Medical Policy

Genetic Testing for Hereditary Breast/Ovarian Cancer Syndrome (BRCA1 or BRCA2)

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- Policy: Medicare
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Policy Number: 245
BCBSA Reference Number: 2.04.02
NCD/LCD: Local Coverage Determination (LCD): Molecular Pathology Procedures (L35000)

Related Policies
- Genetic Cancer Susceptibility Panels Using Next Generation Sequencing, #574
- Moderate Penetrance Variants Associated With Breast Cancer in Individuals at High Breast Cancer Risk, #722

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

PATIENTS WITH CANCER OR WITH PERSONAL HISTORY OF CANCER

Genetic testing for BRCA1 and BRCA2 variants in cancer-affected individuals may be considered MEDICALLY NECESSARY under any of the following circumstances:

- Individual from a family with a known BRCA1 or BRCA2 variant.
- Personal history of breast cancer and one or more of the following:
  - Diagnosed age ≤ 45 years
  - Two primary breast cancers when first 1st cancer diagnosis occurred age at ≤50 years
  - Diagnosed at age ≤50 years AND:
    - One or more 1st-, 2nd-, or 3rd-degree relative(s) with breast cancer at any age, pancreatic cancer or prostate cancer, or
    - Unknown or limited family history
  - Diagnosed at age ≤60 years with a triple-negative estrogen receptor-negative, progesterone receptor-negative, human epidermal growth factor receptor 2-negative breast cancer
  - Diagnosed at any age AND ≥1 1st-, 2nd-, or 3rd-degree relative with breast cancer diagnosed ≤ 50 years
  - Diagnosed at any age AND 1 or more 1st-, 2nd-, or 3rd-degree relative(s) with breast cancer
  - Diagnosed at any age AND 1 or more 1st-, 2nd-, or 3rd-degree relative(s) with epithelial ovarian, fallopian tube, or primary peritoneal cancer
Diagnosed at any age AND 2 or more 1st-, 2nd-, or 3rd-degree relatives with pancreatic cancer or prostate cancer or prostate cancer at any age

- 1st-, 2nd-, or 3rd-degree male relative with breast cancer
- Ethnicity associated with deleterious founder mutations (eg, Ashkenazi Jewish descent)

- Personal history of epithelial ovarian, fallopian tube, or primary peritoneal cancer
- Personal history of male breast cancer
- Personal history of pancreatic cancer or prostate cancer at any age AND 1 or more 1st-, 2nd-, or 3rd-degree relatives with either of the following:
  - Breast cancer ≤50
  - Ovarian, fallopian tube, or primary peritoneal cancer at any age
- Personal history of pancreatic cancer or prostate cancer at any age AND 2 or more 1st-, 2nd-, or 3rd-degree relatives with breast, pancreatic or prostate cancer at any age.
- For pancreatic cancer, if Ashkenazi Jewish ancestry (no additional affected relative is needed).

**PATIENTS WITHOUT CANCER OR WITHOUT HISTORY OF CANCER**

Genetic testing for *BRCA1* and *BRCA2* variants of **cancer-unaffected individuals** may be considered **MEDICALLY NECESSARY** under any of the following circumstances:

- Individual from a family with a known *BRCA1* or *BRCA2* variant,
- 1st- or 2nd-degree blood relative meeting any criterion listed above for Patients with Cancer,
- 3rd-degree blood relative with breast cancer and/or ovarian, fallopian tube, or primary peritoneal cancer AND 2 or more 1st-, 2nd-, or 3rd-degree relatives with breast cancer (≥1 at age ≤50 years) and/or ovarian, fallopian tube, or primary peritoneal cancer.

For familial assessment, 1st-, 2nd-, and 3rd-degree relatives are blood relatives on the same side of the family (maternal or paternal).

- 1st-degree relatives are parents, siblings, and children.
- 2nd-degree relatives are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half-siblings.
- 3rd-degree relatives are great-grandparents, great-aunts, great-uncles, great-grandchildren, and first cousins.

For familial assessment, prostate cancer is defined as Gleason score ≥7.

For example, fewer than 2 first- or second-degree female relatives having lived beyond age 45 in either lineage. In families with a large number of unaffected female relatives, the likelihood of variant detection may be very low.

Testing for Ashkenazi Jewish or other founder mutation(s) should be performed first: High-Risk Ethnic Groups.

**High-Risk Ethnic Groups**

Testing of eligible individuals who belong to ethnic populations in which there are well-characterized founder mutations should begin with tests specifically for these variants. For example, founder mutations account for approximately three-quarters of the *BRCA* variants found in Ashkenazi Jewish populations. When testing for founder mutations is negative, comprehensive variant analysis should then be performed.

Genetic testing for *BRCA1* and *BRCA2* variants in cancer-affected individuals or of cancer-unaffected individuals with a family history of cancer when criteria above are not met is considered **INVESTIGATIONAL**.

Genetic testing in minors for *BRCA1* and *BRCA2* variants is considered **INVESTIGATIONAL**.

*Current U.S. Preventive Services Task Force guidelines recommend screening women with any family history of breast, ovarian, tubal, or peritoneal cancer. Women with positive screening results should receive genetic counseling and, if indicated after counseling, *BRCA* testing (grade B recommendation).
Recommended screening tools designed to identify a family history that may be associated with an increased risk for potentially harmful variants in BRCA1 or BRCA2 are:

- Ontario Family History Assessment Tool (FHAT)
- Manchester Scoring System
- Referral Screening Tool (RST)
- Pedigree Assessment Tool (PAT)
- Family History Screen (FHS-7).

**Medicare HMO BlueSM and Medicare PPO BlueSM Members**

Medical necessity criteria and coding guidance for Medicare Advantage members living in Massachusetts can be found through the link below.

