

## MEDICAL POLICY

|               |                                                          |
|---------------|----------------------------------------------------------|
| POLICY TITLE  | PLACENTAL/UMBILICAL CORD BLOOD AS A SOURCE OF STEM CELLS |
| POLICY NUMBER | MP 9.001                                                 |

|                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| CLINICAL BENEFIT | <input type="checkbox"/> MINIMIZE SAFETY RISK OR CONCERN.<br><input checked="" type="checkbox"/> MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS.<br><input type="checkbox"/> ASSURE APPROPRIATE LEVEL OF CARE.<br><input type="checkbox"/> ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS.<br><input checked="" type="checkbox"/> ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET.<br><input type="checkbox"/> ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE. |
| Effective date:  | 10/1/2026                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |

### POLICY

Transplantation of cord blood stem cells from related or unrelated donors may be considered **medically necessary** in individuals with an appropriate indication for allogeneic stem-cell transplant.

Transplantation of cord blood stem cells from related or unrelated donors is considered **investigational** in all other situations as there is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Collection and storage of cord blood from a neonate may be considered **medically necessary** when an allogeneic transplant is imminent in an identified recipient with a diagnosis that is consistent with the possible need for allogeneic transplant.

Prophylactic collection and storage of cord blood from a neonate may be considered **investigational** when proposed for some unspecified future use as an autologous stem-cell transplant in the original donor, or for some unspecified future use as an allogeneic stem-cell transplant in a related or unrelated donor.

### POLICY GUIDELINES

Refer to the medical policy for specific conditions/diseases that have individual selection criteria for which allogeneic stem cell transplantation may be considered medically necessary.

#### ***Cross-References:***

MP 9.039 Hematopoietic Cell Transplantation for Chronic Myeloid Leukemia  
 MP 9.040 Hematopoietic Cell Transplantation for Acute Myeloid Leukemia  
 MP 9.042 Hematopoietic Cell Transplantation for Non-Hodgkin Lymphomas  
 MP 9.043 Hematopoietic Cell Transplantation for Hodgkin Lymphoma  
 MP 9.046 Hematopoietic Cell Transplantation for Waldenstrom Macroglobulinemia  
 MP 9.047 Hematopoietic Cell Transplantation for Epithelial Ovarian Cancer  
 MP 9.048 Hematopoietic Cell Transplantation Miscellaneous Solid Tumors in Adults  
 MP 9.050 Hematopoietic Cell Transplantation for CNS Embryonal Tumors and Ependymoma  
 MP 9.052 Hematopoietic Cell Transplantation in the Treatment of Germ-Cell Tumors  
 MP 9.053 Hematopoietic Cell Transplantation for Autoimmune Diseases  
 MP 9.055 Allogeneic HCT for Genetic Diseases and Acquired Anemias  
 MP 9.056 Allogeneic HCT for Myelodysplastic Syndromes and Myeloproliferative Neoplasms

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### MP 9.041 Hematopoietic Cell Transplantation for Acute Lymphoblastic Leukemia

#### PRODUCT VARIATIONS

This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations. Please see additional information below.

**FEP PPO** - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

[https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies\\_](https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies_)

#### DESCRIPTION/BACKGROUND

##### Hematopoietic Cell Transplantation

Hematopoietic cell transplantation (HCT) is a procedure in which hematopoietic stem cells are intravenously infused to restore bone marrow and immune function in cancer patients who receive bone marrow-toxic doses of cytotoxic drugs with or without whole-body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or a donor (allogeneic HCT [allo-HCT]). These cells can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. In allogeneic stem cell transplantation, immunologic compatibility between donor and patient is a critical factor for achieving a successful outcome. Compatibility is established by typing of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. HLA refers to the gene complex expressed at the HLA-A, -B, and -DR (antigen-D related) loci on each arm of chromosome 6. An acceptable donor will match the individual at all or most of the HLA loci.

##### Conditioning for Hematopoietic Cell Transplantation

##### Conventional Conditioning

The conventional ("classical") practice of allo-HCT involves administration of cytotoxic agents (e.g., cyclophosphamide, busulfan) with or without total body irradiation at doses sufficient to cause bone marrow ablation in the recipient. The beneficial treatment effect of this procedure is due to a combination of the initial eradication of malignant cells and subsequent graft-versus-malignancy effect mediated by non-self-immunologic effector cells. While the slower graft-versus-malignancy effect is considered the potentially curative component, it may be overwhelmed by existing disease in the absence of pretransplant conditioning. Intense conditioning regimens are limited to patients who are sufficiently medically fit to tolerate substantial adverse effects. These include opportunistic infections secondary to loss of endogenous bone marrow function and organ damage or failure caused by cytotoxic drugs. Subsequent to graft infusion in allo-HCT, immunosuppressant drugs are required to minimize graft rejection and graft-versus-host disease, which increases susceptibility to opportunistic infections.

