HEMATOPOIETIC CELL TRANSPLANTATION FOR GENETIC DISEASES AND ACQUIRED ANEMIAS

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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HEMATOPOIETIC CELL TRANSPLANTATION FOR GENETIC DISEASES AND ACQUIRED ANEMIAS (cont.)

**Description:**

Hematopoietic Cell Transplantation (HCT):
Hematopoietic stem cells form blood and immune cells. HCT is a procedure in which hematopoietic stem cells are infused into a recipient with deficient bone marrow function. Bone marrow stem cells may be obtained from the transplant recipient (autologous HCT) or a donor (allogeneic HCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood and placenta shortly after a delivery. HCT may also be referred to as bone marrow transplant (BMT) or stem cell transplantation (SCT).

High-Dose Chemotherapy (HDC):
HDC is the administration of myelotoxic agents at doses sufficient to cause bone marrow failure. Myeloablative chemotherapy eradicates cancerous cells from the blood and bone marrow and inhibits the immune response against the donor bone marrow. HDC may be given with or without total body radiation.

Nonmyeloablative Chemotherapy With Allogeneic Hematopoietic Cell Transplantation (HCT):
Nonmyeloablative or reduced-intensity conditioning (RIC) is the administration of a lower dose of chemotherapy that is sufficient to eradicate the hematopoietic cells but does not completely destroy the bone marrow. RIC regimens attempt to reduce adverse effects secondary to bone marrow toxicity and allow for relatively prompt hematopoietic recovery. Nonmyeloablative chemotherapy may also be referred to as RIC, “mini transplant” or “transplant lite”.

**Donor Types:**
- Allogeneic: From a third-party donor

**Criteria:**

All stem cell transplants will be reviewed by the medical director(s) and/or clinical advisor(s).

- HDC with allogeneic HCT for an individual with a genetic disease or acquired anemia is considered **medically necessary** with documentation of ALL of the following:

  1. **ONE** of the following:

    **Bone Marrow Failure Syndromes:**
    - Aplastic anemia including hereditary (including Fanconi anemia, dyskeratosis congenital, Shwachman-Diamond syndrome, Diamond-Blackfan syndrome) or acquired (e.g., secondary to drug or toxin exposure) forms.

    **Genetic Disorders Affecting Skeletal Tissue:**
    - Infantile malignant osteopetrosis (Albers-Schonberg disease or marble bone disease).
HEMATOPOIETIC CELL TRANSPLANTATION FOR GENETIC DISEASES AND ACQUIRED ANEMIAS (cont.)

Criteria: (cont.)

- HDC with allogeneic HCT for an individual with a genetic disease or acquired anemia is considered medically necessary with documentation of ALL of the following: (cont.)

1. ONE of the following: (cont.)

   Hemoglobinopathies:
   - Homozygous beta-thalassemia (i.e., thalassemia major)
   - Sickle cell anemia

   Inherited Metabolic Disease:
   - Alpha-mannosidosis
   - Aspartylglucosaminuria
   - Cerebral X-linked adrenoleukodystrophy (childhood onset)
   - Farber lipogranulomatosis
   - Fucosidosis
   - Galactosialidosis
   - Gaucher types 1 and 3
   - GM1 gangliosidosis
   - Globoid-cell leukodystrophy
   - Hurler
   - Lysosomal and peroxisomal storage disorders
   - Maroteaux-Lamy
   - Metachromatic leukodystrophy
   - Mucolipidos
   - Mucopolysaccharidosis (including Hunter, Sanfilippo, Morquio syndromes)
   - Mucolipidosis II (I-cell disease)
   - Multiple sulfatase deficiency
   - Neuronal ceroid lipofuscinosis
   - Niemann-Pick disease
   - Sly syndromes
   - Slylidosis
   - Wolman disease
HEMATOPOIETIC CELL TRANSPLANTATION FOR GENETIC DISEASES AND ACQUIRED ANEMIAS (cont.)

Criteria: (cont.)

- HDC with allogeneic HCT for an individual with a genetic disease or acquired anemia is considered medically necessary with documentation of ALL of the following: (cont.)

1. **ONE** of the following: (cont.)

   Lymphocyte Immunodeficiencies:
   - Adenosine deaminase deficiency
   - Artemis deficiency
   - Calcium channel deficiency
   - CD 40 ligand deficiency
   - Cernunnos/X-linked lymphoproliferative disease deficiency
   - CHARGE syndrome with immune deficiency
   - Common gamma chain deficiency
   - Deficiencies in CD 45, CD3, CD8
   - DiGeorge syndrome
   - DNA ligase IV deficiency syndrome
   - Interleukin-7 receptor alpha deficiency
   - Janus-associated kinase 3 deficiency
   - Major histocompatibility class II deficiency
   - Omenn syndrome
   - Purine nucleoside phosphorylase deficiency
   - Recombinase-activating gene 1/2 deficiency
   - Reticular dysgenesis
   - Winged helix deficiency
   - Wiskott-Aldrich syndrome
   - X-linked lymphoproliferative disease
   - Zeta-chain-associated protein-70 deficiency

Phagocytic Deficiencies:
- Chédiak-Higashi syndrome
- Chronic granulomatous disease
- Griscelli syndrome, type 2
- Hemophagocytic lymphohistiocytosis
- Interferon-gamma receptor deficiencies
- Leukocyte adhesion deficiency
- Severe congenital neutropenias
- Shwachman-Diamond syndrome
HEMATOPOIETIC CELL TRANSPLANTATION FOR GENETIC DISEASES AND ACQUIRED ANEMIAS (cont.)

