Medical Necessity Guideline

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<thead>
<tr>
<th>Medical Necessity Guideline (MNG) Title: Genetic Testing Hereditary Breast and Ovarian Cancer Syndrome Effective</th>
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<tbody>
<tr>
<td>MNG #: 006</td>
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<tr>
<td>Clinical: ☒</td>
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<tr>
<td>Medicare Benefit: ☐ Yes ☒ No</td>
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<td>Last Revised Date: 1/25/2019</td>
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OVERVIEW:
The Plan considers breast cancer susceptibility genetic mutation testing for hereditary breast cancer and ovarian cancer (HBOC) syndrome with site-specific BRCA1/BRCA2 gene testing, comprehensive BRCA1/BRCA2 gene sequencing analysis, multi-site 3 BRCA testing (for a member of Ashkenazi Jewish descent), and/or large genomic rearrangement testing of BRCA1 and BRCA2 genes to be medically necessary for all symptomatic or at-risk members when the Plan’s applicable medical criteria are met for the specified test.

Prior authorization is required for all molecular and chromosomal genetic testing except for prenatal genetic screening tests for a member with any pregnancy diagnosis code; see applicable policies for complete guidance.

DEFINITIONS:
- **Ashkenazi Jewish**: A term for people of eastern European Jewish heritage. The Ashkenazi Jewish population is at risk for specific genetic mutations due to ethnic background.
- **BRCA Genetic Variant Testing**: Test that uses DNA analysis to identify inherited mutations in genes associated with hereditary breast and ovarian cancer (HBOC) syndrome. This includes testing of BRCA1 genes, BRCA2 genes, and multi-site 3 BRCA testing (i.e., testing of three [3] common BRCA1 and BRCA2 founder variants in individuals of Ashkenazi Jewish descent).
- **BRCA1/2/3/4**: Genetic mutations which increase a person’s risk of breast cancer (and possibly certain other cancers)
- **Close Relative**: A blood relative that includes first, second, and third degree relatives.
- **First Degree Relative**: A blood relative of an individual who shares approximately 50% of his/her genes defined as a biological parent, full sibling, or child.
- **Gleason Score**: System of grading prostate cancer tissue, with scores ranging from 2 to 10 to indicate how likely it is that a tumor will spread. A low Gleason score of 2 to 4 means the cancer cells are similar to normal prostate tissue and the tumor is less like to spread quickly. A score of 8 to 10 indicates that the cancer cells have very few features of a normal cell and are likely to be aggressive. A score of 5 to 7 indicates intermediate risk.
- **Hereditary Breast and Ovarian Cancer (HBOC) Syndrome**: Condition caused by a germline pathogenic variant in BRCA1 or BRCA2, and is characterized by an increased lifetime risk for breast cancer, ovarian cancer, prostate cancer, and pancreatic cancer. Individuals with BRCA2 pathogenic variants may also be at an increased risk for melanoma. An increased likelihood of a BRCA1 or BRCA2 pathogenic variant is suspected on the basis of certain personal and family history characteristics, and a diagnosis of HBOC is made following molecular genetic testing in an individual or family with germline BRCA1 or BRCA2 pathogenic variant.
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- **Second Degree Relative**: A blood relative of an individual who shares approximately 25% of his/her genes defined as a biological grandparent, grandchild, aunt, uncle, nephew, niece, or half-sibling.
- **Third Degree Relative**: A blood relative of an individual who shares 12.5% of his/her genes as defined as a biological first cousin, great grandmother, or great grandfather.
- **Triple Negative Breast Cancer**: Any breast cancer that does not express the genes for estrogen receptor (ER), progesterone receptor (PR) or Her2/neu. This subtype of breast cancer is clinically characterized as more aggressive and less responsive to standard treatment and is associated with poorer overall patient prognosis.

**DECISION GUIDELINES**:
The guidelines included in this Plan policy are applicable to CCA members only if there are no criteria established for the specified service in a Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) on the date of the prior authorization request. Review the member’s product-specific benefit documents at [link to CCA plan documents here] to determine coverage.

