Genetic Testing: BRCA-Related Breast and/or Ovarian Cancer Syndrome Medical Necessity Guideline

Medical Necessity Guideline (MNG) Title: Genetic Testing: BRCA-Related Breast and/or Ovarian Cancer Syndrome		
MNG #: 109	**☒ SCO ☒ One Care** **☒ MA Medicare Premier** **☒ MA Medicare Value** **☒ RI Medicare Preferred** **☒ RI Medicare Value** **☒ RI Medicare Maximum**	**Prior Authorization Needed?** **☒ Yes (always required)** **☐ Yes (only in certain situations. See this MNG for details)** **☐ No**
Clinical: ☒	**Operational: ☐**	**Informational: ☐**
Benefit Type: **☒ Medicare** **☒ Medicaid**	**Approval Date:** 9/1/2022;	**Effective Date:** 12/24/2022;
Last Revised Date: **11/9/2023**	**Next Annual Review Date:** 9/1/2023; 11/9/2024	**Retire Date:**

OVERVIEW:

Breast cancer gene 1 (BRCA1) and breast cancer gene 2 (BRCA2) are *tumor suppressor genes that* help to control cell growth. When there are pathogenic (harmful) variations (or mutations) in these genes, there is a markedly increased susceptibility to the development of *hereditary breast and ovarian cancer syndrome (HBOC)*. This can lead to the development of breast and ovarian *cancer*, and an increased incidence of tumors in the fallopian tubes, pancreas, male breast, testicle(s), and prostate. A pathogenic variant in BRCA1 or BRCA2 can be inherited from either parent by a *germline mutation* or acquired through *somatic alteration*.

BRCA1 and BRCA2 testing can help to identify individuals at an increased risk for breast and ovarian cancers, to inform decisions on risk reduction (via further screening and prevention strategies), and to guide subsequent medical management options. Selection for this type of testing is based on a combination of factors, which includes, having a personal history of breast or ovarian cancer (at any age), personal history of other cancers (e.g., pancreatic cancer) in the absence of a family history, family history of BRCA-related cancers, ancestry, and whether a pathogenic or likely pathogenic variant has been previously identified in a family member. However, the American College of Medical Genetics and Genomics suggests that less than 20% of patients with breast and ovarian cancer who meet the national criteria for inherited cancer testing undergo testing. There is an ongoing need to improve identification and testing among high-risk populations and to reduce existing barriers for these patients to access testing.

Coverage criteria outlined in this MNG pertain to cisgender individuals. There is incomplete data on the lifetime risk of developing BRCA1/2-associated cancers in trans and nonbinary persons. CCA recognizes that the risks and screening for BRCA1/2-associated cancers for trans and nonbinary persons depend on individual circumstances, including hormonal and surgical interventions performed for gender affirmation. As such, CCA will review requests for BRCA1/2 testing in trans and nonbinary persons on an individual, person-centered, and case-by-case basis.

Genetic Testing: BRCA-Related Breast and/or Ovarian Cancer Syndrome
Medical Necessity Guideline

DEFINITIONS:
Breast cancer: In the context of the MNG, refers to both invasive and ductal carcinoma in situ.

Cancer: Disease that results from genetic alterations that result in deregulation of pathways that are important for various cellular functions. These include cell growth, maintenance of DNA integrity, cell cycle progression, and apoptosis.

Close blood relatives: Includes first, second, and third-degree relatives on the same side of the family. First-degree relatives refer to parents, siblings, and children. Second-degree relatives refer to half-siblings, aunts/uncles, grandparents, grandchildren, and nieces/nephews affected on the same side of the family. Third-degree relatives refer to first cousins, great-aunts/uncles, great-grandchildren, and great-grandparents affected on the same side of the family.

Germline mutation or variant: A gene change in a body's reproductive cell (egg or sperm) that becomes incorporated into the DNA of every cell in the body of the offspring.

Hereditary breast and ovarian cancer syndrome (HBOC): An inherited genetic condition, usually linked to pathogenic variations in the BRCA1 and BRCA2 genes, that increases the likelihood of the development of breast, ovarian, ductal, peritoneal, melanoma, prostate, and testicular cancers. Other genes that have been linked to HBOC are CDH1, PALB2, PTEN, and TP53.

High-risk group prostate cancer: (one or more of the following):
- cT3a
- Gleason score 8 to 10
- PSA level of more than 20.

Ovarian cancer: In the context of the MNG, includes fallopian tube and primary peritoneal cancers.

PARP-inhibitor: Type of targeted therapy that may also be called a poly (ADP-ribose) polymerase inhibitor. PARP is a substance that blocks an enzyme in cells and can help repair DNA when it becomes damaged. In cancer treatment, PARP inhibitors may help to keep cancer cells from repairing their damaged DNA, which causes them to die.

Somatic alteration: An alteration in DNA that occurs after conception. Somatic mutations can occur in any of the body's cells with the exception of the germ cells (sperm and egg). This means that these alterations are not passed down to children. However, these mutations can (but not always) cause cancer or other diseases.

