BAPTIST HEALTH PLAN

Coverage Guidelines

Genetic Testing and Counseling for BRCA1 and BRCA2 for Breast and Ovarian Cancer Risk

Disclaimer:
Please note that Baptist Health Plan Coverage Guidelines may be updated throughout the year. A printed version may not be most up to date version available. The health plan reserves the right to review and update this policy as needed. Refer to the website to ascertain that you are utilizing the most current available version. Clinical guideline policies are not intended to serve as treatment guidelines or treatment recommendation. Treating providers must use their own clinical judgment in rendering care to their patient population.

DEFINITION

The BRCA1 and BRCA2 gene have been isolated by researchers as a major cause of hereditary breast and epithelial ovarian cancer.¹ These genes have also been less commonly associated with other cancer types including fallopian tube, pancreatic, early onset prostate and primary peritoneal cancers. Most BRCA1 breast cancers and many BRCA2 breast cancers are classified as triple-negative breast cancer.² As opposed to hormone positive breast cancer, triple-negative breast cancer is not activated by changes in hormones like estrogen and progestin. The survival rates are inferior for triple-negative cancer and it has a significantly higher rate of relapse within three to five years. Also, triple negative cancer has a higher incidence in younger women as opposed to hormone positive breast cancers, which are more common in older women stimulated by hormone changes associated with menopause.³ Ovarian cancer risk is also significant for both the BRCA1 and BRCA2.⁴

COVERAGE CRITERIA

Genetic sequencing testing for hereditary breast and/or ovarian cancer is medically necessary for any of the following:

- Member has a personal history of epithelial ovarian cancer at any age
- Member has a personal history of male breast cancer
- Member has a personal history of breast cancer at any age with one of the following:
  - A first-, second- or third-degree relative on the same side of the family* diagnosed with breast cancer at 50 years of age or younger; or
  - Two or more first-, second- or third-degree relatives on the same side of the family*
Genetic Testing and Counseling for BRCA1 and BRCA2
for Breast and Ovarian Cancer Risk

11/30/16; 09/11/14

1. Member has a personal history of breast cancer at age 45 years or younger
2. Member has a personal history of breast cancer at age 50 years or younger, when any one of the following applies:
   a. A first-, second- or third-degree relative on the same side of the family* diagnosed with breast cancer at any age, or
   b. A first-, second- or third-degree relative on the same side of the family diagnosed with pancreatic cancer, or
   c. A relative on the same side of the family with prostate cancer as defined by a Gleason score of 7 or greater, or
   d. A Member with bilateral breast cancer, or two primary breast cancers with the first diagnosed at age 50 or younger, or
   e. A Member with limited family structure or unavailable of family history
3. Member has a confirmed diagnosis of a triple-negative breast cancer type diagnosed at age 60 or younger
4. Member has a personal history of prostate cancer at any age as defined by the Gleason score of 7 or greater with any of the following:
   a. A first-, second- or third-degree relative on the same side of the family* with ovarian carcinoma, including fallopian tube and primary peritoneal cancers at any age; or
   b. A first-, second- or third-degree relative on the same side of the family* with breast cancer at 50 years or younger; or
   c. Two or more relatives on the same side of the family* with cancers of the breast, pancreatic or prostate cancer as defined by a Gleason score of 7 or greater at any age
5. Member has a personal history of pancreatic cancer any age with any of the following:
   a. A first-, second- or third-degree relative on the same side of the family* with ovarian carcinoma, including fallopian tube and primary peritoneal cancers at any age; or
   b. A first-, second- or third-degree relative on the same side of the family* with breast cancer at 50 years or younger; or
   c. Two or more relatives on the same side of the family* with cancers of the breast, pancreatic or prostate cancer as defined by a Gleason score of 7 or greater at any age; or

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* Member is of an ethnicity with higher mutation frequency; or

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Member is of Ashkenazi Jewish ancestry

Genetic sequencing testing and counseling should only be considered for members without a personal history of breast or ovarian cancer when an affected family member is unavailable for testing and when any of the following criteria are satisfied:

- Members who have a third-degree relative on the same side of the family* with breast cancer and/or ovarian carcinoma, including fallopian tube and primary peritoneal cancers and:
  - Two or more first-, second- or third-degree relatives with breast cancer on the same side of the family* with at least one presenting at 50 years or younger and/or ovarian carcinoma

- Members who have a first- or second-degree blood relative on the same side of the family* with a personal history of epithelial ovarian cancer at any age

- Members who have a first- or second-degree blood relative with a personal history of male breast cancer