**Clinical Coverage Criteria**:
**Genetic Testing for Breast and Ovarian Cancer**:

1. The results of the genetic test will significantly alter the medical management of the Member (documentation required).
   
   **AND**

2. The recommendation for testing is based on a review of risk factors, clinical presentation and family history, and is supported by consultation with a healthcare provider with expertise in genetic counseling (documentation of appropriate expertise required).
   
   **AND**

3. Member must meet the criteria in at least one of the below sections Multi-site 3 BRCA Genetic Testing for Members of Ashkenazi Decent

   **1. Multi-site 3 BRCA Genetic Testing for Members of Ashkenazi Decent**
   
   For Members of Ashkenazi descent with or without a Personal History of Breast Cancer, CCA may authorize Multi-site BRCA3 testing for Members with ONE of the following risks:

   a. Personal history of a primary breast cancer, epithelial ovarian/fallopian tube/primary peritoneal cancer, pancreatic cancer, or aggressive prostate cancer (defined as having a Gleason score of 7 or greater) at any age.

   b. No personal history of breast or epithelial ovarian/fallopian tube/primary peritoneal cancer and ONE of the following risks:
      
      i. Family history of breast or epithelial ovarian/fallopian tube/primary peritoneal cancer, diagnosed at any age, in any first-degree relative.
      
      ii. Family history of breast or epithelial ovarian/fallopian tube/primary peritoneal cancer, diagnosed at any age, in at least two second-degree relatives.
      
      iii. A first-degree relative with a known BRCA1or BRCA2 mutation
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FULL PANEL BRCA1 & BRCA2 GENETIC TESTING FOR MEMBERS NOT OF ASHKENAZI DESCENT

CCA may authorize BRCA 1 & BRCA 2 for Members when ONE of the following is met:

1. A known BRCA 1/2 pathogenic/likely pathogenic variant within the family (see “Type of BRCA Testing Ordered”)
2. Personal history of male breast cancer
3. Personal history of breast cancer and one or more of the following:
   i. Diagnosis at or before age 45
   ii. Diagnosis after age 45 and at or before age 50 and one of the following risks:
      a. An additional breast cancer primary at any age
      b. Family history of breast cancer, diagnosed at any age, in one or more first, second or third-degree relatives
      c. Family history of one or more first, second, or third-degree relatives with aggressive prostate cancer (defined as having a Gleason score of 7 or greater)
      d. An unknown or limited family history. A limited family history is defined as an individual with fewer than two first or second degree female relatives having lived beyond age 45 in either lineage.
      e. Diagnosed at or before age 60 with triple negative breast cancer. Triple negative breast cancer is defined as breast cancer in which the tumor does not have receptors for any of the following: estrogen, progesterone or human epidermal growth factor receptor 2 (HER2)
      f. Diagnosed at any age and one of the following:
         1. One or more first, second or third-degree relative with breast cancer diagnosed at or before age 50
         2. One or more first, second, or third degree relative with epithelial ovarian/fallopian tube/primary peritoneal cancer
         3. One or more first, second, or third degree relative with male breast cancer
         4. One or more first, second, or third degree relative with metastatic prostate cancer
         5. One or more first, second, or third degree relative with pancreatic cancer
         6. Two or more additional breast cancer diagnoses for Member at any age.
         7. Two or more breast cancer diagnoses (individuals or breast cancer primaries*) in a first, second or third-degree relative at any age
   g. Personal history of pancreatic cancer
   h. Personal history of metastatic prostate cancer

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1 Two breast cancer primaries includes bilateral (contralateral) disease or two or more clearly separate ipsilateral primary tumors diagnosed at either the same or different times. 4. Personal history of epithelial ovarian/fallopian tube/primary peritoneal cancer
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i. Personal history of aggressive (Gleason score of 7 or greater) prostate cancer and one of the following:

j. One or more first, second, or third degree relative with epithelial ovarian/fallopian tube/primary peritoneal cancer, pancreatic cancer, or metastatic prostate cancer diagnosed at any age

k. One or more first, second, or third degree relative with breast cancer diagnosed before age 50

l. Two or more first, second, or third degree relatives with breast or prostate cancer (any grade) diagnosed at any age

