Quartz

Genetic Testing for Breast, Ovarian, Pancreatic or Prostate Cancer Syndromes Including BRCA

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Policy

The Medical Management Department reviews referral requests for prior authorization of genetic testing for BRCA related-breast, ovarian, pancreatic or prostate cancer syndromes.

This Medical Policy does not constitute medical advice. When deciding coverage, the enrollee's specific plan document must be referenced. The terms of an enrollee's plan document (Certificate of Coverage [COC] or Summary Plan Description [SPD]) may differ from this Medical Policy. In the event of a conflict, the enrollee's specific benefit plan document supersedes this Medical Policy. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements, and the plan benefit coverage prior to use of this Medical Policy. Other Policies and Coverage Determination Guidelines may apply. Quartz reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary.

Procedure

I. Documentation Required:

To facilitate the authorization process, referral requests **MUST** include **ALL** the following:

A. Clinical record of patient detailed family history, and any completed risk assessment tools;
B. Record of appropriate conventional clinical diagnostic studies/tests/interventions including results of those tests;
C. Results of previously completed genetic testing;
D. Documentation of the performance of pre-test genetic counseling and informed consent discussion for testing.
E. Genetic counseling must be performed by a qualified, appropriately trained practitioner with **ONE** of the following backgrounds:

1. Board certified/Board eligible (BC/BE) genetics counselor;
2. BC/BE medical geneticist;
3. Genetic nurse credentialed as either a genetic clinical nurse or advanced practice nurse in genetics;
4. Specialist with expertise in cancer genetics to include an oncologist, surgical oncologist, or other physician or advanced practice professional with documented training and expertise in cancer genetics.
5. The person providing the counseling cannot be employed by a commercial genetic testing laboratory except those employed by/contracted by a laboratory that is part of an integrated health system which routinely delivers health care services beyond just the laboratory test itself.

II. Medical Necessity Criteria for Specific Genetic Tests:

A. Personal History of Breast or Ovarian Cancer

Single or multigene testing for susceptibility of breast or ovarian cancer in adults including the following gene mutations, ATM, BARD1, BRIP1, BRCA1, BRCA2, **(**Comprehensive BRAC*Analysis* test CPT 81162 & Large deletion/duplication testing (rearrangements) CPT 81164) CDH1, CHEK2, NBN, NF1, PALB2, PTEN, RAD51C, RAD51D, STK11, and/or TP53, is considered medically necessary when associated with genetic counseling (see Documentation Required) and **ANY** of the following:

1. Personal history of breast (includes invasive and ductal carcinoma in situ) cancer and **ONE** or more of the following:
   - **a.** Diagnosed at age ≤ 45 **OR**
   - **b.** Diagnosed at age 46-50 with at least **ONE** of the following:
     - i. ≥ 1 close blood relative with breast, ovarian, pancreatic, or prostate cancer at any age; **OR**
     - **ii.** an additional breast cancer primary at any age**; OR**
     - **iii.** an unknown or limited family history (see definition); **OR**
   - **c.** Diagnosed at age ≤ 60 with triple negative breast cancer (ER-, PR-, HER2-); **OR**
   - **d.** Diagnosed at any age with **ONE** of the following:
     - **i.** ≥ 2 additional diagnoses of breast cancer at any age in patient and/or close blood relatives; **OR**
     - **ii.** ≥ 1 close blood relative with:
       - a) Ovarian/fallopian tube/primary peritoneal cancer**; OR**
       - b) Breast cancer diagnosed ≤ age 50; **OR**
       - c) Male breast cancer; **OR**
       - d) Metastatic or intraductal/cribiform histology or high or very-high risk group prostate cancer, **OR**
       - e) Pancreatic cancer
   - e. Patient is of Ashkenazi Jewish ancestry or other ethnic population at increased risk of founder mutations; **OR**
   - f. A mutation is identified on tumor genomic testing that has clinical implications if also identified in the germline (NOTE: test only for the tumor mutation presence in germline testing).

   NOTE: Patients of Ashkenazi Jewish ancestry with no known familial mutation, must be tested for the 3 Ashkenazi Jewish founder-specific mutations (Multisite 3 BRAC*Analysis* test - CPT 81212) first before any comprehensive testing will be authorized. Comprehensive genetic testing may be considered if ancestry also includes non-Ashkenazi Jewish relatives or if other BRCA-related criteria are met. Founder mutations exist in other populations including (but not limited to) Icelandic and French-Canadian ancestry.
2. Personal history of epithelial ovarian cancer including fallopian tube and primary peritoneal cancers; **OR**

