Policy Statement

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.

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 is 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.

The transplantation of Hepatitis C Virus (HCV)-viremic solid organs (kidney, lung, heart, liver, small bowel, pancreas) to a HCV non-viremic recipient with a plan to use direct-acting antiviral treatment for HCV is considered **investigational**.

Policy Guidelines

The American Society of Transplantation Consensus Conference on the use of hepatitis C viremic donors in solid organ transplantation concluded that the transplantation of organs from HCV viremic donors into HCV-negative recipients should be conducted only under monitored IRB-approved protocols and studies. (See Supplemental Information).

Please refer to the Blue Shield of California Medical Policy site to search for specific conditions and diseases that have associated medical policies with patient selection criteria regarding situations for which allogeneic stem cell transplantation may be considered medically necessary.

Description

This evidence review 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 herein; they are discussed in the disease-specific evidence reviews.

Related Policies

- Allogeneic Hematopoietic Cell Transplantation for Genetic Diseases and Acquired Anemias
- Allogeneic Hematopoietic Cell Transplantation for Myelodysplastic Syndromes and Myeloproliferative Neoplasms
- Hematopoietic Cell Transplantation for Acute Lymphoblastic Leukemia
- Hematopoietic Cell Transplantation for Acute Myeloid Leukemia
- Hematopoietic Cell Transplantation for Autoimmune Diseases
• Hematopoietic Cell Transplantation for Central Nervous System Embryonal Tumors and Ependymoma
• Hematopoietic Cell Transplantation for Chronic Myeloid Leukemia
• Hematopoietic Cell Transplantation for Epithelial Ovarian Cancer
• Hematopoietic Cell Transplantation for Hodgkin Lymphoma
• Hematopoietic Cell Transplantation for Miscellaneous Solid Tumors in Adults
• Hematopoietic Cell Transplantation for Non-Hodgkin Lymphomas
• Hematopoietic Cell Transplantation for Waldenström Macroglobulinemia
• Hematopoietic Cell Transplantation in the Treatment of Gem Cell Tumors
• High-Dose Rate Temporary Prostate Brachytherapy

**Benefit Application**

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

**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.

**Rationale**

**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 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 been created 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 neonate cord blood for some unspecified future use in the unlikely event that the child develops a condition that would require autologous transplantation. Also, some neonate cord blood is collected and stored for use by a sibling in whom an allogeneic transplant is anticipated due to a history of leukemia or other condition requiring an 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.1 Two major organizations have created accreditation standards for cord blood banks in the U.S.: the American Association of Blood Banks 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

**Literature Review**

This review was informed by a 1996 and a 2001 Blue Cross Blue Shield Association Technology Evaluation Center (TEC) Assessment, which addressed the use of placental and umbilical cord blood in children and adults, respectively.4,5

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

**Cord Blood as Source of Stem Cells for Stem Cell Transplant**

**Clinical Context and Therapy Purpose**

The purpose of using placental and umbilical cord blood as a source of stem cells is to provide an alternative to or an improvement on existing donor sources in patients with an appropriate indication for allogeneic stem cell transplant.

The question addressed in this evidence review is: Does the use of placental and umbilical cord blood as a source of stem cells for individuals with an indication for allogeneic stem cell transplantation result in an improvement in net health outcomes? The following PICOTS were used to select literature to inform this review.

**Patients**

The relevant population of interest are individuals with an appropriate indication for allogeneic stem cell transplant.
Interventions
The test being considered is placental or umbilical cord blood as a source of stem cells for allogeneic stem cell transplantation.

Comparators
Comparators of interest include stem cells from other donor sources.

Outcomes
The general outcomes of interest are overall survival (OS), disease-specific survival, resource utilization, and treatment-related mortality.

Timing
The timing of follow-up is initially the first post-transplant year for successful engraftment and monitoring relevant outcomes. Follow-up is life-long for successful transplantation.

Setting
Patients with an appropriate indication for allogeneic stem cell transplant are managed by a transplant specialist in an inpatient clinical setting.

Study Selection
Methodologically credible studies were selected using the following principles:
   a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
   b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
   c. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
   d. Studies with duplicative or overlapping populations were excluded.