**Local Coverage Determination (LCD): Molecular Pathology Procedures (L35000)**

For medical necessity criteria and coding guidance for Medicare Advantage members living outside of Massachusetts, please see the Centers for Medicare and Medicaid Services website for information regarding your specific jurisdiction at https://www.cms.gov.

**Prior Authorization Information**

**Inpatient**

- For services described in this policy, precertification/preauthorization is required for all products if the procedure is performed inpatient.

**Outpatient**

- For services described in this policy, see below for products where prior authorization might be required if the procedure is performed outpatient.

<table>
<thead>
<tr>
<th>Product</th>
<th>Prior Authorization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial Managed Care (HMO and POS)</td>
<td>*Prior authorization is required.</td>
</tr>
<tr>
<td>Commercial PPO and Indemnity</td>
<td>Prior authorization is not required.</td>
</tr>
<tr>
<td>Medicare HMO BlueSM</td>
<td>Prior authorization is not required.</td>
</tr>
<tr>
<td>Medicare PPO BlueSM</td>
<td>Prior authorization is not required.</td>
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</tbody>
</table>

*Providers must submit the notification request for prior authorization in Clear Coverage™*

- To submit a notification in Clear Coverage, log on to our provider website, www.bluecrossma.com/provider, and go to eTools>Clear Coverage (Genetic Testing).
- Click Go now to open Clear Coverage.

The Clear Coverage e-tool is the only method by which providers may obtain prior authorization for HMO and POS members who have primary care providers in Massachusetts.

**CPT Codes / HCPCS Codes / ICD Codes**

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:
### CPT Codes

<table>
<thead>
<tr>
<th>CPT codes:</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>81162</td>
<td>BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis</td>
</tr>
<tr>
<td>81211</td>
<td>BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants in BRCA1 (ie, exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)</td>
</tr>
<tr>
<td>81212</td>
<td>BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants</td>
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<tr>
<td>81213</td>
<td>BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; uncommon duplication/deletion variants</td>
</tr>
<tr>
<td>81215</td>
<td>BRCA1 (breast cancer 1) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant</td>
</tr>
<tr>
<td>81217</td>
<td>BRCA2 (breast cancer 2) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant</td>
</tr>
</tbody>
</table>

### 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 variants 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, 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. For this evidence review, we refer collectively to both as **hereditary breast and/or 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 cancer, *BRCA* variants are responsible only for a proportion of affected families. *BRCA* gene variants are inherited in an autosomal dominant fashion through 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.

### Summary

Hereditary breast and ovarian cancer syndrome describes the familial cancer syndromes related to variants in the *BRCA* genes (*BRCA1* located on chromosome 17q21, *BRCA2* located on chromosome 13q12-13). Families with hereditary breast and ovarian cancer syndrome have an increased susceptibility to the following types of cancer: breast cancer occurring at a young age, bilateral breast cancer, male breast cancer, ovarian cancer (at any age), cancer of the fallopian tube, primary peritoneal cancer, prostate cancer, pancreatic cancer, gastrointestinal cancers, melanoma, and laryngeal cancer.

For individuals who have cancer or a personal or family cancer history and meet criteria suggesting a risk of hereditary breast and ovarian cancer syndrome who receive genetic testing for a *BRCA1* or *BRCA2* variant, the evidence includes a TEC Assessment and studies of variant prevalence and cancer risk. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and quality of life. The accuracy of variant testing has been shown to be high. Studies of lifetime risk of cancer for carriers of a *BRCA* variant have shown a risk as high as 85%. Knowledge of *BRCA* variant status in individuals at risk of a *BRCA* variant may impact health care decisions to reduce risk, including intensive surveillance, chemoprevention, and/or prophylactic intervention. In individuals with *BRCA1* or *BRCA2* variants, prophylactic mastectomy and oophorectomy have been found to significantly increase disease-
specific survival and overall survival. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

### Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/2018</td>
<td>BCBSA National medical policy review.</td>
</tr>
<tr>
<td></td>
<td>First medically necessary policy statement updated to reflect changes to NCCN recommendation. Effective 4/1/2018.</td>
</tr>
<tr>
<td>12/2016</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
<tr>
<td>1/2016</td>
<td>Clarified coding information.</td>
</tr>
<tr>
<td>6/2015</td>
<td>Local Coverage Determination (LCD): Molecular Pathology Procedures (L34506) added.</td>
</tr>
<tr>
<td>4/2015</td>
<td>BCBSA National medical policy review.</td>
</tr>
<tr>
<td></td>
<td>CHEK2 removed from policy and from policy statements. Policy statement addressing type of testing (ie, large genomic rearrangements) deleted (now addressed in testing strategy). Title changed to reflect focus on hereditary breast and ovarian cancer syndrome (HBOC). Effective 4/1/2015.</td>
</tr>
<tr>
<td>10/2014</td>
<td>Clarified coding information.</td>
</tr>
<tr>
<td>8/2014</td>
<td>BCBSA National medical policy review.</td>
</tr>
<tr>
<td></td>
<td>New investigational indications described. Effective 8/1/2014.</td>
</tr>
<tr>
<td>6/2013</td>
<td>BCBSA National medical policy review.</td>
</tr>
<tr>
<td></td>
<td>New medically necessary indications described. Effective 6/1/2013.</td>
</tr>
<tr>
<td></td>
<td>Changes to policy statements.</td>
</tr>
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### Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
- Medical Policy Terms of Use
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines

### References

1. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). BRCA1 and BRCA2 testing to determine the risk of breast and ovarian cancer. TEC Assessments. 1997;Volume 12:Tab 4.


