

GENETIC TESTING FOR HEREDITARY BREAST AND/OR OVARIAN CANCER SYNDROME (HBOC)

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INSTRUCTIONS FOR USE

This Medical Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Medical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Medical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Medical Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

Essential Health Benefits for Individual and Small Group

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits (“EHBs”). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

COVERAGE RATIONALE

Definitions

Please note, for the purpose of this policy:

1. Close blood relatives are defined as follows:
 - a. First degree relatives include parents, siblings and offspring

- b. Second degree relatives include half-brothers/sisters, aunts/uncles, grandparents, grandchildren and nieces/nephews
 - c. affected on the same side of the family
 - d. Third degree relatives include first cousins, great-aunts/uncles, great-grandchildren and great grandparents affected on same side of family
2. A breast cancer diagnosis includes either invasive carcinomas or non-invasive (in situ) ductal carcinoma types.
 3. Ovarian cancer also includes fallopian tube cancers and primary peritoneal carcinoma.
 4. Limited family history is defined as having fewer than two known first-degree or second-degree female relatives or female relatives surviving beyond 45 years of age on either or both sides of the family. (e.g., individual who is adopted)
 5. Documentation of personal and family history, in the form of a pedigree drawing/diagram utilizing standardized nomenclature, should be in the contemporaneous medical records submitted with the testing request (i.e., request form).
 6. For the statements that include age guidelines, a person is considered to be 45 years of age up until the day before their 46th birthday, and a person is considered to be 50 years of age up until the day before their 51st birthday.
 7. Two breast primary cancers include cancers appearing at the same time (synchronous) and one is not a metastasis of the other; or primary cancers developing at different times (metachronous or asynchronous). The tumors may be in one or two breasts.
 8. Gleason scoring is a system of grading prostate cancer tissue based on how it looks under a microscope. Gleason scores range from 2 to 10 and indicate how likely it is that a tumor will spread. A low Gleason score means the cancer tissue is similar to normal prostate tissue and the tumor is less likely to spread. A high Gleason score means the cancer tissue is very different from normal and the tumor is more likely to spread.
 9. HBOC-associated malignancies include prostate cancer (Gleason score ≥ 7), pancreatic cancer or melanoma. The presence of these malignancies does not necessarily justify BRCA testing. For example, a female with breast cancer over age 50 whose sister had melanoma at 40 and whose father has prostate cancer (Gleason score ≥ 7) would meet criteria. In another example, a female with breast cancer over age 50 whose maternal aunt had pancreatic cancer and whose paternal uncle had prostate cancer (Gleason score ≥ 7) would not meet criteria because the aunt and uncle are on different sides of the family.
 10. Triple-negative breast cancer refers to any breast cancer that does not show expression of estrogen receptors (ER), progesterone receptors (PR) or HER2/neu. This subtype of breast cancer is clinically characterized as more aggressive and less responsive to standard treatment and is associated with poorer overall patient prognosis. It is diagnosed more frequently in younger women, women with *BRCA1* mutations and those belonging to African-American and Hispanic ethnic groups.
 11. A founder mutation is a gene mutation observed with high frequency in a group that is or was geographically or culturally isolated, in which one or more of the ancestors was a carrier of the mutant gene. This phenomenon is often called a founder effect (National Cancer Institute website).

Genetic Counseling

For benefit plans that allow for medical necessity review, genetic counseling is required by an independent (not employed by a genetic testing lab) genetics provider prior to genetic testing for BRCA mutations in order to inform persons being tested about the benefits and limitations of a specific genetic test as applied to a unique person. Genetics providers employed by or contracted with a laboratory that are part of an integrated health system that routinely delivers health care services beyond the laboratory testing itself are considered independent. Genetic testing for BRCA mutations requires documentation of medical necessity by **ONE** of the following who has evaluated the member and intends to engage in post-test follow-up counseling:

- Board-Eligible or Board-Certified Genetic Counselor (CGC)
- Advanced Genetics Nurse (AGN-BC)
- Genetic Clinical Nurse (GCN)
- Advanced Practice Nurse in Genetics (APNG)
- A Board-Eligible or Board-Certified Clinical Geneticist
- A physician with experience in cancer genetics (Defined as providing cancer risk assessment on a regular basis and having received specialized ongoing training in cancer genetics. Educational seminars offered by commercial laboratories about how to perform genetic testing are not considered adequate training for cancer risk assessment and genetic counseling.)

