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.
<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.</td>
</tr>
<tr>
<td></td>
<td>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 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**
### 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

#### Evidence Review
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

Bone Marrow Disorders

A variety of malignant diseases and nonmalignant bone marrow disorders are treated with myeloablative therapy followed by infusion of allogeneic stem and progenitor cells collected from immunologically compatible donors, either from family members or an unrelated donor identified through a bone marrow donor bank. In some cases, a suitable donor is not found.

Blood harvested from the umbilical cord and placenta shortly after delivery of neonates contains stem and progenitor cells capable of restoring hematopoietic function after myeloablation. This cord blood has been used as an alternative source of allogeneic stem cells. Cord blood is readily available and is thought to be antigenically "naive," thus potentially minimizing the incidence of graft-versus-host disease and permitting the broader use of unrelated cord blood transplants. Unrelated donors are typically typed at low resolution for human leukocyte antigen–A and –B and at high resolution only for human leukocyte antigen–DR; human leukocyte antigen matching at 4 of 6 loci is considered acceptable. Under this matching protocol, an acceptable donor can be identified for almost any patient.

Several cord blood banks have now been developed in the United States and Europe. In addition to obtaining cord blood for specific related or unrelated patients, some cord blood banks collect and store neonatal cord blood for some unspecified future use in the unlikely event that the child develops a condition that would require autologous transplantation. Also, some cord blood is collected and stored from a neonate for use by a sibling in whom an allogeneic transplant is anticipated due to a history of leukemia or other condition requiring allogeneic transplant.

Standards and accreditation for cord blood banks are important for assisting transplant programs in knowing whether individual banks have quality control measures in place to address issues such as monitoring cell loss, change in potency, and prevention of product mix-up. Two major organizations have created accreditation standards for cord blood banks in the US: the American Association of Blood Banks (AABB) and the International NetCord
Foundation/Foundation for the Accreditation of Cellular Therapy (NetCord/FACT). Both the AABB and the NetCord/FACT have developed and implemented a program of voluntary inspection and accreditation for cord blood banking. The AABB and the NetCord/FACT publish standards for cord blood banks that define the collection, testing, processing, storage, and release of cord blood products.²

**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. 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. 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>
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</thead>
<tbody>
<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>none</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. 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.

U.K. Consensus Recommendations on Umbilical Cord Blood Transplantation

A consensus conference in the United Kingdom (2015) issued the following recommendation on umbilical cord blood transplantation:

We recommend that UCB [umbilical cord blood] ... be considered as an alternative source of HSC [hematopoietic stem cells] for transplantation for those patients without a suitably matched sibling or unrelated donor, defined as 'standard' or 'clinical option' transplants within the BSBMT [British Society of Blood and Marrow Transplantation] transplant indications tables.
American College of Obstetricians and Gynecologists

The American College of Obstetricians and Gynecologists (2015) published an opinion on umbilical cord blood banking.\textsuperscript{25} The statement discussed counseling patients about options for umbilical cord blood banking, as well as benefits and limitations of this practice. The relevant recommendations include the following:

- “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.”
- “The routine storage of umbilical cord blood as ‘biologic insurance’ against future disease is not recommended.”

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\textsuperscript{26}:

- Public banking of cord blood is “encouraged.”
- Storing cord blood for autologous (ie, 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.³

References


### History

<table>
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<tr>
<th>Date</th>
<th>Comments</th>
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<tr>
<td>05/05/97</td>
<td>Add to Surgery Section - New Policy</td>
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<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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<td>Date</td>
<td>Comments</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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<tr>
<td>06/09/06</td>
<td>Disclaimer and Scope update - No other changes.</td>
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<td>12/11/07</td>
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<td>05/13/08</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>01/25/12</td>
<td>Code 38232 added.</td>
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<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>02/15/13</td>
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<td>02/27/14</td>
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<td>03/21/14</td>
<td>Update Related Policies. Add 8.01.15 and delete 8.01.514.</td>
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<tr>
<td>04/18/14</td>
<td>Update Related Policies. Delete 8.01.20 and add 8.01.529.</td>
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<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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### Comments

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<tr>
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</thead>
<tbody>
<tr>
<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>
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<td>08/09/16</td>
<td>Update Related Policies. Remove 8.01.27 as it was archived.</td>
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<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>
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</tbody>
</table>

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Email AppealsDepartmentInquiries@Premera.com

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U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, DC 20201, 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at

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