Related Allogeneic Cord Blood Transplant
The first cord blood transplant involved a child with Fanconi anemia; results were reported in 1989. Subsequently, other cord transplants have been performed in matched siblings. The results of these transplants have demonstrated that cord blood contains sufficient numbers of hematopoietic stem and progenitor cells to reconstitute pediatric patients. Lower incidences of acute and chronic graft-versus-host disease (GVHD) have been observed when cord blood, compared with bone marrow, was used as the source of donor cells. This led to the idea that cord blood could be banked and used as a source of unrelated donor cells, possibly without full human leukocyte antigen matching.

Unrelated Allogeneic Cord Blood Transplant
The first prospective evaluation of unrelated cord blood transplant was the Cord Blood Transplantation study, published in 2005. The Cord Blood Transplantation study was designed to examine the safety of unrelated cord blood transplantation in infants, children, and adults. Two-year event-free survival was 55% in children with high-risk malignancies and 78% in children with nonmalignant conditions. Across all groups, the cumulative incidence of engraftment by day 42 was 80%. Engraftment and survival were adversely affected by lower cell doses, pretransplant cytomegalovirus seropositivity in the recipient, non-European ancestry, and higher human leukocyte antigen mismatching. This slower engraftment led to longer hospitalizations and greater utilization of medical resources. In the Cord Blood Transplantation study, outcomes in adults were inferior to the outcomes achieved in children.

Zhang et al (2012) published a meta-analysis of studies comparing unrelated donor cord blood transplantation with unrelated donor bone marrow transplantation in patients who had acute leukemia. Reviewers identified 7 studies (total n=3389 patients). Pooled event rates of engraftment failure (n=5 studies) were 18% (127/694 patients) in the cord blood transplant group and 6% (57/951 patients) in bone marrow transplant groups. The rate of engraftment graft failure
was significantly higher in cord blood transplant recipients (p<0.001). However, rates of acute GVHD were significantly lower in the cord blood transplant group. Pooled event rates of GVHD (n=7 studies) were 34% (397/1179 patients) in the cord blood group and 44% (953/2189 patients) in the bone marrow group (p<0.001). Relapse rates, reported in all studies, did not differ significantly between groups. Several survival outcomes, including OS, leukemia-free survival, and nonrelapse mortality, favored the bone marrow transplant group.

Also, numerous retrospective and registry studies have generally found that unrelated cord blood transplantation is effective in both children and adults with hematologic malignancies and children with a variety of nonmalignant conditions. For example, a study by Liu et al (2014) compared outcomes after unrelated donor cord blood transplantation with matched-sibling donor peripheral blood transplantation. The study included patients ages 16 years or older who had hematologic malignancies. Seventy patients received unrelated cord blood, and 115 patients received human leukocyte antigen-identical peripheral blood stem cells, alone or in combination with bone marrow. Primary engraftment rates were similar in the 2 groups (97% in the cord blood group, 100% in the peripheral blood stem cell group). Rates for most outcomes, including grades III and IV acute GVHD and 3-year disease-free survival, were also similar between groups. However, the rate of chronic GVHD was lower in the unrelated donor cord blood group. Specifically, limited or extensive chronic GVHD occurred in 12 (21%) of 58 evaluable patients in the cord blood group and in 46 (42%) of 109 evaluable patients in the peripheral blood stem cell group (p=0.005).

**Haplo-Cord Blood Transplantation**

Haplo-cord transplants involve a combination of donated cord blood stem cells and half-matched (haploidentical) cells from a related donor.

Mo et al (2016) reported on outcomes after umbilical cord blood and haploidentical hematopoietic cell transplantation in 129 children younger than 14 years old. The 2-year probability of OS was 82% (95% confidence interval [CI], 72.2% to 91.8%) in the haploidentical hematopoietic cell transplantation group and 69.9% (95% CI, 58.0% to 81.2%) in the cord blood group. The difference in OS rates between groups was not statistically significant (p=0.07). The 2-year incidence of relapse was also similar in both groups: 16% (95% CI, 6.1% to 26.1%) in the haplo-HCT group and 24.1% (95% CI, 12.5% to 37.5%) in the cord blood group (p=0.17).