3. Personal history of male breast cancer; **OR**
4. BRCA1/2 pathogenic/likely pathogenic variant detected by tumor profiling on any tumor type in the absence of germline pathogenic/likely pathogenic variant analysis; **OR**
5. Patients with BRCA-related cancers who may benefit from testing to determine eligibility for targeted treatments (see pharmacogenomics policy);
6. The patient has at least a >5% probability of carrying a pathogenic BRCA1 or BRCA2 gene mutation as determined using a validated risk assessment tool (e.g., Ontario Family History Assessment Tool, Manchester Scoring System, Referral Screening Tool, Pedigree Assessment Tool, 7-Question Family History Screening Tool (FHS-7), International Breast Cancer Intervention Study Instrument (Tyler-Cuzick), BRCAPro, CanRisk); **OR**
7. Personal history of breast cancer with a known familial BRCA1/BRCA2 gene mutation (patients with a known familial BRCA1/BRCA2 gene mutation must be tested for the single known mutation first before comprehensive testing will be authorized); **OR**
8. Individual meets criteria for Li-Fraumeni syndrome or Cowden syndrome/PTEN hamartoma tumor syndrome (see Genetics Testing policy), **OR**
9. An individual who does not meet criteria themselves but has one or more first or second-degree blood relatives who meet the above criteria (except for targeted treatment testing criteria). Preference is for the family member to be tested first, **OR**

Lynch syndrome genetic testing (mutations in MLH1, MSH2, MSH6, PMS2 or EPCAM) is considered medically necessary in patients with a personal history of ovarian cancer when associated with genetic counseling or the patient meets criteria for Lynch Syndrome testing found in policy C.6.07 Genetic Testing.

B. Personal or Family History of Prostate Cancer

BRCA1 and BRCA2 (Comprehensive BRAC*Analysis* test CPT 81162 & Large deletion/duplication testing (rearrangements) CPT 81164**), PALB2, ATM, and CHEK2 genetic testing** are considered medically necessary when associated with genetic counseling and **ANY** of the following criteria are met:

1. Strong family history with at least **ONE** of the following:
   a. Known germline DNA repair gene abnormalities, especially BRCA2 mutation or Lynch syndrome (MLH1, MSH2, MSH6, or PMS2); **OR**
   b. A first degree relative with prostate cancer who meets any of the personal history of prostate cancer criteria below; **OR**
   c. The patient has at least a >5% probability of carrying a BRCA1 or BRCA2 gene mutation as determined using a validated risk assessment tool (e.g., Ontario Family History Assessment Tool, Manchester Scoring System, Referral Screening Tool, Pedigree Assessment Tool, 7-Question Family History Screening Tool (FHS-7), International Breast Cancer Intervention Study Instrument (e.g., Tyler-Cuzick), BRCAPro, CanRisk); **OR**

2. Personal history of prostate cancer with at least **ONE** of the following:
    a. Ashkenazi Jewish ancestry, **OR**
    b. Prostate cancer is regional or metastatic in nature; **OR**
    c. Prostate cancer has intraductal/cribiform histology, **OR**
    d. Prostate cancer is considered high risk or very high risk, **OR**
    e. 2 or more close blood relatives with breast or prostate (any grade) cancer at any age; **OR**
    f. 1 or more close relatives with breast cancer at age ≤50; or ovarian cancer; pancreatic cancer; or metastatic, intraductal/cribiform prostate cancer at any age; **OR**
    g. Brother, father or multiple family members with prostate cancer (but not clinically localized Grade Group 1 cancer) at age 60 or younger or who died from prostate cancer, **OR**
    h. ≥3 cancers on the same side of the family, especially diagnoses at age ≤50 years: bile duct, breast, colorectal, endometrial, gastric, kidney, melanoma, ovarian, pancreatic, prostate cancer (but not clinically localized Grade Group 1) small bowel or urothelial cancer; **OR**
    i. Family history of known germline DNA repair gene abnormalities, especially BRCA1/2 mutation or Lynch syndrome (MLH1, MSH2, MSH6, or PMS2);
    j. A mutation identified on tumor genomic testing that has clinical implications if also identified in the germline (NOTE: test only for the tumor mutation presence in germline testing).

NOTE: Patients of Ashkenazi Jewish ancestry with no known familial mutation, must be tested for the 3 Ashkenazi Jewish founder-specific mutations (Multisite 3 BRAC*Analysis* test - CPT 81212) first before any comprehensive testing will be authorized. Comprehensive genetic testing may be considered if ancestry also includes non-Ashkenazi Jewish relatives or if other BRCA-related criteria are met. Founder mutations exist in other populations including (but not limited to) Icelandic and French-Canadian ancestry.

Lynch syndrome genetic testing (mutations in MLH1, MSH2, MSH6, PMS2 or EPCAM) is considered medically necessary in patients with a personal history of prostate cancer when associated with genetic counseling and the patient meets one of the following:

1. Patient meets criteria Lynch Syndrome testing found in policy C.6.07 Genetic Testing, OR
2. Patient has high-risk, very high-risk, regional or metastatic prostate cancer.

Patients with a familial BRCA1/BRCA2, PALB2, ATM, or FANCA gene mutation or with a family history of Lynch Syndrome (known mutations in MLH1, MSH2, MSH6, PMS2 or EPCAM) should be tested for the single known mutation first before comprehensive testing will be authorized.

