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]
2. HLA-haploidentical donor selection criteria includes all of the following:  
- 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 includes:  
  - 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*

**EXCLUSIONS**

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 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).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.

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.

<table>
<thead>
<tr>
<th>CPT</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td>There are no specific codes for haploidentical transplantation</td>
</tr>
<tr>
<td>HCPCS</td>
<td>Description</td>
</tr>
<tr>
<td>-------</td>
<td>-------------</td>
</tr>
<tr>
<td>N/A</td>
<td>There are no specific codes for haploidentical transplantation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10</th>
<th>Description: [For dates of service on or after 10/01/2015]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any/All</td>
<td></td>
</tr>
</tbody>
</table>

**REFERENCES**

**Government Agency**


**Peer Reviewed Publications**


Professional Society Guidelines

   • Acute Myeloid Leukemia. Version 3.2020 Accessed at: 
29. National Cancer Institute:

Other Resources
- Fuchs E, Luznik L. HLA-haploidentical hematopoietic cell transplantation.
23. IRO Peer Review: Advanced Medical Review: Policy reviewed by practicing MD board certified Oncology, Hematology. 2/25/20.

Revision/Review History:
4/23/20: New Policy