Medical Policy

Genetic Testing for Hereditary Breast and Ovarian Cancer Syndrome

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Product Applicability

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Notes:
+ Disclaimer and audit information is located at the end of this document.
◊ The guidelines included in this Plan policy are applicable to members enrolled in Senior Care Options only if there are no criteria established for the specified service in a Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) on the date of the prior authorization request. Review the member’s product-specific benefit documents at www.SeniorsGetMore.org to determine coverage guidelines for Senior Care Options.

Policy Summary

The Plan considers breast cancer susceptibility genetic mutation testing for hereditary breast cancer and ovarian cancer (HBOC) syndrome with site-specific BRCA1/BRCA2 gene testing, comprehensive BRCA1/BRCA2 gene sequencing analysis, multi-site 3 BRCA testing (for a member of Ashkenazi Jewish descent), and/or large genomic rearrangement testing of BRCA1 and BRCA2 genes to be medically necessary for all symptomatic or at-risk members when the Plan’s applicable medical criteria are met for the specified test. See the Plan’s Genetic Testing and Pharmacogenetics medical policy, policy number OCA 3.727, rather than this Plan policy for medically necessary indications for BRCA1 and
BRCA2 mutation testing using tumor profiling to identify the presence of BRCA1 and BRCA2 gene mutations to predict the effectiveness of cancer treatment. **Plan prior authorization is required for all molecular and chromosomal genetic testing** except for prenatal genetic screening tests for a member with one (1) of the pregnancy diagnosis codes specified in the Applicable Coding section in any of the following policies when applicable Plan criteria are met: *Genetic Testing Guidelines and Pharmacogenetics* medical policy, policy number OCA 3.7272; *Chromosomal Microarray Analysis for Unexplained Intellectual Disabilities and/or Multiple Congenital Anomalies* medical policy, policy number OCA 3.573; or *Genetic Testing for Fragile X-Associated Disorders* medical policy, policy number OCA 3.571. Biochemical genetic tests used to study the amount or activity level of proteins to indicate changes to the DNA require prior authorization only when the test is included in the Applicable Coding section of a Plan genetic testing medical policy.

BRCA1 or BRCA2 mutation testing for types of cancer other than breast cancer and ovarian cancer is considered experimental and investigational. It will be determined during the Plan’s standard prior authorization process if the service is considered experimental and investigational for the requested use. See the Plan’s *Experimental and Investigational Treatment* medical policy, policy number OCA 3.12, for the product-specific definitions of experimental or investigational treatment. Refer to the Plan’s *Medically Necessary* medical policy, policy number OCA 3.14, for the product-specific definitions of medically necessary treatment.

The Plan supports the National Comprehensive Cancer Network (NCCN) guidelines for genetic counseling for all genetic tests conducted with Plan members; NCCN recommends that adequate pre-test counseling (including but not limited to preparing the patient for possible outcomes of testing including positive results) and post-test genetic counseling be provided by a health care professional with expertise in genetics. Genetic counseling provided to a Plan member (and/or guardian if the member is under the age of 18) should be documented in the member’s medical record and conducted by an appropriately trained practitioner with expertise and experience in genetics, including a provider acting within the scope of his/her license and practice, clinical geneticist, or genetic counselor.

See the following Plan policies for additional prior authorization guidelines for genetic testing available at [www.bmchp.org](http://www.bmchp.org) for BMC HealthNet Plan members (or at [www.SeniorsGetMore.org](http://www.SeniorsGetMore.org) for Senior Care Options members) and [www.wellsense.org](http://www.wellsense.org) for Well Sense Health Plan members:

1. *Chromosomal Microarray Analysis for Unexplained Intellectual Disabilities and/or Multiple Congenital Anomalies*, policy number OCA 3.573

2. *Gene Expression Profiling of Tumor Tissue to Predict Cancer Recurrence with Risk Stratification (Including Oncotype DX™ and Other Tests)*, policy number OCA 3.572

3. *Genetic Testing for Familial Malignant Melanoma*, policy number OCA 3.78


Genetic Testing for Hereditary Breast and Ovarian Cancer Syndrome

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5. Genetic Testing Guidelines and Pharmacogenetics, policy number OCA 3.727
6. Genetic Testing for Hereditary Colorectal Cancer, policy number OCA 3.64
7. Genetic Testing for Hereditary Thrombophilia, policy number OCA 3.728
8. Preimplantation Genetic Testing (Preimplantation Genetic Diagnosis and Pregenetic Screening), policy number OCA 3.726

Description of Item or Service

Genetic Testing for Breast and Ovarian Cancer: A blood test to check for specific changes (mutations) in genes that help control normal cell growth, specifically the BRCA1 and BRCA2 genes, to determine if an individual has an increased susceptibility to hereditary breast cancer and ovarian cancer. (Note: Studies have reported additional cancers associated with BRCA mutations; however, the type, magnitude of risk, and sex differences remain to be clarified and are not included in this Plan policy.) See the Medical Policy Statement section and Limitations section of this policy for applicable Plan medical criteria. Types of BRCA testing include:

1. Standard BRCA Testing:
   a. Standard BRCA testing with site-specific BRCA1/BRCA2 gene testing is used for an at-risk individual from families transmitting a previously identified BRCA1 or BRCA2 gene variant known to be deleterious (i.e., testing for BRCA1/BRCA2 familial variant). An example of this test includes BRACAnalysis® by Myriad Genetics Inc.
   
   b. Standard BRCA testing with comprehensive BRCA1/BRCA2 gene sequencing analysis (complete/full gene sequencing) with reflex to large genomic rearrangement testing is used for at-risk individuals when no deleterious BRCA1 or BRCA2 sequence variant has been identified in the family. An example of this test includes the Comprehensive BRACAnalysis® (Reflex) by Myriad Genetics Inc.

   c. Multi-site 3 BRCA testing (sometimes referred to as multi-site BRCA3 testing) is a targeted analysis that tests for three (3) common BRCA1 and BRCA2 founder variants in Ashkenazi (Eastern European) Jewish population/ancestry (with or without comprehensive BRCA1/BRCB2 gene sequencing) for an individual (regardless of gender) who is of Ashkenazi Jewish descent. An example of this test includes the Multisite 3 BRACAnalysis® by Myriad Genetics Inc.

2. Large Genomic Rearrangement Testing:

Large genomic rearrangement testing is conducted on individuals who have completed standard BRCA testing who are at risk for hereditary breast cancer and ovarian cancer and no
variant BRCA1/BRCA2 gene has been identified in the individual’s family. The test includes complete sequencing of the BRCA1 and BRCA2 genes and an additional procedure to identify five (5) common large rearrangements in the BRCA1 gene. It is recommended that testing be conducted on the affected family member with the highest likelihood of a BRCA1/BRCA2 mutation (as specified in the Medical Policy Statement section of this policy). An example of this test includes BRACAnalysis® Large Rearrangement Test or BART (Myriad).

Medical Policy

The medical necessity for genetic testing is based on the Plan member’s ability to meet the applicable medical criteria included in this policy; see the member’s applicable benefit documents for a list of covered services available at www.bmchp.org for BMC HealthNet Plan members (or at www.SeniorsGetMore.org for Senior Care Options members) and www.wellsense.org for Well Sense Health Plan members. See the Plan’s Genetic Testing and Pharmacogenetics medical policy (policy number OCA 3.727) rather than this policy for medically necessary indications for BRCA1 and BRCA2 mutation testing using tumor profiling to identify the presence of BRCA1 and BRCA2 gene mutations to predict the effectiveness of specific chemotherapy agents or anti-cancer treatment (e.g., BRACAnalysis CDx® by Myriad Genetic Laboratories, Inc.).

