GENETIC TESTING FOR BCR-ABL1 IN 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.
GENETIC TESTING FOR BCR-ABL1 IN LEUKEMIA (cont.)

Description:

BCR-ABL1 is an abnormal fusion gene that is formed when pieces of two chromosomes break off and trade places. The changed chromosome with the fusion gene on it is called the Philadelphia chromosome. The BCR-ABL1 fusion gene is found in most individuals with chronic myelogenous leukemia (CML) and in some individuals with acute lymphoblastic leukemia (ALL) or acute myelogenous leukemia (AML). Treatment for these diseases include Imatinib (Gleevec®), a tyrosine kinase inhibitor (TKI) and ABL inhibitors, including dasatinib (Sprycel®) and nilotinib (Tasigna®).

Genetic testing of the BCR-ABL1 fusion gene is performed to confirm the diagnosis of CML, for monitoring disease progression or remission during and after treatment and for identification of ABL kinase domain point mutations related to drug resistance when there is inadequate response or loss of response to tyrosine kinase inhibitors or disease progression.

Definitions:

Genetic Testing:
Analysis of DNA, RNA, chromosomes, proteins and certain metabolites in order to detect alterations related to an inherited disorder.

Gene:
A hereditary unit consisting of segments of DNA that occupies a specific location on chromosomes. Genes undergo mutation when their DNA sequence changes.

Genetic Counseling:
Instruction that provides interpretation of genetic tests and information about courses of action that are available for the care of an individual with a genetic disorder or for future family planning.

Affected Individual:
An individual displaying signs or symptoms characteristic of a suspected or specific inherited disorder.

Unaffected Individual:
An individual who displays no signs or symptoms characteristic of a suspected or specific inherited disorder.

Screening:
Genetic screening is the testing of an individual with no symptoms for a specific inherited disorder to determine if the individual carries an abnormal gene. Screening can be used to predict risk or potential risk for the individual or their offspring.
GENETIC TESTING FOR BCR-ABL1 IN LEUKEMIA (cont.)

Criteria:

- Genetic testing and/or counseling of an **unaffected** individual, regardless of risk factors is considered **screening** and **not eligible for coverage**.

- Genetic testing and/or counseling of an **affected** individual to confirm a disease when confirmation of the diagnosis would not impact the care and/or management is considered **not medically necessary** and **not eligible for coverage**.

Chronic Myelogenous Leukemia (CML):

- BCR-ABL1 qualitative genetic testing and/or counseling for the presence of the fusion gene is considered **medically necessary** for the diagnosis of CML.

- BCR-ABL1 genetic testing and/or counseling for messenger RNA transcript levels by quantitative real-time reverse transcription-polymerase chain reaction (RT-PCR) at baseline prior to initiation of treatment and at intervals during therapy is considered **medically necessary** for monitoring of CML treatment response and remission.

- Genetic testing and/or counseling to evaluate ABL kinase domain point mutations for tyrosine kinase inhibitor resistance is considered **medically necessary** when there is inadequate initial response to treatment or any sign of loss of response and/or when there is progression of the disease to the accelerated or blast phase.

- Repeat genetic testing is considered **medically necessary** only when indicated for monitoring of treatment response to medication.

- Genetic testing and/or counseling to evaluate ABL kinase domain point mutations for monitoring in advance of signs of treatment failure or disease progression 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.
GENETIC TESTING FOR BCR-ABL1 IN LEUKEMIA (cont.)

Criteria: (cont.)

Acute Lymphocytic Leukemia (ALL) and Acute Myeloid Leukemia (AML):

- BCR-ABL1 genetic testing and/or counseling by real time polymerase chain reaction (RT-PCR) is considered medically necessary to confirm the diagnosis of Philadelphia chromosome positive (Ph+) acute lymphocytic leukemia (ALL) or Ph+ acute myeloid leukemia (AML) and/or to monitor ALL or AML treatment response.

- Repeat genetic testing is considered medically necessary only when indicated for monitoring of treatment response to medication.

- If above criteria not met, BCR-ABL1 genetic testing and/or counseling by real time polymerase chain reaction (RT-PCR) 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.

Resources:

Literature reviewed 04/12/16. 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 04/16/13 may be requested from the BCBSAZ Medical Policy and Technology Research Department.

GENETIC TESTING FOR BCR-ABL1 IN 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 nliníigíí Blue Cross Blue Shield of Arizona haadá yit’éego bina’ííldikgo éí doodago Háida bígíí aniłyeedígíí t’áadoo le’é yina’ííldikgo beehaz’áanii hólp díí t’áá hazaadk’ehjí háhá a’doololgo beehaz’á doo bąąh ilinígoóó. Ata’ halne’ilígíí koi’bíchí’ hodíílníinh 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於插件項目的名稱 Blue Cross Blue Shield of Arizona 方面的問

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 thể thông tin bằng ngôn ngữ của mình miễn phí. Đế nói chuyển 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 المسؤولة بلغتك من دون أي تكلفة. للتحدث مع مرجم التصل ب 877-475-4799.
GENETIC TESTING FOR BCR-ABL1 IN LEUKEMIA (cont.)

Multi-Language Interpreter Services: (cont.)

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

Korean: 만약 원하는 언어로 진행이 되지 않는다면 제의하는 언어로 실시할 수 있는 권리가 있습니다. 그렇게 통역사와 얘기하기 위해서는 877-475-4799로 전화해주시오.

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 имеет 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々でも、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:

آگر شما یا کسی که شما به او کمک می‌کنید، سوال دار می‌وزرید اطلاعاتی به زبان خود را به طور رایگان دریافت نمایید 877-475-4799.

Assyrian:

Blue Cross Blue Shield of Arizona مخاطبان تنها 877-475-4799 را می‌توانند به این شکل تماس بگیرند.

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 prevodijom, nazovite 877-475-4799.

Thai: หากคุณ หรือคุณคิดถึงตามความหมายในภาษา Blue Cross Blue Shield of Arizonaคุณจะได้รับความช่วยเหลือและข้อมูลภาษา ของคุณโดยไม่เก็บค่าใช้จ่าย ที่ 877-475-4799.