

Medical Coverage Policy



Genetic Testing: Hereditary Breast and/or Ovarian Cancer

Device/Equipment Drug Medical Surgery Test Other

Effective Date:	7/1/2001	Policy Last Updated:	05/07/2013
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Prospective review is recommended/required. Please check the member agreement for preauthorization guidelines.

Prospective review is not required.

Description:

Hereditary breast and ovarian cancer (HBOC) syndrome describes the familial cancer syndromes that are related to mutations in the *BRCA* genes. 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 features 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 *BRCA* 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, 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.

Germline mutations in the *BRCA1* and *BRCA2* genes are responsible for the cancer susceptibility in the majority of HBOC families, especially if ovarian cancer or male breast cancer are features. However, in site-specific breast cancer, *BRCA* mutations are responsible for only 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 kinase2) 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.

In identifying families with a high risk of mutation in the *BRCA1* or *BRCA2* gene, both maternal and paternal family histories are important, but each lineage must be considered separately. Any of the following scenarios indicates a high risk of *BRCA1* or *BRCA2* mutation. In assessing risk of a mutation for those affected with cancer, the overall family history (one lineage) including the affected person is considered.

Recent definitions of high-risk have been published, including the 2012 revised recommendations from National Comprehensive Cancer Network (NCCN). The high-risk criteria largely represent NCCN hereditary breast and/or ovarian cancer syndrome testing criteria with some modifications based on additional guidelines and review of evidence. See Risk Factors in Medical Criteria.

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.

Based on published studies, a substantial minority of clinically significant BRCA mutations will be large genomic rearrangements that are not detected by sequence analysis. These mutations will be missed if BART testing (BRCAAnalysis® Rearrangement Test) is not performed. Myriad Genetics Laboratories BART test includes analysis for five common BRCA1 genomic rearrangements (large deletions and duplications) in their full testing. Testing for detectable rearrangements beyond these five, is offered free of charge by Myriad to highest risk women (i.e., an affected proband with breast cancer before age 50, and two close relatives with breast cancer under age 50, or ovarian cancer). Clinical guidelines, such as NCCN, consider BART testing as part of comprehensive BRCA testing and do not require additional criteria other than a negative sequence result. Therefore, testing for genomic rearrangements of *BRCA1* and *BRCA2* with BART may be considered medically necessary as part of comprehensive BRCA analysis, when testing for standard mutations on sequence analysis is negative.

Mutations other than *BRCA1* and *BRCA2* have been reported to be associated with an increased risk of breast cancer. While 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 not medically necessary as there is as there is no proven efficacy.

The use of genetic testing for *BRCA* mutations has limited or no clinical utility in minors. This is because there is no change in management for minors as a result of knowledge of the presence or absence of a deleterious mutation. Therefore, genetic testing on minors for *BRCA1* or *BRCA2* mutations is considered not medically necessary as there is no proven efficacy.

Medical Criteria:

Cancer-affected Individuals: All Products

Genetic testing for *BRCA1* and *BRCA2* mutations in cancer-affected individuals may be considered **medically necessary** under any of the following circumstances:

- Women who are affected with breast cancer or pancreatic cancer, and are from families with a high risk of *BRCA1* or *BRCA2* mutation as defined in the Policy Guidelines, OR;
- Women who are affected with breast cancer or pancreatic cancer who are not from families with a high risk of *BRCA1* or *BRCA2* mutation, as defined in Policy Guidelines, but are affected with any one of the following:
 - early onset breast cancer;
 - two breast primary cancers with the first cancer diagnosis occurring prior to age 50 years;
 - triple negative breast cancer (neither express estrogen receptor and progesterone receptor, nor overexpress HER2) diagnosed at younger than age 60;
 - two or more close blood relatives with pancreatic cancer at any age
- Women affected with epithelial ovarian cancer/fallopian tube /primary peritoneal cancer, OR;
- Men affected with breast cancer at any age, OR;
- Those affected with breast cancer who are from an ethnic background, e.g., Ashkenazi Jewish descent, associated with deleterious founder mutations.

Unaffected adults: Commercial Products only

Genetic testing for *BRCA1* and *BRCA2* mutations of unaffected adults may be considered **medically necessary** under any of the following circumstances:

- Unaffected individuals (male or female) from families with a known *BRCA1* or *BRCA2* mutation, OR;
- Unaffected individuals from families with a high risk of *BRCA1* or *BRCA2* mutation based on a family history, where it is not possible to test an affected family member for a mutation.
- Unaffected individuals in populations at risk for specific founder mutations due to ethnic background, e.g., Ashkenazi Jewish descent, and with one or more relatives with breast, epithelial ovarian, fallopian tube, or primary peritoneal cancer at any age

Risk Factors:

A personal or family history suggesting genetic cancer susceptibility requires at least one of the following criteria to be present:

