



# 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, three generation pedigree analysis, 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, Ovarian, or Pancreatic Cancer

BRCA1 and BRCA 2 genetic testing for susceptibility of breast, ovarian, or pancreatic cancer for adults (Comprehensive BRCA*Analysis* test CPT 81162) 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  $\leq 45$  **OR**
  - b. Diagnosed at age 46-50 with at least **ONE** of the following (i-iv)
    - i  $\geq 1$  close blood relative with breast cancer at any age; **OR**
    - ii  $\geq 1$  close blood relative with prostate cancer (Gleason score of  $\geq 7$ ); **OR**
    - iii an additional breast cancer primary at any age; **OR**
    - iv. an unknown or limited family history (see definition); **OR**
  - c. Diagnosed at age  $\leq 60$  with triple negative breast cancer (ER-, PR-, HER2-); **OR**
  - d. Diagnosed at any age with **ONE** of the following:
    - i.  $\geq 2$  additional diagnoses of breast cancer at any age in patient and/or close blood relatives; **OR**
    - ii.  $\geq 1$  close blood relative with:
      - a) Ovarian/fallopian tube/primary peritoneal cancer; **OR**
      - b) Breast cancer diagnosed  $\leq$  age 50; **OR**
      - c) Male breast cancer; **OR**
      - d) Metastatic prostate cancer, **OR**
      - e) Pancreatic cancer
  - e. Patient is of Ashkenazi Jewish ancestry or other ethnic population at increased risk of founder mutations; **OR**

**NOTE:** Patients of Ashkenazi Jewish ancestry with no known familial mutation, must be tested for the 3 Ashkenazi Jewish founder-specific mutations (Multisite 3 BRCA*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 ovarian cancer including fallopian tube and primary peritoneal cancers; **OR**
3. Personal history of male breast cancer; **OR**
4. Personal history of pancreatic cancer at any age; **OR**
5. Personal history of metastatic prostate cancer; **OR**
6. Personal history of high-grade prostate cancer (Gleason score  $\geq 7$ ) at any age and **ONE** of the following:
  - a.  $\geq 1$  close blood relatives with ovarian cancer, pancreatic cancer, or metastatic prostate cancer at any age or breast cancer at age  $\leq 50$ , **OR**
  - b.  $\geq 2$  close blood relatives with breast or prostate cancer (any grade) at any age; **OR**
  - c. Ashkenazi Jewish ancestry (see Note above); **OR**
7. 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**
8. Patients with BRCA-related cancers who may benefit from testing to determine eligibility for targeted treatments (see pharmacogenomics policy);

9. The patient has at least a 10% 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, FHS-7, PENN II Risk Model); **OR**
10. Personal history of breast or ovarian 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**
11. An individual who does not meet criteria themselves but has one or more first or second-degree blood relatives who meet the above criteria. Preference is for the family member to be tested first.

**B. Personal History of Prostate Cancer**

**BRCA1 and BRCA2** (Comprehensive BRCA*Analysis* test CPT 81162), **PALB2, ATM, CHEK2, and FANCA genetic testing** are considered medically necessary when associated with genetic counseling and **ANY** of the following criteria are met:

1. Strong family history with:
  - a. Brother, father or multiple family members with prostate cancer at age 60 or younger, **OR**
  - b. Known germline DNA repair gene abnormalities, especially BRCA2 mutation or Lynch syndrome (MLH1, MSH2, MSH6, or PMS2); **OR**
  - c. 2 or more close blood relatives with breast, pancreatic or ovarian cancer at any age; **OR** Prostate cancer is castration-resistant; **OR**
2. Prostate cancer is regional or metastatic in nature; **OR**
3. Prostate cancer is considered high or very high risk when **ONE** of the following are met:
  - a. Gleason score of 7 or higher, **OR**
  - b. Stage T3a, T3b or T4, **OR**
  - c. PSA > 20ng/dL.

**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 has 2 or more close blood relatives with colorectal, endometrial, gastric, ovarian, pancreatic, small bowel, urothelial, kidney, or bile duct cancer at any age.

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, Ovarian, Pancreatic or Prostate Cancer**

BRCA1 and BRCA2 genetic testing for susceptibility to breast or ovarian cancer (CPT® code 81211) is considered medically necessary when associated with genetic counseling (see Documentation Required) and **ANY** of the following criteria are met:

1. The family member is **ANY** of the following:
  - a. First- or second-degree blood relative meeting any of the personal history of cancer criteria in II.A. above; **OR**
  - b. Third-degree blood relative who has breast and/or ovarian/fallopian tube/primary peritoneal cancer and who has ≥ 2 close blood relatives with breast cancer (at least one diagnosed ≤ age 50) and/or ovarian/fallopian tube/primary peritoneal cancer; **OR**
2. The patient has at least a 10% 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, FHS-7, PENN II Risk Model); **OR**
3. Individual from a family with a known deleterious BRCA1/BRCA 2 gene mutation.

