CLINICAL MEDICAL POLICY	
Policy Name:	BRCA1 and BRCA2 Genetic Mutation Testing
Policy Number:	MP-011-MD-PA
Responsible Department(s):	Medical Management
Provider Notice/Issue Date:	02/01/2024; 05/01/2023; 07/01/2022; 06/18/2021; 05/25/2020; 06/17/2019; 03/18/2019; 04/15/2018; 08/01/2016
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Products:	Highmark Wholecare℠ Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 14

Policy History

Date	Activity
03/01/2024	Provider Effective date
01/22/2024	PARP Approval
11/15/2023	QI/UM Committee review
11/15/2023	Urgent Review: Per PA DHS TAG determination, the following CPT codes will be listed as an Option #3 (*Approved with [or denied due to] Limited/Minimal Evidence of Effectiveness - Will require Program Exception)*: 81432 & 81433. These codes will require a Program Exception for approval. Updated 'Governing Bodies Approval' section with TAG determination information.
06/01/2023	Provider Effective date
04/18/2023	PARP Approval
03/15/2023	QI/UM Committee review
03/15/2023	Annual Review: No changes to clinical criteria. Reformatted 'Procedures' section. Removed the word 'covered', replaced with 'medically necessary'. Updated 'Summary of Literature' and 'Reference Sources' sections.
08/01/2022	Provider Effective date
05/17/2022	PARP Approval
03/16/2022	QI/UM Committee review

03/16/2022	Annual Review: No changes to clinical criteria. Reformatted Procedure section numbering. Updated Summary of Literature and Reference Sources sections. Added the following CPT codes: 81432, and 81433. Added the following ICD-10 codes: C56.3, Z17.0 & Z17.1. Removed the following ICD-10 codes: C48.1, C48.2, C48.8, C50.029, C50.119, C50.129, C50.219, C50.229, C50.319, C50.329, C50.419, C50.429, C50.519, C50.529, C50.619, C50.629, C50.819, C50.829, C50.919, C50.929, C56.9, C57.00, C57.4, C79.60, C79.61, C79.62, C79.81, D01.7, D05.00, D05.10, D05.80, D05.90, D07.30, Z15.01, Z15.02, Z80.0, Z80.3, Z80.41, Z80.42, Z85.44, Z85.45, & Z85.49.
04/20/2016	Policy approved at QI/UM Meeting

Disclaimer

Highmark Wholecare℠ medical policy is intended to serve only as a general reference resource regarding coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

Policy Statement

Highmark Wholecare may provide coverage under the laboratory section of the medical benefits of the Company's Medicaid products for medically necessary BRCA testing.

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

The qualifications of the policy will meet the standards of the National Committee for Quality Assurance (NCQA) and the Commonwealth of Pennsylvania (PA) Department of Human Services (DHS) and all applicable state and federal regulations.

(Current applicable PA HealthChoices Agreement Section V. Program Requirements, B. Prior Authorization of Services, 1. General Prior Authorization Requirements.)

Definitions

Prior Authorization Review Panel (PARP) – A panel of representatives from within the Pennsylvania Department of Human Services who have been assigned organizational responsibility for the review, approval and denial of all PH-MCO Prior Authorization policies and procedures.

Close Relative – For the purpose of familial assessment, includes first-, second- and third-degree relatives on the same side of the family (maternal or paternal).

First-degree Relatives – Include parents, children, siblings, and half-siblings.

Second-degree Relatives – Include grandparents, aunts, uncles, nieces, nephews, grandchildren, and half-siblings.

Third-degree Relatives – Include great-grandparents, great-aunts, great-uncles, great-grandchildren, and first cousins.

Triple-negative Breast Cancer – The term used to describe breast cancer cells that do not have estrogen receptors, progesterone receptors, or large of amounts of HER/neu protein. Also called ER-negative PR-negative HER2/neu-negative and ER-PR-HER2/neu-negative.

CHEK2 – A gene on chromosome 22q that encodes a kinase enzyme and influences a person's susceptibility to breast cancer.