The Plan considers genetic testing for susceptibility to hereditary breast cancer and ovarian cancer (HBOC) syndrome to be medically necessary for a member (regardless of gender) when applicable Plan criteria are met for the specified test and documented in the medical record, as specified below in item I for standard BRCA testing (e.g., BRACAnalysis® by Myriad Genetics, Inc.) and/or item II for the large genomic rearrangement test (e.g., BRACAnalysis® Large Rearrangement Test/BART by Myriad Genetics, Inc.).

I. Standard BRCA Test (e.g., BRACAnalysis®):

A standard BRCA test is a genetic test used to determine the risk of hereditary breast and ovarian cancer by identifying a BRCA gene mutation. The gene analysis of BRCA1 and BRCA2 includes gene sequencing of the two (2) genes and analysis for large rearrangements. Rearrangements are evaluated for deletions, duplications, or additions of nucleotides in the gene sequence. (Note: BRCA1 and BRCA2 testing for an individual who is not of Ashkenazi Jewish descent typically starts with gene sequencing of the two [2] genes.) Multi-site BRCA3 testing is considered medically necessary for a member (regardless of gender) of Ashkenazi Jewish descent with or without a personal history of breast cancer.

The Plan considers the standard BRCA test (e.g., BRACAnalysis®) to be medically necessary when BOTH of the following applicable criteria are met, as specified below in item A and item B (for site-specific BRCA1/BRCA2 gene testing, comprehensive BRCA1/BRCA2 gene sequencing analysis, or multi-site BRCA3 testing).
A. Test results will be used to make clinical management decisions for an adult Plan member age 18 or older (on the date of service); AND

B. ONE (1) of the following applicable criteria must be met for the member (regardless of gender), as specified below in item 1 (testing for site-specific BRCA1/BRCA2 gene testing or comprehensive BRCA1/BRCA2 gene sequencing analysis when the member has a personal history related to hereditary breast and/or ovarian cancer syndrome), item 2 (testing for site-specific BRCA1/BRCA2 gene testing or comprehensive BRCA1/BRCA2 gene sequencing analysis when the member with no personal history of hereditary breast and/or ovarian cancer syndrome), or item 3 (multi-site BRCA3 testing related to Ashkenazi Jewish descent):

1. **Criteria for Site-specific BRCA1/BRCA2 Gene Testing or Comprehensive BRCA1/BRCA2 Gene Sequencing Analysis for a Plan Member with a Personal History Related to Hereditary Breast and Ovarian Cancer Syndrome (Affected Individual):**

The Plan member meets at least ONE (1) of the following applicable medical criteria when the member has a personal history related to hereditary breast and ovarian cancer syndrome, as specified below in items a through g:

a. Member (regardless of gender) age 18 or older on the date of service is biologically related to a family with a known deleterious BRCA1 and/or BRCA2 gene mutation (with or without a personal history of breast cancer and/or ovarian cancer); OR

b. **Personal History of Breast Cancer:**

The Plan member (regardless of gender) has a personal history of breast cancer, including invasive breast carcinoma or ductal carcinoma in situ breast cancer, and at least ONE (1) of the following criteria is met, as specified below in items (1) through (4):

(1) Member diagnosed with breast cancer at 45 years of age or younger; OR

(2) Member’s breast cancer diagnosed at 50 years of age or younger and at least ONE (1) of the following applicable criteria is met, as specified below in items (a) through (e):

(a) Member has an additional breast cancer primary (i.e., two [2] or more breast primaries, including bilateral disease or cases where there are two [2] or more clearly separate ipsilateral primary tumors) when the breast cancer diagnosis occurred at 50 years of age or younger; OR
(b) Member diagnosed with breast cancer at 50 years of age or younger with one (1) or more close blood relative (i.e., close blood relative includes first, second, and/or third degree relative) with breast cancer at any age; OR

(c) Member diagnosed with breast cancer at 50 years of age or younger with one (1) or more close blood relative (i.e., close blood relative includes first, second, and/or third degree relatives) with pancreatic cancer at any age; OR

(d) Member diagnosed with breast cancer at 50 years of age or younger with one (1) or more close blood relative (i.e., close blood relative includes first, second, and/or third degree relatives) with prostate cancer (Gleason score ≥7 or metastatic) at any age; OR

(e) Member diagnosed with breast cancer at 50 years of age or younger with an unknown or limited family history;† OR

† Note: The treating provider must use clinical judgment when determining the appropriateness of genetic testing for hereditary breast and ovarian cancer syndrome when the member has a limited family history. All other applicable Plan criteria must be met. The National Comprehensive Cancer Network (NCCN) defines a limited family history as fewer than two (2) first or second degree female relatives (including relatives born with female reproductive organs and/or with typical female karyotype with two [2] X chromosomes, if known) surviving beyond 45 years of age on either the maternal or paternal side.

(3) Member diagnosed with breast cancer at 60 years of age or younger with a triple negative breast cancer; OR

(4) Member’s breast cancer diagnosed at any age and at least ONE (1) of the following applicable criteria is met, as specified below in items (a) through (e):

(a) Member diagnosed with breast cancer at any age with two (2) or more close blood relatives (i.e., close relative includes first, second, and/or third degree relative on the same side of the family) with breast cancer, pancreatic cancer, and/or prostate cancer (Gleason score ≥7 or metastatic) at any age; OR

(b) Member diagnosed with breast cancer at any age with one (1) or more close blood relative (i.e., close relative includes first, second, and/or third degree relative on the same side of the family) with breast cancer diagnosed at 50 years of age or younger; OR

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c. **Personal History of Ovarian Cancer:**

   Member has a personal history of ovarian cancer (including epithelial ovarian cancer, fallopian tube cancer, and/or primary peritoneal cancer) at any age; OR

d. **Personal History of Male Breast Cancer:**

   Member has a personal history of male breast cancer (including personal history of breast cancer in a member born with male reproductive organs and/or with a typical male karyotype with only one [1] X chromosome) at any age; OR

e. **Personal History of High-Grade Prostate Cancer:**

   Member has a personal history of high-grade prostate cancer (Gleason score ≥ 7) at any age and at least ONE (1) of the following criteria is met related to family medical history, as specified below in items (1) through (3):

   (1) Member has one (1) or more close blood relatives (i.e., close blood relative includes first, second and third degree relatives on the same side the family) with a

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Note: Testing for Ashkenazi Jewish founder-specific mutation(s) should be performed first, when applicable. See item 3 below for criteria for multi-site 3 BRCA testing. A member who is of Ashkenazim Jewish descent who has a negative multi-site 3 BRCA test, the Plan considers comprehensive BRCA1/BRCA2 gene sequencing analysis (reflex testing) to be medically necessary with or without a personal history of breast cancer.
history of ovarian cancer (including epithelial ovarian cancer, fallopian tube cancer, and/or primary peritoneal cancer) at any age; OR

(2) Member has one (1) or more close blood relatives (i.e., close blood relative includes first, second and third degree relatives on the same side the family) with a history of breast cancer diagnosed at 50 years of age or younger; OR

