Policy Description

BRCA1 and BRCA2 are two distinct tumor suppressor genes involved in a common DNA repair process (Roy, Chun, & Powell, 2012). Germline mutations of BRCA genes are associated with an increased risk of breast and ovarian cancer, as well as other cancer types including pancreatic, and prostate cancer to a lesser extent (Paul & Paul, 2014).

Related Policies

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<tr>
<th>Policy Number</th>
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Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual’s benefit coverage at the time of the request.

Consideration of both maternal and paternal family histories is necessary in the evaluation of individuals for risk of carrying a mutation in the BRCA1 or BRCA 2 gene; each lineage must be considered separately.

1. BRCA 1 and 2 testing should be offered for individuals meeting any of the criteria described in 2 through 4 below if the individual
   a. Has received genetic counseling AND
   b. Is at least 18 years of age.

2. BRCA 1 and 2 testing in an individual from a family with a known deleterious BRCA 1/BRCA 2 gene mutation MEETS COVERAGE CRITERIA and is limited to the known familial mutation. If the specific familial mutation is unknown, testing for large genomic rearrangements of BRCA1 and BRCA2 MEETS COVERAGE CRITERIA

3. BRCA 1 and 2 testing MEETS COVERAGE CRITERIA when an individual with cancer meets any of the following criteria:
a. Has a history of ovarian carcinoma (See Note 1), fallopian tube, or primary peritoneal cancer

b. Has a history of male breast cancer

c. Has a history of metastatic prostate cancer with radiographic evidence of or biopsy-proven disease

d. Has a personal history of high-grade prostate cancer with Gleason score $\geq 7$ at any age AND at least one of the following:

   i. $>1$ close blood relative (See Note 2) with ovarian carcinoma (See Note 1), pancreatic cancer, or metastatic prostate cancer at any age or breast cancer $<50$ years of age; OR

   ii. Two close blood relatives (See Note 2) with breast cancer or prostate cancer of any grade at any age; OR

   iii. Is of Ashkenazi Jewish ancestry (See Note 3).

e. Has a personal history of pancreatic cancer

f. Diagnosed with breast cancer at age $\leq 45$ years of age

g. Diagnosed with breast cancer between ages 46 and 50 years and one of the following:

   i. An additional breast cancer primary at any age

   ii. At least one close blood relative (See Note 2) with breast cancer at any age

   iii. At least one close blood relative (See Note 2) with high-grade (Gleason score $\geq 7$) prostate cancer

   An unknown or limited family history

h. Diagnosed with breast cancer at any age and one of the following:

   i. At least one close blood relative (See Note 2) with:

      1) Breast cancer diagnosed by age 50 years; or

      2) Ovarian carcinoma (See Note 1); or

      3) Male breast cancer; or

      4) Metastatic prostate cancer; or

      5) Pancreatic cancer

   ii. Two or more additional diagnoses of breast cancer at any age in patient and/or in close blood relatives (See Note 2)

   i. Diagnosed with breast cancer at age $\leq 60$ years and triple negative breast cancer (estrogen receptor/ER negative, progesterone receptor/PR negative and human epidermal growth factor/HER-2 negative)

   j. An individual with ethnicity associated with high mutation frequency (as in Ashkenazi Jewish persons) no additional family history may be required* (See Note 3)
k. Has a *BRCA 1* or *2* mutation detected by tumor profiling in the absence of germline mutation testing

l. Testing for mutations in the *BRCA1* and *BRCA2* genes is limited to once per lifetime unless a patient with ovarian cancer is undergoing treatment with a PARP (PolyADP-ribose polymerase) inhibitor or a patient has HER2-negative recurrent or metastatic breast cancer eligible for single agent therapy with a PARP inhibitor (eg. Olaparib), testing for additional clinically relevant mutations is warranted.

