GENETIC TESTING FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME

▪ BRCA1
▪ BRCA2

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 HEREDITARY BREAST AND OVARIAN CANCER
SYNDROME (cont.)

Description:

Hereditary breast and ovarian cancer (HBOC) and some cases of hereditary site-specific breast cancer describe the familial cancer syndromes that are related to variants in the BRCA genes.

Families suspected of having HBOC syndrome are characterized by an increased susceptibility to breast cancer occurring at a young age, bilateral breast cancer, male breast cancer, ovarian cancer at any age as well as cancer of the fallopian tube and primary peritoneal cancer. Other cancers, such as prostate cancer, pancreatic cancer, gastrointestinal cancers, melanoma and laryngeal cancer occur more frequently in HBOC families.

Hereditary site-specific breast cancer families are characterized by early onset breast cancer with or without male cases, but without ovarian cancer.

Variants in the BRCA1 and BRCA2 genes are responsible for the cancer susceptibility in the majority of HBOC families, especially if ovarian cancer or male breast cancer are features. However, in site-specific breast cancer, BRCA variants are responsible for only a proportion of affected families and research to date has not yet identified other moderate or high-penetrance gene variants that account for disease in these families.

Comprehensive variant analysis includes sequencing the coding regions and intron/exon splice sites, as well as tests to detect common large deletions and rearrangements that can be missed with sequence analysis alone. Additional testing to detect uncommon large rearrangements may be performed on exceptionally high risk individuals that have tested negative for BRCA 1 and 2 variants.

Commercially available genetic tests used to detect common and/or uncommon large gene rearrangements include, but are not limited to:

- Integrated Genetics a LabCorp® Specialty Testing Group BRCAssureSM
- Myriad Genetics, Inc. BRACAnalysis CDx®
- Myriad Genetics, Inc. BRACAnalysis® Large Rearrangement Test (BART™)
- Myriad Genetics, Inc. Comprehensive BRACAnalysis® Test
- Myriad Genetics, Inc. Integrated BRACAnalysis® Test
- Quest Diagnostics®, Inc. BRCAvantage™
GENETIC TESTING FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME (cont.)

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.

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.
GENETIC TESTING FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME (cont.)

Definitions: (cont.)

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 BRCAplus™, see BCBSAZ Medical Coverage Guideline #O863, “Genetic Testing With Cancer Susceptibility Panels Using Next Generation Sequencing”.

For genetic testing for CHEK2 mutations, see BCBSAZ Medical Coverage Guideline #O946, “Genetic Testing for Moderate Penetration Variants Associated With Breast Cancer in Individuals at High Breast Cancer Risk”.

- Genetic testing and counseling for BRCA1 and BRCA2 variants in cancer is considered medically necessary for an affected individual with documentation of ANY of the following:

  1. Individual from a family with a known BRCA1/BRCA2 variant
  2. Personal history of breast cancer and ANY of the following:

    • Diagnosed at age less than or equal to 45 years
    • Two primary breast cancers with the first diagnosis occurring at or before age 50
    • Diagnosed at age less than or equal to 60 years with a triple negative (ER-, PR-, HER2-) breast cancer
    • Diagnosed at age less than or equal to 50 years and ANY of the following:

      - Greater than or equal to one 1\textsuperscript{st}, 2\textsuperscript{nd}, or 3\textsuperscript{rd} degree relative(s) with breast cancer at any age, pancreatic cancer or prostate cancer
      - Unknown or limited family history

    • Diagnosed at any age AND greater than or equal to one 1\textsuperscript{st}, 2\textsuperscript{nd}, or 3\textsuperscript{rd} degree relative(s) with breast cancer diagnosed at age less than or equal to 50 years
    • Diagnosed at any age AND greater than or equal to two 1\textsuperscript{st}, 2\textsuperscript{nd}, or 3\textsuperscript{rd} degree relatives with breast cancer at any age
    • Diagnosed at any age AND greater than or equal to one 1\textsuperscript{st}, 2\textsuperscript{nd}, or 3\textsuperscript{rd} degree relative(s) with ANY of the following:

      - Fallopian tube cancer
      - Epithelial ovarian cancer
      - Primary peritoneal cancer
GENETIC TESTING FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME (cont.)

Criteria: (cont.)

➢ Genetic testing and counseling for BRCA1 and BRCA2 variants in cancer is considered medically necessary for an affected individual with documentation of ANY of the following: (cont.)

2. Personal history of breast cancer and ANY of the following: (cont.)
   • Diagnosed at any age AND greater than or equal to two 1st, 2nd, or 3rd degree relatives with ANY of the following:
     - Pancreatic cancer diagnosed at any age
     - Prostate cancer diagnosed at any age
   • 1st, 2nd, or 3rd degree male relative with breast cancer
   • Ethnicity associated with deleterious founder mutations, e.g., Ashkenazi Jewish descent. Testing for Ashkenazi Jewish or other founder mutation(s) should be performed first. When testing for founder mutations is negative, comprehensive variant analysis should then be performed.

