BAPTIST HEALTH PLAN

Coverage Guidelines

Large Genomic Rearrangement Testing for BRCA1 and BRCA2 for Breast and Ovarian Cancer Risk

Disclaimer:
Please note that Baptist Health Plan updates Coverage Guidelines 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 genes have been proven as a major cause of hereditary breast and ovarian cancer. BRCA1 and BRCA2 have also been associated with several other cancer types including fallopian tube and primary peritoneal cancers. Genetic testing for BRCA1 and BRCA2 have significant clinical importance due to the association of these genes with triple-negative breast cancer, which is usually a more aggressive form of breast cancer with low rates of survival and high rates of recurrence. Also, triple-negative breast cancer is more likely to present in younger women. Ovarian cancer risk is also significant for both the BRCA1 and BRCA2.

Genetic testing for BRCA1 and BRCA2 is conducted using a sequence variant test. In some cases in which the presence of BRCA1 or BRCA2 is suspected but sequence testing yields a negative result, large genomic rearrangement testing may be desirable. Myriad Labs first developed this test, called the BRACAnalysis® Large Rearrangement Test (BART). Other large genomic rearrangement testing has since been developed by other labs to detect deletion/duplication analysis. Examples include, but not all inclusive, BRCAssure by LabCorp, BRCAAdvantage by Quest Diagnostics, and BRCA1/2 Del/Dup Analysis by GeneDx Inc. Although different methodologies are used in different labs and based on the limited information available from different labs, there does not appear to be any substantive difference between test offerings.

COVERAGE CRITERIA

Genetic testing for large genomic rearrangement using the BRACAnalysis Large...
Rearrangement Test (BART) may be medically necessary for members who meet all of the following criteria:

- Member meets criteria for *BRCA1* and *BRCA2* testing as defined by “Genetic Testing for BRCA1 and BRCA2 for Breast and Ovarian Cancer Risk;” and
- Member completes sequence testing for *BRCA1* and *BRCA2* and yields a negative result.

**MEDICAL BACKGROUND**

Hereditary breast and ovarian cancer (HBOC), which is characterized by a significantly increased risk for breast and ovarian malignancies, is typically caused by pathogenic variants in one of the breast cancer susceptibility genes, *BRCA1* and *BRCA2*. *BRCA1* (located on chromosome 17 at band q21) and *BRCA2* (located on chromosome 13 at band q12.3) are categorized as tumor suppressor genes and encode proteins that function in the repair of DNA damage. Overall, it is estimated that 1 in 300 to 1 in 800 individuals in the general population, approximately 3% to 5% of breast cancer patients, and up to 10% of ovarian cancer patients carry a deleterious variant in one of these two genes. The prevalence of *BRCA1*/2 gene variants, however, varies depending on ethnicity, with a frequency as high as 1 in 40 for individuals of Ashkenazi Jewish (AJ) descent. Studies suggest that disease-causing sequence variants in either *BRCA1* or *BRCA2* are detected in 12.5% to 50% of individuals with an elevated risk of HBOC, and that large genomic rearrangements may be identified in up to 5.9% of this patient population. The majority of studies involving patients with possible HBOC report a *BRCA1*/2 variant frequency between 14.5% and 33%, including a study of women referred specifically for early-onset breast cancer. The highest rate of positive test results (50%) was in a population of women with triple negative breast cancer and either an early diagnosis (< 50 years of age) or a significant family history; the lowest (5.9%) was in a population of patients with ductal or lobular carcinoma in situ only. When sequence testing yields a negative result despite the presence of cancer risk, many recommend following up negative sequence test results with large genome rearrangement testing as a means of capturing additional *BRCA1* and *BRCA2* cases. In a study by Judkins et al (2012), the prevalence of *BRCA1*/2 LRs was investigated in 48,456 patients with diverse clinical histories and ancestries, and they were referred for clinical molecular testing for suspicion of hereditary breast and ovarian cancer. The study showed that large rearrangements comprised between 6 and 10% of all clinically significant mutations in *BRCA1* and *BRCA2*. In addition, the study demonstrated that there was significant difference in the prevalence and types of large rearrangements in patients of different ancestries. These large arrangement mutations were significantly more common in those of Latin American and Caribbean descent. This study supports performing large arrangement testing in conjunction with full gene sequencing as an appropriate strategy for clinical *BRCA1* and *BRCA2* analysis.

**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 BRACAnalysis Large Rearrangement Test (BART).

Indiana – No legislative mandates were found for coverage of genetic testing for BRACAnalysis Large Rearrangement Test (BART).

Tennessee – No legislative mandates were found for coverage of genetic testing for BRACAnalysis Large Rearrangement Test (BART).

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. 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

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.

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
<th>Coverage Information</th>
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</thead>
<tbody>
<tr>
<td>81162</td>
<td>BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., 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>
</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 (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 all criteria are met.</td>
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<tr>
<td>81212</td>
<td>BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC,</td>
<td>Is medically necessary</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
<td>Coverage Information</td>
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</tr>
<tr>
<td>81213</td>
<td><strong>6174delT variants</strong> when all criteria are met.</td>
<td></td>
</tr>
<tr>
<td>81214</td>
<td><strong>BRCA1 (breast cancer 1)</strong> (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants (i.e., exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 8121404 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)</td>
<td>Is medically necessary when all criteria are met.</td>
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<tr>
<td>81215</td>
<td><strong>BRCA1 (breast cancer 1)</strong> (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant</td>
<td>Is medically necessary when all criteria are met.</td>
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<td>81216</td>
<td><strong>BRCA2 (breast cancer 2)</strong> (eg, hereditary breast and ovarian cancer) gene analysis</td>
<td>Is medically necessary when all criteria are met.</td>
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<td>81217</td>
<td><strong>BRCA2 (breast cancer 2)</strong> (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant</td>
<td>Is medically necessary when all criteria are met.</td>
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**ICD.10 Diagnosis Codes**

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>C50.011-C50.929</td>
<td>Malignant neoplasm of breast [male/female]</td>
<td>Is medically necessary when all criteria are met.</td>
</tr>
<tr>
<td>D05.00-D05.92</td>
<td>Carcinoma in situ, breast [invasive and ductal carcinoma in situ (DCIS) – lobular carcinoma in situ (LCIS) is not included]</td>
<td>Is medically necessary when all criteria are met.</td>
</tr>
<tr>
<td>Z15.01</td>
<td>Genetic susceptibility to malignant neoplasm of breast.</td>
<td>Is medically necessary when all criteria are met.</td>
</tr>
<tr>
<td>Z80.3</td>
<td>Family history of malignant neoplasm of breast.</td>
<td>Is medically necessary when all criteria are met.</td>
</tr>
</tbody>
</table>
Z85.00-Z85.9  Personal history of malignant neoplasm  Is medically necessary when criteria are met.

REFERENCES


SEARCH TERMS

BRCA
Breast
Cancer

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