Hsu et al (2018) reported on patients with lymphoma or chronic lymphoblastic leukemia who underwent haplo-cord allogeneic stem cell transplantation. Forty-two patients treated between 2007 and 2016 were included in the analysis. After a median survivor follow-up of 42 months, the median 3-year GVHD relapse-free survival, progression-free survival, and OS were 53% (95% CI: 36-68%), 62% (95% CI: 44-75%), and 65% (95% CI: 48-78%), respectively. The cumulative incidence of relapse was 12% at 100 days and 19.5% at 1 year.

**Double Unit Cord Blood Transplantation**

Transplantation of two umbilical cord blood units (or double-unit transplants) has been evaluated as a strategy to overcome cell dose limitations with one cord blood unit in older and heavier patients. Initial experience at a university showed that using two units of cord blood for a single transplant in adults improved rates of engraftment and OS. Although cell doses are higher with double-unit transplants, studies published to date have found that survival rates are similar to transplants using single-cord blood units, and there is some suggestion of higher rates of GVHD (see Tables 1 and 2).

### Table 1. Summary of Key Trial Characteristics

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Active</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wagner et al (2014)</td>
<td>19, 1</td>
<td>1</td>
<td>Patients (age range, 1-21 y) who had high-risk acute leukemia, chronic myeloid leukemia, or myelodysplastic syndrome for whom there were 2 HLA-matched cord blood units available</td>
<td>2 units</td>
<td>1 unit</td>
<td></td>
</tr>
</tbody>
</table>

HLA: human leukocyte antigen.
Table 2. Summary of Key Trial Results (N=224)

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>Treatment</th>
<th>Dates</th>
<th>Participants</th>
<th>Am 1</th>
<th>Am 2</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wagner et al (2014)19,</td>
<td>Single unit (95% CI), %</td>
<td>2002-2004</td>
<td>Single unit</td>
<td>73 (63 to 80)</td>
<td>0.17</td>
<td>0.011</td>
</tr>
<tr>
<td></td>
<td>Double unit (95% CI), %</td>
<td>2004-2009</td>
<td>Double unit</td>
<td>65 (56 to 74)</td>
<td>0.011</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Cl: confidence interval; DFS: disease-free survival; GVHD: graft-versus-host disease; OS: overall survival.

Results of observational studies are similar to those of the Wagner et al (2014) RCT (see Tables 3 and 4). In a study by Scaradavou et al (2013), there was a significantly higher risk of acute GVHD (grade II-IV) in recipients of double-cord blood units treated during the first several years of observation.20 In the later period (2004-2009), rates of acute GVHD (grade II-IV) did not differ significantly between single and double units of cord blood. An analysis by Baron et al (2017) found no significant differences between single- and double- cord blood transplantation for relapse or nonrelapse mortality, with a trend (p=0.08) toward a higher incidence of GVHD with double units.21

Table 3. Summary of Key Observational Study Characteristics

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Study Type</th>
<th>Dates</th>
<th>Participants</th>
<th>Am 1</th>
<th>Am 2</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scaradavou et al (2013)20.</td>
<td>Comparative cohort</td>
<td>2002-2004</td>
<td>Single unit</td>
<td>6.14 (2.54 to 14.87)</td>
<td>&lt;0.001</td>
<td>0.30</td>
</tr>
<tr>
<td>Baron et al (2017)21.</td>
<td>Registry</td>
<td>2004-2014</td>
<td>Adults with first CBT for AML or ALL</td>
<td>Double unit</td>
<td>0.9 (0.6 to 1.3)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

ALL: acute lymphocytic leukemia; AML: acute myeloid leukemia; CBT: cord blood transplantation.

Table 4. Summary of Key Observational Study Results

<table>
<thead>
<tr>
<th></th>
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<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Scaradavou et al (2013)20.</td>
<td>Single unit</td>
<td>172</td>
<td>28%</td>
<td>6.14 (2.54 to 14.87)</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Double unit</td>
<td>362</td>
<td>36%</td>
<td>0.9 (0.6 to 1.3)</td>
<td>0.08</td>
<td></td>
</tr>
</tbody>
</table>

CI: confidence interval; GVHD: graft-versus-host disease; HR: hazard ratio

Section Summary: Cord Blood as Source of Stem Cells for Stem Cell Transplant

A number of observational studies and meta-analyses of observational studies have compared outcomes after cord blood transplantation with stem cells from a different source. One meta-analysis found similar survival outcomes and lower GVHD after cord blood transplantation than bone marrow transplantation. Also, an RCT has compared single- and double-unit cord blood transplantation and found similar outcomes.