C. Family History of Breast or Ovarian Cancer

Single or multigene testing for susceptibility of breast or ovarian cancer in adults including the following gene mutations, ATM, BARD, BRCA1 and BRCA2, BRIP1, CDH1, CHEK2, NBN, NF1,

PALB2, PTEN, RAD51C, RAD51D, STK11, and/or TP53, genetic testing for susceptibility to breast or ovarian cancer is considered medically necessary when associated with genetic counseling (see Documentation Required) and **ANY** of the following criteria are met:

1. First- or second-degree blood relative meeting any of the personal history of cancer criteria in II.A. above except patients having testing for targeted treatment decisions only; **OR**
2. The patient has at least a >5% probability of carrying a BRCA1 or BRCA2 gene mutation as determined using a validated risk assessment tool (e.g., Ontario Family History Assessment Tool, Manchester Scoring System, Referral Screening Tool, Pedigree Assessment Tool, 7-Question Family History Screening Tool (FHS-7), International Breast Cancer Intervention Study Instrument (e.g., Tyler-Cuzick), BRCAPro, CanRisk); **OR**
3. Individual from a family with a known deleterious BRCA1/BRCA 2 gene mutation.

D. Personal history of Exocrine Pancreatic Cancer Susceptibility Screening

Genetic testing for a genetic susceptibility to pancreatic cancer including the following tests, ATM, BRCA1, BRCA2, CDKN2A, MLH1, MSH2, MSH6, EPCAM, PALB2, PMS2, STK11, and/or TP53 is considered medically necessary for patients with confirmed exocrine pancreatic cancer when associated with genetic counseling.

Additionally, in patients with a history of recurrent pancreatitis genetic testing including PRSS1, SPINK1 and CFTR is considered medically necessary for patients with confirmed exocrine pancreatic cancer when associated with genetic counseling.

NOTE: Patients with a known familial pathogenic/likely pathogenic germline variant should be tested for the known mutation first.

E. Family history of Exocrine Pancreatic Cancer Susceptibility Screening

Genetic testing for a genetic susceptibility to exocrine pancreatic cancer including the following tests, ATM, BRCA1, BRCA2, CDKN2A, MLH1, MSH2, MSH6, EPCAM, PALB2, STK11, and/or TP53 is considered medically necessary when associated with genetic counseling if **ANY** of the following are met:

1. A known pathogenic/likely pathogenic germline (familial) variant in a exocrine pancreatic cancer susceptibility gene (ATM, BRCA1, BRCA2, CDKN2A, MLH1, MSH2, MSH6, EPCAM, PALB2, STK11, and/or TP53) AND a family history of pancreatic cancer (first-degree or second-degree relative) from the same side of the family as the germline pathogenic/likely pathogenic variant. Testing of first-degree relatives of a person with exocrine pancreatic cancer with unknown gene status should only be done if it is impossible to test the individual who has pancreatic cancer; **OR**
2. A family history of exocrine pancreatic cancer in ≥2 first-degree relatives from the same side of the family, even in the absence of a known pathogenic/likely pathogenic variant, **OR**

3. A family history of exocrine pancreatic cancer in ≥3 first- and/or second-degree relatives from the same side of the family, even in the absence of a known pathogenic/likely pathogenic variant.

NOTE: Patients with a known familial pathogenic/likely pathogenic germline variant should be tested for the known mutation first.

III. Indications Considered Experimental, Investigational or not Medically Necessary (*Not an all-inclusive list)*

1. Genetic testing for BRCA-related or other genetic-related breast or ovarian cancer syndrome before age 18 years old;

2. Testing of unaffected individuals with no significant family history of cancer or no known genetic mutations in the family;

3. Multigene testing for hereditary breast or ovarian cancer not listed above as medically necessary.

HCPCS/CPT Codes

81162	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (ie, detection of large gene arrangements)
81163	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81164	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81165	BRCA1 (BRCA1, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81166	BRCA1 (BRCA1, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (i.e., detection of large gene rearrangements)
81167	BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (i.e., detection of large gene rearrangements)
81212	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants)
81215	BRCA1 (BRCA1, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant
81216	BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81217	BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant
81403	PALB2 site specific analysis; TP53 site specific analysis

81405	TP53 gene sequence and deletion / duplication
81406	PALB2 gene sequence and deletion/duplication
81307	PALB2 gene analysis; full gene sequence
81308	PALB2 known familial variant
81432	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence panel, must include at least 10 genes always including BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, TP53
81433	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11

References

CMS LCD Title Molecular Pathology Procedures L35000; National Government Services.

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National Comprehensive Cancer Network (NCCN); Clinical Practice Guidelines in Oncology;

- Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. V2.2021. Accessed May 19, 2021.
- Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. V1.2021. Accessed May 19, 2021.
- Pancreatic Adenocarcinoma. V2.2021. Accessed May 19, 2021.
- Prostate Cancer. V2.2021. Accessed May 19, 2021.

Pritchard CC, et al. Inherited dna-repair gene mutations in med with metastatic prostate cancer. New Engl J Med. 2016; 375:443-453.

U.S. Preventive Services Task Force. Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: U.S. Preventive Services Task Force recommendation statement. J Am Med Assoc. 2019;322(7):652-665.