Medical Policy
Genetic Testing for Hereditary Breast and/or Ovarian Cancer

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

Related Policies
- Genetic Cancer Susceptibility Panels Using Next Generation Sequencing, #574

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

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,
- 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.

Testing for genomic rearrangements of the BRCA1 and BRCA2 genes in patients who meet criteria for BRCA testing whose testing for point mutations is negative may be MEDICALLY NECESSARY.

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.

Testing for CHEK2 genetic abnormalities (mutations, deletions, etc.) in affected and unaffected patients with breast cancer irrespective of the family history 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.

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.
Outpatient

<table>
<thead>
<tr>
<th>Coverage Type</th>
<th>Coverage Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial Managed Care (HMO and POS)</td>
<td>No</td>
</tr>
<tr>
<td>Commercial PPO and Indemnity</td>
<td>No</td>
</tr>
<tr>
<td>Medicare HMO Blue℠</td>
<td>No</td>
</tr>
<tr>
<td>Medicare PPO Blue℠</td>
<td>No</td>
</tr>
</tbody>
</table>

CPT Codes / HCPCS Codes / ICD-9 Codes
The following codes are included below for informational purposes. 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.

CPT Codes

<table>
<thead>
<tr>
<th>CPT codes</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<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>
</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

Hereditary breast and ovarian cancer (HBOC) syndrome describes the familial cancer syndromes that are related to mutations in the BRCA genes (BRCA1 located on chromosome 17q21 and BRCA2 located on chromosome 13q12-13). Identification of patients with BRCA mutations may lead to enhanced screening and/or surveillance that could lead to improved outcomes.

Several genetic syndromes with an autosomal dominant pattern of inheritance that feature breast cancer have been identified. Of these, 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, 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 policy, both will be referred to collectively as hereditary breast and/or ovarian cancer.

Germline mutations 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 mutations are responsible only for a proportion of affected families and research to date has not yet identified other moderate or high-penetrance gene mutations that account for disease in these families. BRCA gene mutations 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 mutation in cancer cases and to identify family members with increased cancer risk. Family members without existing cancer who are found to have BRCA mutations can consider preventive interventions for reducing risk and mortality.

CHEK2 (cell cycle checkpoint kinase 2) is also involved with DNA repair and human cancer predisposition, like BRCA1 and BRCA2. CHEK2 is normally activated in response to DNA double-stranded breaks. CHEK2 regulates the function of BRCA1 protein in DNA repair and also exerts critical roles in cell cycle control and apoptosis. The CHEK2 mutation, 1100delC in exon 10 has been associated with familial breast cancers.

Summary

The presence of a BRCA1 or BRCA2 mutation confers a high lifetime risk for breast and ovarian cancer among affected women. These mutations may be gene sequence variations or large rearrangements/deletions. Knowledge of mutation status in individuals at risk of a BRCA mutation may impact healthcare decisions to reduce risk. Risk-reducing options include intensive surveillance, chemoprophylaxis, prophylactic mastectomy, or prophylactic oophorectomy. Criteria for testing high-risk women have been developed by National Comprehensive Cancer Network (NCCN), the U.S. Preventive Services Task Force (USPSTF) and other review bodies. Definitions of high-risk vary somewhat, and there is not widespread agreement on the optimal criteria that should be used for defining high-risk. When testing high-risk women, health outcomes are improved; therefore, testing high-risk women for BRCA1 and BRCA2 mutations may be considered medically necessary.

Mutations other than BRCA1 and BRCA2 have been reported to be associated with an increased risk of breast cancer. Although a number of these, for example the CHEK2 mutation, have been confirmed to be associated with increased risk, clinical utility of testing for these non-BRCA mutations has not been demonstrated. Therefore, genetic testing for mutations other than BRCA1 and BRCA2 to determine risk of breast and/or ovarian cancer is considered investigational.

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/2014</td>
<td>Clarified coding information</td>
</tr>
</tbody>
</table>

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
3. 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.