Triple negative breast cancer: Breast cancer in which the tumor does not have the following receptors: estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2.

Tumor suppressor gene: A tumor suppressor gene encodes a protein that acts to regulate cell division. When it is inactivated by a mutation, the protein it encodes is not produced or does not function properly. This results in uncontrolled cell division which may contribute to the development of cancer.

Genetic Testing: BRCA-Related Breast and/or Ovarian Cancer Syndrome
Medical Necessity Guideline

Unknown or limited family history: In the context of the MNG, defined as having fewer than two known first-degree or second-degree female relatives or female relatives surviving beyond 45 years of age on either or both sides of the family (e.g., member was adopted).

Very-high-risk group prostate cancer (one or more of the following):

- cT3b or cT4
- Biopsy tissue shows areas with Gleason score 9 or 10
- More than 4 biopsy pieces with Gleason score 8 to 10
- 2 or 3 of the features found in the high-risk group (see above)

DECISION GUIDELINES:

Clinical Coverage Criteria:

Commonwealth Care Alliance (CCA) follows applicable Medicare and Medicaid regulations and uses InterQual Smart Sheets, when available, to review prior authorization requests for medical necessity. This Medical Necessity Guideline (MNG) applies to all CCA Products unless a more expansive and applicable CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), or state-specific medical necessity guideline exists.

1. Commonwealth Care Alliance may cover BRCA1 and BRCA2 genetic testing for a biologically related individual from a family with a known BRCA1 or BRCA2 pathogenic/likely pathogenic variant (P/LP) when **all** the following criteria are met:
    a. The results of genetic testing will be clinically useful in the clinical management of the member; and
    b. The member has a close blood relative with a known BRCA1 or BRCA2 pathogenic/likely pathogenic variant; and
    c. There is documentation of the known familial variant and relationship of the carrier(s) to the member.

2. Commonwealth Care Alliance may cover BRCA1 and BRCA2 genetic testing for an individual with a current diagnosis or a personal history of cancer when the BRCA variant status is unknown and when **all** the following criteria are met:
    a. The results of genetic testing will be clinically useful in the clinical management of the member; and
    b. One of the following criteria is met:
        i. Member has a personal history of breast cancer **AND** one or more of the following:
            I. Diagnosed at age ≤ 50 years; or
            II. Diagnosed at any age with an additional primary breast cancer; or
            III. Diagnosed at any age with triple negative breast cancer; or
            IV. Diagnosed at any age with male breast cancer; or
            V. Diagnosed at any age with ≥ 1 close blood relative with female breast cancer (age ≤ 50 years), ovarian cancer, pancreatic cancer, metastatic prostate cancer, high grade-risk group prostate

cancer or male breast cancer, **or** ≥3 diagnoses of breast and/or prostate cancer (any grade) on the same side of the family including the member with breast cancer; or

VI. Diagnosed with lobular breast cancer and with personal or family history of diffuse gastric cancer; or

VII. Member with first- or second-degree blood relative meeting one of criteria 2biI-2biVI; or

VIII. Ashkenazi Jewish ancestry; or

IX. Unknown/limited family history; or

X. There is documentation that member has a probability of >5% of a BRCA1/2 P/LP variant based on prior probability models (e.g., Tyrer-Cuzick, BRCAPro, CanRisk)

[OR]

ii. Member has a personal history of prostate cancer diagnosed at any age **AND** one or more of the following:

I. Ashkenazi Jewish ancestry; or

II. ≥ 1 close blood relative(s) with ovarian cancer, pancreatic cancer, breast cancer (age ≤ 50 years), triple negative breast cancer, male breast cancer or metastatic or high/very high-risk group prostate cancer; or

III. ≥3 close blood relatives with prostate cancer (any grade) and/or breast cancer on the same side of the family including the member with prostate cancer

[OR]

iii. Member has a personal history of male breast cancer, ovarian carcinoma, pancreatic cancer, high- or very-high-risk group prostate cancer or metastatic prostate cancer

[OR]

iv. BRCA1 or 2 pathogenic/likely pathogenic variant detected by tumor-profiling and has clinical implications if also identified in the germline.

3. Commonwealth Care Alliance may cover BRCA1 and BRCA2 genetic testing for an individual with no current diagnosis or personal history of a BRCA-related cancer with an unknown variant status, when the following criteria are met:

a. The results of genetic testing will be clinically useful in the clinical management of the member; and

b. One of the following criteria is met:

i. Member's affected family member is unavailable for testing; or

ii. Member has first- or second-degree blood relative with epithelial ovarian cancer at any age; or

iii. Member has first- or second-degree blood relative meeting one of criteria 2biI-2biVI; or

iv. There is documentation that genetic counseling was completed and a determination that the member has a probability of >2.5% of a BRCA1/2 P/LP variant based on prior probability models (eg, Tyrer-Cuzick, BRCAPro, CanRisk)

4. Commonwealth Care Alliance may cover BRCA1 and BRCA2 genetic testing when member is being considered for treatment with a PARP-inhibitor (Lynparza, Rubraca and Talzenna) and requested testing is required per FDA label indications and usage.