(3) Member has at least two (2) relatives with a history of breast cancer (diagnosed at 51 years of age or older), pancreatic cancer at any age, and/or prostate cancer (Gleason score ≥ 7 or metastatic) at any age; OR

f. **Personal History of Metastatic Prostate Cancer:**

Member has a personal history of metastatic prostate cancer (with radiographic evidence of or biopsy-proven disease) at any age; OR

g. **Personal History of Pancreatic Cancer:**

Member (regardless of gender) has a personal history of pancreatic cancer at any age and at least ONE (1) of the following criteria is met related to family medical history, as specified below in items (1) through (3):

(1) Member has one (1) or more close blood relatives (i.e., close blood relative includes first, second and third degree relatives on the same side the family) with a history of ovarian cancer (including epithelial ovarian cancer, fallopian tube cancer, and/or primary peritoneal cancer) at any age or breast cancer diagnosed at 50 years of age or younger; OR

(2) Member has at least two (2) relatives with a history of breast cancer, pancreatic cancer, and/or prostate cancer (Gleason score ≥ 7) at any age; OR

(3) Member with a personal history of pancreatic cancer at any age and is of Ashkenazi Jewish ancestry; OR

2. **Criteria for Site-specific BRCA1/BRCA2 Gene Testing or Comprehensive BRCA1/BRCA2 Gene Sequencing Analysis for a Plan Member with No Personal History Related to Hereditary Breast and Ovarian Cancer Syndrome (Unaffected Individual):**

When the member (regardless of gender) has no personal history related to hereditary breast and ovarian cancer syndrome, ALL of the following criteria must be met for medically necessary BRCA1/BRCA2 genetic testing, as specified below in items a through c:
a. It is the clinical judgment of the treating provider that the member age 18 or older on the date of service (regardless of gender) has a reasonable likelihood of a mutation, considering the unaffected Plan member’s current age and family history, as specified below in item b; AND

b. The member (regardless of gender) meets at least ONE (1) of the following applicable criteria related to family history, as specified below in items (1) or item (3):

(1) First or Second Degree Blood Relative:

The Plan member has a first or second degree blood relative that meets at least ONE (1) of the criteria listed above in items B1a through B1g †; OR

† Note: The criteria specified in items B1a through B1g also apply to an affected individual, i.e., a Plan member with a personal history related to hereditary breast and ovarian cancer syndrome.

(2) Third Degree Blood Relative:

The Plan member has a third degree blood relative that meets BOTH of the following criteria, as specified below in item (a) and item (b):

(a) Third degree blood relative of member who has breast cancer (including invasive breast carcinoma or ductal carcinoma in situ breast cancer) and/or ovarian cancer (including epithelial ovarian cancer, fallopian tube cancer, and/or primary peritoneal cancer; AND

(b) Third degree blood relative of member has two (2) or more close blood relatives (i.e., close blood relative includes first, second and third degree relatives on the same side the family) with breast cancer (at least one [1] with breast cancer diagnosed at 50 years of age or younger) and/or ovarian cancer (including epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer) at any age; OR

(3) Ashkenazi Jewish Descent:

The Plan considers comprehensive BRCA1/BRCA2 gene sequencing analysis (reflex testing) to be medically necessary for a member (regardless of gender) age 18 or older on the date of service who is of Ashkenazi (Eastern European) Jewish descent and has had a negative multi-site 3 BRCA test result (with or without a personal history of breast cancer); AND
c. Each of the Plan member’s affected blood relatives is not available and/or not willing to be tested.

3. **Criteria for Multi-Site 3 BRCA Testing:**

Multi-site 3 BRCA testing (sometimes referred to as multi-site BRCA3 testing) is considered medically necessary for an individual (regardless of gender) who is of Ashkenazi Jewish descent. The Plan considers comprehensive BRCA1/BRCA2 gene sequencing analysis (reflex testing) to be medically necessary after a negative multi-site BRCA3 test (with or without a personal history of breast cancer).

II. **Large Genomic Rearrangement Test (e.g., BRACAnalysis® Large Rearrangement Test or BART):**

Large genomic rearrangement test is a blood test used to detect rare, large rearrangements of DNA in the BRCA1 and BRCA2 genes that are not evaluated in the standard, comprehensive BRCA test (e.g., BRACAnalysis® by Myriad Genetics, Inc.). This additional test is used for a member (regardless of gender) who has a strong family history of breast or ovarian cancer or is at high risk for hereditary breast cancer and ovarian cancer (HBOC) syndrome. It is estimated that about one (1) percent of individuals who meet the family history criteria for large genomic rearrangement testing (e.g., BRACAnalysis® Large Rearrangement Test or BART) will have a mutation detected by the test.

The Plan considers large genomic rearrangement test (e.g., BRACAnalysis® Large Rearrangement Test or BART) to be medically necessary when ALL of the following criteria are met, as specified below in items A through C:

A. Plan member meets the testing criteria in item I above for the standard BRCA test (e.g., BRACAnalysis®) but had negative results from that testing; AND

B. Plan member has no known familial BRCA1/BRCA2 gene mutations; AND

C. Testing is conducted on ONE (1) of the following, as specified below as item 1 or item 2:

1. An affected family member with the highest likelihood of a BRCA1/BRCA2 mutation; OR

2. A non-affected Plan member ONLY if the affected family member with the highest likelihood of a BRCA1/BRCA2 mutation is not available and/or not willing to be tested.

**Limitations**

1. The Plan does NOT cover genetic testing for BRCA1 and BRCA2 mutations for members less than age 18 on the date of service because it is considered investigational and there are no

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recommended preventive interventions for this age group. The National Society of Genetic Counselors (NSGC) “encourages deferring predictive genetic testing of minors for adult-onset conditions when results will not impact childhood medical management or significantly benefit the child.”

2. BRCA1 or BRCA2 mutation testing for indications other than identifying if a member has an increased susceptibility to hereditary breast cancer and ovarian cancer (HBOC) syndrome and/or BRCA1 or BRCA2 mutation testing that is not consistent with guidelines included the Medical Policy Statement section of this policy is considered investigational and not supported by scientific evidence.

3. The Plan considers genetic testing to identify a member with an increased susceptibility to hereditary breast cancer and ovarian cancer (HBOC) syndrome to NOT be medically necessary unless the type of genetic test is specified as medically necessary according to the applicable guidelines in Medical Policy Statement section of this policy (i.e., only site-specific BRCA1/BRCA2 gene testing, comprehensive BRCA1/BRCA2 gene sequencing analysis, multi-site 3 BRCA testing [for a member of Ashkenazi Jewish descent], and/or large genomic rearrangement testing of BRCA1 and BRCA2 genes would be considered medically necessary when applicable Plan criteria are met).

4. An unaffected member (i.e., no personal history of breast cancer) is not eligible for BRCA1/BRCA2 gene mutation testing if an affected blood relative is available and willing to be tested.

5. The Plan considers genetic testing for the KRAS-variant (e.g. PreOvar by Mira Dx Inc.) in order to determine genetic susceptibility to ovarian cancer to be experimental or investigational.