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The success of autologous HCT is predicated on the potential of cytotoxic chemotherapy, with or without radiotherapy, to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of the bone marrow with presumably normal hematopoietic stem cells obtained from the patient before undergoing bone marrow ablation. Therefore, autologous HCT is typically performed as consolidation therapy when the individual's disease is in complete remission. Individuals who undergo autologous HCT are also susceptible to chemotherapy-related toxicities and opportunistic infections before engraftment but not graft-versus-host disease.

### Reduced-Intensity Conditioning Allogeneic Hematopoietic Cell Transplantation

Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses of cytotoxic drugs or less intense regimens of radiotherapy than are used in traditional full-dose myeloablative conditioning treatments. Although the definition of RIC is variable, with numerous versions employed, all regimens seek to balance the competing effects of relapse due to residual disease and non-relapse mortality. The goal of RIC is to reduce disease burden and to minimize associated treatment-related morbidity and non-relapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. RIC regimens range from nearly total myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Individuals who undergo RIC with allo-HCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full donor chimerism. In this review, the term reduced-intensity conditioning will refer to all conditioning regimens intended to be nonmyeloablative.

### Regulatory Status

According to the U.S. Food and Drug Administration (FDA), cord blood stored for potential use by an individual unrelated to the donor meets the definitions of "drug" and "biological products." As such, products must be licensed under a biologics license application or an investigational new drug application before use. Facilities that prepare cord blood units only for autologous and/or first- or second-degree relatives are required to register and list their products, adhere to Good Tissue Practices issued by the FDA, and use applicable processes for donor suitability determination.

### RATIONALE

#### SUMMARY OF EVIDENCE

For individuals who have an appropriate indication for allogeneic stem cell transplant who receive cord blood as a source of stem cells, the evidence includes a number of observational studies, a meta-analysis of observational studies, and randomized controlled trials (RCTs). Relevant outcomes are overall survival, disease-specific survival, resource utilization, and treatment-related mortality. A meta-analysis of observational studies found similar survival outcomes and lower graft-versus-host disease after cord blood transplantation than bone marrow transplantation, but a recent RCT showed improved survival outcomes with haploidentical bone marrow transplantation over umbilical cord blood transplantation. In another RCT, survival rates were similar after single- and double-unit cord blood transplantation. The

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evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have an unspecified potential future need for stem cell transplant who receive prophylactic collection and storage of cord blood, the evidence includes no published studies. Relevant outcomes are overall survival, disease-specific survival, resource utilization, and treatment-related mortality. No evidence was identified on the safety or effectiveness of autologous cord blood transplantation from prophylactically stored cord blood for the treatment of malignant neoplasms. The evidence is insufficient to determine the effects of the technology on health outcomes.

### DEFINITIONS

**CORD BLOOD** refers to the blood remaining in the umbilical cord and placenta following the birth of an infant **HEMATOPOIETIC** relates to the production and formation of blood cells.

**MYELOABLATIVE** refers to treatment designed to destroy most blood and cancer cells

### DISCLAIMER

*Capital Blue Cross' medical policies are used to determine coverage for specific medical technologies, procedures, equipment, and services. These medical policies do not constitute medical advice and are subject to change as permitted by law or applicable clinical evidence from independent treatment guidelines. Treating providers are solely responsible for medical advice and treatment of members. These policies are not a guarantee of coverage or payment. Payment of claims is subject to a determination regarding the member's benefit program and eligibility on the date of service, and a determination that the services are medically necessary and appropriate. Final processing of a claim is based upon the terms of contract that applies to the members' benefit program, including benefit limitations and exclusions. If a provider or a member has a question concerning this medical policy, please contact Capital Blue Cross' Provider Services or Member Services.*

### CODING INFORMATION

**Note:** This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

#### Covered when medically necessary:

| Procedure Codes |       |       |  |  |  |  |  |
|-----------------|-------|-------|--|--|--|--|--|
| S2140           | S2142 | S2150 |  |  |  |  |  |

Please reference the appropriate Hematopoietic Cell Transplantation (HCT) policy for the specific diagnoses for which allogeneic cell transplantation may be considered medically necessary.

