GENETIC TESTING FOR MODERATE PENETRANCE VARIANTS ASSOCIATED WITH BREAST CANCER IN INDIVIDUALS AT HIGH BREAST CANCER RISK

- ATM
- CHEK2
- PALB2

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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GENETIC TESTING FOR MODERATE PENETRANCE VARIANTS ASSOCIATED WITH BREAST CANCER IN INDIVIDUALS AT HIGH BREAST CANCER RISK (cont.)

Description:

Genes Associated with a Moderate Penetrance of Breast Cancer:
PALB2 (partner and localizer of BRCA2) is a tumor suppressor gene which encodes for the PALB2 protein. The PALB2 protein assists BRCA2 in DNA repair and tumor suppression.

CHEK2 (checkpoint kinase 2) is activated in response to DNA double-strand breakage and plays a role in cell-cycle control, DNA repair, and apoptosis.

ATM (ataxia-telangiectasia [AT] mutated, is associated with the autosomal recessive condition AT. This condition is characterized by progressive cerebellar ataxia with onset between the ages of 1 and 4 years, telangiectasias of the conjunctivae, oculomotor apraxia, immune defects and cancer predisposition.

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 MODERATE PENETRANCE VARIANTS ASSOCIATED WITH BREAST CANCER IN INDIVIDUALS AT HIGH BREAST CANCER RISK (cont.)

Definitions: (cont.)

Familial Assessment:
1st, 2nd, and 3rd degree relatives are blood relatives on the same side of the family (maternal or paternal).

- 1st Degree Relative: Blood-related sibling, parent or child.
- 2nd Degree Relative: Blood-related relative removed by one generation, e.g., grandparent, grandchild, aunt/uncle, niece/nephew or half siblings.
- 3rd Degree Relative: Blood-related relative removed by two generations, e.g., great-grandparent, great-grandchild, great-aunt/uncle, grandniece/nephew or first cousin.

Founder Mutation:
A gene mutation observed with high frequency in a group that is or was geographically or culturally isolated, in which one or more of the ancestors was a carrier of the mutant gene. Three known founder mutations in individuals of known Ashkenazi Jewish descent are 185delAG and 5182insC in BRCA1; 6174delT in BRCA2.

Gleason Score:
A system of grading prostate cancer tissue based on how it looks under a microscope. Gleason scores range from 2 to 10 and indicate how likely it is that a tumor will spread. For the purpose of familial assessment, prostate cancer is defined as Gleason score greater than or equal to 7.

Criteria:

For PANEXIA™, see BCBSAZ Medical Coverage Guideline #O890, “Genetic Testing With Genetic Panels”.

For PALB2 genetic testing performed as part of a cancer susceptibility panel, see BCBSAZ Medical Coverage Guideline #O863, “Genetic Testing With Cancer Susceptibility Panels Using Next Generation Sequencing”.

For genetic testing for BRCA 1 and BRCA 2 mutations, see BCBSAZ Medical Coverage Guideline #O662, “Genetic Testing for Hereditary Breast and Ovarian Cancer Syndrome”.

GENETIC TESTING FOR MODERATE PENETRANCE VARIANTS ASSOCIATED WITH BREAST CANCER IN INDIVIDUALS AT HIGH BREAST CANCER RISK (cont.)

Criteria: (cont.)

- Genetic testing and counseling for PALB2 variants for breast cancer risk assessment is considered medically necessary for an affected individual with documentation of ALL of the following:

1. ONE of the following:
   - Individual from a family with a known sequence variant in a cancer susceptibility gene
   - Personal history of breast cancer and ANY of the following:
     - Diagnosed at age less than or equal to 50 years
     - Triple negative (ER-, PR-, HER2-) breast cancer diagnosed less than or equal to 60 years
     - Two breast cancer primaries in a single individual
     - Diagnosed with breast cancer at any age and ANY of the following:
       a. Greater than or equal to one 1st, 2nd, or 3rd degree blood relative with breast cancer diagnosed at less than or equal 50 years of age
       b. Greater than or equal to one 1st, 2nd, or 3rd degree blood relative with invasive ovarian cancer at any age
       c. Greater than or equal to two 1st, 2nd, or 3rd degree blood relative with breast cancer and/or pancreatic cancer at any age
       d. Populations at increased risk due to founder mutations
   - Personal history of male breast cancer
   - Personal history of breast, ovarian, or pancreatic cancer at any age AND Ashkenazi Jewish decent
   - Personal history of ovarian cancer
   - Personal history and/or family history of three or more of the following (especially if diagnosed at age less than or equal to 50 years and can include multiple primary cancers in same individual):
     - Breast cancer
     - Prostate cancer (Gleason score greater than or equal to 7)
     - Melanoma
     - Sarcoma
     - Adrenocortical carcinoma
     - Brain tumors
     - Leukemia
     - Diffuse gastric cancer
     - Colon cancer
     - Endometrial cancer
     - Thyroid cancer
     - Kidney cancer
     - Dermatologic manifestations
     - Macrocephaly
     - Hamartomatous polyps of GI tract