m. BRCA 1/2 pathogenic/likely pathogenic variant detected by tumor profiling on any tumor type in the absence of germline pathogenic/likely pathogenic variant analysis

n. A Member who does not meet any of the criteria outlined above but who has one or more first or second-degree relative meeting any of the above criteria

o. A combination of three or more first or second-degree relatives with breast cancer regardless of age at diagnosis

p. A third degree blood relative who has breast cancer and/or ovarian/fallopian tube/primary peritoneal cancer AND who has two or more first, second or third-degree relatives with breast cancer (one or more at or before age 50) and/or ovarian/fallopian tube/primary peritoneal cancer

LIMITATIONS/EXCLUSIONS:

1. The Plan does NOT cover genetic testing for BRCA1 and BRCA2 mutations for members less than age 18 on the date of service because it is considered investigational and there are no recommended preventive interventions for this age group. The National Society of Genetic Counselors (NSGC) “encourages deferring predictive genetic testing of minors for adult-onset conditions when results will not impact childhood medical management or significantly benefit the child.”

2. BRCA testing for any indications other than those above noted is considered experimental, investigational or unproven, and is therefore not medically necessary.

3. An unaffected member (i.e., no personal history of breast cancer) is not eligible for BRCA1/BRCA2 gene mutation testing if an affected blood relative is available and willing to be tested.

AUTHORIZATION:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not signify whether 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. Other Policies and Coverage Determination Guidelines may apply. This Medical Necessity Guideline is subject to all applicable laws and regulations, 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).
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<table>
<thead>
<tr>
<th>CPT Codes</th>
<th>Description: Codes Covered When Medically Necessary</th>
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<tr>
<td>81162</td>
<td>BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis</td>
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| 81211     | BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants in BRCA1 (i.e., exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)  
Plan note: See criteria in the Plan’s Genetic Testing and Pharmacogenetics medical policy, policy number OCA 3.727, for medically necessary indications for BRCA1 and BRCA2 mutation testing using tumor profiling to predict the effectiveness of cancer treatment (e.g., BRACAnalysis CDx®). |
| 81212     | BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants  
Plan note: Code may be used for multisite 3 BRCA testing. |
| 81213     | BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; uncommon duplication/deletion variants  
Plan note: Code used for large genomic rearrangement test (e.g., BRACAnalysis® Large Rearrangement Test or BART) and multisite 3 BRCA testing. |
| 81214     | BRCA1 (breast cancer 1) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants (i.e., exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb) |
| 81215     | BRCA1 (breast cancer 1) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant |
| 81216     | BRCA2 (breast cancer 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis |
| 81217     | BRCA2 (breast cancer 2) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant |

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<th>CPT Codes</th>
<th>Description: Codes Considered Not Medically Necessary for Genetic Testing for Hereditary Breast Cancer and Hereditary Ovarian Cancer (and Plan Medical Director Review is Required, as Specified in the Limitations Section)</th>
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<tr>
<td>81432</td>
<td>Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence and analysis panel, must include sequencing of at least 14 genes, including, BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, and TP53</td>
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<tr>
<td>81433</td>
<td>Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11</td>
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<tr>
<th>HCPCS Codes</th>
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<td>None</td>
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## REGULATORY NOTES:


8. The American College of Obstetricians and Gynecologists (ACOG). Committee on Genetics. Committee
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62. Myriad Genetic Laboratories, Inc. BRACAnalysis®. Accessed at:
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http://myriadgenetics.eu/products/bracanalysis/


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RELATED REFERENCES:

NA

ATTACHMENTS:

| EXHIBIT A: |
| EXHIBIT B |

REVISION LOG:

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APPROVALS:

Thomas A. Amoroso, MD  Medical Director, Utilization Management
CCA Senior Clinical Lead [Print]  Title [Print]

Signature  1/11/2019  Date

CCA Senior Operational Lead [Print]  Title [Print]

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CCA CMO or Designee [Print]  Title [Print]
Medical Necessity Guideline

1/19/2019

Signature: [Signature]

Date: ______________________