Gleason Scoring – A system of grading prostate cancer tissue based on microscopic review. The scores range from 2 to 10 that indicate the likelihood of tumor spread. A low Gleason Score indicates that the tumor is less likely to spread, while a high Gleason Score indicates that the tumor is more likely to spread.

Procedures

1. The following general criteria must be met for ALL patients when ordering BRCA1/BRCA2 genetic testing:
    A. The results of the BRCA testing will provide support in the clinical management of the patient; AND
    B. The BRCA testing must be FDA approved.

2. The following is specific BRCA1/BRCA2 genetic testing medical necessity criteria that must be met:
    A. For patients with no personal history of cancer, ALL of the following conditions must be met:
        1) The patient must have a blood-related family member (defined as first-, second-, or third-degree relative) with a known BRCA1/BRCA2 gene mutation/variant ; AND
        2) Testing should be limited to the known target BRCA1/BRCA2 mutation in the family; AND
        3) Further BRCA1/BRCA2 testing will be considered medically necessary if test results are negative AND the patient meets the other criteria listed in this policy.

    B. For patients with active cancer or a personal history of cancer, ANY ONE of the following conditions must be met:
        1) Diagnosed with bilateral breast cancer between the ages of 50 and 65; OR
        2) Personal history of breast cancer diagnosed at $\leq$ 45 years of age; OR
        3) Personal history of breast cancer diagnosed between 46 to 60 years of age with ANY of the following:
            a) Limited or unknown family history; OR
            b) A second breast cancer at any age; OR
            c) One or more close blood relatives with breast cancer at any age; OR
            d) A close blood relative with breast, ovarian, pancreatic, or prostate cancer at any age; OR
        4) Triple-negative breast cancer diagnosed at age ≤ 60 (ER-, PR-, HER2-); OR
        5) Patient is of Ashkenazi Jewish ancestry; OR
        6) One or more close blood relatives with breast cancer at age ≤ 50 or ovarian cancer, pancreatic cancer, metastatic, intraductal/cribriform histology, or high- or very high- risk group prostate cancer at any age; OR

7) High-grade prostate cancer (Gleason score ≥ 7) with ANY of the following:
    a) Two or more close relatives with breast or prostate cancer (any grade), at any age; OR
    b) One or more close relatives with ANY of the following:
        I. Breast cancer at age ≤ 50; OR
        II. Ovarian cancer at any age; OR
        III. Pancreatic cancer at any age; OR
        IV. Metastatic or intraductal/cribriform prostate cancer at any age; OR
8) A patient diagnosed at any age with ANY of the following:
    a) Three or more total diagnoses of breast cancer in the patient and/or close blood relatives; OR
    b) Male breast cancer; OR
    c) Epithelial ovarian cancer, including fallopian tube or peritoneal cancer; OR
    d) Pancreatic (exocrine) cancer.

C. BRCA1/BRCA2 genetic testing is considered medically necessary in unaffected or affected individual who otherwise does not meet any of the criteria listed above but who has a 2.5% to 5% probability of BRCA1/BRCA2 pathogenic variant based on prior probability modes (e.g., Tyrer-Cuzick, BRCAPro, or Penn ll models).

Note: Generally, genetic testing for a particular disease should be performed once per lifetime; however, there are rare instances in which testing may be performed more than once in a lifetime such as when previous testing methodology is inaccurate or a new discovery has added significant relevant mutations for a disease. Repeat BRCA testing with an FDA-approved test (i.e., FoundationFocus) can be performed for women with ovarian cancer who had another brand of BRCA test and are being considered for treatment with rucaparib (Rubraca) after two or more previous lines of chemotherapy.

Note: CPT codes 81432 and 81433 require a Program Exception. The ordering physician must provide a supporting statement indicating why the requested therapy is medically necessary, and the alternative options have been or are likely to be ineffective, adversely affect patient compliance, or cause an adverse reaction.