4. Testing for individuals without cancer (note the significant limitation interpreting test results in persons unaffected by cancer) **MEETS COVERAGE CRITERIA ONLY** if family members affected by breast, ovarian (See Note 1), pancreatic, metastatic prostate cancer, fallopian tube, or primary peritoneal cancers are not available for testing **AND:**

   a) Individual has a first- or second-degree relative meeting any of the criteria in #3; **OR**

   b) Women who have family members with breast, ovarian, tubal, or peritoneal cancer with positive screening results from a tool (See Note 4) designed to identify a family history that may be associated with an increased risk for potentially harmful mutations in breast cancer susceptibility genes (*BRCA1* or *BRCA2*).

5. Testing for *BRCA 1* and *BRCA 2* **DOES NOT MEET COVERAGE CRITERIA** for the following:

   a) Genetic testing in minors < 18 years of age

   b) General population screening

   c) In all other situations not specified above

6. Testing family members for a variant of unknown significance is considered **EXPERIMENTAL AND INVESTIGATIONAL.**

**Note 1:** Ovarian cancer excluding germline tumors

**Note 2:** Close blood relatives include 1st-degree relatives (e.g., parents, siblings, and children), 2nd-degree relatives (e.g., grandparents, aunts, uncles, nieces, nephews, grandchildren, and half-siblings), and 3rd-degree relatives (great-grandparents, great-aunts, great-uncles, great-grandchildren, and first cousins), all of whom are on the same side of the family.

**Note 3:** Testing of Ashkenazi Jewish individuals without a known familial mutation should be initially limited to the three known founder mutations (185delAG and 518insC in *BRCA1*; 617delT in *BRCA2*). If testing is negative for founder mutations, comprehensive genetic testing may be considered. Comprehensive genetic testing can also be considered if ancestry also include non-Ashkenazi Jewish relatives or if other BRCA-related criteria are met. In addition, before August 2006, testing for large deletions and rearrangements was not performed, thus some patients with familial breast cancer who had negative BRCA testing before this time may consider repeat testing for the rearrangements.

**Note 4:** According to the USPSTF recommendation in 2013, the risk tools include the Ontario Family History Assessment Tool, Manchester Scoring System, Referral Screening Tool, Pedigree Assessment Tool, and FHS-7. They do not specifically state the preference of one tool over any of the others listed; however, the USPSTF specifically states, “To determine which patients would benefit from BRCA risk assessment, primary care providers should not use general breast cancer risk assessment models (for example, the National Cancer Institute Breast Cancer Risk Assessment Tool, which is based on the Gail model) because they are not designed to determine which women should receive genetic counseling or BRCA testing (USPSTF, 2013).” The USPSTF does not specifically list what constitutes an increased risk within the recommendation.
**Scientific Background**

BRCA1 and BRCA2 are critical genes in the process of homologous recombination repair of double-strand DNA breaks (Walsh, 2015). Both genes are very large (occupying about 70 kb) and encode a combined total of 49 exons. They are considered tumor suppressor genes and a loss of function on either gene increases the cancer risk (Pan & Xie, 2017). BRCA1 is thought to regulate c-Abl kinase activity (as loss of BRCA1 results in a constitutively activated c-Abl kinase) whereas BRCA2 is thought to regulate Rad51, which repairs DNA damage such as chromosomal breaks (Yoshida & Miki, 2004).

Different regions of mutation may confer different types of risk. For example, BRCA2 has an area called the ovarian cancer cluster region (OCCR) in which mutations predispose the patient for ovarian cancer. Mutations outside the OCCR are more likely to result in breast cancer compared to mutations in the OCCR. On BRCA1, mutations closer to the 3’ end of the gene may result in higher risk than mutations closer to the 5’ end (Meric-Bernstam et al., 2013). Other gene defects that affect homologous recombination include hypermethylation of RAD51C or ATR mutation. However, these are considered to have a phenotype of “BRCAness” and behave like BRCA-deficient genes even if the BRCA gene itself is normal (Walsh, 2015).

