TITLE: GENETIC TESTING FOR SUSCEPTIBILITY TO HEREDITARY BREAST AND / OR OVARIAN CANCER

EFFECTIVE DATE: November 20, 2017

This policy was developed with input from specialists in oncology, hematology and cancer genetics and endorsed by the Medical Policy Committee.

IMPORTANT INFORMATION – PLEASE READ BEFORE USING THIS POLICY
These services may or may not be covered by all Medica plans. Please refer to the member's plan document for specific coverage information. If there is a difference between this general information and the member’s plan document, the member’s plan document will be used to determine coverage. With respect to Medicare and Minnesota Health Care Programs, this policy will apply unless these programs require different coverage. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Medica utilization management policy may call the Medica Provider Service Center toll-free at 1-800-458-5512.

Medica utilization management policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

PURPOSE
To promote consistency between reviewers in utilization management decision-making by providing the criteria that generally determine the medical necessity of genetic testing for susceptibility to hereditary breast and ovarian cancer. The Coverage Issues box below outlines the process for addressing the needs of individuals who do not meet these criteria.

BACKGROUND
I. Definitions
   A. BRCA1 and BRCA2 (BReast CANcer) are genes that suppress tumor development in many areas throughout the body. A mutation in either of these genes may cause their tumor suppressing properties to malfunction and may be indicative of a predisposition for hereditary breast and ovarian cancer.
   B. BRACAnalysis® Rearrangement Test (BART) is a molecular diagnostic test that detects rare, large rearrangements of deoxyribonucleic acid (DNA) in the BRCA1 and BRCA2 genes. It is intended for patients with a strong family history of breast and ovarian cancer. The test can be performed with blood drawn in the laboratory, doctor’s office, hospital, or clinic and is referred to as reflex testing.
   C. Close blood relative includes first, second, or third degree blood relatives (for this policy only). First degree relative is a relative with whom one half of an individual’s genes are shared (i.e., parent, sibling, offspring). Second degree relative is a relative with whom one quarter of an individual’s genes is shared (i.e., grandparent, grandchild, uncle, aunt, nephew, niece, half-sibling). Third degree relatives are defined as great-grandparents, great-aunts, great-uncles, great-grandchildren, and first cousins.
   D. Founder mutation: A gene mutation observed in high frequency in a specific population (frequently referenced in the literature as “founder population”) due to the presence of that gene mutation in a single ancestor or small number of ancestors.
   E. A genetic counselor is a health professional with specialized training and clinical experience in the areas of medical genetics and counseling that has completed an accredited Masters or Doctorate Degree program and has been certified by the American Board of Genetic Counseling or the American Board of Medical Genetics. Genetic counselors work as members of a health care team providing information and support to individuals and/or families who have birth defects or genetic disorders or who may be at risk for a variety of inherited conditions. Genetic counseling services may be provided both before and after genetic testing and include, but are not limited to the following services:
      1. The collection, documentation and interpretation of family and medical histories to assess the risk of
Genetic Testing for Susceptibility to Hereditary Breast and/or Ovarian Cancer
Medica Policy No. III-DIA.04

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disease occurrence or recurrence
1. Education regarding inheritance and the nature, risks, and potential outcomes of genetic testing
2. Assessment and review of the psychological and societal risks and benefits of genetic testing
3. Supportive counseling to promote informed consent
4. Identification of and referral to appropriate support services

F. **Limited Family History** is defined as fewer than two first or second degree female relatives or female relatives surviving beyond 45 years in either lineage.

G. A **medical geneticist** is a licensed physician with specialty training in medical genetics and counseling who has been certified by the American Board of Medical Genetics. In addition to genetic counseling, the medical geneticist can conduct physical examinations, make diagnoses of genetic disorders, and manage the clinical care of these disorders.

H. **Multigene panel testing** is genetic testing that uses next-generation sequencing to test multiple genes simultaneously, and is also called multiple-gene panel testing and multiple-gene testing.

I. **Multisite 3 BRACAnalysis** is performed in individuals of Ashkenazi Jewish ethnicity to analyze BRCA 1 and 2 genes for three mutations indicating susceptibility to breast and ovarian cancer. Two of these mutations are in BRCA-1 (del187AG and 5385insC) and one mutation is in BRCA-2 (6174delT).

J. **Next-generation sequencing (NGS)**, also known as massively parallel or high through-put sequencing, is an automated method of sequencing DNA, that can process many genes at one time. Using NGS, DNA sequencing is less costly and less time-consuming than traditional manual DNA sequencing.

K. **Single site test** is performed when a gene mutation has been previously identified in another family member; this test examines a small portion of the DNA specifically for that mutation.

L. **Triple negative phenotype** is an individual whose tumor tissue test is negative for estrogen-receptor, progesterone-receptor and HER2 expression.

M. A **variant**, also known as a gene mutation, is a permanent alteration in the DNA sequence that makes up a gene, such that the sequence differs from what is found in most people. They are also known as benign DNA variants where the alteration in the DNA sequence does not cause a change in the function of the gene. Mutations can vary in size; they can affect a single DNA base pair or be due to small deletions or insertions or rearrangements of DNA base pairs. Larger duplication and/or deletions of varying sizes include segments of a chromosome that can include multiple genes.

