



MEDICAL COVERAGE GUIDELINES
SECTION: MEDICINE

ORIGINAL EFFECTIVE DATE: 04/12/16
LAST REVIEW DATE: 01/22/19
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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.

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

Description:

Acute lymphoblastic leukemia (ALL) is a cancer that starts from white blood cells (lymphocytes) in the bone marrow. It can spread to other parts of the body such as the brain and spinal cord (central nervous system), lymph nodes, liver, spleen and testicles. ALL may also be referred to as acute lymphocytic leukemia.

HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE LYMPHOBLASTIC LEUKEMIA (cont.)

Description: (cont.)

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".

Definitions:

Donor Types:

- Allogeneic: From a third-party donor
- Autologous: From an individual's own bone marrow and/or circulating blood

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.

HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE LYMPHOBLASTIC LEUKEMIA (cont.)

Criteria:

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

Pretransplantation Evaluation:

Human Leukocyte Antigen (HLA) typing and Matched Unrelated Donor (MUD) searches may be approved by the coordinator if 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 status¹ 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)**.

¹ Performance status tables are located at the end of the Criteria section.

HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE LYMPHOBLASTIC LEUKEMIA (cont.)

Criteria: (cont.)

Adult Acute Lymphoblastic Leukemia:

- HDC with allogeneic HCT for an adult with acute lymphoblastic leukemia is considered **medically necessary** with documentation of **ALL** of the following:
 1. Pretransplantation evaluation criteria above is met
 2. **ONE** of the following:
 - First complete or partial remission for any risk level of relapse
 - Second or greater remission
 - Refractory
 - Relapsed
 - Relapse after a prior course of HDC with autologous HCT

- HDC with allogeneic HCT for an adult with acute lymphoblastic leukemia for all other indications 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.

HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE LYMPHOBLASTIC LEUKEMIA (cont.)

Criteria: (cont.)

Adult Acute Lymphoblastic Leukemia: (cont.)

- Nonmyeloablative reduced-intensity conditioning (RIC) with allogeneic HCT for an adult with acute lymphoblastic leukemia is considered **medically necessary** with documentation of **ALL** of the following:
 1. Pretransplantation evaluation criteria above is met
 2. Complete marrow and first or second extramedullary remission
 3. Medically unable to tolerate HDC

- Nonmyeloablative reduced-intensity conditioning (RIC) with allogeneic HCT for individuals with acute lymphoblastic leukemia for all other indications 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.

- HDC with autologous HCT for an adult with acute lymphoblastic leukemia is considered **medically necessary** with documentation of **ALL** of the following:
 1. Pretransplantation evaluation criteria above is met
 2. First complete or partial remission but at high risk of relapse

- HDC with autologous HCT for an adult with acute lymphoblastic leukemia for all other indications 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.

Indications include, *but are not limited to*:

- Second or greater remission
- Refractory

HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE LYMPHOBLASTIC LEUKEMIA (cont.)

Criteria: (cont.)

Childhood Acute Lymphoblastic Leukemia:

- HDC with allogeneic HCT for a child with acute lymphoblastic leukemia is considered **medically necessary** with documentation of **ALL** of the following:
 1. Pretransplantation evaluation criteria above is met
 2. **ONE** of the following:
 - First complete or partial remission but at high risk of relapse
 - Second or greater remission
 - Refractory

- HDC with allogeneic HCT for a child with acute lymphoblastic leukemia is considered **medically necessary** with documentation of **ALL** of the following:
 1. Pretransplantation evaluation criteria above is met
 2. Relapse after a prior course of HDC with autologous HCT

- HDC with allogeneic HCT for a child with acute lymphoblastic leukemia for all other indications 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.

- HDC with autologous HCT for a child with acute lymphoblastic leukemia is considered **medically necessary** with documentation of **ALL** of the following:
 1. Pretransplantation evaluation criteria above is met
 2. **ONE** of the following:
 - First complete or partial remission but at high risk of relapse
 - Second or greater remission
 - Refractory

HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE LYMPHOBLASTIC LEUKEMIA (cont.)

Criteria: (cont.)

Childhood Acute Lymphoblastic Leukemia: (cont.)

- HDC with autologous HCT for a child with acute lymphoblastic leukemia for all other indications or if above criteria not met is considered **experimental or investigational²** 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.
- ² 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 |



MEDICAL COVERAGE GUIDELINES
SECTION: MEDICINE

ORIGINAL EFFECTIVE DATE: 04/12/16
LAST REVIEW DATE: 01/22/19
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE LYMPHOBLASTIC LEUKEMIA (cont.)

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 |



MEDICAL COVERAGE GUIDELINES
SECTION: MEDICINE

ORIGINAL EFFECTIVE DATE: 04/12/16
LAST REVIEW DATE: 01/22/19
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE LYMPHOBLASTIC LEUKEMIA (cont.)

Resources:

Literature reviewed 02/20/18. 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 06/26/13 may be requested from the BCBSAZ Medical Policy and Technology Research Department.

1. 8.01.32 BCBS Association Medical Policy Reference Manual. Hematopoietic Stem-Cell Transplantation for Acute Lymphoblastic Leukemia. Re-issue date 01/11/2018, issue date 04/30/2000.



MEDICAL COVERAGE GUIDELINES
SECTION: MEDICINE

ORIGINAL EFFECTIVE DATE: 04/12/16
LAST REVIEW DATE: 01/22/19
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE LYMPHOBLASTIC LEUKEMIA (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 nilinígíí Blue Cross Blue Shield of Arizona haada yit'éego bina'idilkidgo éí doodago Háida bíjá anilyeedígíí t'áadoo le'é yina'idilkidgo beehaz'áanii hólo díí t'áa hazaadk'ehjí háká a'doowołgo bee haz'ą doo baqah ilinígóó. Ata' halne'ígíí kojį' bich'į' hodilnih 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.

