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

EFFECTIVE DATE: October 21, 2019

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 utilization management reviewers by providing the criteria that determines the medical necessity.

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/or ovarian cancer.
B. BRACAnalysis® Rearrangement Test (BART) is a molecular diagnostic test that detects rare, large rearrangements of deoxyribonucleic acid (DNA) in the BRCA 1 and BRCA 2 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. BRCA-related ovarian cancer are cancers are associated with epithelial, non-mucinous histology. Lynch syndrome can be associated with both non-mucinous and mucinous epithelial tumors. Specific types of non-epithelial ovarian cancers and tumors can also be associated with other rare syndromes (e.g., sex-cord tumors, Peutz-Jeghers syndrome, Sertoli-Leydig tumors, DICER1-related tumors).
D. 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.
E. 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.
F. 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. A list of states issuing licenses for genetic counselors can be found at https://www.nsgc.org/p/cm/ld/fid=19. 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 disease occurrence or recurrence
2. Education regarding inheritance and the nature, risks, and potential outcomes of genetic testing
3. Assessment and review of the psychological and societal risks and benefits of genetic testing
4. Supportive counseling to promote informed consent
5. Identification of and referral to appropriate support services.

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

H. 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.

I. 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.

J. Multiple breast cancer primaries are two or more breast tumors that can include either bilateral (contralateral) disease or two or more clearly separate ipsilateral primary tumors. The diagnoses could be made either synchronously or asynchronously.

K. 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).

L. 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.

M. Single site test is performed when a single gene mutation has been previously identified in another family member. A single site test examines a small portion of DNA specifically for the mutation previously found in the individual’s family member.

N. Triple negative phenotype is an individual whose tumor tissue test is negative for estrogen-receptor (ER), progesterone-receptor (PR) and HER2 expression.

O. A gene 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. Mutations range in size; they can affect anywhere from a single DNA base pair to a large segment of a chromosome that includes multiple genes.

BENEFIT CONSIDERATIONS

1. Prior authorization is required for genetic testing for susceptibility to hereditary breast and/or ovarian cancer. Please see the prior authorization list for product specific prior authorization requirements.

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 coverage policy, Genetic and Pharmacogenetic Testing.

3. The Pre-Ovar KRAS Variant Test for susceptibility to ovarian cancer is investigatory 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 Medica coverage policy, Genetic Testing and Pharmacogenetic Testing).

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. If the Medical Necessity and Benefit Considerations are met, Medica will authorize benefits within the limits in the member’s plan document.

8. If it appears that the Medical Necessity and Benefit Considerations 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.
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 a family history (regardless of degree of relatedness) indicating an increased likelihood of carrying a pathogenic variant in a breast/ovarian cancer-related susceptibility gene (e.g., BRCA1, BRCA2, CHEK2, PALB2, ATM).
C. A board-certified and licensed (where required) genetic counselor, medical geneticist, oncologist, obstetrician/gynecologist (Ob/Gyn), surgeon, oncology nurse, or other health professional with expertise and experience in cancer genetics, independent of the laboratory performing the test, has reviewed and documented family history or 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).

NOTE: For individuals with documented Ashkenazi Jewish ancestry, no further family history beyond ancestry is required prior to genetic counseling.

D. The test is ordered by a physician with expertise in the diagnosis and/or management of breast and ovarian cancer; or a physician assistant or nurse practitioner if working in a practice specializing in Ob/Gyn, surgery, oncology, or other practice with expertise in cancer genetics; or a 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 or more of the following criteria are met:

1. The individual to be tested has a personal history of breast cancer and one or more of the following criteria are met:
   a. A female diagnosed with breast cancer at or before age 50.
   b. A female diagnosed at or before age 60 with triple negative breast cancer (ER-, PR-, HER2-).
   c. A female diagnosed at any age with more than one breast cancer primary.
   d. A female diagnosed at any age when one or more of the following criteria are met:
      1) One or more close blood relative (first- second-, or third-degree blood relative) diagnosed with one or more of the following:
         a) Breast cancer at or before age 50
         b) Invasive ovarian cancer
         c) Male breast cancer
         d) Pancreatic cancer
         e) Prostate cancer.
      2) Two or more close blood relatives diagnosed with breast cancer at any age.
   e. Individual is of Ashkenazi Jewish ancestry.
      NOTE: No additional family history required; See B., above.

2. The individual to be tested has a personal history of non-breast cancer and one of the following diagnoses is met:
   a. Ovarian cancer
   b. Fallopian tube cancer
   c. Peritoneal cancer, primary
   d. Pancreatic cancer
   e. Metastatic prostate cancer.