Prophylactic Collection and Storage Of Cord Blood

Clinical Context and Therapy Purpose

The purpose of prophylactic collection and storage of placental or umbilical cord blood stem cells is to provide an alternative donor source for individuals without or with an unspecified potential future need for stem cell transplant.

The question addressed in this evidence review is: Does the prophylactic collection and storage of placenta and umbilical cord blood stem cells provide an alternative donor source for stem cell transplant?
individuals without or with an unspecified potential future need for stem cell transplantation improve net health outcomes.

The following PICOTS were used to select literature to inform this review.

**Patients**
The relevant population of interest are individuals without or with an unspecified potential future need for stem cell transplant.

**Interventions**
The test being considered is prophylactic collection and storage of placental or umbilical cord blood stem cells.

**Comparators**
Comparators of interest include usual care without prophylactic storage of cord blood.

**Outcomes**
The general outcomes of interest are OS, disease-specific survival, resource utilization, and treatment-related mortality.

**Timing**
The future use of stored stem cells is unknown and, thus, the follow-up time period to transplant is indeterminate.

**Setting**
Collection and preservation of placental or umbilical cord for future use is carried out at the time of labor and delivery and is carried out by commercial service providers.

**Study Selection**
Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

No studies have compared outcomes after prophylactic collection and storage of cord blood from a neonate for individuals who have an unspecified future need for transplant with standard care without cord blood collection and storage.

Also, although blood banks are collecting and storing neonate cord blood for potential future use, data on the use of cord blood for autologous stem cell transplantation are limited. A 2017 position paper from the American Academy of Pediatrics noted that there is little evidence of the safety or effectiveness of autologous cord blood transplantation for treatment of malignant neoplasms. Also, a 2009 survey of pediatric hematologists noted few transplants had been performed using cord blood stored in the absence of a known indication.

**Section Summary: Prophylactic Collection and Storage of Cord Blood**
There is a lack of published evidence comparing outcomes after prophylactic collection and storage of cord blood from a neonate for individuals who have an unspecified future need for transplant with standard care without cord blood collection and storage.
Summary of Evidence
For individuals who have an appropriate indication for an 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 an RCT comparing outcomes after single- or double-cord blood units. The relevant outcomes are OS, disease-specific survival, resource utilization, and treatment-related mortality. The meta-analysis of observational studies found similar survival outcomes and lower GVHD 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.

Supplemental Information
Practice Guidelines and Position Statements
The American Society of Transplantation (2017) convened a consensus conference of experts to address issues related to the transplantation of hepatitis C virus (HCV) viremic solid organs into HCV non-viremic recipients.27 Key findings and recommendations are summarized in Table 5.

Table 5. American Society of Transplantation Consensus Conference - Use of HCV Viremic Donors

<table>
<thead>
<tr>
<th>Content Area</th>
<th>Key Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Definition of HCV positive</td>
<td>HCV – viremic reflecting a positive NAT should be adopted</td>
</tr>
<tr>
<td>2. Data interpretation</td>
<td>HCV antibody status alone limits interpretation of outcomes of transplantation of HCV “positive” organs</td>
</tr>
<tr>
<td>3. Transmission and Treatment</td>
<td>Highest risk for unexpected HCV transmission is associated with organ donation from a person who injected drugs within the eclipse or pre-viremic period</td>
</tr>
<tr>
<td>4. OPTN policy</td>
<td>No current policies prevent transplantation of HCV-viremic organs into HCV non-viremic recipients</td>
</tr>
<tr>
<td>5. Ethical considerations</td>
<td>Transplantation of HCV-viremic organs into HCV non-viremic recipients should be conducted under site specific IRB approved protocols with multi-step informed consent.</td>
</tr>
</tbody>
</table>

American Academy of Pediatrics
A position statement on cord blood banking for potential future transplantation was published by the American Academy of Pediatrics in 2017.22 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.

U.K. Consensus Recommendations on Umbilical Cord Blood Transplantation
A consensus conference in the United Kingdom (2015) issued the following recommendation on UCB transplantation24:

“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 UCB banking. The statement discussed counseling patients on options for UBC banking, as well as the benefits and limitations of this practice. The relevant recommendations included 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:

1. Public banking of cord blood is “encouraged.”
2. Storing cord blood for autologous (i.e., personal) use “is not recommended.”
3. “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.”