Documentation Requirements

- Three generation pedigree
- UnitedHealthcare genetic counseling attestation form.

BRCA Testing Criteria

Note: National Comprehensive Cancer Network (NCCN) guidelines state that meeting one or more of these criteria warrants further personalized risk assessment, genetic counseling and consideration of genetic testing.

Comprehensive *BRCA1/BRCA2* genetic testing includes sequencing of both *BRCA1* and *BRCA2* genes and analysis for large genomic rearrangements, either concurrently or sequentially. NCCN guidelines emphasize the need for comprehensive testing for individuals who meet the testing criteria for *BRCA1/BRCA2* and have no known familial *BRCA1/BRCA2* mutations who have undergone accurate risk assessment and genetic counseling.

- I. *BRCA1* and *BRCA2* testing is proven and medically necessary for women with a personal history of breast cancer in the following situations and where gene testing results will impact medical management:
 - A. Breast cancer diagnosed at age 45 or younger with or without family history; or
 - B. Breast cancer diagnosed at age 50 or younger with:
 1. An additional primary breast cancer; or
 2. At least one close blood relative with breast cancer at any age; or
 3. At least one close blood relative with pancreatic cancer; or
 4. At least one close blood relative with prostate cancer (Gleason score ≥ 7); or
 5. An unknown or limited family history (see [Definitions](#) section for further clarification of limited family history).
 - C. Breast cancer diagnosed at any age with:
 1. At least one close blood relative with breast cancer diagnosed at age 50 or younger; or
 2. At least two close blood relatives on the same side of the family with breast cancer at any age; or
 3. At least one close blood relative with ovarian cancer at any age; or
 4. At least two close blood relatives on the same side of the family with pancreatic and/or prostate cancer (Gleason score ≥ 7) at any age; or
 5. Close male blood relative with breast cancer; or
 6. At least one close blood relative who has a *BRCA1* or *BRCA2* mutation (Testing should be targeted to the known *BRCA1/BRCA2* mutation in the family. Further *BRCA1/BRCA2* testing should only be pursued if the results are negative and the patient otherwise meets testing criteria); or
 7. Ashkenazi Jewish or ethnic groups associated with founder mutations. Testing for Ashkenazi Jewish founder-specific mutations should be performed first. Further *BRCA1/BRCA2* testing should only be pursued if the results are negative and the patient otherwise meets testing criteria without considering Ashkenazi Jewish ancestry.
 - D. Triple-negative breast cancer diagnosed at age 60 or younger.
- II. *BRCA1* and *BRCA2* testing is proven and medically necessary for women with a personal history of ovarian cancer.
- III. *BRCA1* and *BRCA2* testing is proven and medically necessary for women and men with a personal history of pancreatic cancer at any age and at least one close blood relative on the same side of the family with ovarian cancer at any age or breast cancer (\leq age 50 years) or two relatives with breast, pancreatic and/or prostate cancer (Gleason score ≥ 7) at any age.
- IV. *BRCA1* and *BRCA2* testing for Ashkenazi Jewish founder-specific mutations is proven and medically necessary for women and men with a personal history of pancreatic cancer and Ashkenazi Jewish ancestry.
- V. *BRCA1* and *BRCA2* testing is proven and medically necessary for men with a personal history of prostate cancer (Gleason score ≥ 7) at any age and at least one close blood relative on the same side of the family with ovarian cancer at any age or breast cancer (\leq age 50 years) or two relatives with breast, pancreatic and/or prostate cancer (Gleason score ≥ 7) at any age.
- VI. *BRCA1* and *BRCA2* testing is proven and medically necessary for men with a personal history of breast cancer.
- VII. *BRCA1* and *BRCA2* screening tests are proven and medically necessary for men and women without a personal history of breast or ovarian cancer with at least one of the following familial risk factors only when there are no family members affected with a BRCA associated cancer available for testing (see Note below):
 - A. At least one first- or second-degree blood relative meeting any of the above criteria (I-VI); or
 - B. At least one third-degree blood relative with breast cancer and/or ovarian cancer who has at least 2 close blood relatives with breast cancer (at least one with breast cancer at age 50 or younger) and/or ovarian cancer; or

- C. A known *BRCA1/BRCA2* mutation in a blood relative (defined as first-, second- or third-degree relative). Testing should be targeted to the known *BRCA1/BRCA2* mutation in the family. Further *BRCA1/BRCA2* testing should only be pursued if the results are negative and the patient otherwise meets testing criteria.