3. The individual to be tested does not meet the above criteria (E.1. and E.2) and one of the following criteria are met:
   a. Family history of a close blood relative with known positive BRCA1 or BRCA2 mutation.
   b. One or more of the following criteria are met:
      1) The individual to be tested has a first- or second-degree relative meeting one or more of the following criteria:
         a) Breast cancer at or before age 45
         b) Ovarian cancer
         c) Fallopian tube cancer
         d) Peritoneal cancer, primary
e) Male breast cancer
f) Pancreatic cancer
g) Metastatic prostate cancer
h) At least two breast cancer primaries in a single family member
i) At least two blood relatives with breast cancer primaries on the same side of the family and at least one relative diagnosed at or before age 50.

2) The individual to be tested has a third degree blood relative with breast cancer and/or BRCA-related ovarian cancer and that third degree relative has at least two close blood relatives with breast cancer and/or BRCA-related ovarian cancer.

3) Family history on the same side of the family of three or more of the following diagnoses: Breast cancer (including lobular breast cancer), sarcoma, adrenocortical carcinoma, brain tumor, leukemia, colon cancer, endometrial cancer, thyroid cancer, kidney cancer, macrocephaly, gastrointestinal cancer, hamartomatous polyps of the gastrointestinal tract, lobular breast cancer, diffuse gastric cancer, ovarian sex chord tumors, pancreatic cancer, testicular sertoli cell tumors, dermatologic manifestations, childhood skin pigmentation.

NOTE: Can include diagnosis in the individual to be tested, as well as multiple primary cancers in the same individual.

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. Results of BRCA1 and BRCA2 testing were negative.

B. One or more of the following criteria are met:
   1. The individual to be tested has a personal history of breast cancer and one of the following criteria are met:
      a. A female diagnosed with breast cancer at or before age 50.
      b. A female diagnosed with breast cancer at or before age 60 with triple negative breast cancer (ER-, PR-, HER2-).
      c. A female diagnosed at any age with more than one breast cancer primary.
      d. A female diagnosed with breast cancer at any age when one or more of the following criteria are met:
         1) One or more close blood relative (first-, second-, or third-degree blood relative) diagnosed with one of the following:
            a) Breast cancer at or before age 50
            b) Invasive ovarian cancer
            c) Male breast cancer
            d) Pancreatic cancer
            e) Prostate cancer.
         2) Two or more close blood relative diagnosed with breast cancer at any age.
      3) Individual is of Ashkenazi Jewish Ancestry
         NOTE: No additional family history required; See B., above.
   2. The individual to be tested has a personal history of non-breast cancer and one of the following diagnoses are met:
      a. Ovarian cancer
      b. Fallopian tube cancer
      c. Peritoneal cancer, primary
      d. Pancreatic cancer
      e. Metastatic prostate cancer.
   3. The individual to be tested does not meet the above criteria (E.1. and E.2.) but has a blood relative meeting one or more of the following criteria:
      a. The individual to be tested has a first- or second-degree blood relative with one or more of the following criteria:
         1) Breast cancer at or before age 45
         2) Ovarian cancer
         3) Fallopian tube cancer
         4) Peritoneal cancer, primary
5) Male breast cancer
6) Pancreatic cancer
7) Metastatic prostate cancer
8) At least two breast cancer primaries in a single family member
9) At least two blood relatives with breast cancer primaries on the same side of the family and at least one diagnosed at or before age 50.

b. The individual to be tested has a third-degree blood relative with breast cancer and/or BRCA-related ovarian cancer and that third-degree blood relative has at least two close blood relatives with breast cancer and/or ovarian cancer.

c. Family history on the same side of the family of three or more of the following diagnoses: Breast cancer (including lobular breast cancer), sarcoma, adrenocortical carcinoma, brain tumor, leukemia, colon cancer, endometrial cancer, thyroid cancer, kidney cancer, dermatologic manifestations, macrocephaly, gastrointestinal cancer, hamartomatous polyps of the gastrointestinal tract, lobular breast cancer, diffuse gastric cancer, ovarian sex chord tumors, pancreatic cancer, testicular sertoli cell tumors, childhood skin pigmentation.

NOTE: Can include diagnosis in the individual to be tested, as well as multiple primary cancers in the same individual.

Centers for Medicare & Medicaid Services (CMS)
- For Medicare members, refer to the following, as applicable at: http://www.cms.hhs.gov/mcd/search.asp

Document History

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References:

Pre-9-2015 Medical Policy Committee (MPC)

09/2015 MPC
47. Isaacs C, Fletcher SW, Peshkin BN. Genetic testing for hereditary breast and ovarian cancer syndrome. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2015.
52. Peshkin BN, Isaacs C. Genetic risk assessment for individuals at risk for hereditary breast and ovarian cancer syndrome. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2015.
54. Peshkin BN, Isaacs C. Interpretation of uninformative BRCA1/BRCA2 genetic testing results for hereditary breast and ovarian cancer. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2015.

11/2016 MPC


09/2017 MPC


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

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


09/2018 MPC


09/2019 MPC


86. Peshkin BN, Isaacs C. Genetic counseling and testing for those at risk of hereditary breast and ovarian cancer. Last updated May 16, 2019. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2019.