentical transplantation

HCPCS	Description
	N/A There are no specific codes for haploidentical transplantation

ICD-10	Description: [For dates of service on or after 10/01/2015]
	Any/All

REFERENCES

Government Agency

- Centers for Medicare & Medicaid Services (CMS). Medicare Coverage Database. National coverage determination (NCD) Search. Accessed at: <https://www.cms.gov/medicare-coverage-database/new-search/search.aspx>
- NIH U.S. National Library of Medicine. Clinical Trials. Double Cord versus Haploidentical (BMT CTN 1101). Accessed at: <https://clinicaltrials.gov/ct2/show/NCT01597778>

Peer Reviewed Publications

- 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.

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Professional Society Guidelines

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 - Adult Hodgkin's Lymphoma Treatment. Accessed at: <http://www.cancer.gov/types/lymphoma/hp/adult-hodgkin-treatment-pdq>
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Other Resources

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REVIEW REVISION HISTORY

- 4/23/20: New Policy
 4/5/21: Policy reviewed, no changes to criteria. Updated references.