The overall prevalence of disease related mutations in these genes is estimated to be 1 in 300 for BRCA1 and 1 in 800 for BRCA2 (NCCN, 2018a). Although the probability of cancer development in carriers is variable, estimates of penetrance in individuals with a pathogenic variant in BRCA1 or BRCA2 range from 46% to 87% lifetime risk for breast cancer, and 16.5% to 63% lifetime risk for ovarian cancer (Petrucci, Daly, & Pal, 2016). BRCA1 and BRCA2 mutations account for about 5 – 10% of breast cancers and 10 – 18% of ovarian cancers (Walsh, 2015). BRCA mutations are inherited in an autosomal dominant fashion and are highly penetrant (Isaacs, 2018).

It is clinically important to recognize these carriers to guide management of cancer and identify unaffected women with a BRCA mutation who will benefit from enhanced surveillance, tailor care to improve outcomes, and more efficiently use health-care resources. This has the potential to have a significant individual and population health impact on morbidity and mortality if these women adhere to guidelines for managing cancer risk (Buchanan et al., 2017). For example, BRCA deficient cancers are often targeted for a certain class of drugs called poly(ADP-ribose) polymerase (PARP) inhibitors. These inhibitors target enzymes responsible for the base excision repair pathway. A cell can survive with the loss of either the base excision repair pathway or the homologous recombination mechanism, but not both. Since BRCA-deficient cells already have a faulty homologous recombination mechanism, the BRCA-deficient cell dies when the PARP inhibitor shuts down the base excision repair pathway. BRCA-deficient cells have been shown to be affected 1000 times more by these PARP inhibitors than wild-type cells (Walsh, 2015).

Numerous proprietary tests exist for the assessment of BRCA or its related genes such as RAD51. For example, gene panels such as Ambry Genetics’ panel include 25 genes such as BRCA1, BRCA2, CHEK2, ATM, RAD51C, and BRIP1. This test is performed by next generation sequencing or Sanger sequencing (except for EPCAM) with a turnaround time of 2-3 weeks. Ambry has several proprietary tests such BRCAplus and BreastNext (Ambry, 2018).

**Validity and Utility**

A study performed by Kuchenbaecker et al assessed the cumulative risk of breast and ovarian cancer based on mutation position. A sample of 9856 patients was analyzed, with 6036 patients carrying a BRCA1 mutation and 3820 with a BRCA2 mutation. 5046 patients were unaffected by either type of cancer and 4810 had breast cancer, ovarian cancer, or both at baseline. The breast cancer assessment was based on 3886 carriers, and the ovarian cancer assessment was based on 5066 women. The authors evaluated the cumulative risk of breast cancer to 80 years to be 72% for BRCA1 mutation carriers and 69% for BRCA2 carriers. Cumulative risk for ovarian cancer to 80 years was found to be 44% for BRCA1 carriers and 17% for BRCA2 carriers. BRCA2 mutations outside the OCCR were found to have a higher risk of breast cancer than mutations inside it (hazard ratio: 1.93 for OCCR ranges 5’ to c.2830, c.2831 to c.6401,
c.6402 to 3) but no difference in overall ovarian cancer risk. Mutations closer to the 3’ or 5’ ends of BRCA1 were found to have a higher risk of breast cancer compared to the middle third of the gene and the third closest to the 3’ end had the highest hazard ratio of 1.51 compared to the third closest to the 5’ end (1.43) (Kuchenbaecker et al., 2017).

A meta-analysis of 44 articles was performed to assess the difference in risk factors between BRCA1 and BRCA2 carriers. Factors such as breastfeeding, coffee, infertility, and more were examined between both genotypes, and the only risk factor that revealed an association of any kind was age at first live birth for BRCA1 carriers. Breast cancer risk was found to decrease for BRCA1 women over 30 compared to women under 30, and the same was found for women from 25-29 compared to women under 25. However, the authors stressed that more research was required (Friebel, Domchek, & Rebbeck, 2014).