6. The Plan considers disease-targeted ATM, BRIP1, CDH1, CHEK2, NBN, PALB2, RAD51C, RAD51D, and/or STK11 genes to determine susceptibility to hereditary breast cancer and ovarian cancer (HBOC) syndrome to be experimental and investigational due to insufficient clinical utility of testing. (Note: Clinical alternatives to ATM, BRIP1, CDH1, CHEK2, NBN, PALB2, RAD51C, RAD51D, and/or STK11 genes genetic testing for breast cancer include a comprehensive medical work-up, including clinical breast examination, followed by mammogram, ultrasound, or magnetic resonance imaging [MRI], as appropriate. Fine-needle aspiration or biopsy of suspicious abnormalities will allow for a definitive pathologic diagnosis of breast cancer. An accurate and complete family history will help identify patients at high risk for familial breast cancer and genetic testing according to the Medical Policy Statement section of this Plan policy.)

7. The Plan considers the use of a risk assessment test based on the presences of multiple common genetic changes known as single nucleotide polymorphisms (SNPs) to be experimental and investigational when used to predict susceptibility to breast and/or ovarian cancer syndrome; examples include but are not limited to the OncoVue® Breast Cancer Risk Test.
8. Multigene Panel Testing:

The most common hereditary causes of breast and ovarian cancer are variants in the breast cancer 1 (BRCA1) and breast cancer 2 (BRCA2) genes. However, many familial breast cancer and hereditary ovarian cancer cases do not have variants in BRCA1 or BRCA2. A large number of other genes have been implicated as contributing to familial cases, with some having a greater contribution than others; many of these additional genes have also been associated with other cancers and diseases. Many laboratories have developed and now offer multigene testing panels for hereditary breast and ovarian cancer that vary in methodology and the types of genes included within the panels.

The use of a multigene testing panel is generally considered to NOT be medically necessary as an alternative to, or in addition to, disease-targeted BRCA1/BRCA2 testing to predict susceptibility to hereditary breast and/or ovarian cancer syndrome due to limited data on clinical validity and clinical utility of multigene testing. Examples of such testing include but are not limited to the following: BRCAplus (Ambry Genetics Corp.), BRCAvantage Plus (BRCA1, BRCA2, TP53, STK11, PTEN, CDH1, PALB2) (Quest Diagnostics), Breast Ovarian Cancer NGS Panel (Fulgent Diagnostics), Breast/Ovarian Cancer Panel (GeneDx Inc.), BreastNext Next Gen Cancer Panel (Ambry Genetics Corp.), BreastTrue High Risk Panel (Pathway Genomics Corp.), BROCA Cancer Risk Panel (University of Washington Laboratory Medicine), CancerNext Next-Gen Cancer Panel (Ambry Genetics Corp.), Color Hereditary Cancer Test (Color Genomics Inc.), High/Moderate Risk Panel (GeneDx Inc.), genTrue (True Health Diagnostics), iGene Cancer Panel (ApolloGen Molecular Diagnostics Laboratory), Invitae Breast Cancer High-Risk Panel (Invitae), myRisk® Hereditary Cancer (Myriad Genetic Laboratories, Inc.), OvaNext Next-Gen Cancer Panel (Ambry Genetics Corp.), Preventest (GeneID Advanced Molecular Diagnostics LLC), and VistaSeq Hereditary Cancer Panel (Laboratory Corporation of America).

If the treating provider is recommending multigene panel testing rather than, or in addition to, condition-targeted genetic testing, Plan Medical Director review is required. For multigene panel testing to be considered medically necessary, medical record documentation must be submitted to the Plan with the prior authorization request demonstrating that ALL of the following criteria are met (and after approval by a Plan Medical Director), with criteria specified below in items a through g:

a. A recommendation for multigene panel testing for the member by an independent Board-Certified or Board-Eligible Medical Geneticist, an American Board of Medical Genetics or American Board of Genetic Counseling-certified Genetic Counselor not employed by a commercial genetic testing laboratory, or a genetic nurse credentialed as either a Genetic Clinical Nurse (GCN) or an Advanced Practice Nurse in Genetics (APGN) by either the Genetic Nursing Credentialing Commission (GNCC) or the American Nurses Credentialing

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Center (ANCC) who is not employed by a commercial genetic testing laboratory; this provider has a documented evaluation of the member which includes a completed 3-generation pedigree and intends to engage in post-test follow-up counseling; AND

b. Member meets criteria for genetic testing outlined in the Medical Policy Statement section of this policy; AND

c. All genes included in the multigene panel are relevant to the personal medical history, biological family medical history, and/or treatment plan for the member being tested and there are professional society management guidelines or National Comprehensive National Comprehensive Cancer Network (NCCN) guidelines (with applicable references provided with the prior authorization request) documenting the clinical utility of testing for the members who test positive for any and all genes in the panel; AND

d. The results of the requested multigene panel will directly impact the treatment plan and clinical decision-making process for the member being tested; AND

e. There are no other known causative circumstances or factors (e.g., environmental exposures, injury, infection) that can explain the member’s symptoms or medical condition; AND

f. Multigene panel testing is more practical testing to diagnose the member’s condition than the separate single gene tests or targeted panels that would be recommended (with supporting documentation provided); AND

g. The member’s clinical presentation does not fit a well-described syndrome for which single-gene testing, targeted panel testing, or chromosomal microarray analysis is currently available for the member’s condition or is not clinically appropriate for the member (with supporting clinical documentation provided).

The Plan considers the multigene panel testing to be medically necessary only when ALL of the criteria outlined above (in items a through g) are met; disease-targeted genetic testing is considered medically necessary as an alternative when Plan criteria are met in the Medical Policy Statement section (and according to guidelines specified in the Limitations section of this policy). See the Genetic Testing Guidelines and Pharmacogenetics medical policy, policy number OCA 3.727, for guidelines related to multigene panel testing to determine response to drug metabolism and adjuvant therapy and the use of multigene panels to determine hereditary cancer susceptibility for other types of cancer.

Review the Plan’s Genetic Testing Guidelines and Pharmacogenetics medical policy, policy number OCA 3.727, for Plan guidelines for genetic testing indications that may not be included in this Plan policy, including BRCA1 and BRCA2 mutation testing using tumor profiling to identify the presence of BRCA1 and BRCA2 gene mutations to predict the effectiveness of specific chemotherapy agents or anti-cancer drugs.
treatment. An example of such testing includes Tumor BRACAnalysis CDx® (Myriad Genetic Laboratories, Inc.) used to detect the presences of BRCA1 or BRCA2 gene mutation in ovarian tumor tissue (using blood samples). BRACAnalysis CDx® is used with a member with advanced ovarian cancer when treatment with Lynparza (olaparib) is being considered, and the member has NOT had previous BRCA mutation testing (or meets applicable criterion for repeating BRCA1 and BRCA2 testing). Refer to the Plan’s *Medically Necessary* medical policy, policy number OCA 3.14, for the product-specific definitions of medically necessary treatment. See the Plan’s *Experimental and Investigational Treatment* medical policy, policy number OCA 3.12, for the product-specific definitions of experimental or investigational treatment.

Definitions

**Ashkenazi Jewish:** A term for people of eastern European Jewish heritage. The Ashkenazi Jewish population is at risk for specific genetic mutations due to ethnic background.

**BRCA Genetic Variant Testing:** Test that uses DNA analysis to identify inherited mutations in genes associated with hereditary breast and ovarian cancer (HBOC) syndrome. This includes testing of BRCA1 genes, BRCA2 genes, and multi-site 3 BRCA testing (i.e., testing of three [3] common BRCA1 and BRCA2 founder variants in individuals of Ashkenazi Jewish descent).

