# MEDICAL POLICY

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

| CLINICAL BENEFIT | ☐ MINIMIZE SAFETY RISK OR CONCERN.<br>☒ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS.<br>☐ ASSURE APPROPRIATE LEVEL OF CARE.<br>☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS.<br>☒ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET.<br>☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE. |
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| **Effective Date:** | **3/1/2025** |



## I. POLICY

Transplantation of cord blood stem cells from related or unrelated donors may be considered **medically necessary** in patients 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 patient 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 Extracranial 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**
**MP 9.041 Hematopoietic Cell Transplantation for Acute Lymphoblastic Leukemia**

## II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. 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 .**

## III. DESCRIPTION/BACKGROUND

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### 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 patient 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.

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 patient's disease is in complete remission. Patients 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. Patients 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 a patient 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.

## IV. RATIONALE

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### 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 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.

## V. DEFINITIONS

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**ALLOGENEIC** refers to having a different genetic constitution but belonging to the same species, i.e., involves a donor and a recipient.

**AUTOLOGOUS** means originating within an individual, i.e., self-donation**.**

**CORD BLOOD** refers to blood from the cord that connects the circulatory system of the fetus to the placenta.

**HEMATOPOIETIC** pertains to or effecting the production and development of blood cells.

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

## VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member’s health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits, and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and

providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

## VII. DISCLAIMER

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*Capital Blue Cross' medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.*

## VIII. CODING INFORMATION

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**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 | | | | | | | |
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| 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.

## IX. REFERENCES

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## X. POLICY HISTORY

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| **MP 9.001** | **02/26/2020 Consensus Review.** No coding or reference updates. No change |

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| | to policy statements. |
| | **02/25/2021 Consensus Review.** No changes to policy statements. Description/Background section and references updated. |
| | **07/19/2022 Consensus Review.** No change in policy statement. References updated and coding reviewed. NCCN statement added. |
| | **09/28/2023 Consensus Review.** No change in policy statement. References updated. Coding reviewed, no changes. |
| | **10/22/2024 Minor Review.** 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. |
| | **01/15/2025 Administrative Update.** Removed NCCN statement |

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