- Individual from a family with a known deleterious *BRCA1/BRCA2* mutation
- Personal history of breast cancer plus one or more of the following:
 - Diagnosed at an early age (see definition, following)
 - Diagnosed at age ≤ 50 years with at least one close blood relative (see definition, following) with breast cancer at age ≤ 50 years and/or at least one close blood relative with epithelial ovarian/fallopian tube/primary peritoneal cancer at any age
 - Two breast primaries when the first breast cancer diagnosis occurred prior to age 50 years
 - Diagnosed age < 60 years with a triple negative breast cancer
 - Diagnosed age < 50 years with a limited family history
 - Diagnosed at any age, with ≥ 2 close blood relatives with breast and/or epithelial ovarian/fallopian tube/primary peritoneal cancer at any age
 - Close male relative with breast cancer
 - For an individual of ethnicity associated with higher mutation frequency (e.g., Ashkenazi Jewish) no additional family history may be required
- Personal history of epithelial ovarian/fallopian tube/primary peritoneal cancer
- Personal history of male breast cancer
- Personal history of breast and/or ovarian cancer at any age with ≥ 2 close blood relatives with pancreatic cancer at any age
- Personal history of pancreatic cancer at any age with ≥ 2 close blood relatives with breast and/or ovarian cancer and/or pancreatic cancer at any age
- Family history only:
 - Close blood relative meeting any of the above criteria*

Early age at diagnosis refers generally to diagnosis before age 40 to 45 years; an exact cutoff for testing affected individuals without known family history but with cancer diagnosis at an early age has not been established, although guidelines of the American College of Medical Genetics suggest age 45 years or younger.

*Close blood relative typically refers to first-degree (parent, full sibling, or offspring) and second-degree (grandparent, grandchild, uncle, aunt, niece, nephew, or half-sibling) relatives in diseases associated with high penetrance gene mutations such as *BRCA1* and *BRCA2* mutations. Accommodation may be made to include third-degree relatives (first cousin, great grandparent

or great grandchild) in some cases, e.g., limited family history, particularly in tracing hereditary breast and ovarian and related cancers in the paternal lineage.

Policy:

Prior authorization is required for BlueCHIP for Medicare and recommended for all other lines of business.

Commercial

Genetic testing for BRCA1 and BRCA2 mutations, and BART testing is considered **medically necessary** when the above listed medical criteria has been met. For all other indications, unless they meet the criteria above, genetic testing is considered **not medically necessary** as there is insufficient peer-reviewed literature that demonstrates the efficacy of this testing.

Testing for *CHEK2* abnormality (mutations, deletions, etc.) in affected and unaffected patients with breast cancer, irrespective of the family history is considered **not medically necessary** as there is insufficient peer-reviewed literature that demonstrates the efficacy of this testing.

BlueCHIP for Medicare

Genetic testing for BRCA1 and BRCA2 mutations, and BART testing is considered **medically necessary** when the above listed medical criteria for cancer affected individuals has been met. For all other indications, unless they meet the criteria above, genetic testing is considered **not medically necessary** as there is insufficient peer-reviewed literature that demonstrates the efficacy of this testing.

Testing for *CHEK2* abnormality (mutations, deletions, etc.) in affected patients with breast cancer, irrespective of the family history is considered **not medically necessary** as there is insufficient peer-reviewed literature that demonstrates the efficacy of this testing.

For unaffected individuals genetic screening is not covered as Medicare excludes all screening (not just genetic screening) with certain statutory exceptions. Blue CHIP for Medicare provides no additional benefits for genetic screening.

For all products

Testing for genomic rearrangements of the *BRCA1* and *BRCA2* genes may be considered **medically necessary** in patients who meet criteria for *BRCA* testing, whose testing for point mutations is negative.

Genetic testing in minors for *BRCA1* and *BRCA2* mutations is considered **not medically necessary** as there is insufficient peer-reviewed literature that demonstrates the efficacy of this testing.

Coverage:

Medicare excludes all screening (not just genetic screening) with certain statutory exceptions. Blue CHIP for Medicare provides no additional benefits for genetic screening. **Only** if the patient exhibits signs or symptoms of the disease, would the test not be considered screening.

Benefits may vary between groups/contracts. Please refer to the appropriate Evidence of Coverage, Subscriber Agreement, or Benefit Booklet for applicable genetic testing benefits/coverage.

Coding:

The following codes are covered when the medical criteria has been met.

81211, 81212, 81213, 81214, 81215, 81216, 81217

Brac analysis rearrangement test (BART):

Brac analysis rearrangement test (BART) should be reported using an unlisted code as at this time there is no code specific to the test.

Also known as:

None

Related Topics:

Genetic Testing

Published:

Provider Update, July 2013

Provider Update, April 2012

Provider Update, April 2011

Provider Update, November 2009

Provider Update, February 2009

Provider Update, November 2008

Policy Update, January 2008

Policy Update, August 2006

Policy Update, July 2001

References:

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- II. Genetic/Familial High-Risk Assessment: Breast and Ovarian (V.1.2012). *National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology*. Available online at: http://www.nccn.org/professionals/physician_gls/PDF/genetics_screening.pdf.
- III. ACOG Practice Bulletin No. 103: Hereditary breast and ovarian cancer syndrome. *Obstet Gynecol* 2009; 113(4):957-66.

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History:

April 2013 - annual review with text changes

Jan 2013 - codes deleted:

83890 83891 83892 83893 83894 83896 83897 83898 83900 83902 83903 83906
S3818

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