- Members who have a first- or second-degree blood relative on the same side of the family* with a personal history of breast cancer at any age with one of the following:
  - A first-, second- or third-degree relative diagnosed with breast cancer at 50 years of age or younger; or
  - Two or more first-, second- or third-degree relatives diagnosed with breast cancer at any age; or
  - A first-, second- or third-degree relative diagnosed with ovarian carcinoma, including fallopian tube and primary peritoneal cancers; or
  - Two or more first-, second- or third-degree relatives diagnosed with pancreatic cancer and/or prostate cancer as defined by a Gleason score of 7 or greater at any age; or
  - A first-, second- or third-degree male relative diagnosed with breast cancer; or
  - Member is of an ethnicity with higher mutation frequency

- Members who have a first- or second-degree blood relative on the same side of the family* with a personal history of breast cancer at 45 years or younger

- Members who have a first- or second-degree blood relative on the same side of the family* with a personal history of breast cancer at age 50 years or younger, with any of the following:
  - A first-, second- or third-degree relative diagnosed with breast cancer at any age, or
  - A first-, second- or third-degree relative diagnosed with pancreatic cancer, or
  - A relative with prostate cancer as defined by a Gleason score of 7 or greater, or
  - Has bilateral breast cancer, or two primary breast cancers with the first diagnosed at age 50 or younger, or

- Members who have a first- or second-degree blood relative on the same side of the family** with a confirmed diagnosis of a triple-negative breast cancer type diagnosed at age 60 or
younger \(5\)

- Members who have a first- or second-degree blood relative on the same side of the family* with a personal history of prostate cancer at any age as defined by the Gleason score of 7 or greater with any of the following:
  - A first-, second- or third-degree relative with ovarian carcinoma, including fallopian tube and primary peritoneal cancers at any age; or
  - A first-, second- or third-degree relative with breast cancer at 50 years or younger; or
  - Two or more relatives with cancers of the breast, pancreatic or prostate cancer as defined by a Gleason score of 7 or greater at any age

- Members who have a first- or second-degree blood relative on the same side of the family* with a personal history of pancreatic cancer at any age with any of the following:
  - A first-, second- or third-degree relative with ovarian carcinoma, including fallopian tube and primary peritoneal cancers at any age; or
  - A first-, second- or third-degree relative with breast cancer at 50 years or younger; or
  - Two or more relatives on the same side of the family* with cancers of the breast, pancreatic or prostate cancer as defined by a Gleason score of 7 or greater at any age; or *Close blood relatives include first-, second-, and third-degree relatives on the same side of the family. \(6\)
  - Member is of Ashkenazi Jewish ancestry \(7\)

Full gene sequencing using the BRACAnalysis® Large Rearrangement Test (BART\textsuperscript{TM}) is medically necessary following a negative result from genetic sequencing testing. Please refer to Baptist Health Plan’s Coverage Guideline titled BART Testing for BRCA1 and BRCA2 for Breast and Ovarian Cancer Risk.

Genetic testing for \textit{BRCA1} and \textit{BRCA2} is not currently considered medically necessary in any of the following situations. It is considered either experimental/ investigational and/or knowledge of the results will not impact treatment or health outcomes:

- CA-125 blood test for routine screening for breast cancer \(8\)
- CA-125 blood test for routine screening for ovarian cancer. \(9\)

**MEDICAL BACKGROUND**

Breast cancer (BC) is among the most common type of cancer diagnosed in women in the US, second only to skin cancer. Invasive BC occurs at a rate of in 1 of 8 (12%) women. Overall BC mortality has steadily declined since 1989, especially in women younger than 50 years old. BC publicity coupled with screening programs have been largely successful identifying cancer in early stages, and treatment courses have improved in both tolerability and effectiveness. Still, BC represents the second leading cause of cancer death in women after lung cancer. Mortality due to breast cancer occurs at a rate of 1 in 36 (3%) with an estimated 246,660 women are expected to be diagnosed with invasive BC in the US in 2016 and over 40,000 are expected to die from the disease. \(10\)
Up to 10% of BC cases demonstrate a genetic component as noted by a disproportionate family burden of BC and other cancers, multiple recurring primary BCs in the same person, or the presence of BC along with ovarian cancer within the same person or close family. Cases like these led researchers to isolate the genetic susceptibility genes. The breast cancer 1 susceptibility gene (BRCA1) is located on chromosome 17 at band q21. Genetic alterations in BRCA1 are estimated to be responsible for 45% to 90% of BC cases in women with a strong family history of breast and/or ovarian cancers. Women found to carry BRCA1 are at an increased risk of developing breast cancer prior to 40 years of age. The breast cancer 2 susceptibility gene (BRCA2) is located on chromosome 13 at band q12. Genetic alterations in BRCA2 are estimated to be responsible for 35% of BC cases in women with a strong family history of breast and/or ovarian cancers. The protein encoded by BRCA2 was discovered in 1991.