Note: NCCN guidelines state that significant limitations of interpreting test results for an individual without a cancer diagnosis should be discussed. If there are no living family members with breast or ovarian cancer available for testing, consider testing family members affected with other cancers associated with *BRCA1/BRCA2*, such as prostate cancer (Gleason score ≥ 7), pancreatic cancer or melanoma. Testing of individuals without a cancer diagnosis should only be considered when there is no affected family member available for testing (NCCN, 2016).

VIII. *BRCA1* and/or *BRCA2* testing is unproven and not medically necessary for all other indications including: 1) screening for breast or ovarian cancer risk for individuals not listed in the proven indications above or 2) for risk assessment of other cancers. Further evidence is needed to establish the clinical utility of testing in other populations.

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

CPT Code	Description
81162	<i>BRCA1, BRCA2</i> (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis
81211	<i>BRCA1, BRCA2</i> (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants in <i>BRCA1</i> (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)
81212	<i>BRCA1, BRCA2</i> (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants
81214	<i>BRCA1</i> (breast cancer 1) (e.g., 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 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)
81215	<i>BRCA1</i> (breast cancer 1) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant
81216	<i>BRCA2</i> (breast cancer 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81217	<i>BRCA2</i> (breast cancer 2) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant
81432	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 14 genes, including ATM, <i>BRCA1, BRCA2, BRIP1, CDH1, MLH1, MSH2, MSH6, NBN, PALB2, PTEN, RAD51C, STK11, and TP53</i>
81433	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for <i>BRCA1, BRCA2, MLH1, MSH2, and STK11</i>
96040	Medical genetics and genetic counseling services, each 30 minutes face-to-face with patient/family
Large Genomic Rearrangements	
81213	<i>BRCA1, BRCA2</i> (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; uncommon duplication/deletion variants

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HCPCS Code	Description
S0265	Genetic counseling, under physician supervision, each 15 minutes

DESCRIPTION OF SERVICES

About 5% to 10% of breast cancer cases are thought to be genetic. A majority of hereditary breast cancers are associated with inherited mutations in one of the breast-cancer-susceptibility genes: *BRCA1* and *BRCA2*. Hereditary breast and ovarian cancers cluster in families and tend to occur at relatively young ages. Women who carry *BRCA1* and *BRCA2* mutations have an increased lifetime risk of about 80% for individuals who live to age 70. In the contralateral breast, the lifetime risk of cancer is about 40%, and for ovarian cancer, the lifetime risk is about 40% with the *BRCA1* mutation and 20% with the *BRCA2* mutation. Individuals with these mutations are also at increased risk of certain other cancers but to a lesser degree than for breast and ovarian cancer (ECRI, 2015).

According to the NCCN, comprehensive genetic testing includes full sequencing of *BRCA1/BRCA2* and detection of large genomic rearrangements and may be indicated for individuals at exceptionally high risk as determined through cancer risk assessment and counseling (NCCN, 2016).

CLINICAL EVIDENCE

A GeneReviews® chapter on hereditary breast and ovarian cancer addresses BRCA mutations and the risk of developing certain cancers. An increased likelihood of a *BRCA1* or *BRCA2* mutation is suspected on the basis of certain personal and family history characteristics and various clinical criteria (Petrucci et al., 2013).

In a Cochrane systematic review, Hilgart et al. (2012) evaluated the impact of cancer genetic risk-assessment services on patients at risk of familial breast cancer. In this update, the authors included five new trials, bringing the total number of included studies to eight. The included trials provided data on 1973 participants and assessed the impact of cancer genetic risk assessment on outcomes including perceived risk of inherited cancer, and psychological distress. The review suggests that cancer genetic risk-assessment services help to reduce distress, improve the accuracy of the perceived risk of breast cancer and increase knowledge about breast cancer and genetics. The review found favorable outcomes for patients after risk assessment for familial breast cancer.

Warlam-Rodenhuis et al. (2005) completed a 1000 patient prospective study to determine predictive factors linked to *BRCA1/BRCA2*. The family history of breast cancer was the highest predictive factor of a positive BRCA test. The next highest predictive factor was age. Nearly 30% of BRCA carriers had no family history of breast or ovarian cancer and an additional 50% of the mutation carriers had no affected first-degree relatives with breast cancer suggesting that BRCA screening based on family history alone would miss a considerable proportion of mutation carriers. The frequency of BRCA mutations in patients diagnosed before the age of 45 years indicated that this age was a useful selection criterion.