A study using next generation sequencing (NGS) to identify BRCA mutations was performed by Lang et al. 4034 patients were screened (2991 breast cancer patients, 1043 healthy controls). BRCA mutations were found in 247 of the breast cancer patients or 8.3%. 13.9% (16/115) of the BRCA1 mutations were of the “c.5470_5477del” variation, and several clinical characteristics such as high KI67 index and high tumor grade were related to BRCA mutations, BRCA2 carriers were also found to have poorer disease free survival among HER2 positive patients (Lang et al., 2017).

**Guidelines and Recommendations**

**National Comprehensive Cancer Network (NCCN, 2019)**

NCCN guidelines titled *Genetic/Familial High-Risk Assessment: Breast and Ovarian Version 3.2019* (NCCN, 2018b, 2019) list the following testing criteria for further genetic risk evaluation:

- "Individual from a family with a known BRCA 1/2 pathogenic/likely pathogen variant, including such variants found on research testing"

- Personal history of breast cancer + one or more of the following:
  - Diagnosed ≤45 y
  - Diagnosed 46 – 50 y with:
    - An additional breast cancer primary at any age
    - ≥1 close blood relative with breast cancer at any age
    - ≥1 close blood relative with high-grade (Gleason score ≥7) prostate cancer
    - An unknown or limited family history
  - Diagnosed ≤60 y with:
    - Triple-negative breast cancer
  - Diagnosed at any age with:
    - ≥1 close blood relative with:
      - Breast cancer diagnosed ≤50 y; or
      - Ovarian carcinoma; or
      - Male breast cancer; or
      - Metastatic prostate cancer; or
      - Pancreatic cancer
    - ≥2 additional diagnoses of breast cancer at any age in patient and/or in close blood relatives
• Ashkenazi Jewish ancestry

• Personal history of ovarian carcinoma

• Personal history of male breast cancer

• Personal history of pancreatic cancer

• Personal history of metastatic prostate cancer

• Personal history of high-grade prostate cancer (Gleason score $\geq 7$) at any age with
  o $\geq 1$ close blood relatives [sic] with ovarian carcinoma, pancreatic cancer, or metastatic prostate cancer at any age or breast cancer $< 50$ y; or
  o $\geq 2$ close blood relatives with breast, or prostate cancer (any grade) at any age; or

• Ashkenazi Jewish ancestry

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

• Regardless of family history, some individuals with an $BRCA$-related cancer may benefit from genetic testing to determine eligibility for targeted treatment

• An individual who does not meet the other criteria but with $\geq 1$ first- or second-degree blood relative meeting any of the above criteria. The significant limitations of interpreting test results for an unaffected individual should be discussed.”

The NCCN states, “two breast cancer primaries includes bilateral (contralateral) disease or two or more clearly separate ipsilateral primary tumors diagnosed either synchronously or asynchronously (NCCN, 2019).”

When there is a known deleterious mutation in a family member, the NCCN recommends that genetic testing in additional family members should be limited to known familial mutations.

In patients with unknown familial BRCA mutation and who meet testing criteria, the NCCN suggests to start testing in the affected family member first because this individual has the highest likelihood of a positive result. NCCN recommends that “unless the affected individual is a member of an ethnic group with known founder gene mutations, comprehensive genetic testing (i.e. full gene sequencing and detection of large gene rearrangements) should be performed (NCCN, 2018a)”.

For individuals with significant family history on both maternal and paternal sides, NCCN states that “the possibility of a second deleterious mutation in the family should be considered, and full sequencing may be indicated, even if a mutation has already been identified in a relative (NCCN, 2018b)”. Furthermore, in the situation of an unaffected family member with a significant family history, NCCN recommends that “the testing of the unaffected individual (or of unaffected family members) should only be considered when no affected family member is available for testing. In such cases, the unaffected individual or unaffected close relative with the highest likelihood of testing positive for the mutation should be tested. A negative test result in such cases, however, is considered indeterminate (NCCN, 2018b).”