3. Genetic Counseling
   Pre- and post-test genetic counseling is required to be performed by an independent (not employed by a genetic testing lab) genetic specialist/counselor prior to genetic testing for mutations. This service is necessary in order to inform persons being tested about the benefits and limitations of a specific genetic test for the specific patient. Genetic testing for mutation requires documentation of medical necessity from one of the following providers who has evaluated the patient and intends to see the patient after testing has been performed for counseling:
   - Board Eligible or Board Certified Genetic Counselor
   - Advanced Genetics Nurse
   - Genetic Clinical Nurse
   - Advanced Practice Nurse in Genetics
   - Board Eligible or Board Certified Clinical Geneticist
   - A physician with experience in cancer genetics
   - A physician specializing in the care for the indication(s) for genetic testing

4. When services are not medically necessary
    - For conditions other than those listed above because the scientific evidence has not been established.
    - Genetic testing in minors for BRCA1/BRCA2 mutations does not meet the definition of medical necessity. There is no change in management for minors as a result of knowledge of the presence or absence of a deleterious mutation.
    - Use of the CHEK2 is considered not medically necessary because the efficacy of this test in determining an individual's risk of cancer has not yet been proven.
    - Genetic screening in the general population is considered not medically necessary.
    - Direct-to-consumer saliva genetic testing kits for BRCA1/BRCA2 are considered not medically necessary.
    - Screening for cancer risk in individuals not identified in the covered services section are considered not medically necessary.
    - BRCA1/BRCA2 genetic testing is not considered medically necessary when used to confirm a direct-to-consumer genetic testing result without the individual meeting the indications above.
    - Large genomic rearrangement testing (CPT code 81213) used to identify individuals at risk for BRCA1/BRCA2 related cancers is not typically medically necessary (e.g., BART™). Therefore, requests for this service will require case-by-case physician review only when both sequencing and testing for common large rearrangements have been performed and are negative.

5. Place of Service
   The proper place of service for BRCA/BRCA2 genetic testing is outpatient.

6. Post-payment Audit Statement
   The medical record should include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Wholecare℠ at any time pursuant to the terms of your provider agreement.
7. Related Policies
    - MP-010-MD-PA Testing for Genetic Disease
    - MP-074-MD-PA Oncologic Genetic Testing Panels

Governing Bodies Approval

Genetic testing is regulated under the Clinical Laboratory Improvement Amendments (CLIA) Act of 1998.

Examples of Performing Laboratories
Myriad Genetic Laboratories (Salt Lake City, UT) offers the BRACAnalysis CDx®, which is an FDA-approved blood test used to identify patients with germline BRCA1/2 mutations who are eligible for certain targeted therapies. This test provides results for patients with metastatic pancreatic cancer, metastatic breast cancer, ovarian cancer, and metastatic prostate cancer.

Quest Diagnostics (Madison, NJ) offers BRCAvantage™ that includes sequencing of BRCA1/BRCA2 and a multiplex ligation-dependent probe amplification assay to detect both common and uncommon gene rearrangements.

LabCorp (Burlington, NC) offers the BRCAssure℠ suite of tests which includes: targeted BRCA1/BRCA2 analysis for known BRCA1 or BRCA2 mutations; a founder mutation panel for Ashkenazi Jewish patients (3 mutations); comprehensive BRCA1/BRCA2 analysis (full gene sequencing plus analysis of common and

uncommon large rearrangements); and deletion/duplication analysis of uncommon large rearrangements only (without sequencing) for use when comprehensive analysis is negative.

CMS

The Centers for Medicare and Medicaid Services (CMS) has no published National Coverage Determinations (NCD) for BRCA testing. CMS has published the following guidance:

- Local Coverage Determination (LCD) BRCA1 and BRCA2 Genetic Testing (L36715)
- Local Coverage Determination (LCD) Biomarkers Overview (L35062)
- Local Coverage Article (LCA) Billing and Coding: BRCA1 and BRCA2 Genetic Testing (A56542)

The Pennsylvania Department of Human Services Technology Assessment Group (TAG) workgroup meets quarterly to discuss issues revolving around new technologies and technologies or services that were previously considered to be a program exception. During this meeting, decisions are made as to whether or not certain technologies will be covered and how they will be covered. TAG's decisions are as follow:

- Option #1: Approved - Will be added to the Fee Schedule
- Option #2: Approved as Medically Effective - Will require Program Exception
- Option #3: Approved with (or denied due to) Limited/Minimal Evidence of Effectiveness - Will require Program Exception
- Option #4: Denied - Experimental/Investigational

As of August 2023, the TAG workgroup assigned hereditary breast cancer-related disorders analysis panels an Option # 3, specifically for CPT codes 81432 and 81433.