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### REFERENCES

1. Food and Drug Administration (FDA). Cord Blood Banking: Information for Consumers. 2012 July 23;
2. Wall DA. Regulatory issues in cord blood banking and transplantation. *Best Pract ResClin Haematol*. Jun 2010; 23(2): 171-7. PMID 20837328
3. NetCord-FACT. International standards for cord blood collection banking and release of information accreditation manual. Seventh Edition Draft.
4. Gluckman E, Broxmeyer HA, Auerbach AD, et al. Hematopoietic reconstitution in a patient with Fanconi's anemia by means of umbilical-cord blood from an HLA-identical sibling. *N Engl J Med*. Oct 26, 1989; 321(17): 1174-8. PMID 2571931
5. Wagner JE, Rosenthal J, Sweetman R, et al. Successful transplantation of HLA-matched and HLA-mismatched umbilical cord blood from unrelated donors: analysis of engraftment and acute graft-versus-host disease. *Blood*. Aug 01, 1996; 88(3): 795-802. PMID 8704232
6. Broxmeyer HE, Douglas GW, Hangoc G, et al. Human umbilical cord blood as a potential source of transplantable hematopoietic stem/progenitor cells. *Proc Natl Acad Sci U S A*. May 1989; 86(10): 3828-32. PMID 2566997
7. Kurtzberg J, Cairo MS, Fraser JK, et al. Results of the cord blood transplantation (COBLT) study unrelated donor banking program. *Transfusion*. Jun 2005; 45(6): 842-55. PMID 15934981
8. Martin PL, Carter SL, Kernan NA, et al. Results of the cord blood transplantation study (COBLT): outcomes of unrelated donor umbilical cord blood transplantation in pediatric patients with lysosomal and peroxisomal storage diseases. *Biol Blood Marrow Transplant*. Feb 2006; 12(2): 184-94. PMID 16443516
9. Kurtzberg J. Update on umbilical cord blood transplantation. *Curr Opin Pediatr*. Feb 2009; 21(1): 22-9. PMID 19253461
10. Zhang H, Chen J, Que W. A meta-analysis of unrelated donor umbilical cord blood transplantation versus unrelated donor bone marrow transplantation in acute leukemia patients. *Biol Blood Marrow Transplant*. Aug 2012; 18(8): 1164-73. PMID 22289799
11. Rocha V, Cornish J, Sievers EL, et al. Comparison of outcomes of unrelated bone marrow and umbilical cord blood transplants in children with acute leukemia. *Blood*. May 15, 2001; 97(10): 2962-71. PMID 11342418
12. Kato K, Choi I, Wake A, et al. Treatment of patients with adult T cell leukemia/lymphoma with cord blood transplantation: a Japanese nationwide retrospective survey. *Biol Blood Marrow Transplant*. Dec 2014; 20(12): 1968-74. PMID 25172635
13. Liu HL, Sun ZM, Geng LQ, et al. Similar survival, but better quality of life after myeloablative transplantation using unrelated cord blood vs matched sibling donors in adults with hematologic malignancies. *Bone Marrow Transplant*. Aug 2014; 49(8): 1063-9. PMID 24842525
14. Fuchs EJ, O'Donnell PV, Eapen M, et al. Double unrelated umbilical cord blood versus HLA-haploidentical bone marrow transplantation (BMT CTN 1101). *Blood*. Aug 31, 2020. PMID 32870242

