



MEDICAL COVERAGE GUIDELINES
SECTION: MEDICINE

ORIGINAL EFFECTIVE DATE: 11/05/14
LAST REVIEW DATE: 10/16/18
LAST CRITERIA REVISION DATE: 11/08/16
ARCHIVE DATE:

HEMATOPOIETIC CELL TRANSPLANTATION

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 (cont.)

Description:

Hematopoietic Cell Transplantation (HCT):

Hematopoietic stem cells form blood and immune cells. HCT is a procedure in which hematopoietic 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 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
- Autologous: From an individual's own bone marrow and/or circulating blood
- Syngeneic: From an identical twin

Definitions:

Refractory/Primary Refractory:

The disease is resistant to treatment and does not achieve a complete remission.

Relapse:

The recurrence of a disease or symptoms after apparent recovery.

Remission:

Period of time when cancer is responding to treatment or is under control. In complete remission, all signs and symptoms of the disease have disappeared.

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HEMATOPOIETIC CELL TRANSPLANTATION (cont.)

Criteria:

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

A. Hematopoietic Cell Transplant:

CONDITION	MEDICALLY NECESSARY	EXPERIMENTAL OR INVESTIGATIONAL ¹
		¹ See Criteria C for Rationale
Chronic granulomatous disease	<ul style="list-style-type: none"> ➤ Nonmyeloablative reduced-intensity conditioning (RIC) with allogeneic SCT 	
Granulocytic Sarcoma Also known as: <ul style="list-style-type: none"> - Chloroma - Extramedullary myeloid tumor - Myeloblastoma - Myeloid Sarcoma 	<ul style="list-style-type: none"> ➤ HDC with allogeneic HCT must meet Criteria B and ANY of the following: <ol style="list-style-type: none"> 1. To induce remission 2. Following first remission in chemoresponsive disease ➤ Nonmyeloablative reduced-intensity conditioning (RIC) with allogeneic HCT for individual who meets criteria for allogeneic HCT but is medically unable to tolerate HDC 	<ul style="list-style-type: none"> ➤ HDC with autologous HCT
HIV Associated Lymphoma	<ul style="list-style-type: none"> ➤ HDC with autologous HCT with ALL of the following: <ol style="list-style-type: none"> 1. Current use of HAART 2. Undetectable HIV viral load 3. First remission or chemosensitive lymphoma in relapse 	<ul style="list-style-type: none"> ➤ HDC with allogeneic HCT

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Criteria: (cont.)

A. Hematopoietic Cell Transplant: (cont.)

CONDITION	MEDICALLY NECESSARY	EXPERIMENTAL OR INVESTIGATIONAL ¹
Promyelocytic Leukemia, Acute (APL)	<ul style="list-style-type: none"> ➤ HDC with allogeneic or autologous HCT for ANY of the following: <ol style="list-style-type: none"> 1. 1st complete remission 2. Primary refractory 3. Relapsed 	<p>¹ See Criteria C for Rationale</p> <ul style="list-style-type: none"> ➤ HDC with allogeneic HCT for relapse after a prior course of HDC with autologous HCT if autologous HCT was less than 6 months ago
Paroxysmal Nocturnal Hemoglobinuria (PNH)	<ul style="list-style-type: none"> ➤ HDC with allogeneic or syngeneic HCT for ANY of the following: <ol style="list-style-type: none"> 1. Refractory 2. Life threatening complications (i.e., blood clots, progression to aplastic anemia or acute myelogenous leukemia) 	



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Criteria: (cont.)

B. Pretransplantation Evaluation:

- Human Leukocyte Antigen (HLA) typing and Matched Unrelated Donor (MUD) searches may be approved by the coordinator if the prior medical necessity criteria are met. HLA typing may use serologic tissue and/or DNA (gene) for more precise matching. The psychosocial criteria listed below must only be met prior to the actual transplant procedure.
- Pretransplantation evaluation with documentation of **ALL** of the following:
 1. Psychosocial screen with documentation of **ALL** of the following:
 - Drug/alcohol screen with documentation of **ONE** of the following:
 - No drug/alcohol abuse by history
 - Drug and alcohol free for a period greater than or equal to 6 months
 - Behavioral health disorder screening with documentation of **ONE** of the following:
 - No behavioral health disorder by history and physical exam
 - Behavioral health disorder treated
 2. Adequate social/family support
 3. Performance status² with documentation of **ONE** of the following:
 - Karnofsky score greater than or equal to 70%
 - Eastern Cooperative Oncology Group (ECOG) score 0-2
 - For ages 10 or under: Lansky Play score greater than or equal to 70. A Lansky Play score less than 70 **will be reviewed by the medical director(s) and/or clinical advisor(s)**.

² Performance status tables are located at the end of the Criteria section.



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Criteria: (cont.)

C. Experimental or Investigational Procedures:

- Transplant procedures described as experimental or investigational in Criteria A are considered ***experimental or investigational***¹ 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.

Performance Status Tables:

Eastern Cooperative Oncology Group (ECOG) Score (Also known as Zubrod Score):

0	Asymptomatic. Fully active, able to carry on all pre-disease performance without restriction.
1	Symptomatic, fully ambulatory. Restricted in physically strenuous activity but able to carry out work of a light or sedentary nature.
2	Symptomatic, in bed less than 50% of the day. Capable of all self-care but unable to carry out any work activities.
3	Symptomatic, in bed or chair more than 50% of the day but not bedridden. Capable of only limited self-care.
4	Bedridden. Cannot perform any self-care.
5	Dead

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Criteria: (cont.)

Performance Status Tables: (cont.)