Program Exception

CPT codes 81432 and 81433 require a Program Exception. The ordering physician must provide a supporting statement indicating why the requested therapy is medically necessary, and the alternative options have been or are likely to be ineffective, adversely affect patient compliance, or cause an adverse reaction.

Summary of Literature

It has been estimated that between 5% and 10% of breast cancers are thought to be the direct result from defects in genes inherited from a parent. The majority of hereditary breast cancers are associated with inherited mutations in one of the breast-cancer-susceptibility genes, BRCA1 or BRCA2. Individuals that carry the BRCA1 and the BRCA2 mutations have an increased lifetime risk of about 80% for those who live to age 70. In the contralateral breast, the lifetime risk of cancer is about 40%, and for ovarian cancer, the lifetime risk is approximately 40% with the BRCA1 mutation and 20% with the BRCA2 mutation. The BRCA mutations can be transmitted via maternal and/or paternal lineage. However, not all who inherit the genetic mutation develop cancer (ECRI, 2015).

Hereditary breast and ovarian cancer syndrome is a familial cancer syndrome that is related to mutations in the BRCA genes located on chromosomes 17q21 (BRCA1) and 13q12.3 (BRCA2). Identification of patients with the genetic mutation can result in enhanced screening and surveillance which could lead to improved outcomes. The characteristics of BRCA1 and BRCA2 genes are different and are considered together since their similarities outweigh their differences. There are commercial tests available for BRCA1 and BRCA2 mutation assessment. There are four types of BRCA genetic testing and are described as: full sequence analysis of BRCA1 and BRCA2 genes, deletion/duplication, known familial mutation testing, and Ashkenazi Jewish founder mutation testing.

The American College of Obstetricians and Gynecologists' (ACOG) Committee on Genetics recommends that a hereditary cancer risk assessment should be used to identify patients and families who may be at risk of developing certain types of cancer. Assessments should be performed by an OB-GYN or other provider and should be updated regularly. The assessment should include personal and family history, including pathology, imaging reports, and evaluation of other medical risk factors for cancer. If the hereditary cancer assessment suggests an increased risk of hereditary cancer syndrome, the patient should be referred to a genetic cancer specialist or a health care provider with expertise in genetics. The specialist will gather the patient's family history information, risk assessment, education, and counseling, which may lead to genetic testing and tailored cancer screening or risk reduction measures, or both. ACOG also recommends counseling before and after genetic testing to discuss rationale for any genetic testing, disclose results, define other cancer risks, identify educational needs, and secure referrals if necessary for ongoing management (ACOG, 2019).

Prior to genetic testing, an expanded family medical history which includes first-, second-, and third-degree relatives is an essential and integral component to identify men and women who may be candidates for genetic counseling and for BRCA testing for specific risk interventions. Family medical history should include all types of cancers, age of cancer diagnosis, risk-reducing surgeries, carcinogen exposure, and documentation records of primary cancers.

A variety of tools have been developed to determine the probability of identifying BRCA1 and BRCA2 gene variants. These tools assist in identifying suitable candidates for testing. Examples of available Screening Tools include:

- Ontario Family History Assessment Tool (FHAT)
- Manchester Scoring System
- Referral Screening Tool (RST)
- Pedigree Assessment Tool (PAT)
- FHS-7

Available resources concur that widespread screening of the general population for BRCA gene mutations is not recommended, nor for screening individuals that are unaffected with no personal or family history of breast and/or ovarian cancer, or in individuals younger than 18 years of age. There is no established clinical utility for the use of genetic testing for BRCA mutations in individuals younger than 18 years of age. This is due to the fact that there is no change in the management of this particular age group with the knowledge of the presence or absence of this genetic mutation. There is also the risk of potential harm related to stigmatization and discrimination based on BRCA testing. The Society of Gynecologic Oncologists (Lancaster et al., 2014) have documented that the risk of developing breast or ovarian cancer in an individual younger than age 21 is very low, regardless of families with inherited cancer susceptibility as a result of hereditary breast and ovarian cancer syndrome.

