BRCA 1 and 2 Genetic Testing (Sequence Analysis/Rearrangement)

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Definitions

Close blood relative	1st, 2nd, or 3rd degree relative (a parent, full sibling, half sibling, child, grandparent, great-grandparent, grandchild, aunt, great aunt, uncle, great uncle, nephew, niece or first cousin).
Limited family history	Fewer than two first- or second-degree female relatives or female relatives surviving beyond 45 years in either lineage (maternal and paternal).

Related Medical Guidelines

MYvantage® Hereditary Comprehensive Cancer Panel

Guideline

A. BRCA 1 and 2 genetic testing (sequencing analysis, founder mutations) is considered medically necessary when results will directly impact surveillance or treatment and one or more of the following criteria are met:

- Individual from a family with a known deleterious *BRCA1/ BRCA2* gene mutation
- Personal history of breast cancer (includes invasive and ductal carcinoma in situ) + one or more of the following:
  - Diagnosed ≤ 45 y
  - Diagnosed 46–50 y with:
    - An additional breast cancer primary at any age (Note: Two breast cancer primaries includes bilateral [contralateral] disease or two or more clearly separate ipsilateral primary tumors either synchronously or asynchronously)
    - ≥ 1 close blood relative with breast cancer at any age
    - ≥ 1 close blood relative with ovarian cancer at any age

        - ≥ 1 relative with prostate cancer (Gleason score ≥ 7 or metastatic)
        - Pancreatic cancer at any age
        - An unknown or limited family history
- Diagnosed ≤ 60 y with:
    - Triple negative breast cancer
- Diagnosed at any age with:
    - ≥ 2 close blood relatives with breast cancer at any age
    - ≥ 1 close blood relative with pancreatic cancer
    - ≥ 1 close blood relative with metastatic prostate cancer
    - ≥ 1 close blood relative with breast cancer diagnosed ≤ 50 y
    - ≥ 1 close blood relative with ovarian carcinoma
    - A close male blood relative with breast cancer
    - For an individual of ethnicity associated with higher mutation frequency (eg, Ashkenazi Jewish) no additional family history may be required (Note: Testing for Jewish Ashkenazi founder-specific mutation[s] should be performed first. 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)
- Personal history of ovarian carcinoma
- Personal history of male breast cancer
- Personal history of high-grade prostate cancer (Gleason score ≥ 7) at any age with ≥ 1 close blood relative with ovarian carcinoma at any age or breast cancer ≤ 50 y or two relatives with breast, pancreatic, or prostate cancer (Gleason score ≥ 7or metastatic) at any age
- Personal history of metastatic prostate cancer (radiographic evidence of or biopsy-proven disease)
- Personal history of exocrine pancreatic cancer
- Personal history of pancreatic cancer or any first degree relative of an individual with pancreatic cancer
- BRCA1/2 pathogenic mutation detected by tumor profiling on any tumor type in the absence of germline mutation analysis
- Family history only (significant limitations of interpreting test results for an unaffected individual should be discussed):
    - First- or second-degree blood relative meeting any of the above criteria
    - Third-degree blood relative who has breast cancer and/or ovarian carcinoma (includes fallopian tube and primary peritoneal cancers) and who has ≥ 2 close blood relatives with breast cancer (at least one with breast cancer ≤ 50 y) and/or ovarian carcinoma
- Unaffected/asymptomatic member with positive family history of hereditary breast and ovarian cancer (HBOC) syndrome

B. Members are eligible for BRCA 1 and 2 rearrangement testing if the criteria for comprehensive sequence analysis are met and the analysis is negative.

Limitations/Exclusions

Authorization should initially be for the mutation(s) specific to the ethnic group in question (e.g., Multisite 3 BRACAnalysis [or equivalent testing for founder mutations] for members of Ashkenazi descent). If multisite screening is negative, additional genetic testing (e.g., comprehensive sequence analysis) would be warranted if the member meets the remainder of the criteria above.

Requests that do not meet the testing criteria will be reviewed by a Medical Director.

Revision History

May 13, 2022	Clarified personal history of pancreatic cancer RE 1st degree relative with pancreatic cancer and ovarian carcinoma Removed personal history of pancreatic and Ashkenazi Jewish ancestry prerequisite (as having pancreatic cancer, irrespective of ethnicity, is supported for testing)
Mar. 12, 2021	Updated commensurate with V1.2021 NCCN criteria
Mar. 8, 2019	Updated commensurate with V3.2019 NCCN criteria
Feb. 9, 2018	Updated commensurate with V1.2018 NCCN criteria
Dec. 9, 2016	Expanded coverage to unaffected/asymptomatic members with positive family history of HBOC Syndrome

Applicable Procedure Codes

81162	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (ie, detection of large gene rearrangements)
81163	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81164	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81165	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81166	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81167	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81212	BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants
81215	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant
81216	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81217	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant

Applicable ICD-10 Diagnosis Codes

C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast

C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola, unspecified male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast

C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.9	Malignant neoplasm of unspecified ovary
D05.10	Intraductal carcinoma in situ of unspecified breast
D05.11	Intraductal carcinoma in situ of right breast
D05.12	Intraductal carcinoma in situ of left breast
D05.80	Other specified type of carcinoma in situ of unspecified breast
D05.81	Other specified type of carcinoma in situ of right breast
D05.82	Other specified type of carcinoma in situ of left breast
D05.90	Unspecified type of carcinoma in situ of unspecified breast

D05.91	Unspecified type of carcinoma in situ of right breast
D05.92	Unspecified type of carcinoma in situ of left breast
Z15.01	Genetic susceptibility to malignant neoplasm of breast
Z15.02	Genetic susceptibility to malignant neoplasm of ovary
Z80.3	Family history of malignant neoplasm of breast
Z80.41	Family history of malignant neoplasm of ovary
Z85.3	Personal history of malignant neoplasm of breast
Z85.43	Personal history of malignant neoplasm of ovary
Z86.000	Personal history of in-situ neoplasm of breast

References

1. National Comprehensive Care Network. Genetic/Familial High-Risk Assessment: Breast Ovarian, and Pancreatic. Version 2.2022. https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf. Accessed May 23, 2022.
2. Specialty-matched clinical peer review.