Of the 10 percent of breast cancer cases that have a familial basis, around 40 percent to 50 percent are due to mutations in BRCA1 and BRCA2. Since the discovery of BRCA1 and BRCA2, a few additional genes have been identified as associated with hereditary breast and ovarian cancer (HBOC) syndrome that include but are not limited to ATM, BRIP1, CDH1, CHEK2, NBN, PALB2, RAD51C, RAD51D, and STK11 genes; the clinical utility of genetic testing for variants in other associated genes (i.e., other than BRCA1/BRCA2 genes) have not been established. BRCA genes include the following:

1. **BRCA1:** A specific gene on chromosome 17 that normally helps to suppress cell growth associated with an autosomal dominant cancer predisposition syndrome thought to account for the majority of inherited forms of breast and ovarian cancer along with BRCA2.

2. **BRCA2:** A specific gene on chromosome 13 that normally helps to suppress cell growth associated with an autosomal dominant cancer predisposition syndrome thought to account for the majority of inherited forms of breast and ovarian cancer along with BRCA1.

3. **BRCA3 and BRCA4:** At least two other genes, BRCA3 and BRCA4, are suspected to be associated with hereditary breast and ovarian cancer (HBOC) syndrome, but the clinical validity and clinical utility of such findings have not been established. The phenotype of these targeted families varies, but appears to include ductal carcinoma in situ and later onset breast cancers (similar to BRCA2) with lower penetrance and a smaller family history of associated conditions. The latest guidelines from the National Comprehensive Cancer Network for BRCA-related breast and/or ovarian cancer syndrome include genetic testing criteria for BRCA1 gene variants, BRCA2 mutations, and multi-site 3 BRCA testing for individuals of Ashkenazi Jewish descent.

Genetic Testing for Hereditary Breast and Ovarian Cancer Syndrome

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(also referred to as multi-site BRCA3 testing); there is no reference to BRCA3 testing or BRCA4 testing.

Close Relative: A blood relative that includes first, second, and third degree relatives.

First Degree Relative: A blood relative of an individual who shares approximately 50% of his/her genes defined as a biological parent, full sibling, or child.

Genetic Testing: According to U.S. Library of Medicine, genetic testing is defined as a type of medical test that identifies changes in chromosomes, genes, or proteins. The results of a genetic test can confirm or rule out a suspected genetic condition or help determine a person’s chance of developing or passing on a genetic disorder. More than 1,000 genetic tests are currently in use, and more are being developed. Several methods can be used for genetic testing:

1. Molecular genetic tests (or gene tests) study single genes or short lengths of DNA to identify variations or mutations that lead to a genetic disorder.

2. Chromosomal genetic tests analyze whole chromosomes to see if there are large genetic changes, such as an extra copy of a chromosome or missing DNA, that cause a genetic condition.

3. Biochemical genetic tests study the amount or activity level of proteins; abnormalities in either can indicate changes to the DNA that result in a genetic disorder.

Gleason Score: System of grading prostate cancer tissue, with scores ranging from 2 to 10 to indicate how likely it is that a tumor will spread. A low Gleason score of 2 to 4 means the cancer cells are similar to normal prostate tissue and the tumor is less like to spread quickly. A score of 8 to 10 indicates that the cancer cells have very few features of a normal cell and are likely to be aggressive. A score of 5 to 7 indicates intermediate risk.

Hereditary Breast and Ovarian Cancer (HBOC) Syndrome: Condition caused by a germline pathogenic variant in BRCA1 or BRCA2, and is characterized by an increased lifetime risk for breast cancer, ovarian cancer, prostate cancer, and pancreatic cancer. Individuals with BRCA2 pathogenic variants may also be at an increased risk for melanoma. An increased likelihood of a BRCA1 or BRCA2 pathogenic variant is suspected on the basis of certain personal and family history characteristics, and a diagnosis of HBOC is made following molecular genetic testing in an individual or family with germline BRCA1 or BRCA2 pathogenic variant.

Multigene Panel Tests: Tests that evaluate more than one (1) gene simultaneously to detect changes in gene expression most commonly associated with certain diseases and other genes that may have limited evidence of an association to the disorder. Multigene panel tests may involve traditional exon-by-exon sequencing of targeted genes to identify genetic variants or use next-generation sequencing. Each laboratory establishes its own set of criteria for selecting the genes represented in a panel, even

Genetic Testing for Hereditary Breast and Ovarian Cancer Syndrome

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Genetic Testing for Hereditary Breast and Ovarian Cancer Syndrome

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when panels are used for the same or similar clinical indications. The lack of regulatory oversight of genetic testing means that laboratories can change the components of a panel at any time, making it difficult to evaluate the clinical utility of multigene panel tests.

Multisite BRCA3 Testing: Targeted analysis that tests for three (3) common BRCA1 and BRCA2 founder variants in Ashkenazi Jewish population. This test only applies to this population.

Next-Generation Sequencing (NGS or Massively Parallel Sequencing): Genetic testing that involves sequencing of millions of DNA fragments using the following three (3) levels of molecular analysis: (1) Disease-targeted gene panels to sequence genes with an established role in the targeted disease, (2) exome sequencing of coding regions of the genome to include less common variants associated with the disease (i.e., a coding region is the segment of a gene that contains a protein-coding sequence called an exon in all 22,000 genes of the human genome); and (3) genome sequencing of both the coding and non-coding regions of the genome (i.e., the non-coding regions in between exons are called introns). Multiple sequencing platforms and different processes result in variability in test results among laboratories.

Second Degree Relative: A blood relative of an individual who shares approximately 25% of his/her genes defined as a biological grandparent, grandchild, aunt, uncle, nephew, niece, or half-sibling.

Single Nucleotide Polymorphisms (SNPs): The most common type of genetic variation among individuals. Each SNP represents a difference in a single DNA building block, called a nucleotide. SNPs occur normally throughout a person’s DNA; normally these variations are found in the DNA between genes. If more than one (1) percent of a population does not carry the same nucleotide at a specific position in the DNA sequence, then this variation can be classified as a SNP. Most SNPs have no effect on health or development. When there is sufficient scientific evidence to support the clinical utility of testing, SNPs may help predict an individual’s response to certain drugs, susceptibility to environmental factors, risk of developing particular diseases, and/or susceptibility to genetic diseases within families.

Third Degree Relative: A blood relative of an individual who shares 12.5% of his/her genes as defined as a biological first cousin, great grandmother, or great grandfather.

Triple Negative Breast Cancer: Any breast cancer that does not express the genes for estrogen receptor (ER), progesterone receptor (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.