Genetic Counseling

The current NCCN guidelines for genetic counseling services recommends that the decision to offer genetic testing involve three related stages: 1) pre-test counseling done prior to ordering testing; 2) consideration of the most appropriate tests to order; and 3) post-test counseling done when results are disclosed. It is recommended that a genetic counselor, clinical geneticist, oncologist, surgeon, oncology nurse, or other health professional with expertise and experience in cancer genetics be involved at each stage whenever possible. Testing should be considered in appropriate high-risk individuals where it is likely to impact the risk management and/or treatment of the tested individuals and/or their at-risk family members (NCCN, 2021).

The National Society of Genetic Counselors (NSGC) has recommended that genetic testing be performed utilizing the informed decision-making process (Berliner et al., 2013). Issues included in the process should include the following:

- Obtaining all pertinent personal medical and family history data
- Psychosocial assessment
- Discussion of cancer and mutation risk and how personalized risk estimates are derived
- Facilitation of the informed consent process through discussion of the risks, benefits, limitations, and likelihood of identifying a mutation with genetic susceptibility testing
- Result disclosure, when appropriate
- Discussion of medical management options
- Review of issues related to genetic discrimination

Cell cycle checkpoint kinase 2 (CHEK2) involves DNA repair and human cancer predisposition similar to BRCA1 and BRCA2. CHEK2 is normally activated in response to DNA double strand breaks, and it regulates the function of BRCA1 protein in DNA repair. CHEK2 also exerts critical roles in cell cycle control and apoptosis. The CHEK2 mutation is identified as 1100delC in exon 10 and has been associated with familial breast cancers. CHEK2 mutations account for approximately one-third of mutations identified in BRCA-negative patients, however, the CHEK2 mutations are rare, making accurate estimates of risk less precise.

A study (Tung et al., 2015) performed an assessment of the frequency of pathogenic mutations among patients with breast cancer that had been referred for BRCA1/2 testing. The study included two cohorts. Cohort 1 consisted of 1,781 patients referred for BRCA1/2 testing between November 2012 and April 2013. A total of 241 (13.5%) individuals were found to have a mutation in at least one of the 25 genes tested, 162 in BRCA1/2, and 76 in at least one of the other genes. Of the mutation-positive, BRCA1/2-negative patients, the most common mutation identified was in CHEK2 (n=29), accounting for approximately one-third of the additional mutations identified in BRCA-negative patients, and 12% of mutations overall. The second cohort consisted of 377 samples from patients who were referred to Beth Israel Deaconess Medical Center for genetic testing between 1998 and 2013 and had previously tested negative for BRCA1/2. Mutations were identified in additional genes in 14 women, of which CHEK2 was the most frequent (n=5), comprising approximately 33% of mutations identified in mutation-positive, BRCA-negative patients.

Despite studies showing that the CHEK2 mutation appears to account for one-third of mutations identified in BRCA1/2-negative patients, it is relatively rare. Accurate risk estimates, which have been studied in population- and family-based case controls, are subject to bias.

National Comprehensive Cancer Network guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian (v.2.2021) recommends annual mammogram for carriers of a pathogenic or likely pathogenic CHEK2 variant beginning at 40 years of age, with consideration of annual breast MRI. There are no data on the benefit of risk-reducing mastectomy for carriers of a pathogenic CHEK2 variant, but this procedure may be considered based on family history.

Additional studies are needed to determine if patients with a CHEK2 mutation have a risk that is similar to the risk with a high-penetration mutation. Clinical management recommendations for individuals with breast cancer and CHEK2 mutation are not standardized. The evidence is not sufficient to determine the effects of this technology on health outcomes.