Criteria: (cont.)

➢ HDC with allogeneic HCT for an individual with a genetic disease or acquired anemia is considered *medically necessary* with documentation of ALL of the following: (cont.)

1. **ONE** of the following: (cont.)

   - **Primary Immunodeficiencies:**
     - Absent or defective T cell function (e.g., severe combined immunodeficiency, Wiskott-Aldrich syndrome, X-linked lymphoproliferative syndrome)
     - Absent or defective natural killer function (e.g. Chédiak-Higashi syndrome)
     - Absent of defective neutrophil function (e.g. Kostmann syndrome, chronic granulomatous disease, leukocyte adhesion defect)

   - **Other Immunodeficiencies:**
     - Autoimmune lymphoproliferative syndrome
     - Cartilage hair hypoplasia
     - CD25 deficiency
     - Hyper IgD and IgE syndromes
     - Immunodeficiency, centromeric instability and facial dysmorphism syndrome
     - Immunodysregulation, polyendocrinopathy enteropathy X-linked syndrome
     - Nuclear factor-κ B (NF-κB) essential modulator deficiency
     - NF-κB inhibitor, NF-κB-a deficiency
     - Nijmegen breakage syndrome

➢ HCT for an individual with a genetic disease or acquired anemia for all other indications not previously listed or if above criteria not met is considered experimental or investigational based upon:

1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
2. Insufficient evidence to support improvement of the net health outcome, and
3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives.

1 Although specific transplantation procedures may be considered experimental or investigational and therefore not eligible for coverage under standard medical benefits, these procedures may be eligible for coverage based upon Arizona Revised Statutes §20-2326 concerning Cancer Clinical Trials.
HEMATOPOIETIC CELL TRANSPLANTATION FOR GENETIC DISEASES AND ACQUIRED ANEMIAS (cont.)

Resources:

Literature reviewed 11/07/17. We do not include marketing materials, poster boards and non-published literature in our review.

The BCBS Association Medical Policy Reference Manual (MPRM) policy is included in our guideline review. References cited in the MPRM policy are not duplicated on this guideline.

Resources prior to 12/10/13 may be requested from the BCBSAZ Medical Policy and Technology Research Department.

HEMATOPOIETIC CELL TRANSPLANTATION FOR GENETIC DISEASES AND ACQUIRED ANEMIAS (cont.)

Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ’s Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ’s Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: 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 http://www.hhs.gov/ocr/office/file/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe’é atah nílínígíí Blue Cross Blue Shield of Arizona haada ylt’éego bina’ídííkidgo éí doodago Háida bíjá aniyeedííí t’aadowó le’é yína’ídííkidgo bæheæz’æænií hólo dúuí t’aa hazaad’ehí háká a’doowolgo bee hæ’á doo baaíh ilínígö. Ata’ halné’íígií koj’ bich’é’ hodiilíhí 877-475-4799.

Chinese: 如果您，或是您正在协助的对象，有关于插入项目的名称 Blue Cross Blue Shield of Arizona 方面的问题，您有权利免费以您的母语得到帮助和讯息。洽询一位翻译员，请拨电话 在此插入数字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thợ dịch viên, xin gọi 877-475-4799.

Arabic:

إن كان لديك أو أدى شخص تساءله أسئلة بخصوص Blue Cross Blue Shield of Arizona للحصول على المساعدة والمعلومات الضرورية باتجاه من دون أي تكلفة. للتحدث مع متزوج اتصل ب. 877-475-4799
HEMATOPOIETIC CELL TRANSPLANTATION FOR GENETIC DISEASES AND ACQUIRED ANEMIAS (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutulungan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuha ng tulong at impormasyon sa iyong wika ng walang gastos. Upang makausap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관해서 질문이 있다면 귀하의 도움과 정보를 귀하의 언어로 바꿀 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 동역사와 얘기하기 위해서는 877-475-4799로 전화하십시오.

French: Si vous, ou quelqu’un que vous êtes en train d’aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d’obtenir de l’aide et l’information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizonaについてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799 までお電話ください。

Farsi:

ازمانه، یا کسی که شما به او کمک می‌کنید، سوال در مورد اطلاعات به زبان خود را به طور رایگان دریافت نمایید 877-475-4799.

Assyrian:

Blue Cross Blue Shield of Arizona . نهش بو نهش بو، 877-475-4799.

Serbo-Croatian: Ukoliko Vi ili neko kome Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da bespletno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodiocem, nazovite 877-475-4799.

Thai: หากคุณหรือคนที่คุณช่วยเหลือถามคำถามเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณสามารถจะได้รับความช่วยเหลือและข้อมูลภาษา ของคุณโดยไม่มีค่าใช้จ่าย ด้วยหมายเลข โทร 877-475-4799