**D. BRCAAnalysis Large Rearrangement Test (BART) – (CPT 81164)**

BRCAAnalysis Large Rearrangement Test (BART) is medically necessary when associated with genetic counseling (see Documentation Required) and **BOTH** the following are met:

1. Patient has met the medical necessity criteria for Genetic Testing for BRCA1 and BRCA 2 in Section II.A of this policy (Comprehensive BRCAAnalysis test CPT 81162 is completed); **AND**
2. Patient has negative BRCA1 and BRCA2 genetic test results;

Patients with a new diagnosis of breast cancer who meet criteria for BRCA genetic testing and in whom the results will impact initial breast cancer treatment decisions (e.g., type of surgical procedure) may undergo simultaneous BRCA1/2 and BART testing.

**E. Li-Fraumeni Syndrome (TP53 gene mutation) - (CPT 81403, 81405)**

Genetic testing for the TP53 gene mutation is medically necessary when associated with genetic counseling (see Documentation Required) and **ANY** of the following are met. (Patients with a known familial mutation must be tested for the single known mutation first. If unknown, comprehensive TP53 testing of patient or, if unaffected, the family member with the highest likelihood of mutation should be considered.)

1. Patient is from a family with a known TP53 mutation; **OR**
2. Classic Li-Fraumeni syndrome (LFS) including **ALL** the following:
  - a. Patient is age < 45 with a sarcoma; **AND**
  - b. A first degree relative diagnosed at age < 45 with cancer; **AND**
  - c. An additional first or second degree relative in the same lineage with cancer diagnosed at age < 45, or a sarcoma at any age; **OR**
3. Chompret criteria including **ANY** of the following:
  - a. Patient with a tumor from LFS tumor spectrum (soft tissue sarcoma, osteosarcoma, brain tumor, breast cancer, adrenocortical carcinoma, leukemia, lung bronchoalveolar cancer) at age < 46, **AND** at least one first or second degree relative with any of the aforementioned cancers (other than breast cancer if the proband has breast cancer) at age < 56 or with multiple primaries at any age; **OR**
  - b. Patient with multiple tumors (except multiple breast tumors), two of which belong to LFS tumor spectrum with the initial cancer occurring at age < 46; **OR**
  - c. Patient with adrenocortical carcinoma, choroid plexus carcinoma or rhabdomyosarcoma of embryonic anaplastic subtype, at any age of onset, regardless of the family history; **OR**.
  - d. Breast cancer diagnosed at age ≤ 30.

**F. PALB2 (CPT 81403, 81406)**

PALB2 genetic testing is medically necessary when associated with genetic counseling (see Documentation Required) and **ALL** the following are met:

1. Medical history is consistent with hereditary breast cancer and meets **ANY** of the following:
  - a. Personal history of breast cancer and at least **ONE** of the following:
    - i. Breast cancer diagnosed at age ≤ 45; **OR**
    - ii. Breast cancer diagnosed at age ≤ 50 with **ONE** of the following:
      - 1) An additional breast cancer primary (Two breast cancer primaries includes bilateral (contralateral) disease or ≥ 2 clearly separate ipsilateral primary tumors occurring synchronously or asynchronously); **OR**
      - 2) ≥ 1 close blood relative with breast cancer at any age; **OR**

- 3) An unknown or limited family history; **OR**
  - b. Triple negative breast cancer diagnosed at age ≤ 60; **OR**
  - c. Breast cancer diagnosed at any age with **ONE** of the following:
    - i. ≥ 1 close blood relative with breast cancer diagnosed at age ≤ 50; **OR**
    - ii. ≥ 2 close blood relatives with breast cancer at any age; **OR**
    - iii. ≥ 2 close blood relatives with pancreatic and/or prostate cancer (Gleason score ≥ 7) at any age; **OR**
    - iv. A close male blood relative with breast cancer; **OR**
  - d. Men with a personal history of breast cancer; **OR**
  - e. Personal history of pancreatic cancer with ≥ 1 close blood relative with **ANY** of the following:
    - i. Breast cancer diagnosed at age ≤ 50; **OR**
    - ii. Invasive ovarian cancer at any age; **OR**
    - iii. Pancreatic cancer at any age; **OR**
  - f. First or second-degree blood relative meeting **ANY** of the above criteria; **AND**
  - g. Patient has prostate cancer and meets criteria in section B. above.
2. Negative BRCA 1 and BRCA 2 testing.

**NOTE:** Patients with a new diagnosis of breast cancer who meet criteria for both BRCA and PALB2 testing and in whom the results will impact initial breast cancer treatment decisions (e.g., type of surgical procedure) may undergo simultaneous BRCA1/2, BART, and PALB2 testing.

**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;
4. Multigene testing for hereditary breast or ovarian cancer not listed above as medically necessary.

**HCPCS/CPT Codes**

81162	BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (Comprehensive)
81163	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81164	Large deletion/duplication testing (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, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; (Ashkenazi Jewish Screen)

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
81403	PALB2 site specific analysis; TP53 site specific analysis
81405	TP53 gene sequence and deletion / duplication
81406	PALB2 gene sequence and deletion/duplication

## **References**

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

Hayes, Inc. Genetic Test Evaluation Overview: PALB2-Associated Hereditary Breast Cancer for Hereditary Breast Cancer, August 21, 2014. Accessed September 7, 2017.

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Moyer VA; 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. *Ann Intern Med*. 2014; 160(4):271-281.

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