LIMITATIONS/EXCLUSIONS:

Genetic Testing: BRCA-Related Breast and/or Ovarian Cancer Syndrome Medical Necessity Guideline

1. Commonwealth Care Alliance will limit diagnostic genetic testing for a disease to one test per lifetime. Repeat testing will require review from a CCA Medical Director to assess for medical necessity. A duplicate genetic test for an inherited condition may be covered if there is uncertainty about the validity of the existing test result or if repeat testing of somatically acquired variants may be required to inform appropriate therapeutic decision-making.
2. Commonwealth Care Alliance will not cover and does not consider genetic tests that meet **ANY** of the following criteria as medically necessary:
    a. Testing for the purposes of surveillance and assessment of risks for other cancers unrelated to BRCA1 and BRCA2.
    b. Testing is performed primarily for the medical management of a family member.
    c. When the only indication for testing is family history and clinical judgement indicates that the member does not have a reasonable likelihood of having a BRCA-pathogenic/likely pathogenic variant, considering the member's current age and the age of female unaffected relatives who link the member with the affected relatives; *or*
    d. The member has been previously tested and there is certain validity of the test result.

AUTHORIZATION:

The following list(s) of codes is provided for reference purposes only and may not be all inclusive. Listing a code in this guideline does not signify that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. This Medical Necessity Guideline is subject to all applicable Plan Policies and Guidelines, including requirements for prior authorization and other requirements in Provider's agreement with the Plan (including complying with Plan's Provider Manual specifications).

CPT Code	Description	Coverage	
		SCO/ One Care	Medicare Advantage
81162	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (ie, detection of large gene arrangements)	✓	✓
81163	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, 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 (i.e., detection of large gene rearrangements)	✓	✓

Genetic Testing: BRCA-Related Breast and/or Ovarian Cancer Syndrome
Medical Necessity Guideline

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 (i.e., detection of large gene rearrangements	✓	✓
81167	BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (i.e., 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) gene analysis; full sequence analysis	✓	✓
81217	BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant	✓	✓
81479	Unlisted Molecular Pathology (Limited coverage may be provided)	✓	

REGULATORY NOTES:

Medical Necessity Guidelines are published to provide a better understanding of the basis upon which coverage decisions are made. CCA makes coverage decisions on a case-by-case basis by considering the individual member's health care needs. If at any time an applicable CMS LCD or NCD or state-specific MNG is more expansive than the criteria set forth herein, the NCD, LCD, or state-specific MNG criteria shall supersede these criteria.

This MNG references the specific regulations, coverage, limitations, service conditions, and/or prior authorization requirements in the following:
1. MassHealth, Guidelines for Medical Necessity Determination for Genetic Testing for Hereditary Breast and/or Ovarian Cancer.
2. MassHealth, 130 CMR 401.000: Independent Clinical Laboratory Services, Subchapter 4.
3. MassHealth, 101 CMR 320.000: Clinical Laboratory Services.
4. Medicare, Local Coverage Determination (L35000): Molecular Pathology Procedures.
5. Medicare, Local Coverage Article (A56199): Billing and Coding: Molecular Pathology Procedures.

Disclaimer

This Medical Necessity Guideline is not a rigid rule. As with all of CCA's criteria, the fact that a member does not meet these criteria does not, in and of itself, indicate that no coverage can be issued for these services. Providers are advised,

however, that if they request services for any member who they know does not meet our criteria, the request should be accompanied by clear and convincing documentation of medical necessity. The preferred type of documentation is the letter of medical necessity, indicating that a request should be covered either because there is supporting science indicating medical necessity (supporting literature (full text preferred) should be attached to the request), or describing the member's unique clinical circumstances, and describing why this service or supply will be more effective and/or less costly than another service which would otherwise be covered. Note that both supporting scientific evidence and a description of the member's unique clinical circumstances will generally be required.

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REVISION LOG:

REVISION DATE	DESCRIPTION
12/31/23	Utilization Management Committee approval
11/9/23	Updates to Clinical Coverage Criteria to align with NCCN Clinical practice guidelines in oncology: Genetic/familial high-risk assessment: Breast, ovarian, and pancreatic V2.2024.

APPROVALS:

David Mello	Senior Medical Director, Utilization Review and Medical Policy
CCA Senior Clinical Lead [Print]	**Title [Print]**
	12/31/2023
Signature	**Date**
Charlotte Finn	Medical Policy Manager
CCA Senior Operational Lead [Print]	**Title [Print]**
Charlotte Finn	12/1/2023
Signature	**Date**
Nazlim Hagmann	Chief Medical Officer
CCA CMO or Designee [Print]	**Title [Print]**

Genetic Testing: BRCA-Related Breast and/or Ovarian Cancer Syndrome
Medical Necessity Guideline

Signature

12/1/2023

Date