Karnofsky Performance Score:

100%	Able to carry on normal activity, no evidence of disease.
90%	Able to carry on normal activity, minor signs or symptoms of disease.
80%	Normal activity with effort, some signs and symptoms of disease.
70%	Cares for self, unable to carry on normal activity or to work.
60%	Requires occasional assistance from others but able to care for most needs
50%	Requires considerable assistance from others and frequent medical care
40%	Disabled, requires special care and assistance.
30%	Severely disabled, hospitalization indicated, death not imminent.
20%	Very sick, hospitalization indicated, active support treatment necessary.
10%	Moribund
0%	Dead

Lansky Play Score (Also known as Lansky Play - Performance Scale):

100	Fully active, normal.
90	Minor restrictions in physically strenuous activity
80	Active, but tires more quickly.
70	Both greater restriction of and less time spent in play activity
60	Up and around, but minimal active play; keeps busy with quieter activities.
50	Gets dressed but lies around much of the day, no active play but able to participate in all quiet play and activities.
40	Mostly in bed; participates in quiet activities.
30	In bed; needs assistance even for quiet play.
20	Often sleeping; play entirely limited to very passive activities.
10	No play; does not get out of bed.
0	Unresponsive



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Resources:

Resources published prior to 2006 may be requested from the BCBSAZ Medical Policy and Technology Research Department.

Literature reviewed 11/28/17. We do not include marketing materials, poster boards and non-published literature in our review.

1. Clinical Trials.gov. Cyclophosphamide and rATG With Hematopoietic Stem Cell Support in Systemic Scleroderma. Accessed 01/16/2008.
2. Duarte RF, Salgado M, Sanchez-Ortega I, et al. CCR5 Delta32 homozygous cord blood allogeneic transplantation in a patient with HIV: a case report. *The lancet. HIV*. Jun 2015;2(6):e236-242.
3. External Consultant. Hematology. 07/2008.
4. External Consultant Review. Hematology. 01/2008.
5. FDA Oncology Tools. Performance Status. Accessed 01/22/2007.
6. Holter Chakrabarty JL, Rubinger M, Le-Rademacher J, et al. Autologous is superior to allogeneic hematopoietic cell transplantation for acute promyelocytic leukemia in second complete remission. *Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation*. Jul 2014;20(7):1021-1025.
7. InterQual® Care Planning Procedures. Transplantation, Allogeneic Stem Cell.
8. InterQual® Care Planning Procedures. Transplantation, Autologous Stem Cell.
9. Krishnan A, Zaia JA. HIV-associated non-Hodgkin lymphoma: viral origins and therapeutic options. *Hematology. American Society of Hematology. Education Program*. Dec 5 2014;2014(1):584-589.
10. Matsui T, Hidaka M, Kiyokawa T, Murayama T, Kawano F. Successful treatment of bulky granulocytic sarcoma of the retroperitoneum with high-dose chemotherapy and autologous peripheral blood stem cell transplantation. *Journal of clinical and experimental hematopathology : JCEH*. 2013;53(3):235-239.



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Resources: (cont.)

11. Tan D, Wong GC, Koh LP, et al. Successful treatment of primary granulocytic sarcoma by non-myeloablative stem cell transplant. *Leuk Lymphoma*. 2006 Jan 2006;47(1):159-162.
12. UpToDate.com. Chronic Granulomatous Disease: Treatment and Prognosis. 07/14/2015.
13. UpToDate.com. Treatment of relapsed or refractory acute promyelocytic leukemia in adults. 09/13/2015.
14. UpToDate.com. Treatment and prognosis of paroxysmal nocturnal hemoglobinuria. 03/21/2016.
15. UpToDate.com. AIDS-related lymphomas: Treatment of systemic lymphoma. 02/09/2016.



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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 nilínigíí Blue Cross Blue Shield of Arizona haada yit'éego bina'idííkidgo éí doodago Háida bíjá anilyeedígíí t'áadoo le'é yina'idííkidgo beehaz'áanii hólg díí t'áa hazaadk'ehjí háká a'doowołgo bee haz'ą doo baqah ilínígóó. Ata' halne'ígíí kojí' bich'í' hodíilnih 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 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 thông dịch viên, xin gọi 877-475-4799.

Arabic:

إن كان لديك أو لدى شخص تساعد أسئلة بخصوص Blue Cross Blue Shield of Arizona، فلديك الحق في الحصول على المساعدة والمعلومات الضرورية بلغتك من دون أية تكلفة. للتحدث مع مترجم اتصل بـ 877-475-4799.

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Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutulangan, 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 Arizona 에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 통역사와 얘기하기 위해서는 877-475-4799 로 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:

اگر شما، یا کسی که شما به او کمک میکنید، سوال در مورد Blue Cross Blue Shield of Arizona، داشته باشید حق این را دارید که کمک و اطلاعات به زبان خود را به طور رایگان دریافت نمایید 877-475-4799 [تماس حاصل نمایید].

Assyrian:

Blue Cross Blue Shield of Arizona، ئەگەر تۆنێک یان کێسێک وێهێنێت، ئەتوانێت بە ئەزەزێکی بێهەنە وێهێنێت، ئەگەر تۆنێک یان کێسێک وێهێنێت، ئەتوانێت بە ئەزەزێکی بێهەنە وێهێنێت، ئەگەر تۆنێک یان کێسێک وێهێنێت، ئەتوانێت بە ئەزەزێکی بێهەنە وێهێنێت. 877-475-4799.

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

Thai: หากคุณ หรือคนที่คุณกำลังช่วยเหลือถามเกี่ยวกับ Blue Cross Blue Shield of Arizona คนมีสิทธิที่จะได้รับความช่วยเหลือและขอมลในภาษา ของคุณได้โดยไม่มีค่าใช้จ่าย โปรดขงสอบถาม โทร 877-475-4799