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15. Mo XD, Tang BL, Zhang XH, et al. Comparison of outcomes after umbilical cord blood and unmanipulated haploidentical hematopoietic stem cell transplantation in children with high-risk acute lymphoblastic leukemia. *Int J Cancer*. Nov 01, 2016; 139(9): 2106-15. PMID 27356906
16. Hsu J, Artz A, Mayer SA, et al. Combined Haploidentical and Umbilical Cord Blood Allogeneic Stem Cell Transplantation for High-Risk Lymphoma and Chronic Lymphoblastic Leukemia. *Biol Blood Marrow Transplant*. Feb 2018; 24(2): 359-365. PMID 29128555
17. Poonsombudlert K, Kewcharoen J, Prueksapraopong C, et al. Post transplant cyclophosphamide based haplo-identical transplant versus umbilical cord blood transplant; a meta-analysis. *Jpn J Clin Oncol*. Oct 01, 2019; 49(10): 924-931. PMID 31265729
18. Li D, Li X, Liao L, et al. Unrelated cord blood transplantation versus haploidentical transplantation in adult and pediatric patients with hematological malignancies-A meta-analysis and systematic review. *Am J Blood Res*. 2020; 10(1): 1-10. PMID 32206440
19. Wu R, Ma L. Haploidentical Hematopoietic Stem Cell Transplantation Versus Umbilical Cord Blood Transplantation in Hematologic Malignancies: A Systematic Review and Meta-Analysis. *Cell Transplant*. Jan-Dec 2020; 29: 963689720964771. PMID 33040595
20. Barker JN, Weisdorf DJ, DeFor TE, et al. Transplantation of 2 partially HLA-matched umbilical cord blood units to enhance engraftment in adults with hematologic malignancy. *Blood*. Feb 01, 2005; 105(3): 1343-7. PMID 15466923
21. Wagner JE, Eapen M, Carter S, et al. One-unit versus two-unit cord-blood transplantation for hematologic cancers. *N Engl J Med*. Oct 30, 2014; 371(18): 1685-94. PMID 25354103
22. Scaradavou A, Brunstein CG, Eapen M, et al. Double unit grafts successfully extend the application of umbilical cord blood transplantation in adults with acute leukemia. *Blood*. Jan 31, 2013; 121(5): 752-8. PMID 23223509
23. Baron F, Ruggeri A, Beohou E, et al. Single- or double-unit UCBT following RIC in adults with AL: a report from Eurocord, the ALWP and the CTIWP of the EBMT. *J Hematol Oncol*. Jun 21, 2017; 10(1): 128. PMID 28637512
24. Shearer WT, Lubin BH, Cairo MS, et al. Cord Blood Banking for Potential Future Transplantation. *Pediatrics*. Nov 2017; 140(5). PMID 29084832
25. Thornley I, Eapen M, Sung L, et al. Private cord blood banking: experiences and views of pediatric hematopoietic cell transplantation physicians. *Pediatrics*. Mar 2009; 123(3): 1011-7. PMID 19255033
26. ACOG Committee Opinion No. 771: Umbilical Cord Blood Banking. *Obstet Gynecol*. Mar 2019; 133(3): e249-e253. PMID 30801478
27. Ballen KK, Barker JN, Stewart SK, et al. Collection and preservation of cord blood for personal use. *Biol Blood Marrow Transplant*. Mar 2008; 14(3): 356-63. PMID 18275904
28. Dholaria B, Savani BN, Hamilton BK, et al. Hematopoietic Cell Transplantation in the Treatment of Newly Diagnosed Adult Acute Myeloid Leukemia: An Evidence-Based Review from the American Society of Transplantation and Cellular Therapy. *Biol Blood Marrow Transplant*. Sep 20, 2020. PMID 32966881

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29. Chao, N. J. *Selection of an Umbilical Cord Blood Graft for Hematopoietic Cell Transplantation*. UpToDate [online serial]. Waltham, MA: UpToDate; Literature through May 2026, last updated Mar 20, 2024.
30. Chao, N. J. *Collection and Storage of Umbilical Cord Blood for Hematopoietic Cell Transplantation*. UpToDate [online serial]. Waltham, MA: UpToDate; Literature through May 2026, last updated Nov 17, 2025.
31. Devi S, Bongale AM, Tefera MA, Dixit P, Bhanap P. *Fresh Umbilical Cord Blood-A Source of Multipotent Stem Cells, Collection, Banking, Cryopreservation, and Ethical Concerns*. *Life (Basel)*. 2023;13(9):1794. Published 2023 Aug 23. doi:10.3390/life13091794

### POLICY HISTORY

|                 |                                                                                                                                                                                                         |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>MP 9.001</b> | <b>02/26/2020 Consensus Review.</b> No coding or reference updates. No change to policy statements.                                                                                                     |
|                 | <b>02/25/2021 Consensus Review.</b> No changes to policy statements. Description/Background section and references updated.                                                                             |
|                 | <b>07/19/2022 Consensus Review.</b> No change in policy statement. References updated and coding reviewed. NCCN statement added.                                                                        |
|                 | <b>09/28/2023 Consensus Review.</b> No change in policy statement. References updated. Coding reviewed, no changes.                                                                                     |
|                 | <b>10/22/2024 Minor Review.</b> Updated "Prophylactic collection and storage of cord blood from a neonate for unspecified future use" from NMN to INV. References updated. Coding reviewed, no changes. |
|                 | <b>01/15/2025 Administrative Update.</b> Removed NCCN statement.                                                                                                                                        |
|                 | <b>08/14/2025 Consensus Review.</b> No change to policy stance. Updated references.                                                                                                                     |
|                 | <b>10/29/2025 Administrative Update.</b> Removed Benefit Variations Section and updated Disclaimer.                                                                                                     |
|                 | <b>06/03/2026 Consensus Review.</b> No changes to policy statement. Updated formatting, cross-references, product variations, background, definitions, disclaimer, and references. No coding changes.   |

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