NCCN also mentions that “certain large genomic rearrangements are not detectable by a primary sequencing assay, thereby necessitating supplementary testing in some cases... Therefore, the NCCN Guidelines Panel emphasizes the need for comprehensive
testing, which encompasses full BRCA1/2 sequencing and detection of large gene rearrangements (NCCN, 2018b).”

**The U.S. Preventive Services Task Force (USPSTF)** (Moyer, 2014) recommends that primary care providers screen women “who have family members with breast, ovarian, tubal, or peritoneal cancer with 1 of several screening tools designed to identify a family history that may be associated with an increased risk for potentially harmful mutations in breast cancer susceptibility genes (BRCA1 or BRCA2). Women with positive screening results should receive genetic counseling and, if indicated after counseling, BRCA testing. (B recommendation) The USPSTF recommends against routine genetic counseling or BRCA testing for women whose family history is not associated with an increased risk for potentially harmful mutations in the BRCA1 or BRCA2 genes.”

In February 2019, the USPSTF issued an updated draft recommendation statement for public comment until March 18, 2019, prior to official publication of a final statement. This updated draft reinforces the 2014 recommendation by giving the following B recommendation: "The USPSTF recommends that primary care providers screen women who have family members with breast, ovarian, tubal, or peritoneal cancer or have an ethnicity or ancestry associated with \textit{BRCA1} or \textit{BRCA2} gene mutations with one of several screening tools designed to identify a family history that may be associated with an increased risk for potentially harmful mutations in breast cancer susceptibility genes (\textit{BRCA1} or \textit{BRCA2}). Women with positive screening results should receive genetic counseling and, if indicated after counseling, genetic testing (USPSTF, 2019).” Moreover, they do not recommend (i.e. issue a D recommendation) routine screening, genetic testing, or genetic counseling for women who have no family or personal history of breast cancer or whose ancestry or ethnicity is not associated with a higher risk for potentially pathogenic \textit{BRCA1} or \textit{BRCA2} gene mutations.


**The American College of Obstetricians and Gynecologists** (ACOG, 2017) recommend:

- Evaluating a patient’s risk of hereditary breast and ovarian cancer syndrome should be a routine part of obstetric and gynecologic practice. Initial risk evaluation should include a personal medical history and family history.

- Genetic testing is recommended when the results of a detailed risk assessment that is performed as part of genetic counseling suggest the presence of an inherited cancer syndrome for which specific genes have been identified and when the results of testing are likely to influence medical management.

- The two main genetic testing options for hereditary breast and ovarian cancer syndrome are BRCA mutation testing and multigene panel testing that includes both BRCA and other genetic mutations. Multigene panel testing may be useful when more than one gene may be associated with an inherited cancer syndrome or when a patient has a personal or family history that is consistent with an inherited cancer susceptibility, but single-gene testing has not identified a pathogenic variant.

**The American Society of Breast Surgeons** (ASBS, 2017) have released guidelines on genetic testing for patients with and without breast cancer. They are as follows:

1. Breast surgeons, CGCs and other trained cancer-liaison staff with in-depth knowledge of genetic testing indications, implications, and limitations can provide genetic testing services and recommendations to their patients. Use of specialized risk-assessment services and certified genetic counselors when patient history and
test results are more complex is encouraged. Testing qualified patients can include BRCA1 and BRCA2 only, or additional genes (i.e., panel testing) related to hereditary breast cancer, so long as it is within guidelines, and the provider feels comfortable with recommendations.

2. Patients with a personal history of breast cancer: Always obtain information about family history of cancer. Ideally, a three-generation pedigree including maternal and paternal lineage should be obtained. This information can be used to guide the type of testing to be performed and the selection of patients who may benefit from further counseling with a CGC. Patients with a personal history of breast cancer meet criteria for genetic testing with any of the following characteristics:
   a. Age onset of breast cancer ≤50
   b. Triple-negative tumor (ER-PR-HER2-) and age ≤60
   c. Ashkenazi Jewish heritage and breast cancer at any age
   d. Two or more primary breast cancers (cancers can be asynchronous, synchronous, bilateral, or multicentric)
   e. First-degree relative with breast cancer age ≤50
   f. Two relatives on the same side of the family with breast cancer and/or pancreatic cancer
   g. Family or personal history of ovarian cancer, fallopian cancer, or primary peritoneal cancer
   h. Male breast cancer
   i. Known mutation carrier in the family