The National Institute for Health and Care Excellence (NICE) published guidelines addressing the classification and care of people at risk of familial breast cancer and management of breast cancer and related risks in people with a family history of breast cancer (NICE, 2013).

The U.S. Preventive Services Task Force (USPSTF, 2013) recommends that primary care providers screen women who have family members with breast, ovarian, tubal or peritoneal cancer 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 (*BRCA1* or *BRCA2*). Women with positive screening results should receive genetic counseling and, if indicated after counseling, BRCA testing (Grade B).

Grade B Recommendation: The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.

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 (Grade D).

Grade D Recommendation: The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.

Germline mutations in the tumor suppressor genes *BRCA1* and *BRCA2* have been proven to indicate a drastically increased lifetime risk of breast and ovarian cancers in the individuals who carry them. A number of studies have shown that the third most common cancer associated with these mutations is pancreatic cancer (Greer and Whitcomb, 2007).

Castro et al. (2013) analyzed the tumor features and outcomes of 2,019 patients with prostate cancer (18 *BRCA1* carriers, 61 *BRCA2* carriers and 1,940 noncarriers). The study reported that prostate cancers with germline *BRCA1/2*

mutations were more frequently associated with Gleason ≥ 8 , T3/T4 stage, nodal involvement and metastases at diagnosis than prostate cancers in noncarriers. BRCA mutations were associated with poor survival outcomes. Cause-specific overall survival (CSS) was significantly longer in noncarriers than in carriers. For localized prostate cancer, 5-year CSS and metastasis-free survival (MFS) were significantly higher in noncarriers.

Of 211 Ashkenazi Jewish breast cancer probands with a family history of pancreatic cancer, Stadler et al. (2011) found that 30 (14.2%) harbored a BRCA mutation. Fourteen (47%) of the mutations were in *BRCA1* and 16 (53%) were in *BRCA2*. Patients diagnosed with breast cancer at age ≤ 50 years were found to have a higher *BRCA1/2* mutation prevalence than probands with breast cancer who were diagnosed at age > 50 years (21.1% vs 6.9%). In patients with a first-, second-, or third-degree relative with pancreatic cancer, mutation prevalences were 15.4%, 15.3% and 8.6%, respectively. The authors found that *BRCA1* and *BRCA2* mutations are observed with nearly equal distribution in Ashkenazi Jewish breast-pancreas cancer families, suggesting that both genes are associated with pancreatic cancer risk.

Ferrone et al. (2009) looked at the prevalence of *BRCA1* and *BRCA2* in an unselected group of Jewish patients and compared patients with resected BRCA mutation-associated pancreatic adenocarcinoma (PAC) to PAC patients without mutations. Of the 187 Jewish patients who underwent resection for PAC, tissue was available for 145 patients. Founder mutations for *BRCA1* and *BRCA2* were identified in 5.5% of patients (two with *BRCA1* [1.3%] and six with *BRCA2* [4.1%]). A previous cancer was reported by 24% (35 of 145) of patients with the most common sites being breast cancer (9 of 35; 74%) and prostate cancer (8 of 35; 23%).

Large Genomic Rearrangement (LR) Testing

The prevalence of *BRCA1/2* LRs was investigated in 48,456 patients with diverse clinical histories and ancestries that were referred for clinical molecular testing for suspicion of hereditary breast and ovarian cancer. Prevalence data was analyzed for patients from different risk and ethnic groups. Patients were designated as high-risk (n=25,535) if their clinical history predicted a high prior probability. For these patients, large rearrangement (LR) testing was performed automatically in conjunction with sequencing. Elective patients (n=22,921) did not meet the high-risk criteria, but underwent LR testing if *BRCA1/2* sequencing indicated no known mutations. Overall *BRCA1/2* mutation prevalence among high-risk patients was 23.8% versus 8.2% for the elective group. The mutation profile for high-risk patients was 90.1% sequencing mutations versus 9.9% LRs, and for elective patients, 94.1% sequencing versus 5.9% LRs. The authors noted that this difference may reflect the bias in high-risk patients to carry mutations in *BRCA1*, which has a higher penetrance and frequency of LRs compared with *BRCA2*. Significant differences in the prevalence and types of LRs were found in patients of different ancestries. LR mutations were significantly more common in Latin American/Caribbean patients (Judkins et al., 2012).

