05-82000-30

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Reviewed: 01/28/21

Revised: 02/15/21

Subject: Genetic Testing for BRCA1 or BRCA2 for Hereditary Breast/Ovarian Cancer Syndrome and Other High-Risk Cancers

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Several genetic syndromes with an autosomal dominant pattern of inheritance that feature breast cancer have been identified. Of these, hereditary breast and ovarian cancer (HBOC) and some cases of hereditary site-specific breast cancer have in common causative mutations in BRCA (breast cancer susceptibility) 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, and 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.

Germline variants in the BRCA1 and BRCA2 genes are responsible for the cancer susceptibility in most 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. BRCA gene variants are inherited in an autosomal dominant fashion through either the maternal or paternal lineage. It is possible to test for abnormalities in BRCA1 and BRCA2 genes to identify the specific variant in

cancer cases, and to identify family members at increased cancer risk. Family members without existing cancer who are found to have BRCA variants can consider preventive interventions for reducing risk and mortality.

POSITION STATEMENT:

NOTE: Coverage for genetic testing, screening, and counseling are applicable only under those contracts that include benefits for genetic testing, preventive health services, screening services, and medical counseling.

Genetic testing for BRCA1 and BRCA2 variants **meets the definition of medical necessity** for cancer-affected women or men who meet **ONE** or more of the following criteria:

1. Member with any blood relative with a known pathogenic/likely pathogenic variant in a cancer susceptibility gene (eg. BRCA1, BRCA2, CDH1, PTEN, TP53).
2. Member meeting the criteria below but with previous limited testing (e.g., single gene and/or absent deletion duplication analysis).
3. Personal history of breast cancer and **ONE** or more of the following:
    - Diagnosed at age ≤45 years;
    - Diagnosed age 46-50 years with:
        - An additional breast cancer primary (bilateral disease or two or more clearly separate ipsilateral primary tumors diagnosed either synchronously or asynchronously) at any age
        - ≥1 close blood relative* with breast, ovarian, pancreatic, or prostate cancer at any age
        - An unknown or limited family history.
    - Diagnosed age ≤ 60 years with a triple negative breast cancer;
    - Diagnosed at any age with:
        - ≥1 close blood relative* with:
            - Breast cancer diagnosed ≤50 years; or
            - Ovarian carcinoma (includes fallopian tube & primary peritoneal cancers); or
            - Metastatic, intraductal/cribiform prostate cancer, or high-risk or very-high-risk group**; or
            - Pancreatic cancer.
        - ≥3 total diagnoses of breast cancer in member and/or close blood relative*
        - Ashkenazi Jewish ancestry.
    - Diagnosed at any age with male breast cancer.
4. Personal history of epithelial ovarian carcinoma (includes fallopian tube cancer or peritoneal cancer) at any age.
5. Personal history of exocrine pancreatic cancer at any age.
6. Personal history of metastatic, intraductal/cribiform histology prostate cancer at any age; or high-risk group or very-high-risk group** prostate cancer at any age.

7. Personal history of high-grade prostate cancer (Gleason score ≥ 7) at any age with:
    - ≥1 close blood relative* with ovarian carcinoma, pancreatic cancer, or metastatic, intraductal/cribiform prostate cancer at any age or breast cancer ≤50 years; or
    - ≥2 close blood relatives* with breast or prostate cancer (any grade) at any age; or
    - Ashkenazi Jewish ancestry.
8. Personal history of cancer and a mutation identified on tumor genomic testing that has clinical implications if also identified in the germline.
9. Personal history of cancer and to aid in systemic therapy decision-making, such as for PARP-inhibitors for human epidermal receptor 2 (HER2)-negative metastatic breast cancer, ovarian cancer, prostate cancer, pancreatic cancer; platinum therapy for prostate cancer and pancreatic cancer.

Genetic testing for BRCA1 and BRCA2 variants of cancer-unaffected women or men **meets the definition of medical necessity** under any ONE of the following circumstances:

- An affected or unaffected member with a 1st- or 2nd-degree blood relative* meeting any criterion listed above for Members With Cancer (except members who meet criteria only for systemic therapy decision-making)
- An affected or unaffected member who otherwise does not meet the criteria above but has a probability >5% of a *BRCA1/2* pathogenic variant based on prior probability models (*e.g.,* Tyrer-Cuzick, BRCAPro, Penn ll).

*****Close blood relatives include 1st-, 2nd-, and 3rd- degree relatives on the same side of the family (maternal or paternal): **1st-degree** relatives: parents, siblings, and children; **2nd-degree** relatives: grandparents, aunts, uncles, nieces, nephews, grandchildren, and half-siblings; **3rd-degree** relatives: great-grandparents, great-aunts, great-uncles, great-grandchildren, and first cousins.

***High-risk group**: no very-high-risk features and are T3a (American Joint Committee on Cancer staging T3a=tumor has extended outside of the prostate but has not spread to the seminal vesicles); OR Grade Group 4 or 5; OR prostate specific antigen of 20 ng/ml or greater. Very-high-risk group: T3b-T4 (tumor invades seminal vesicle(s); or tumor is fixed or invades adjacent structures other than seminal vesicles such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall); OR Primary Gleason Pattern 5; OR 2 or 3 high-risk features; OR greater than 4 cores with Grade Group 4 or 5.

BRACAnalysis® Rearrangement Test (BART™) **meets the definition of medical necessity** for individuals that meet the BRCA testing criteria listed above.