3. Patients without a personal history of breast cancer: Patients should be made aware that testing an affected relative first when available can be more informative than testing themselves since a negative result will not give them more insight into their family history. If an affected relative is not available, patients should be reminded of limitations of testing. Ideally, a three-generation pedigree including maternal and paternal lineage should be obtained. This information can be used to guide the type of testing to be performed and the selection of patients who may benefit from further counseling with a CGC. Patients without a personal history of breast cancer meet criteria for genetic testing for the following family history:
   a. First- or second-degree relative with early age onset of breast cancer ≤45
   b. Ashkenazi Jewish heritage and family history of breast cancer at any age
   c. Two or more primary breast cancers (cancers can be asynchronous, synchronous, bilateral, or multicentric) in a single-family member
   d. Two or more relatives on the same side of the family with breast cancer and/or pancreatic cancer
   e. Family or personal history of ovarian cancer, fallopian cancer, or primary peritoneal cancer
   f. Male breast cancer
   g. Known mutation carrier in the family

Referral for cancer genetic consultation is recommended by the American College of Medical Genetics and Genomics and the National Society of Genetic Counselors for individuals with a personal or family history indicative of a hereditary form of cancer.
State and Federal Regulations, as applicable

The Center for Devices and Radiological Health of the Food and Drug Administration (FDA, 2018) granted premarket approval on 1/12/2018 to BRACAnalysis CDx® is an in vitro diagnostic device intended for the qualitative detection and classification of variants in the protein coding regions and intron/exon boundaries of the BRCA1 and BRCA2 genes using genomic DNA obtained from whole blood specimens collected in EDTA. Single nucleotide variants and small insertions and deletions (indels) are identified by polymerase chain reaction (PCR) and Sanger sequencing. Large deletions and duplications in BRCA1 and BRCA2 are detected using multiplex PCR.

Additionally, many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). As an LDT, the U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use.

Applicable CPT/HCPCS Procedure Codes

<table>
<thead>
<tr>
<th>CPT Code Number</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>81162</td>
<td>BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (ie, detection of large gene rearrangements)</td>
</tr>
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<td>81163</td>
<td>BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis</td>
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<td>BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)</td>
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<td>81165</td>
<td>BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis</td>
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<tr>
<td>81167</td>
<td>BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)</td>
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<td>81212</td>
<td>BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants</td>
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<td>81215</td>
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<tr>
<td>81216</td>
<td>BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis</td>
</tr>
<tr>
<td>81217</td>
<td>BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant</td>
</tr>
<tr>
<td>96040</td>
<td>Medical genetics and genetic counseling services, each 30 minutes face-to-face with patient/family</td>
</tr>
<tr>
<td>S0265</td>
<td>Genetic counseling, under physician supervision, each 15 minutes</td>
</tr>
<tr>
<td>CPT Code Number</td>
<td>Code Description</td>
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<tr>
<td>0129U</td>
<td>Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), genomic sequence analysis and deletion/duplication analysis panel (ATM, BRCA1, BRCA2, CDH1, CHEK2, PALB2, PTEN, and TP53)</td>
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<td>0131U</td>
<td>Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), targeted mRNA sequence analysis panel (13 genes) (List separately in addition to code for primary procedure)</td>
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<td>0132U</td>
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<td>PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) mRNA sequence analysis (List separately in addition to code for primary procedure)</td>
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<td>0138U</td>
<td>BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) mRNA sequence analysis (List separately in addition to code for primary procedure)</td>
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*Procedure codes appearing in policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.*

**Evidence-based Scientific References**


**Policy Implementation/Update Information**

1/1/20 New Policy
State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.