Other studies have looked at the results of prostate cancer screening in men with BRCA mutations. The IMPACT study (2011) evaluated the results of screening in 205 men 40 to 69 years of age who were BRCA

mutation carriers and 95 control patients. At the baseline screen, biopsies were performed in 7.0% of patients with a prostate-specific antigen (PSA) level greater than 3.0, and prostate cancer was identified in 3.3%. This resulted in a positive predictive value of 47.6%, which is considerably higher than that estimated for normal-risk men. Also, the grade of tumor identified was intermediate in 67% of cancers and high in 11%. This differs from the expected distribution of cancer grade in average-risk men, with more than 60% expected to have low-grade cancer.

Members of the Jewish community who trace their roots to Central or Eastern Europe are known as Ashkenazi Jews. For centuries, this ethnic population was geographically isolated. The isolation experienced by this population means its members can trace their ancestry back to a small number of members known as "founders."

Approximately one in 40 individuals of Ashkenazi Jewish descent is a carrier for BRCA mutation, leaving these individuals at a higher risk of developing breast and ovarian cancer. This is compared to mutation frequency of one in 500 in the general population. These mutations are inherited in an autosomal dominant pattern, so males and females with such a mutation, whether or not they develop cancer, have a 50% chance of passing on the gene mutation to the next generation. Just as Ashkenazi Jewish women have an increased risk for the BRCA genetic mutation, males of this ethnic population have a higher risk of developing male breast cancer and prostate cancer. Men that inherit the BRCA1/2 gene have a 6% risk of developing breast cancer and are three to seven more times likely than average to develop prostate cancer.

In March 2018, the FDA approved 23andMe home DNA testing for three genetic mutations in BRCA1 and BRCA2 (FDA 2018). Prior to this date, the FDA had banned selling kits to consumers that allow for disease detection. The FDA is cautioning against the use of this testing without proper support. They state that the test does not provide information on a person's overall risk of developing any type of cancer, and the use of the test carries significant risks if the individual uses the results without consulting with a physician and/or genetic counselor. Direct-to-consumer testing is marketed as an aid to consumers to get a better understanding of their individual risk profile for developing breast cancer. The results are provided to the consumer without an individualized analysis of the consumer's family history and risk factors. In addition, the direct-to-consumer testing is limited in scope in that testing for only three specific mutations in the BRCA gene and not for the more than 1,000 other genes that are now associated with breast cancer, which can result in a false sense of security. Other drawbacks include: less than 1% of people have a BRCA1 or BRCA2 mutation which would result in inappropriate testing; false positive results/high error rate; lack of expert input from licensed genetic counselors or physicians; and the potential for the consumer to forgo regular screening for breast cancer with negative test results.

The current U.S. Preventive Services Task Force (USPSTF) recommendations related to risk assessment, genetic counseling, and genetic testing for BRCA-related cancers states that primary care clinicians should assess women with a personal or family history of breast, ovarian, tubal, or peritoneal cancer or who have an ancestry associated with breast cancer susceptibility 1 and 2 (BRCA1/2) gene mutations. This assessment can be accomplished with the use of an appropriate brief familial risk assessment tool. Women with a positive result on the risk assessment tool should receive genetic counseling and, if indicated after counseling, genetic testing (B recommendation). The USPSTF recommends against routine risk assessment, genetic counseling, or genetic testing for women whose personal or family history or ancestry is not associated with potentially harmful BRCA1/2 gene mutations (D recommendation) (USPSTF, 2019).

The American Society of Breast Surgeons (ASBrS) has issued recommendations for genetic testing that medical professionals can use to assess hereditary risk for breast cancer in their patients:

1. Breast surgeons, genetic counselors, and other medical professionals knowledgeable in genetic testing can provide patient education and counseling and make recommendations to their patients regarding genetic testing and arrange testing
2. Genetic testing should be made available to all patients with a personal history of breast cancer.
3. Patients who had genetic testing previously may benefit from updated testing.
4. Genetic testing should be made available to patients without a history of breast cancer who meet NCCN guidelines.
5. Variants of uncertain significance are DNA sequences that are NOT clinically actionable.