BRACAnalysis Rearrangement Test (BART) is considered **experimental or investigational** for all other indications including screening in the general population. There is a lack of clinical data to permit conclusions on the clinical management of the patient and net health outcomes.

Genetic testing for BRCA1 and BRCA2 variants in cancer-affected members or of cancer-unaffected members with a family history of cancer when criteria above are not met is considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes.

Genetic testing in minors for BRCA1 or BRCA variants is considered **experimental or investigational**. There is no change in management for minors as a result of knowledge of the presence or absence of a deleterious variant. In addition, there are potential harms related to stigmatization and discrimination.

Testing for BARD1 variants is considered **experimental or investigational** for all indications. The evidence is insufficient to determine the effects of this testing on health outcomes.

BILLING/CODING INFORMATION:

CPT Coding:

81162	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (ie, detection of large gene rearrangements)
81163	BRCA1 (BRCA1, dna repair associated), BRCA2 (BRCA2, dna repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81164	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81165	BRCA1 (BRCA1, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81166	BRCA1 (BRCA1, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81167	BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81212	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis;185delAG, 5385insC, 6174delT variants
81215	BRCA1 (BRCA1, DNA repair associated) (e.g.,hereditary breast and ovarian cancer) gene analysis; known familial variant
81216	BRCA2 (BRCA2, DNA repair associated) (e.g.,hereditary breast and ovarian cancer) geneanalysis; full sequence analysis
81217	BRCA2 (BRCA2, DNA repair associated) (e.g.,hereditary breast and ovarian cancer) geneanalysis; known familial variant

Genetic Counseling: Genetic counseling is covered in accordance to the member's contract benefits for medical counseling. Pre and post genetic counseling may be considered medically necessary as an adjunct to the genetic tests. The following codes may be reported:

CPT Coding:

96040	Medical genetics and genetic counseling services, each 30 minutes face-to-face with patient/family

HCPCS Coding:

S0265	Genetic counseling, under physician supervision, each 15 minutes

REIMBURSEMENT INFORMATION:

None applicable

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage products:

The following Local Coverage Determination (LCD) was reviewed on the last guideline reviewed date: BRCA1 and BRCA2 Genetic Testing (L36499) located at fcso.com.

DEFINITIONS:

Triple-negative breast cancer: describes breast cancer cells that do not have estrogen receptors, progesterone receptors, or large amounts of HER2/neu protein. Also called ER-negative PR-negative HER2/neu-negative and ER-PR-HER2/neu-.

RELATED GUIDELINES:

Genetic Testing, 05-82000-28
Magnetic Resonance Imaging of the Breast, 04-70540-09
Preventive Services, 01-99385-03
Prophylactic Mastectomy, 02-12000-15

OTHER:

None applicable

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16. National Comprehensive Cancer Network, (NCCN) Clinical Practice Guidelines in Oncology, Genetic/Familial High-Risk Assessment: Breast and Ovarian, Version 2.2021; accessed at nccn.org.
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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy & Coverage Committee on 01/28/21.

GUIDELINE UPDATE INFORMATION:

11/15/03	Annual review. Developed separate policy for Genetic Testing for Inherited BRCA1 and BRCA2 Mutations. Added coverage and non-coverage statement for BRCA testing of men.
07/01/05	HCPCS update. Added S0265.
12/15/05	Biennial review. Coverage statement changed to reflect BCA policy. Non-coverage section reworded. Information added to Description section.
01/01/06	Annual HCPCS coding update: added 83900, 83907, 83908, 83909, and 83914; revised 83898 & 83901.
06/15/06	Revision to include new codes into limitation section.

10/15/06	Revision to coverage statement; definitions added.
01/01/07	Annual HCPCS coding update: added 96040, deleted 99401, 99402, 99403, 99404.
07/15/07	Annual review, coverage statements maintained, guideline reformatted, references updated.
01/01/08	Annual HCPCS coding update: revised 83898, 83900, 83901, and 83908.
01/01/09	Annual HCPCS coding update: descriptor revised for codes 83890, 83891, 83892, 83893, 83894, 83897, 83900, 83903, 83907, 83909, and 83914.
09/15/09	Annual review: position statements updated, description section, guideline title, and references updated.
10/15/09	Reimbursement Information section updated.
08/15/10	Annual review: position statements updated to include “cancer of fallopian tube or primary peritoneal cancer” to be considered along with breast and ovarian cancer in assessing family history; additional position statements added regarding CHEK2 testing and testing for minors; description section and references updated.
04/01/11	Revision; Certificate of Medical Necessity added.
08/15/11	Scheduled review; position statements and references updated; formatting changes.
01/01/12	Annual HCPCS update. Added CPT codes 81211-81217; revised Billing/Coding and Reimbursement Information sections.
04/01/12	Quarterly HCPCS update. Deleted codes S3818-S3823.
08/15/12	Annual review; position statements, description section, and references updated.
11/15/13	Annual review; position statements, program exception, and references updated.
11/15/14	Annual review; position statements and references updated.
07/15/15	Annual Review; position statements, program exception, and references updated.
01/01/16	Annual HCPCS/CPT update; code 81162 added.
08/15/16	Revision; position statement section and references updated.
02/15/17	Revision; position statements and references updated.
02/15/18	Revision; position statements and references updated.
01/01/19	Annual CPT/HCPCS coding update. Added codes 81163, 81167; revised codes 81162, 81212, 81215-81217; deleted codes 81211, 81213, 81214.
02/15/19	Revision; position statements updated and reorganized; policy title, description, and references updated.
02/15/21	Review; position statements and references updated.