3. Personal history of ANY of the following:
   • Fallopian tube cancer
   • Epithelial ovarian cancer
   • Primary peritoneal cancer

4. Personal history of male breast cancer

5. Personal history of pancreatic cancer or prostate cancer at any age AND one or more 1st, 2nd, or 3rd degree relative(s) with ANY of the following: (for pancreatic cancer, if Ashkenazi Jewish ancestry, no additional affected relative is needed)
   • Breast cancer diagnosed at age less than or equal to 50
   • Fallopian tube cancer diagnosed at any age
   • Ovarian cancer diagnosed at any age
   • Primary peritoneal cancer diagnosed at any age
GENETIC TESTING FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME (cont.)

Criteria: (cont.)

- Genetic testing and counseling for BRCA1 and BRCA2 variants in cancer is considered *medically necessary* for an affected individual with documentation of ANY of the following: (cont.)

  6. Personal history of pancreatic cancer or prostate cancer at any age AND two or more 1st, 2nd, or 3rd degree relatives with ANY of the following: (for pancreatic cancer, if Ashkenazi Jewish ancestry, no additional affected relative is needed)
     - Breast cancer at any age
     - Pancreatic cancer at any age
     - Prostate cancer at any age

- Genetic testing and counseling for BRCA1 or BRCA2 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 BRCA1 or BRCA2 variants is considered *medically necessary* for an unaffected individual with documentation of ONE or more of the following:

  1. Individual from a family with a known BRCA1/BRCA2 variant
  2. 1st- or 2nd degree blood relative meeting any criterion listed above for an affected individual
  3. 3rd degree blood relative with breast cancer and/or ovarian/fallopian tube/primary peritoneal cancer AND greater than or equal to two 1st, 2nd, or 3rd degree relatives with breast cancer (greater than or equal to one diagnosed at age less than or equal to 50 years) and/or ovarian/fallopian tube/primary peritoneal cancer.
GENETIC TESTING FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME (cont.)

Criteria: (cont.)

- Genetic testing and counseling for BRCA1 or BRCA2 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 and counseling for **uncommon** large genomic rearrangements (e.g., BART) may be considered **medically necessary** with documentation of **ALL** of the following:
  
  1. Individual meets the above criteria for BRCA1 or BRCA2 testing
  2. Comprehensive testing for BRCA1 or BRCA2 variants (e.g., sequence analysis and testing for the five common large rearrangements) is negative.

Resources:

Literature reviewed 12/19/17. 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.

Resources prior to 12/11/12 may be requested from the BCBSAZ Medical Policy and Technology Research Department.


GENETIC TESTING FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME (cont.)

Resources: (cont.)


5. U.S. Dept. of Health and Human Services. FAQs About Affordable Care Act Implementation Part XII. 02/20/2013.

GENETIC TESTING FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME (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/index.html

Multi-Language Interpreter Services:

Spanish: Sí 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 kweé' átah nilliníi Blue Cross Blue Shield of Arizona haada ylt’éego bina’dílíkidgo éi doodago Háida bígí aniyeeedíí t’áadoo le’é' yina’dílíkidgo beehaz’aáníii hólo díí t’áa hazaadk’éhi háká a’doo wołgo bee ħá’ doo báah ilíngóó. Aта’ halné’ilígií kojí’ bíčh’a’ hodilihíi 877-475-4799.

Chinese: 如果您，或是您正在协助的对象，有关于入插项目的名称 Blue Cross Blue Shield of Arizona 方面的问题，您有权利免费以您的母语得到帮助和讯息。洽询一位翻译员，拨电话 在此插入数字 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 thể thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thợng dịch viên, xin gọi 877-475-4799.

Arabic:

إن كان لديك أو لدى شخص تساعدته أسئلة بخصوص Blue Cross Blue Shield of Arizona المهمة تلائمك من دون أي إلهام للتحدث مع محترف تحويل، نحن في وضعنا للاستجابة للمطلبة 877-475-4799.
GENETIC TESTING FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutuulan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuhang 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 Arizona에 문의하셔 점문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 통역사와 매개하기 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: اگر شما یا کسی که شما به او کمک می‌کنید، سوالات مورد اطلاعات به زبان فارسی را به طور رایگان دریافت نمایید 877-475-4799. [به زبان فارسی]

Assyrian: Blue Cross Blue Shield of Arizona یاری ادبیات و سوالات شما را به زبان عبری و سوئدی می‌پذیرد. 877-475-4799.

Serbo-Croatian: Ukoliko Vi ili neko kom se 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: หากคุณมีคำถามเกี่ยวกับบริการของ Blue Cross Blue Shield of Arizona คุณสามารถเข้าถึงบริการทางโทรศัพท์ 877-475-4799 ได้