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**MEDICAL NECESSITY CRITERIA**

I. Genetic testing for susceptibility to hereditary breast and/or ovarian cancer, using single gene or multigene panels, in individuals NOT previously tested is considered medically necessary when documentation in the medical record indicates that **all of the following** criteria are met:

   A. The member is at least 18 years of age
   B. The individual to be tested has an increased likelihood of carrying a deleterious mutation in the **BRCA 1**, **BRCA 2**, or other breast cancer susceptibility gene(s), (e.g., **CHEK2**, **PALB2**, **ATM**).
   C. A board-certified and licensed (where required) genetic counselor, medical geneticist, or oncologist, independent of the laboratory performing the test, has reviewed and documented family history, created a pedigree, advised the patient of the potential benefits and harms of the testing and implications of the test results, and obtained written informed consent (genetic professionals are not excluded if they are employed by or contracted with a laboratory that is part of an integrated health system which routinely delivers health care services beyond just the laboratory test).
   D. The test is ordered by a physician with expertise in the diagnosis and/or management of breast and ovarian cancer or board-certified and licensed (where required) genetic counselor independent of the laboratory performing the testing (genetic professionals are not excluded if they are employed by or contracted with a laboratory that is part of an integrated health system which routinely delivers health care services beyond just the laboratory test).
   E. **One of the following** criteria are met:
      1. Requesting Individual with Personal History of Cancer
         Personal history of breast cancer and **one or more of the following**:
         a. Diagnosed with breast cancer at or before age 45
         b. Diagnosed with breast cancer at or before age 50 and **one of the following**:
            1) An additional breast cancer primary
            2) One or more close blood relative with breast cancer at any age
            3) One or more close relative with pancreatic cancer
            4) One or more relative with prostate cancer*

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Effective Date: November 20, 2017
5) An unknown or limited family history
c. Diagnosed at or age 60 with triple negative breast cancer.
d. Diagnosed at any age with one of the following:
   1) Two or more close blood relatives with breast cancer, pancreatic cancer, or prostate cancer* at any age
   2) One or more close blood relatives with breast cancer diagnosed at or before age 50
   3) One or more close blood relatives with ovarian cancer
   4) A close male blood relative with breast cancer
   Note: For an individual of ethnicity associated with a higher mutation frequency (e.g., Ashkenazi Jewish) no additional family history may be required.
e. Personal history of ovarian cancer
f. Personal history of male breast cancer
g. Personal history of prostate cancer* at any age with 1 or more close blood relatives with ovarian cancer at any age or breast cancer at or before at 50, or 2 relatives with breast, pancreatic, or prostate cancer* at any age
h. Personal history of pancreatic cancer at any age with 1 or more close blood relatives with ovarian cancer at any age or breast cancer at or before age 50 or two relatives with breast, pancreatic, or prostate cancer* at any age
i. Personal history of pancreatic cancer and Ashkenazi Jewish ancestry
j. BRCA 1/2 mutation detected by tumor profiling in the absence of germline mutation analysis.

2. Requesting Individual with Family History of Known Genetic Mutation
   Family history of a close relative with known positive BRCA1 or BRCA2 mutation.

3. Requesting Individual with Family History of Cancer and one of the following:
a. First or second degree blood relative meeting any of the above criteria
b. Third degree blood relative with breast cancer and/or ovarian cancer and at least two close blood relatives with breast cancer and/or ovarian cancer.

II. Large genomic rearrangement testing (e.g., BART) to identify individuals at risk for BRCA 1 and BRCA 2-related cancers (if the previous test did not include BART) is considered medically necessary when documentation in the medical record indicates that all of the following are met:
   A. The individual meets one or more of the criteria in Section I.
   B. Testing for BRCA 1 and BRCA 2 are negative.

*Gleason score ≥ 7

COVERAGE ISSUES
1. Prior authorization is required for genetic testing for susceptibility to hereditary breast and/or ovarian cancer.
2. This utilization management policy does not apply to genetic testing for BRCA mutation (BRACAnalysis CDx diagnostic test) to assess potential response to Lynparza (olaparib) treatment for advanced ovarian cancer associated with germline BRCA mutations. See Medica utilization management policy, Olaparib (Lynparza®) and Medica coverage policy, Genetic and Pharmacogenetic Testing.
3. The Pre-Ovar KRAS Variant Test for susceptibility to ovarian cancer is investigative and therefore not covered.
4. Genetic testing is excluded and therefore not covered when performed in the absence of symptoms or high risk factors for a genetic disease or when knowledge of genetic status will not affect treatment decisions or screening for the disease (see Genetic Testing and Pharmacogenetic Testing coverage policy).
5. See also related Medica coverage policies: Genetic and Pharmacogenetic Testing and Genetic Testing and TP53 (p53) Testing for Li-Fraumeni Syndrome.
6. Coverage may vary according to the terms of the member’s plan document.
7. For Medicare members, refer to the following, as applicable at: http://www.cms.hhs.gov/mcd/search.asp?
8. If the Medical Necessity and Coverage Criteria are met, Medica will authorize benefits within the limits in the member’s plan document.
9. If it appears that the Medical Necessity and Coverage Criteria are not met, the individual’s case will be reviewed by the medical director or external reviewer. Practitioners are advised of the appeal process in their Medica Providers Administrative Manual.
References:

Pre-9-2015 Medical Policy Committee (MPC):

09/2015 MPC
Genetic Testing for Susceptibility to Hereditary Breast and/or Ovarian Cancer

Medica Policy No. III-DIA.04


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54. Peshkin BN, Isaacs C. Interpretation of uninformative BRCA1/BRC2 genetic testing results for hereditary breast and ovarian cancer. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2015.


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76. Hayes, Inc. *Hayes GTE Synopsis: Ovarian Cancer Focus Panel (Fulgent Genetics).* April 2017. Lansdale, PA.