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 6.

Table 6. 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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<tbody>
<tr>
<td>Ongoing</td>
<td>The Collection and Storage of Umbilical Cord Blood for Transplantation</td>
<td>250,000</td>
<td>Apr 2099</td>
</tr>
<tr>
<td>NCT01728545</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.

References

5. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Transplanting Adult Patients with Hematopoietic Stem Cells from Placental and Umbilical Cord Blood TEC Assessments. 2001;Volume 16:Tab 17. PMID

**Documentation for Clinical Review**

Please provide the following documentation (if/when requested):

- Referring physician history and physical
- Bone marrow transplant consultation report and/or progress notes documenting:
  - Diagnosis (including disease staging) and prognosis
  - Synopsis of alternative treatments performed and results
  - Specific transplant type being requested
- Surgical consultation report and/or progress notes
- Results of completed transplant evaluation including:
  - Clinical history
  - Specific issues identified during the transplant evaluation
  - Consultation reports/letters (when applicable)
  - Correspondence from referring physicians (when applicable)
  - Identification of donor for allogeneic related bone marrow/stem cell transplant (when information available)
- Medical social service/social worker and/or psychiatric (if issues are noted) evaluations including psychosocial assessment or impression of patient’s ability to be an adequate candidate for transplant
- Radiology reports including:
  - Chest x-ray (CXR)
  - PET scan, CT scan and bone survey (as appropriate)
- Cardiology procedures and pulmonary function reports:
  - EKG
  - Echocardiogram
  - Pulmonary function tests (PFTs)
- Biopsy/Pathology reports including:
  - Bone marrow biopsy
  - Lymph node biopsy (as appropriate)
- Laboratory reports
Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

MN/IE

The following services may be considered medically necessary in certain instances and investigational in others. Services may be considered medically necessary when policy criteria are met. Services may be considered investigational when the policy criteria are not met or when the code describes application of a product in the position statement that is investigational.

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
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<tr>
<td>CPT®</td>
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<td>None</td>
</tr>
<tr>
<td>HCPCS</td>
<td>S2140</td>
<td>Cord blood harvesting for transplantation, allogeneic</td>
</tr>
<tr>
<td></td>
<td>S2142</td>
<td>Cord blood-derived stem-cell transplantation, allogeneic</td>
</tr>
<tr>
<td></td>
<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>
<tr>
<td>ICD-10 Procedure</td>
<td>30243X0</td>
<td>Transfusion of Autologous Cord Blood Stem Cells into Central Vein, Percutaneous Approach</td>
</tr>
<tr>
<td></td>
<td>30243X2</td>
<td>Transfusion of Allogeneic Related Cord Blood Stem Cells into Central Vein, Percutaneous Approach</td>
</tr>
<tr>
<td></td>
<td>30243X3</td>
<td>Transfusion of Allogeneic Unrelated Cord Blood Stem Cells into Central Vein, Percutaneous Approach</td>
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<tr>
<td></td>
<td>30243X4</td>
<td>Transfusion of Allogeneic Unspecified Cord Blood Stem Cells into Central Vein, Percutaneous Approach</td>
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</table>

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
<th>Reason</th>
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<tr>
<td>01/07/2011</td>
<td>BCBSA Medical Policy adoption</td>
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<tr>
<td>05/29/2015</td>
<td>Coding update</td>
<td>Administrative Review</td>
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<td>12/04/2015</td>
<td>Policy title change from Placental/Umbilical Cord Blood as a Source of Stem Cells Policy revision without position change</td>
<td>Medical Policy Committee</td>
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<tr>
<td>04/01/2016</td>
<td>Policy revision without position change</td>
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<tr>
<td>03/01/2017</td>
<td>Policy revision without position change</td>
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<td>03/01/2018</td>
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<td>03/01/2019</td>
<td>Policy revision without position change</td>
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<tr>
<td>11/01/2019</td>
<td>Policy revision without position change</td>
<td>Administrative Review</td>
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Definitions of Decision Determinations

**Medically Necessary:** A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

**Investigational/Experimental:** A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state government is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should also be directed to the Transplant Case Management Department. Please call 1-800-637-2066 ext. 3507708 or visit the Provider Portal www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.