Walsh et al. (2006) found that genetic tests used to determine risk for developing hereditary breast cancer failed to detect *BRCA1* and *BRCA2* mutations in approximately 12% of breast cancer patients (n=300) who were members of a family with at least 4 cases of breast cancer and/or ovarian cancer. In this study, researchers retested participants for carrier status of genetic mutations known to influence risk for development of breast cancer using a molecular method not currently cleared for market in the United States known as multiplex ligation-dependent probe amplification (MLPA). Prior to enrollment, all participants had received a negative result from the breast cancer genetic test (Myriad Genetics Inc.) used routinely in the United States. The results of MLPA analysis indicated that 17% of study participants were, in fact, carriers of breast cancer-relevant genetic mutation, with 12% found to have alterations of *BRCA1* or *BRCA2*. Inherited alterations of *BRCA1* were more frequent among participants who were diagnosed with breast cancer prior to 40 years of age (16%) than among those who were older when diagnosed (6.5%). The clinical implications of these findings cannot be generalized to other populations, but results strongly suggest that improved methods for determining breast cancer risk are needed for individuals with strong family histories of breast and/or ovarian cancer.

Unger et al. (2000) assessed the frequency of genomic rearrangements in *BRCA1* in 42 American families with breast and ovarian cancer who were seeking genetic testing and who were subsequently found to be negative for *BRCA1* and *BRCA2* coding-region mutations. The exon 13 duplication was detected in one family, and four families had other genomic rearrangements. A total of 5 (11.9%) of the 42 families with breast/ovarian cancer who did not have *BRCA1* and *BRCA2* coding-region mutations had mutations in *BRCA1* that were missed by conformation-sensitive gel electrophoresis or sequencing. Four of five families with *BRCA1* genomic rearrangements included at least one individual with both breast and ovarian cancer; therefore, 4 (30.8%) of 13 families with a case of multiple primary breast and ovarian cancer had a genomic rearrangement in *BRCA1*. Families with genomic rearrangements had prior probabilities of having a *BRCA1* mutation, ranging from 33% to 97% (mean 70%). In contrast, in families without rearrangements, prior probabilities of having a *BRCA1* mutation ranged from 7% to 92% (mean 37%).

Triple-Negative Breast Cancer

A meta-analysis by Tun et al (2014) reported that a triple-negative phenotype significantly increases the risk of having a *BRCA1* mutation in high-risk breast cancer patients compared with a non-triple-negative phenotype. In a

high-risk population, women with triple negative breast cancer (TNBC) are approximately five and a half times more likely to have a *BRCA1* mutation compared with a non-TNBC phenotype. Approximately two in nine women with TNBC harbor a *BRCA1* mutation. Twelve studies comprising 2533 breast cancer patients were included in the analysis.

A study of 54 women with triple-negative breast cancer aged 40 years or younger, who were not considered candidates for BRCA testing because of the lack of a strong family history, showed five with *BRCA1* mutations and one with a *BRCA2* mutation (11% mutation prevalence) (Young et al. 2009).

Several studies have shown that *BRCA1* breast cancer is more likely to be characterized as triple- negative. Studies have reported *BRCA1* mutations in 9-28% of patients with triple- negative breast cancer. In addition, it appears that among patients with triple-negative disease, BRCA mutation carriers were diagnosed at a younger age compared with non-carriers (NCCN, 2016).

In a cohort of triple-negative breast cancer patients, Gonzalez-Angulo et al. (2011) found a 19.5% incidence of BRCA mutations. Median age was 51 years (27-83 years). The authors recommend that genetic testing be discussed with patients with triple-negative breast cancer.

Almost 10% of women with breast cancer who are younger than age 50 have BRCA mutations. Most of the BRCA-positive women do not have personal or family histories of breast or ovarian cancer and are not of Ashkenazi Jewish ancestry. Using a simulation model, Kwon et al. (2010) evaluated six populations of women younger than 50 with breast cancer, looking at costs and health benefits. The results led the authors to conclude that testing women with triple-negative breast cancers who were younger than 50 years for BRCA mutations should be adopted into current guidelines for genetic testing.

NCCN guidelines present specific criteria for genetic testing for hereditary breast and/or ovarian cancer syndrome. The guidelines address genetic risk assessment, counseling, testing and management based on test results (NCCN, 2016).

