MEDICAL POLICY – 7.01.50
Placental and Umbilical Cord Blood as a Source of Stem Cells

BCBSA Ref. Policy: 7.01.50
Effective Date: April 1, 2020
Last Revised: March 19, 2020
Replaces: N/A

RELATED MEDICAL POLICIES:
None

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Stem cells are cells in our body that have the ability to develop into many different kinds of cells. Stem cells have been used to treat many conditions including such things as diabetes, heart disease, arthritis, spinal cord injuries, and some types of cancer.

Stem cells are found in embryos, adults, and the umbilical cords of newborn babies. They are also found in the placenta (the “after birth”) of a pregnant woman. Stem cells that have been retrieved from the placenta or umbilical cord have been transplanted into patients in order to treat some specific diseases. This policy discusses when the transplantation of placental or umbilical cord stem cells might be considered to be medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria
<table>
<thead>
<tr>
<th>Service</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplantation of cord blood stem cells</td>
<td>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.</td>
</tr>
<tr>
<td>Collection and storage of cord blood</td>
<td>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.</td>
</tr>
<tr>
<td>Prophylactic collection and storage of cord blood</td>
<td>Prophylactic collection and storage of cord blood from a neonate may be considered not medically necessary 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.</td>
</tr>
</tbody>
</table>

**Documentation Requirements**

The patient’s medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:

- For the use of the of stem cells retrieved from the umbilical cord and placenta:
  - Documentation that the stem cells will be used in patients who qualify for a stem cell transplant using donor cells
- For collection and storage of cord blood:
  - Documentation that a transplant using donor cells is imminent for a person diagnosed with a disease that can be treated by using donor cells
## Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S2140</td>
<td>Cord blood harvesting for transplantation, allogeneic</td>
</tr>
<tr>
<td>S2142</td>
<td>Cord blood-derived stem-cell transplantation, allogeneic</td>
</tr>
<tr>
<td>S2150</td>
<td>Bone marrow or blood-derived stem-cells (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications; including: pheresis and cell preparation/storage; marrow ablative therapy; drugs, supplies, hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days of pre-and post-transplant care in the global definition</td>
</tr>
</tbody>
</table>

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## Related Information

### Benefit Application

Through the National Marrow Donor Program’s *Be the Match*, eligible families within the United States can collect and store their neonate’s cord blood unit free of charge. When the stored unit is transplanted, a fee is charged. A family is considered eligible if:

- The sibling of the neonate has been diagnosed with a disease treatable by a related cord blood transplant
- The neonate does not have the same disease as the affected biological sibling (determined after birth)
- The affected sibling and the neonate have the same biological parents

**OR**

- An affected biological parent is enrolled in a clinical or research trial that would accept a haploidentical, related, allogeneic cord blood unit as a treatment option
Description

This policy addresses the collection, storage, and transplantation of placental and umbilical cord blood ("cord blood") as a source of stem cells for allogeneic and autologous stem cell transplantation. Potential indications for the use of cord blood are not addressed in this policy.

Background

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]). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates. Cord blood transplantation is discussed in detail in a separate policy.

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 six. 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 (eg, 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**

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.
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 a randomized controlled trial (RCT) comparing outcomes after single- or double-cord blood units. The relevant outcomes are overall survival, disease-specific survival, resource utilization, and treatment-related mortality. The meta-analysis of observational studies found similar survival outcomes and lower graft-versus-host disease after cord blood transplantation than bone marrow transplantation. In the RCT, survival rates were similar after single- and double-unit cord blood transplantation. The evidence is sufficient to determine that the technology results in a meaningful 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. The 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.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01728545</td>
<td>The Collection and Storage of Umbilical Cord Blood for Transplantation</td>
<td>250,000</td>
<td>Apr 2099</td>
</tr>
<tr>
<td>NCT00012545</td>
<td>Collection and Storage of Umbilical Cord Stem Cells for Treatment of Sickle Cell Disease</td>
<td>99,999,999</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

NCT: national clinical trial
Practice Guidelines and Position Statements

American Academy of Pediatrics

A position statement on cord blood banking for potential future transplantation was published by the American Academy of Pediatrics in 2017.\textsuperscript{22} The Academy recommended cord blood banking for public use, with a more limited role for private cord blood banking for families with a known fatal illness that could be rescued by cord blood transplant.

American College of Obstetricians and Gynecologists

The American College of Obstetricians and Gynecologists (2015; updated 2019) published an opinion on umbilical cord blood (UCB) banking.\textsuperscript{24} The statement discussed counseling patients about options for UCB banking, as well as benefits and limitations of this practice. The relevant recommendations include the following:

- “[UCB] collected from a neonate cannot be used to treat a genetic disease or malignancy in that same individual.”
- The routine collection and storage of [UCB] with a private cord blood bank is not supported by the available evidence.
- “Private [UCB] banking may be considered when there is knowledge of a family member with a medical condition (malignant or genetic) who could potentially benefit from cord blood transplantation.”
- “Public [UCB] banking is the recommended method of obtaining [UCB] for use in transplantation, immune therapies, or other medically validated indications.”
- “Umbilical cord blood collection should not compromise obstetric or neonatal care or alter routine practice for the timing of umbilical cord clamping.”
- “The current indications for cord blood transplant are limited to select genetic, hematologic, and malignant disorders.”
- “If a patient requests information about [UCB] banking, balanced and accurate information regarding the advantages and disadvantages of public and private [UCB] banking should be provided.”
American Society for Blood and Marrow Transplantation