Whole Exome Sequencing (WES)/Whole Genome Sequencing (WGS): WES captures and sequences at a deep level the protein coding regions (called exons) of an individual’s genes using first-generation sequencing techniques or next-generation sequencing to detect disease-causing variants and discover gene targets. While exons represent only 1% of the genome, they account for approximately 85% of disease-causing variants. Through identification of variants across the exome, WES avoids the need to

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run multiple single-gene tests, which require prior information about variants affecting the disease. WES has been performed in a number of cancers, whereby comparison between tumor DNA and normal DNA from the same individual allows identification of variants specific to the tumor, which may provide information used for diagnosis and treatment. WES is targeted sequencing of the subset of the human genome that contains functionally important sequences of protein-coding DNA, while whole genome sequencing (WGS) uses next-generation sequencing techniques to sequence both coding and non-coding regions of the genome. Because WES only evaluates the protein-coding regions of the human genome (exons), WES is a more cost-effective alternative to WGS. WES produces a smaller, more manageable data set with faster turnaround time for analyses than WGS. WGS has the ability to detect structural variations located outside of the exome that may be related to many diseases and cannot be identified with WES. WES and WGS have been proposed to be more efficient than traditional sequencing methods in discovering the genetic causes of diseases, but there remain issues of error rates due to technical challenges and difficulty interpreting potential causative variants from variants of unknown significance generated for each patient. Examples of tests include but are not limited to the following: TruGenome tests (Illumina), Endometrial Cancer Panel (GeneDx), ExomeNext and ExomeNext-Rapid (Ambry Genetics), XomeDx™ test (GeneDx), mtSEEK Whole Mitochondrial Genome Analysis (Courtagen Life Sciences Inc.), and/or nucSEEK Comprehensive Sequence Analysis of Nuclear Mitochondrial Exome (Courtagen Life Sciences, Inc.). According to The American College of Obstetricians and Gynecologists (Committee Opinion Number 682), the routine use of whole genome or whole exome sequencing for prenatal diagnosis is not recommended outside of the context of clinical trials until sufficient peer-reviewed data and validation studies are published. See the Genetic Testing Guidelines and Pharmacogenetics medical policy (policy number OCA 3.727) rather than this policy for Plan guidelines related to WES and WGS.

**Applicable Coding**

The Plan uses and adopts up-to-date Current Procedural Terminology (CPT) codes from the American Medical Association (AMA), International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10) diagnosis codes developed by the World Health Organization and adapted in the United Stated by the National Center for Health Statistics (NCHS) of the Centers for Disease Control under the U.S. Department of Health and Human Services, and the Health Care Common Procedure Coding System (HCPCS) established and maintained by the Centers for Medicare & Medicaid Services (CMS). Because the AMA, NCHS, and CMS may update codes more frequently or at different intervals than Plan policy updates, the list of applicable codes included in this Plan policy is for informational purposes only, may not be all inclusive, and is subject to change without prior notification. Whether a code is listed in the Applicable Coding section of this Plan policy does not constitute or imply member coverage or provider reimbursement. Providers are responsible for reporting all services using the most up-to-date industry-standard procedure and diagnosis codes as published by the AMA, NCHS, and CMS at the time of the service.

Providers are responsible for obtaining prior authorization for the services specified in the Medical Policy Statement section and Limitation section of this Plan policy, even if an applicable code appropriately describing the service that is the subject of this Plan policy is not included in the

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Applicable Coding section of this Plan policy. Coverage for services is subject to benefit eligibility under the member’s benefit plan. Please refer to the member’s benefits document in effect at the time of the service to determine coverage or non-coverage as it applies to an individual member. See Plan reimbursement policies for Plan billing guidelines.

Refer to the Plan’s policy, *Genetic Testing Guidelines and Pharmacogenetics*, policy number OCA 3.727, for additional guidelines regarding genetic testing available at [www.bmchp.org](http://www.bmchp.org) or [www.wellsense.org](http://www.wellsense.org). Plan prior authorization is required for all genetic testing, even when the applicable code for the genetic test is not listed in a Plan policy.

<table>
<thead>
<tr>
<th>CPT Codes</th>
<th>Description: Codes Covered When Medically Necessary</th>
</tr>
</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>
</tr>
</tbody>
</table>
| 81211     | BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., 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)  
Plan note: See criteria in the Plan’s *Genetic Testing and Pharmacogenetics* medical policy, policy number OCA 3.727, for medically necessary indications for BRCA1 and BRCA2 mutation testing using tumor profiling to predict the effectiveness of cancer treatment (e.g., BRACAnalysis CDx®). |
| 81212     | BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants  
Plan note: Code may be used for multisite 3 BRCA testing. |
| 81213     | BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; uncommon duplication/deletion variants  
Plan note: Code used for large genomic rearrangement test (e.g., BRACAnalysis® Large Rearrangement Test or BART) and multisite 3 BRCA testing. |
| 81214     | BRCA1 (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     | BRCA1 (breast cancer 1) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant |
| 81216     | BRCA2 (breast cancer 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis |
| 81217     | BRCA2 (breast cancer 2) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant |

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Genetic Testing for Hereditary Breast and Ovarian Cancer

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<table>
<thead>
<tr>
<th>CPT Codes</th>
<th>Description: Codes Considered Not Medically Necessary for Genetic Testing for Hereditary Breast Cancer and Hereditary Ovarian Cancer (and Plan Medical Director Review is Required, as Specified in the Limitations Section)</th>
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<tbody>
<tr>
<td>81432</td>
<td>Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence and analysis panel, must include sequencing of at least 14 genes, including BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, and TP53</td>
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<tr>
<td>81433</td>
<td>Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11</td>
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<tr>
<th>HCPCS Codes</th>
<th>Description: Codes Covered When Medically Necessary</th>
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<tbody>
<tr>
<td>None</td>
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</table>

Clinical Background Information

There are two (2) major breast cancer predisposition genes known as breast cancer 1 susceptibility gene (BRCA1) and breast cancer 2 susceptibility gene (BRCA2) that have been found in breast cancers. Certain specific family history patterns, including those found in hereditary breast and ovarian cancer (HBOC) syndrome, and some hereditary site-specific breast cancer are associated with an increased risk for mutations in the BRCA1 or BRCA2 gene. Families suspected of having hereditary breast and ovarian cancer (HBOC) syndrome are more susceptible to breast cancer occurring at a young age, bilateral breast cancer, male breast cancer (including breast cancer in an individual born with male reproductive organs and/or with a typical male karyotype with only one [1] X chromosome), ovarian cancer, cancer of the fallopian tube, and primary peritoneal cancer. Other cancers, such as prostate cancer, pancreatic cancer, gastrointestinal cancers, melanoma, laryngeal cancer, occur more frequently in HBOC families. The U.S. Preventive Services Task Force (USPSTF) recommends that primary care providers screen women (including individuals born with female reproductive organs and/or two [2] X chromosomes) 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 (including individuals born with female reproductive organs and/or with typical female karyotype with two [2] X chromosomes) with positive screening results should receive genetic counseling and, if indicated after counseling, BRCA testing.

Single-site BRCA1 or BRCA2 gene testing may be conducted for an at-risk individual from families transmitting a previously identified BRCA1 or BRCA2 gene variant known to be deleterious. Comprehensive BRCA1/BRCA2 gene testing (complete gene sequencing) is completed for at-risk individuals and/or when no deleterious BRCA1 or BRCA2 sequence variant has been identified in the family. BRCA1 and BRCA2 gene testing for HBOC is performed by direct sequence analysis. In addition, testing for large genomic rearrangements may be performed when sequencing is negative. A targeted analysis that tests for three specific variants common among individuals of Ashkenazi Jewish descent may also be performed prior to a comprehensive sequence analysis. Product names for BRCA1/2 testing include the following: BRCA1/2 Genes Sequence and Deletion/Duplication Analyses (Ambry Genetic Testing for Hereditary Breast and Ovarian Cancer Syndrome)