2. Individual has undergone testing for sequence variants in BRCA1 and BRCA2 with negative results
GENETIC TESTING FOR MODERATE PENETRANCE VARIANTS ASSOCIATED WITH BREAST CANCER IN INDIVIDUALS AT HIGH BREAST CANCER RISK (cont.)

Criteria: (cont.)

- Genetic testing and counseling for PALB2 sequence variants for an affected individual 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, and
  4. Insufficient evidence to support improvement outside the investigational setting.

- Genetic testing and counseling for PALB2 variants for breast cancer risk assessment is considered medically necessary for an unaffected individual with documentation of ALL of the following:
  1. ONE of the following:
    - A 1st, 2nd, or 3rd degree relative with ANY of the following:
      - Individual from a family with a known sequence variant in a cancer susceptibility gene
      - Two breast cancer primaries in a single individual
      - Greater than or equal to two individuals with breast cancer primaries on the same side of family with at least one diagnosed at less than or equal 50 years of age
      - Ovarian cancer
      - Male breast cancer
    - 1st or 2nd degree relative diagnosed with breast cancer diagnosed less than or equal to 45 years
    - Family history of three or more of the following (especially if diagnosed at age less than or equal to 50 years and can include multiple primary cancers in same individual):
      - Breast cancer
      - Prostate cancer (Gleason score greater than or equal to 7)
      - Melanoma
      - Sarcoma
      - Adrenocortical carcinoma
      - Brain tumors
      - Leukemia
      - Diffuse gastric cancer
      - Colon cancer
      - Endometrial cancer
      - Thyroid cancer
      - Kidney cancer
      - Dermatologic manifestations
      - Macrocephaly
      - Hamartomatous polyps of GI tract
  2. Individual has undergone testing for sequence variants in BRCA1 and BRCA2 with negative results
GENETIC TESTING FOR MODERATE PENETRANCE VARIANTS ASSOCIATED WITH BREAST CANCER IN INDIVIDUALS AT HIGH BREAST CANCER RISK (cont.)

Criteria: (cont.)

- Genetic testing and counseling for PALB2 sequence variants for an unaffected individual 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, and
  4. Insufficient evidence to support improvement outside the investigational setting.

- Genetic testing or counseling for CHEK2 and ATM variants in the assessment of breast cancer risk 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, and
  4. Insufficient evidence to support improvement outside the investigational setting.

Resources:

Literature reviewed 01/17/17. 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.

GENETIC TESTING FOR MODERATE PENETRANCE VARIANTS ASSOCIATED WITH BREAST CANCER IN INDIVIDUALS AT HIGH BREAST CANCER RISK (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.htm

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.

Nawajo: Díl kwe’é atah nilinigii Blue Cross Blue Shield of Arizona haada yít’éego bina’idilkidgo éi doodago Háiđa bíjá anilyeedigii t’àadoo le’é yina’idlkidgo beehaz’áñìii hóló díl t’à házadd’ehji háká’ a’doowolgo bee haz’á doo bağh illígóló. Ata’ haine’igi kojì bich’i’ hodilinh 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關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, hoặc 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 đổi chuyển với một thống dịch viên, xin gọi 877-475-4799.

Arabic: إن كان لديك أو لدى شخص تساعد أسئلة بخصوص Blue Cross Blue Shield of Arizona ضرورية بلغتك من دون أي تكلفة، للتحدث مع مترجم للحصول على المساعدة والمعلومات 877-475-4799.
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**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 귀하를 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 이용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 통역사와 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:

اطلاعات به زبان خود را به طور رایگان دریافت نمایید 877-475-4799. 

Assyrian:

Blue Cross Blue Shield of Arizona

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 prevodicom, nazovite 877-475-4799.

Thai: หากคุณ หรือผู้ที่คุณช่วยเหลือเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณมีคำถามเกี่ยวกับข้อมูลของคุณในภาษา ของคุณได้ไปที่ 877-475-4799