According to a 2015 updated Hayes Technology report, the abundant data regarding BRCA1/2 gene testing lacks strong analytical validity due to restrictions from the current patent owners. The technical specifications reported by Myriad Genetics and Ambry Genetics claim a sensitivity and specificity rate of both sequence and large rearrangement analysis in excess of 99%.

According to this same report, clinical validity is well studied. In fact, pathogenic BRCA1 and BRCA2 sequence variants may be identified in 12.5% to 50% of individuals with an elevated risk of breast and ovarian cancer. The lifetime risk of BC to age 70 ranged from 46% to 72% for BRCA1 carriers and 38% to 85% for BRCA2 carriers. Also, BRCA1/2-positive individuals were at a four-time greater risk for contralateral breast cancer, which increased even more for those diagnosed with BC before 30 years of age.

The clinical utility of BRCA1/2 testing was also evaluated. Hayes reports that up to 55% of women who tested positive for the BRCA1 or BRCA2 gene variant chose to undergo elective ovary and fallopian tube removal and 44% chose to undergo prophylactic mastectomy. Women who did not choose elective surgeries participated in increased disease screenings such as breast mammography.

Updated practice guidelines published by the National Comprehensive Cancer Network (NCCN) recommend genetic risk evaluation for select patients with a personal history of breast cancer as well as other BRCA1/2 associated cancers. The NCCN is cautious in recommending genetic sequencing testing and counseling in those without a personal history of breast or ovarian cancer, only doing so when an affected family member is available for testing.

REGULATORY INFORMATION

The Departments of Labor, Treasury, and Health and Human Services have issued a rule prohibiting group health plans and health insurance insurers in the group market from:

- Increasing premiums for the group based on the results of one enrollee’s genetic information
- Denying enrollment
- Imposing preexisting condition exclusions
- Conducting other forms of underwriting based on genetic information

Kentucky – No legislative mandates were found for coverage of genetic testing for BRCA1 and BRCA2.
BRCA2.

Indiana – No legislative mandates were found for coverage of genetic testing for BRCA1 and BRCA2.

Tennessee – No legislative mandates were found for coverage of genetic testing for BRCA1 and BRCA2.

Baptist Health Plan Coverage Guidelines are created to provide members and providers with peer-reviewed, current medical information.

State and federal laws/mandates and contract language have priority over Coverage Guidelines and must be taken into consideration before eligibility for coverage is determined.

Baptist Health Plan Coverage Guidelines may or may not mirror Centers for Medicare & Medicaid Services benefits or coverage offered by any other health insurance company.

For self-funded plans, consult individual plan documents. If there is a conflict between this policy and a self-funded plan document, the provisions of the plan document will govern. In addition, coverage for Medicare Advantage members may differ. This is a result of applicable coverage statements by the Center for Medicare and Medicaid Services (CMS). The National Coverage Determinations, Local Coverage Determinations, and Local Medical Review Policies may be found at the CMS website, [http://www.cms.gov](http://www.cms.gov). Please note that for all plans, the member’s health plan benefits that are in effect on the rendered date of service must be used in coverage determinations.

### COVERAGE DETAIL

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<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
<th>Coverage Information</th>
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<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>
<td>Is medically necessary when all criteria are met.</td>
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<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 (i.e., 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>
<td>Is medically necessary when criteria are met</td>
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<td>81212</td>
<td>BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants</td>
<td>Is medically necessary when criteria are met</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</td>
<td>Is medically necessary when used to report</td>
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duplication/deletion variants

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<tr>
<th>ICD.10 Diagnosis Codes</th>
<th>Description</th>
<th>Coverage Information</th>
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<td>All malignancy-related diagnoses, including but not limited to</td>
<td></td>
<td>Is medically necessary when all criteria are met.</td>
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<td>C50.011-C50.929</td>
<td>Malignant neoplasm of breast [male/female]</td>
<td>Is medically necessary when all criteria are met.</td>
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<td>Z15.01</td>
<td>Genetic susceptibility to malignant neoplasm of breast</td>
<td>Is medically necessary when all criteria are met.</td>
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<td>Z80.3</td>
<td>Family history of malignant neoplasm of breast</td>
<td>Is medically necessary when all criteria are met.</td>
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<tr>
<td>Z85.00-Z85.9</td>
<td>Personal history of malignant neoplasm</td>
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</tbody>
</table>


**SEARCH TERMS**

BART
BRCA
Breast
Breast Cancer
Cancer
Family
Genes
Hereditary breast cancer
Inherited
Large gene deletions
Large gene duplications
Large genomic rearrangement
Large rearrangement test (BART)
Malignancy
Malignant
Mammogram
Ovarian cancer
Screening
Triple-negative