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Genetic testing for BRCA1 and BRCA2 is used to determine if an asymptomatic individual has an increased susceptibility for breast and ovarian cancer, or whether the cancer in an affected individual is due to a strong genetic factor. Women (including individuals born with female reproductive organs and/or with typical female karyotype with two [2] X chromosomes) who inherit mutations in BRCA1 and BRCA2 are at increased risk for breast and ovarian cancer and men have an increased risk of both breast and prostate cancer. Because the majority of test results are negative, it is strongly recommended by the National Comprehensive Cancer Network (NCCN) that it is best to consider testing of an affected family member first, especially a family member with early-onset, bilateral disease or multiple primaries because that individual is likely to test positive. If the patient is of Ashkenazi Jewish ancestry, testing for the three common Ashkenazi “founder” mutations is done first. Appropriate genetic counseling helps members to make informed decisions, can improve their knowledge and perception of their risk for breast and ovarian cancer and reduce anxiety. Genetic testing for BRCA1 and BRCA2 mutations is used to assist clinicians in determining whether a patient is at risk for developing primary or recurrent breast or ovarian cancer and can aid in the medical or surgical management or ongoing surveillance (e.g., more frequent mammography, prophylactic mastectomy, and/or oophorectomy, tamoxifen therapy). Genetic testing for BRCA1 and BRCA2 mutations has become an integral part of clinical practice, but testing is generally limited to these two genes and to women (including individuals born with female reproductive organs and/or with typical female karyotype with two [2] X chromosomes) with severe family histories of breast or ovarian cancer. Large genomic rearrangements occur in a small percentage (i.e., less than one [1] percent) of all patients tested for HBOC syndrome.

The Food and Drug Administration (FDA) only regulates genetic tests sold as kits and has practiced enforcement discretion for laboratory-developed tests (LDTs), which represent the majority of genetic tests marketed in the United States. While the Centers of Medicare & Medicaid Services (CMS) does regulate the clinical laboratories in which LDTs are performed, CMS does not evaluate whether the genetic tests are clinically meaningful.

At the time of the Plan’s most recent policy review, the Centers for Medicare & Medicaid Services (CMS) has implemented the following national coverage determinations (NCDs) related to genetic tests: NCD for Colorectal Cancer Screening Tests (210.3) for coverage of immunoassay and guaiac fecal occult blood tests and the Cologuard™ - Multitarget Stool DNA (sDNA) test when CMS applicable criteria are met, NCD for Pharmacogenomic Testing for Warfarin Response (90.1) for medically necessary indications for testing as determined by CMS, and NCD for Cytogenetic Studies (190.3) for...
coverage based on CMS guidelines. Medicare uses a combination of national and local coverage determinations for making coverage decisions for genetic tests. Medicare administrative contractors (MAC) may implement local coverage determinations (LCDs) that apply only within their own jurisdictions. Verify if applicable CMS criteria are in effect (through an NCD, LCD, or other CMS guidelines) for the specified genetic test, product name, site-specific gene analysis, and the indication for testing on the date of the prior authorization request for a Senior Care Options member.

References


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Centers for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD) for Colorectal Cancer Screening Tests (210.3). Effective Date October 9, 2014. Implementation Date September 8, 2015. Accessed at: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=281&ncdver=5&CoverageSelection=Both&ArticleType=All&PoiicyType=Final&s=Massachusetts&KeyWord=colorectal+cancer&KeyWordLookUp=Title&KeyWordSearchType=And&bc=gAAAAABAAAAAA%3d%3d&

Centers for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD) for Cytogenetic Studies (190.3). July 16, 1998. Accessed at: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=198&ncdver=1&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=Massachusetts&KeyWord=cytogenetic&KeyWordLookUp=Title&KeyWordSearchType=And&lcd_id=24308&lccd_version=26&basket=lcd*3a%2424308*3a%2426*3a%24Genetic+Testing*3a%24MAC+-+Part+B*3a%24Noridian+Administrative+Services%257C%257C+LlC+(03102)*3a%24&bc=gAAAACAAAABAAAAAAA%3d%3d&

Genetic Testing for Hereditary Breast and Ovarian Cancer Syndrome

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Centers for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD) for Pharmacogenomic Testing for Warfarin Response (90.1). August 3, 2009. Accessed at: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=333&ncdver=1&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=Massachusetts&KeyWord=warfarin&KeyWordLookUp=Title&KeyWordSearchType=And&lcd_id=24308&lcd_version=26&basket=lcd%3a%24244308%3a%2426%3a%24Genetic+Testing%3a%24MAC+-+Part+B%3a%24Noridian+Administrative+Services%257C%257C+LLC+(03102)%3a%24&bc=gAAAAACAAAA%3d%3d&


Hayes GTE Lab Comparison Table. Comparison of Commercially Available Tests for Hereditary Breast and Ovarian Cancer (BRCA1 and BRCA2). Winifred Hayes, Inc. August 3, 2014.


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Hayes GTE Synopsis. BRCAvantage Plus (BRCA1, BRCA2, TP53, STK11, PTEN, CDH1, PALB2). Winifred Hayes, Inc. December 17, 2015.


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<table>
<thead>
<tr>
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<th>Original Effective Date* and Version Number</th>
<th>Policy Owner</th>
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<td>Regulatory Approval: N/A</td>
<td>10/01/06 Version 1</td>
<td>Medical Policy Manager as Chair of Medical Policy, Criteria, and Technology Assessment Committee (MPCTAC)</td>
<td>Quality and Clinical Management Committee (Q&amp;CMC)</td>
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<td>Internal Approval: 08/01/06</td>
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* Effective Date for the BMC HealthNet Plan Commercial Product(s): 01/01/12
* Effective Date for the Well Sense Heath Plan New Hampshire Medicaid Product(s): 01/01/13
* Effective Date for the Senior Care Options Product(s): 01/01/16
* Policy title 10/01/06 to 03/31/17 was Genetic Testing Hereditary Breast and Ovarian Cancer. Policy title as of 04/01/17 is Genetic Testing Hereditary Breast and Ovarian Cancer Syndrome.