Hayes, Inc.

- Screening All Women with New Diagnoses of Breast Cancer for Hereditary Cancer Risk Variants
    - Clinical Utility Score: **3 Probable**
      For use of genetic testing to detect hereditary cancer high risk gene variants in women with new diagnoses of breast cancer, who are not preselected for other risk factors, to improve disease management. Evidence from 5 studies suggests that using genetic screening for BRCA1/2 (2 studies) and other high risk breast cancer genes (3 studies) for all women with breast cancer consistently identifies a small number of women carrying high risk variants who would not be recognized when clinical criteria are used to select candidates for genetic testing. While the overall quality of the body of evidence is low to moderate, these results for high risk variant carriers are similar across studies and are unlikely to change. BRCA1/2 variant carriers would likely benefit from evidence-supported recommendations for prevention, treatment, and/or surveillance. Carriers of other high risk genes are presumed to benefit similarly for most recommended interventions based on the strength of association with disease.

    - Clinical Utility Score: **2 Uncertain**
      For use of genetic testing to detect hereditary cancer moderate risk gene variants in women with new diagnoses of breast cancer, who are not preselected for other risk factors, to improve disease management. Evidence from 3 studies suggests that using genetic screening for all women with breast cancer identifies a large group of women carrying moderate risk gene variants who would not be recognized when clinical criteria are used to select candidates for genetic testing. However, due to limited low quality evidence and minimal inferential clinical utility, the clinical impact for this group of breast cancer patients is uncertain.

- Multisyndrome Panel Testing to Aid in Management of Patients Suspected of Having a Hereditary Cancer Syndrome
  Based on a review of included abstracts, there appears to be minimal support for the use of multisyndrome panel testing to aid in management of patients suspected of having a hereditary cancer syndrome. Based on a review of professional guidelines, there is weak support both for and against the use of multisyndrome panel testing to aid in management of patients suspected of having a hereditary cancer syndrome.

Coding Requirement

Procedure Codes

CPT Code	Description
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 (i.e., detection of large gene rearrangements)
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; duplication/deletion analysis (i.e., 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, SNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant
81432*	Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 10 genes, always including BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, and TP53
81433*	Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11

*Requires a Program Exception, see '*Governing Bodies Approval*' section above.

Diagnosis Codes

ICD-10 Code	Description
C25.0	Malignant neoplasm of head of pancreas
C25.1	Malignant neoplasm of body of pancreas
C25.2	Malignant neoplasm of tail of pancreas
C25.3	Malignant neoplasm of pancreatic duct
C25.4	Malignant neoplasm of endocrine pancreas
C25.7	Malignant neoplasm of other parts of pancreas

C25.8	Malignant neoplasm of overlapping sites of pancreas
C25.9	Malignant neoplasm of pancreas, unspecified
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
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left 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
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left 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
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left 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
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left 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
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.3	Malignant neoplasm of bilateral ovaries
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C61	Malignant neoplasm of prostate
D05.01	Lobular carcinoma in situ of right breast
D05.02	Lobular carcinoma in situ of left breast
D05.11	Intraductal carcinoma in situ of right breast

D05.12	Intraductal carcinoma in situ of left 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
D05.91	Unspecified type of carcinoma in situ of right breast
D05.92	Unspecified type of carcinoma in situ of left breast
Z17.0*	Estrogen receptor positive status [ER+]
Z17.1*	Estrogen receptor negative status [ER-]
Z85.07	Personal history of malignant neoplasm of pancreas
Z85.3	Personal history of malignant neoplasm of breast
Z85.43	Personal history of malignant neoplasm of ovary
Z85.46	Personal history of malignant neoplasm of prostate

*For diagnosis C50 series codes, report applicable diagnosis code Z17 code for patients 60 years of age or less, to identify estrogen-receptor status.

Reimbursement

Participating facilities will be reimbursed per their Highmark Wholecare℠ contract.

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