Professional Societies

American College of Obstetricians and Gynecologists (ACOG)

In a 2009 practice bulletin (reaffirmed 2015), the ACOG recommended criteria for genetic risk assessment of hereditary breast and ovarian cancer syndrome (HBOC). These recommendations conclude:

- BRCA positive women should be offered salpingo-oophorectomy by age 40 or when childbearing is completed.
- For a risk reducing bilateral salpingo-oophorectomy, all tissue from the ovaries and fallopian tubes should be removed. Thorough visualization of the peritoneal surfaces with pelvic washings should be performed. Complete, serial sectioning of the ovaries and fallopian tubes is necessary, with microscopic examination for occult cancer.
- Genetic risk assessment is recommended for patients with a greater than an approximate 20-25% chance of having an inherited predisposition to breast cancer and ovarian cancer. This includes women with the following:
 - A close relative (mother, sister, daughter, grandmother, granddaughter, aunt or niece) with a known BRCA mutation
 - Personal history of both breast and ovarian cancer
 - Ovarian cancer and a close relative with ovarian cancer or premenopausal breast cancer or both
 - Ovarian cancer and Ashkenazi Jewish ancestry
 - Breast cancer by age 40 years and Ashkenazi Jewish ancestry
 - Breast cancer by age 50 years and a close relative with ovarian cancer or male breast cancer

American Society of Clinical Oncology (ASCO)

An ASCO policy statement recommends that genetic testing for cancer susceptibility be performed when the following three criteria are met: the individual being tested has a personal or family history suggestive of genetic cancer susceptibility; the test can be adequately interpreted; and the test results have accepted clinical utility (ASCO, 2003; Robson et al., 2010).

National Society of Genetic Counselors (NSGC)

The NSGC recommends that genetic testing be performed in the context of an informed decision-making process (Berliner et al., 2013). The process of cancer risk assessment and genetic counseling for hereditary breast and ovarian cancer syndrome requires many steps, including the following:

- Gathering personal medical and family history data
- Psychosocial assessment
- Discussion of cancer and mutation risk and how personalized risk estimates are derived
- Facilitation of the informed consent process through discussion of the risks, benefits, limitations, and likelihood of identifying a mutation with genetic susceptibility testing
- Results disclosure (if applicable)
- Discussion of medical management options
- Review of issues related to genetic discrimination

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Genetic tests are regulated under the Clinical Laboratory Improvement Amendments (CLIA) Act of 1988. More information is available at:

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm124105.htm>.
(Accessed April 15, 2016)

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for genetic testing for hereditary breast and/or ovarian cancer (HBOC) syndrome. Local Coverage Determinations (LCDs) do exist. Refer to the LCDs for [Biomarkers Overview](#), [MoIDX: Molecular Diagnostic Tests \(MDT\)](#), [Molecular Diagnostic Testing](#), [Molecular Pathology Procedures](#), [Genetic Testing](#) and [Molecular Diagnostic Tests \(MDT\)](#).

(Accessed August 14, 2015)

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
08/01/2016	<ul style="list-style-type: none"> • Reformatted and reorganized policy; transferred content to new template • Revised coverage rationale: <ul style="list-style-type: none"> ○ Updated definitions; added language to indicate: <ul style="list-style-type: none"> ▪ A <i>founder mutation</i> is a gene mutation observed with high frequency in a group that is or was geographically or culturally isolated, in which one or more of the ancestors was a carrier of the mutant gene; this phenomenon is often called a founder effect (National Cancer Institute web site) ○ Updated coverage guidelines for genetic counseling; added language to clarify guidelines apply to benefit plans that allow for medical necessity review ○ Updated coverage guidelines BRCA testing: <ul style="list-style-type: none"> ▪ Modified BRCA testing criteria pertaining to the following individuals to indicate BRCA1 and BRCA2 testing is proven and medically necessary for; <ul style="list-style-type: none"> - Women and men with a personal history of pancreatic cancer at any age and at least one close blood relative on the same side of the family <i>with ovarian cancer at any age or breast cancer (≤ age 50 years), or two relatives with breast, pancreatic and/or prostate cancer (Gleason score ≥7) at any age</i> - Men with a personal history of prostate cancer (Gleason score ≥7) at any age and at least one close blood relative on the same side of the family <i>with ovarian cancer at any age or breast cancer (≤ age 50 years), or two relatives with breast, pancreatic and/or prostate cancer (Gleason score ≥7) at any age</i> ▪ Modified notation addressing NCCN testing guidelines; replaced references to “unaffected individual” with “individual without a cancer diagnosis” • Updated list of applicable CPT codes; added 96040 • Added list of applicable HCPCS codes: S0265 • Updated supporting information to reflect the most current clinical evidence and references • Archived previous policy version 2016T0009S