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<th>Summary of Revisions</th>
<th>Revision Effective Date and Version Number</th>
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<td>07/11/07</td>
<td>Annual review, updated criteria, template, added coding and references.</td>
<td>Version 2</td>
<td>07/11/07: MPCTAC 07/24/07: Utilization Management Committee (UMC) 08/13/07: Quality Improvement</td>
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<td>Annual review, updated criteria.</td>
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<td>07/28/09</td>
<td>Annual review, updated references and criteria: The diagnoses of fallopian</td>
<td>Version 4</td>
<td>07/28/09: MPCTAC 07/28/09: UMC 08/26/09: QIC</td>
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<td>tube and primary peritoneal cancer were added to ovarian cancer as criteria</td>
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<td>for testing; for a personal history of breast cancer the diagnosed age was</td>
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<tr>
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<td>changed to &lt; 45 and two breast primaries criteria was added; the qualifying</td>
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<td>criteria for males with breast cancer was removed.</td>
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<td>07/01/10</td>
<td>Annual review, updated references, no changes to clinical criteria.</td>
<td>Version 5</td>
<td>07/21/10: MPCTAC 09/22/10: QIC</td>
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<td>07/01/11</td>
<td>Updated clinical criteria based on the 2011 NCCN guidelines.</td>
<td>Version 6</td>
<td>08/17/11: MPCTAC 09/28/11: QIC</td>
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<td>12/01/11</td>
<td>Added new 2012 codes.</td>
<td>Version 7</td>
<td>12/01/11: MPCTAC 12/01/11: QIC</td>
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<td>07/30/12</td>
<td>Off cycle review for Well Sense Health Plan, revised Description of Service</td>
<td>Version 8</td>
<td>08/03/12: MPCTAC 09/05/12: QIC</td>
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<td>section, reformatted Medical Policy Statement, added clarification regarding</td>
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<td>methodology codes, revised the introductory paragraph in Applicable Coding</td>
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<td>section, deleted diagnosis codes, revised Limitations section.</td>
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<td>08/14/13</td>
<td>Off cycle review for Well Sense Health Plan and merged policy format.</td>
<td>Version 9</td>
<td>08/14/13: MPCTAC (electronic vote) 08/15/13: QIC</td>
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<td>Well Sense Health Plan product; these policy revisions were approved by</td>
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<td>Revised policy title and the following sections: Summary, Description of</td>
<td>Version 10</td>
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<td>Service, Definitions, and Clinical Background. Added clarification regarding</td>
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<td>the use of Tier 1 molecular pathology codes, updated CPT codes to include</td>
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<td>section, and deleted diagnosis codes. Described BRACAnalysis and BART;</td>
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<tr>
<td></td>
<td>added clinical criteria for BART test. Added reference to</td>
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<tr>
<th>Date</th>
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<td>07/01/14</td>
<td>Review for effective date 08/01/14. Updated Summary section and introductory paragraph in the Applicable Coding section. No change to criteria or applicable code list. Added reference.</td>
<td>08/01/14 Version 12</td>
<td>07/24/14: QIC</td>
</tr>
<tr>
<td>10/01/14, 11/01/14, and 12/01/14</td>
<td>Review for effective date 03/01/15. Updated criteria in the Medical Policy Statement and Limitations sections. Revised Summary, Description of Item or Service, Definitions, Clinical Background Information, and References sections. Revised note in Applicable Coding section without changing the applicable code list. Changed policy review calendar.</td>
<td>03/01/15 Version 13</td>
<td>12/10/14: QIC 12/02/14: MPCTAC (electronic vote)</td>
</tr>
<tr>
<td>11/25/15</td>
<td>Review for effective date 01/01/16. Updated template with list of applicable products and notes. Updated Summary and Medical Policy Statement sections without changing criteria. Revised language in the Applicable Coding section.</td>
<td>01/01/16 Version 14</td>
<td>12/09/15: QIC 11/25/15: MPCTAC (electronic vote)</td>
</tr>
<tr>
<td>01/01/16</td>
<td>Review for effective date 05/01/16. Revised criteria in the Medical Policy Statement and Limitations sections. Revised Summary, Description of Item or Service, Definitions, Clinical Background Information, and References sections. Updated applicable code list.</td>
<td>05/01/16 Version 15</td>
<td>02/10/16: QIC 01/11/17: QIC</td>
</tr>
<tr>
<td>09/28/16</td>
<td>Review for effective date 11/01/16. Administrative changes made to clarify language related to gender.</td>
<td>11/01/16 Version 16</td>
<td>10/12/16: QIC 09/30/16: MPCTAC (electronic vote)</td>
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<tr>
<td>12/01/16</td>
<td>Review for effective date 04/01/17. Updated policy title and Summary, Description of Item or Service, Clinical Background Information, References, and Reference to Applicable Laws and Regulations sections. Revised criteria in</td>
<td>04/01/17 Version 17</td>
<td>01/11/17: QIC 12/21/16: MPCTAC</td>
</tr>
</tbody>
</table>
Policy Revisions History

<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
<th>Version</th>
<th>Authorizing Entity</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/01/17</td>
<td>Review for effective date 05/01/17. Revised criteria for multigene panel testing in the Limitations section. Updated definition of WES and WGS.</td>
<td>05/01/17 Version 18</td>
<td>01/18/17: MPCTAC 02/08/17: QIC</td>
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<tr>
<td>12/01/17</td>
<td>Review for effective 01/01/18. Industry-wide update to code description in the Applicable Coding section.</td>
<td>01/01/18 Version 19</td>
<td>Not applicable because industry-wide change in code description.</td>
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<td>12/20/17</td>
<td>Review for effective date 03/09/18. Revised criteria in the Medical Policy Statement and Limitations sections. Updated Summary and References sections.</td>
<td>03/09/18 Version 20</td>
<td>12/20/17: MPCTAC</td>
</tr>
</tbody>
</table>

Last Review Date
12/20/17

Next Review Date
12/01/18

Authorizing Entity
MPCTAC

Other Applicable Policies
Medical Policy - Chromosomal Microarray Analysis for Unexplained Intellectual Disabilities and/or Multiple Congenital Anomalies, policy number OCA 3.573
Medical Policy - Experimental and Investigational Treatment, policy number OCA 3.12
Medical Policy - Gene Expression Profiling of Tumor Tissue to Predict Cancer Recurrence with Risk Stratification (Including Oncotype DX™ and Other Tests), policy number OCA 3.572
Medical Policy - Genetic Testing for Familial Malignant Melanoma, policy number OCA 3.78
Medical Policy - Genetic Testing for Fragile X-Associated Disorders, policy number OCA 3.571
Medical Policy - Genetic Testing Guidelines and Pharmacogenetics, policy number OCA 3.727
Medical Policy - Genetic Testing for Hereditary Colorectal Cancer, policy number OCA 3.64
Medical Policy - Genetic Testing for Hereditary Thrombophilia, policy number OCA 3.728
Medical Policy, Medically Necessary, policy number OCA 3.14

*Plan refers to Boston Medical Center Health Plan, Inc. and its affiliates and subsidiaries offering health coverage plans to enrolled members. The Plan operates in Massachusetts under the trade name Boston Medical Center HealthNet Plan and in other states under the trade name Well Sense Health Plan.
Medical Policy - *Preimplantation Genetic Testing (Preimplantation Genetic Diagnosis and Pregenetic Screening)*, policy number OCA 3.726

**Reference to Applicable Laws and Regulations**


Massachusetts General Law. Chapter 111. Section 70G. (M.G.L. c. 111 sec. 70G.) Genetic information and reports protected as private information; prior written consent for genetic testing. Accessed at: https://malegislature.gov/Laws/GeneralLaws/PartI/TitleXVI/Chapter111/Section70G

**Disclaimer Information:** +

Medical Policies are the Plan’s guidelines for determining the medical necessity of certain services or supplies for purposes of determining coverage. These Policies may also describe when a service or supply is considered experimental or investigational, or cosmetic. In making coverage decisions, the Plan uses these guidelines and other Plan Policies, as well as the Member’s benefit document, and when appropriate, coordinates with the Member’s health care Providers to consider the individual Member’s health care needs.

Plan Policies are developed in accordance with applicable state and federal laws and regulations, and accrediting organization standards (including NCQA). Medical Policies are also developed, as appropriate, with consideration of the medical necessity definitions in various Plan products, review of current literature, consultation with practicing Providers in the Plan’s service area who are medical experts in the particular field, and adherence to FDA and other government agency policies. Applicable state or federal mandates, as well as the Member’s benefit document, take precedence over these guidelines. Policies are reviewed and updated on an annual basis, or more frequently as needed. Treating providers are solely responsible for the medical advice and treatment of Members.

The use of this Policy is neither a guarantee of payment nor a final prediction of how a specific claim(s) will be adjudicated. Reimbursement is based on many factors, including member eligibility and benefits on the date of service; medical necessity; utilization management guidelines (when applicable); coordination of benefits; adherence with applicable Plan policies and procedures; clinical coding criteria; claim editing logic; and the applicable Plan – Provider agreement.