Medical Policy

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

Table of Contents
- Policy: Commercial
- Policy: Medicare
- Authorization Information
- Coding Information
- Description
- Policy History
- Information Pertaining to All Policies
- References

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

Policy

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

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

- Women from a family with a known BRCA1 or BRCA2 mutation,
- Women with a personal history of breast cancer and who are affected with any one of the following:
  - Diagnosed age ≤ 45 years,
  - Two breast primary cancers with first cancer diagnosis occurring prior to age 50
  - Diagnosed age ≤50 years AND:
    - ≥1 1st-, 2nd-, or 3rd-degree relative with breast cancer at any age or,
    - Unknown or limited family history
  - Triple negative breast cancer (neither express estrogen receptor and progesterone receptor, nor overexpress HER2) diagnosed at younger than age 60 or,
  - Diagnosed any age AND ≥1 1st-, 2nd-, or 3rd-degree relative with breast cancer diagnosed ≤ 50 years
  - Diagnosed any age AND ≥2 1st-, 2nd-, or 3rd-degree relatives with breast cancer at any age
  - Diagnosed any age AND ≥1 1st-, 2nd-, or 3rd-degree relative with epithelial ovarian/fallopian tube/primary peritoneal cancer
  - Diagnosed any age AND ≥2 1st-, 2nd-, or 3rd-degree relatives with pancreatic 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
- Women affected with epithelial ovarian cancer/fallopian tube/primary peritoneal cancer,
- Men affected with breast cancer at any age, or
- Personal history of pancreatic cancer or prostate cancer at any age AND ≥2 1st-, 2nd-, or 3rd-degree relatives with any of the following at any age. For pancreatic cancer, if Ashkenazi Jewish ancestry, only 1 additional affected relative is needed.
  - Breast cancer
  - Ovarian/fallopian tube/primary peritoneal cancer
  - Pancreatic or prostate cancer.

Genetic testing for BRCA1 and BRCA2 mutations of cancer-unaffected adults may be MEDICALLY NECESSARY under any of the following circumstances:
- Unaffected individuals (male or female) from families with a known BRCA1 or BRCA2 mutation,
- Unaffected individuals with one or more 1st- or 2nd-degree blood relative meeting any criterion listed above for Patients with Cancer, or
- Unaffected individuals with one or more 3rd-degree blood relative with breast cancer and/or ovarian/fallopian tube/primary peritoneal cancer AND ≥2 1st-, 2nd-, or 3rd-degree relatives with breast cancer (≥1 at age ≤50 years) and/or ovarian/fallopian tube/primary peritoneal cancer.

Genetic testing either for those affected by breast, ovarian, fallopian tube, or primary peritoneal cancer or for unaffected individuals, including those with a family history of pancreatic cancer, unless they meet the above conditions is INVESTIGATIONAL.

Genetic testing in minors for BRCA1 and BRCA2 mutations is INVESTIGATIONAL.

For the purpose of 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.

Current U.S. Preventive Services Task Force (USPSTF) 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.

Recommended screening tools designed to identify a family history that may be associated with an increased risk for potentially harmful mutations in BRCA1 or BRCA2 are:
- Ontario Family History Assessment Tool (FHAT)
- Manchester Scoring System
- Referral Screening Tool (RST)
- Pedigree Assessment Tool (PAT)
- 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
Pre-service approval is required for all inpatient services for all products. See below for situations where prior authorization may be required or may not be required for outpatient services.
Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

<table>
<thead>
<tr>
<th>Outpatient</th>
<th>Commercial Managed Care (HMO and POS)</th>
<th>Yes*</th>
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<tbody>
<tr>
<td></td>
<td>Commercial PPO and Indemnity</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Medicare HMO BlueSM</td>
<td>No</td>
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<tr>
<td></td>
<td>Medicare PPO BlueSM</td>
<td>No</td>
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*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:

<table>
<thead>
<tr>
<th>CPT codes</th>
<th>Code Description</th>
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<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>
</tr>
<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>
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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 \textit{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 mutations in the \textit{BRCA1} and \textit{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, \textit{BRCA} mutations are responsible only for a proportion of affected families. \textit{BRCA} gene mutations are inherited in an autosomal dominant fashion through maternal or paternal lineage. It is possible to test for abnormalities in \textit{BRCA1} and \textit{BRCA2} genes to identify the specific mutation in cancer cases and to identify family members at increased cancer risk. Family members without existing cancer who are found to have \textit{BRCA} mutations can consider preventive interventions for reducing risk and mortality.

Summary
Hereditary breast and ovarian cancer (HBOC) syndrome describes the familial cancer syndromes related to mutations in the \textit{BRCA} genes (\textit{BRCA1} located on chromosome 17q21, \textit{BRCA2} located on chromosome 13q12-13). Families with HBOC syndrome have an increased susceptibility to 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, as well as other cancers, such as prostate cancer, pancreatic cancer, gastrointestinal cancers, melanoma, and laryngeal cancer.

For individuals who have cancer or a personal or family cancer history and meeting criteria suggesting a risk of HBOC syndrome who receive genetic testing for a \textit{BRCA1} or \textit{BRCA2} mutation, the evidence includes a TEC Assessment and studies of mutation prevalence and cancer risk. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, morbid events, quality of life, and treatment-related morbidity. The accuracy of mutation testing has been shown to be high. Studies of lifetime risk of cancer for carriers of a \textit{BRCA} mutation have shown a risk as high as 85%. Knowledge of \textit{BRCA} mutation status in individuals at risk of a \textit{BRCA} mutation may impact health care decisions to reduce risk, including intensive surveillance, chemoprevention, and/or prophylactic intervention. 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>
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<tbody>
<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. CHEK2 removed from policy and from policy statements. Policy statement addressing type of testing (ie, large genomic rearrangements) deleted (now</td>
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| 4 |
addressed in testing strategy). Title changed to reflect focus on hereditary breast and ovarian cancer syndrome (HBOC). Effective 4/1/2015.

<table>
<thead>
<tr>
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<th>Event</th>
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<tr>
<td>10/2014</td>
<td>Clarified coding information.</td>
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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.