On behalf of the American Society for Blood and Marrow Transplantation, Ballen et al (2008) published recommendations related to the banking of umbilical cord blood.²⁵

- Public banking of cord blood is “encouraged.”
- Storing cord blood for autologous (i.e., personal) use is “not recommended.”
- “Family member banking (collecting and storing cord blood for a family member) is recommended when there is a sibling with a disease that may be successfully treated with an allogeneic transplant. Family member banking on behalf of a parent with a disease that may be successfully treated with an allogeneic transplant is only recommended when there are shared HLA [human leukocyte-antigens] between the parents.”

Medicare National Coverage

There is no national coverage determination.

Regulatory Status

According to the U.S. Food and Drug Administration, 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 Food and Drug Administration, and use applicable processes for donor suitability determination.¹

References


<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/05/97</td>
<td>Add to Surgery Section - New Policy</td>
</tr>
<tr>
<td>04/09/02</td>
<td>Replace policy - Policy updated and revised based on 2001 TEC Assessment; cord blood as a source of stem cells no longer restricted to children, considered medically necessary in adults.</td>
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<tr>
<td>09/12/03</td>
<td>Replace policy - Policy updated; statement added about storing cord blood stem cells for later possible use as autologous transplant.</td>
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<td>06/09/06</td>
<td>Disclaimer and Scope update - No other changes.</td>
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<td>12/11/07</td>
<td>Replace policy - Reviewed with literature search; no change to policy statement; references added. Reviewed and recommended by OAP on November 15, 2007.</td>
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<td>05/13/08</td>
<td>Cross Reference Update - No other changes.</td>
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<td>12/08/09</td>
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<td>08/10/10</td>
<td>Replace policy - Policy updated with literature review and extensive revisions. References 1, 2 and 5-19 have been added. The intent of the policy statements has not changed.</td>
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<td>11/10/11</td>
<td>Replace policy – Policy updated with literature review; policy statement unchanged. References 3 and 4 added. Related Policies updated.</td>
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<td>01/25/12</td>
<td>Code 38232 added.</td>
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<td>09/10/12</td>
<td>Update Related Policy – Remove 7.01.503 as it was deleted; Add 8.01.21 and 8.01.22. ICD-10 codes are now effective 10/01/2014.</td>
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<td>Update Related Policies – Add 8.01.20, 8.01.29, 8.01.23, 8.01.27, 8.01.28, 8.01.30.</td>
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<td>Date</td>
<td>Comments</td>
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<tr>
<td>12/19/12</td>
<td>Replace policy. Policy updated with literature review; policy statements unchanged. References 5, 9-11 added. Add Related Policies 8.01.24, 8.01.31 and 8.01.35.</td>
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<tr>
<td>02/01/13</td>
<td>Update Related Policies, change title of policy 8.01.21.</td>
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<tr>
<td>02/15/13</td>
<td>Update Related Policies, change title of policy 8.01.30.</td>
</tr>
<tr>
<td>09/30/13</td>
<td>Update Related Policies. Change title of policy 8.01.31.</td>
</tr>
<tr>
<td>12/04/13</td>
<td>Replace policy. Rationale updated based on a literature review through July 25, 2013. References 4, 5, 19, 20, 26, 29, 30 added; others renumbered or removed. Policy statements unchanged.</td>
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<tr>
<td>01/20/14</td>
<td>Update Related Policies. Change title to 8.01.21.</td>
</tr>
<tr>
<td>02/27/14</td>
<td>Update Related Policies. Change title to 8.01.30.</td>
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<tr>
<td>03/21/14</td>
<td>Update Related Policies. Add 8.01.15 and delete 8.01.514.</td>
</tr>
<tr>
<td>04/18/14</td>
<td>Update Related Policies. Delete 8.01.20 and add 8.01.529.</td>
</tr>
<tr>
<td>06/24/14</td>
<td>Update Related Policies. Delete 8.01.35, 8.01.42 and 8.01.54, then add 8.01.530, 8.01.531 and 8.01.532.</td>
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<td>11/20/14</td>
<td>Annual Review. Policy updated with literature review through July 21, 2014. Policy statements unchanged. References 4, 16-17, and 23 added. ICD-9 and ICD-10 procedure codes removed; these are not utilized in adjudication of the policy.</td>
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<tr>
<td>03/08/16</td>
<td>Annual Review. Policy updated with literature review through December 6, 2015; reference 27 added. Policy statements unchanged.</td>
</tr>
<tr>
<td>08/09/16</td>
<td>Update Related Policies. Remove 8.01.27 as it was archived.</td>
</tr>
<tr>
<td>03/14/17</td>
<td>Annual review. Policy updated with literature review through November 9, 2016; references 17 and 23 added. Removed Related Policies. Removed CPT codes 38232 and 38240. Policy statements unchanged.</td>
</tr>
<tr>
<td>10/27/17</td>
<td>Policy moved to new format; no change to policy statements.</td>
</tr>
</tbody>
</table>
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Toll free 855-332-4535, Fax 425-918-5952, TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

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