



MEDICAL COVERAGE GUIDELINES
SECTION: MEDICINE

ORIGINAL EFFECTIVE DATE: 05/06/15
LAST REVIEW DATE: 06/05/18
LAST CRITERIA REVISION DATE: 06/05/18
ARCHIVE DATE:

HEMATOPOIETIC CELL TRANSPLANTATION FOR SOLID TUMORS OF CHILDHOOD

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 SOLID TUMORS OF CHILDHOOD (cont.)

Description:

Solid tumors of childhood include, but are not limited to the following:

- Desmoplastic small cell
- Ewing's sarcoma/Ewing sarcoma family of tumors (ESFT)
- Neuroblastoma
- Osteosarcoma
- Retinoblastoma
- Rhabdomyosarcoma
- Wilms' tumor

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 SCT) or a donor (allogeneic SCT). 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).

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 (SCT):

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

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.



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Description: (cont.)

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.

Tandem Transplant:

Two successive cycles of high-dose chemotherapy, each followed by infusion of autologous stem cells, whether or not there is evidence of persistent disease following the first treatment.

Criteria:

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

Ewing's Sarcoma:

- HDC with autologous HCT for an individual with Ewing's sarcoma is considered **medically necessary** with documentation of **ANY** of the following:
 1. Initial treatment of high risk Ewing's sarcoma (e.g., metastatic disease, larger tumor size, older age of individual, tumor location)
 2. Refractory disease
 3. Recurrent disease

- The following treatments for an individual with Ewing's sarcoma 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.

These treatments include, *but are not limited to*:

- HDC with autologous HCT as initial treatment of low or intermediate risk Ewing's sarcoma
- HDC with allogeneic (myelo or nonmyeloablative) HCT
- Tandem transplant with autologous HCT
- Salvage allogeneic hematopoietic cell transplantation for pediatric solid tumors that relapse after autologous transplant or fail to respond



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Criteria: (cont.)

Neuroblastoma:

- HDC with autologous HCT for an individual with neuroblastoma is considered **medically necessary** with documentation of **ANY** of the following:
 1. Initial treatment of high risk neuroblastoma (e.g., age older than 1 year, disseminated disease, MYCN oncogene amplification, unfavorable histopathologic findings)
 2. Refractory disease
 3. Recurrent disease
- Tandem transplant with autologous HCT for an individual with high-risk neuroblastoma is considered **medically necessary**.
- The following treatments for an individual with neuroblastoma 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.

These treatments include, *but are not limited to*:

- HDC with autologous HCT as initial treatment of low or intermediate risk neuroblastoma
- HDC with allogeneic (myelo or nonmyeloablative) HCT
- Tandem transplant with autologous HCT excluding tandem transplant with autologous HCT for high-risk neuroblastoma
- Salvage allogeneic hematopoietic cell transplantation for pediatric solid tumors that relapse after autologous transplant or fail to respond



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Criteria: (cont.)

Retinoblastoma:

- HDC with autologous HCT for an individual with metastatic retinoblastoma is considered **medically necessary**
- The following treatments for an individual with retinoblastoma are considered **experimental or investigational¹** 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.

These treatments include, *but are not limited to:*

- HDC with autologous HCT for retinoblastoma without metastasis
- HDC with allogeneic (myelo or nonmyeloablative) HCT
- Tandem transplant with autologous HCT
- Salvage allogeneic hematopoietic cell transplantation for pediatric solid tumors that relapse after autologous transplant or fail to respond

HEMATOPOIETIC CELL TRANSPLANTATION FOR SOLID TUMORS OF CHILDHOOD (cont.)

Criteria: (cont.)

Other Solid Tumors of Childhood:

- HDC with autologous HCT for all other solid tumors of childhood 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.

These solid tumors include, *but are not limited to*:

- Desmoplastic small cell tumor
- Osteosarcoma
- Rhabdomyosarcoma
- Wilms' tumor

- The following treatments for all other solid tumors of childhood not previously listed or if above criteria not met 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.

These treatments include, *but are not limited to*:

- HDC with autologous HCT
- HDC with allogeneic (myelo or nonmyeloablative) HCT
- Tandem transplant with autologous HCT
- Salvage allogeneic hematopoietic cell transplantation for pediatric solid tumors that relapse after autologous transplant or fail to respond

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.



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Resources:

Literature reviewed 06/05/18. 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 05/28/13 may be requested from the BCBSAZ Medical Policy and Technology Research Department.

1. 8.01.34 BCBS Association Medical Policy Reference Manual. Hematopoietic Cell Transplantation for Solid Tumors of Childhood. Re-issue date 02/08/2018, issue date 04/30/2000.
2. Al Balushi Z, Bulduc S, Mulleur C, Lallier M. Desmoplastic small round cell tumor in children: a new therapeutic approach. *J Pediatr Surg*. May 2009;44(5):949-952.
3. Bisogno G, Ferrari A, Rosolen A, et al. Sequential intensified chemotherapy with stem cell rescue for children and adolescents with desmoplastic small round-cell tumor. *Bone Marrow Transplant*. May 2010;45(5):907-911.
4. Children's Oncology Group. In treatment for soft tissue sarcoma 7/2011.
5. Cook RJ, Wang Z, Arora M, et al. Clinical outcomes of patients with desmoplastic small round cell tumor of the peritoneum undergoing autologous HCT: a CIBMTR retrospective analysis. *Bone Marrow Transplant*. Nov 2012;47(11):1455-1458.
6. Hayes-Jordan A, Anderson PM. The diagnosis and management of desmoplastic small round cell tumor: a review. *Curr Opin Oncol*. Jul 2011;23(4):385-389.
7. Jordan AH, Pappo A. Management of desmoplastic small round-cell tumors in children and young adults. *J Pediatr Hematol Oncol*. May 2012;34 Suppl 2:S73-75.
8. Journal of Pediatric Surgery. Desmoplastic small round cell tumor in children: a new therapeutic approach *Journal of Pediatric Surgery*. August 2008;Volume 44.(Issue 5):949-952.
9. National Cancer Institute. Childhood Soft Tissue Sarcoma Treatment (PDQ®) 04/02/2018, 2/15/2017, 4/2/2015, 3/15/2013
10. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Soft Tissue Sarcoma. 03/27/2018 Version 2.2018, 11/30/2012 Version 3.2012.



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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 nilinígíí Blue Cross Blue Shield of Arizona haada yit'éego bina'idííkidgo éí doodago Háida bíjá anilyeedígíí t'áadoo le'é yina'idííkidgo beehaz'ánii hólo díí t'áa hazaadk'ehjí háká a'doowołgo bee haz'ą doo baqah ilinígóó. 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.

