



Geisinger Health Plan Policies and Procedure Manual

Policy: MP097

Section: Medical Benefit Policy

Subject: Genetic Testing for BRCA1, BRCA2 and PALB2 for Breast or Ovarian Cancer

Applicable Lines of Business

Commercial	X	CHIP	X
Medicare	X	ACA	X
Medicaid	X		

I. Policy: Genetic Testing for BRCA1, BRCA2 and PALB2 for Breast or Ovarian Cancer

II. Purpose/Objective:

To provide a policy of coverage regarding Genetic Testing for BRCA1, BRCA2 and PALB2 for Breast or Ovarian Cancer

III. Responsibility:

- A. Medical Directors
- B. Medical Management

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions

Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

- a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
- b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
- c. in accordance with current standards of good medical treatment practiced by the general medical community.
- d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
- e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment

Medically Necessary — A service, item, procedure, or level of care that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

- Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
- Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an

- illness, condition, injury or disability.
- Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age

Triple negative breast cancer: a cancer negative for expression of estrogen and progesterone receptors, and for overexpression of HER2 receptors

Blood Relatives: NCCN defines blood relative as first- (parents, siblings and children), second- (grandparents, aunts, uncles, nieces and nephews, grandchildren and half-siblings), and third degree-relatives (great-grandparents, great-aunts, great uncles, great grandchildren and first cousins) on same side of family

DESCRIPTION:

Approximately 7-10% of all breast cancers, 20-25% of all ovarian cancers, 10-17% of prostate cancers, and 5-10% of pancreas cancers can be attributed to a dominantly inherited susceptibility.

Multi-gene panel testing is the most cost-effective and accurate approach to characterize familial cancer risk. BRCA1 and BRCA2 testing alone is no longer the clinical standard of care. Mutations in BRCA1 and BRCA2 have been identified in up to 50% of the inherited forms of hereditary breast and ovarian cancers, however, additional high- and moderate-risk genes have been discovered that may (1) explain familial cancer risk, (2) provide future cancer risk information, or (3) direct targeted therapeutic options.

Disease-specific panels may change from year to year based on available evidence and technological advancements. Germline multigene panel testing (MGPT) for moderate and high-penetrance cancer susceptibility genes should ultimately include ATM, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, TP53) and full duplication and deletion analysis (i.e., detection of large genomic rearrangements).

Up to 12% of genomic tumor profiling or sequencing tests will reveal a germline pathogenic variant. Some germline variants are highly predictive of response to specific cancer-directed therapies, such as poly-ADP ribose polymerase (PARP) inhibitors in patients with breast or ovarian cancer who have germline BRCA1/2 variants. Some reports suggest up to 50- 60% likelihood that when a BRCA sequencing variant is reported in any tumor type, it will be present in the germline.

Panel testing is considered medically necessary once per lifetime for persons who meet one or more National Comprehensive Cancer Network (NCCN) testing criteria for high-penetrance breast, ovarian, or pancreatic cancer susceptibility gene

INDICATIONS:

The Plan considers molecular susceptibility testing for hereditary breast and ovarian cancer (HBOC) via panel testing, medically necessary in **ANY** of the following indications:

NOTE: STAT testing of BRCA1, BRCA2, and PALB2 may be required in specific clinical scenarios for surgical or therapeutic decision making. Panel testing is considered medically necessary and will be approved for members undergoing this sequential testing.

Members with a personal history of an HBOC-related cancer, at any age, regardless of family history:

- Breast cancer (includes histologic subtypes: invasive lobular, invasive ductal, inflammatory, papillary, and DCIS. (LCIS excluded.)
- Ovarian, fallopian tube, primary peritoneal cancer
- Pancreatic adenocarcinoma
- Prostate adenocarcinoma

Members with any other type of malignancy where somatic (tumor-based) testing demonstrates a BRCA1 or BRCA2 variant within the tumor sample.

Members without a personal history of cancer, but with a family history of meeting ANY ONE of the following criteria:

1. A blood relative with a mutation in a known cancer susceptibility gene, OR.
2. A blood relative with a mutation in a hereditary cancer syndrome gene found on tumor testing who is unable to undergo germline testing, OR

- At least one blood relative with a history of breast cancer diagnosed at 50 years or younger
3. At least one blood relative diagnosed with triple negative breast cancer OR bilateral breast cancer OR two separate breast primaries, at any age
 4. At least one blood relative with any of the following cancers, diagnosed at any age:
 - a. male breast cancer
 - b. epithelial ovarian cancer, fallopian tube, or primary peritoneal cancer
 - c. pancreatic adenocarcinoma
 - d. prostate cancer (metastasis or high-grade diagnosis not required)
 - e. two close relatives with any combination of breast, ovary, pancreas, or prostate cancers
 5. At least 5% mutation probability using a validated risk tool (eg. Tyrer-Cuzick v8, BRCAPro, or CanRisk).
 6. A reported history of Ashkenazi Jewish ancestry with at least one first or second-degree relative with an HBOC cancer (eg. breast, ovarian, pancreas, or prostate cancer) at any age.
 7. The member has a personal or family history suggestive of a rare hereditary cancer syndrome that does not fall into the above criteria. Examples: Li-Fraumeni syndrome (TP53), Peutz-Jeghers syndrome (STK11), or PTEN Hamartoma Tumor syndrome (aka Cowden syndrome, PTEN).
 - a. Combination of any two of the following in a patient or close relative: macrocephaly, cerebellar tumors or adult Lhermitte-Duclose disease, autism spectrum disorder, intellectual disability, macular degeneration of the glans penis, one ganglioneuroma or at least two hamartomas of the GI tract, follicular thyroid cancer, breast cancer, endometrial cancer, or two or more trichilemmomas, oral papillomatosis, verrucous facial papules, or palmo-plantar keratoses.
 - b. Close relative with acute lymphoblastic leukemia (ALL), soft tissue or bone sarcoma, brain cancer, chorioid plexus carcinoma, rhabdomyosarcoma, or adrenocortical carcinoma.

Therapeutic companion testing:

BRCA/PALB2 testing using an FDA-approved companion diagnostic is considered medically necessary when the following criteria are met:

- The member has a diagnosis of cancer; and
- The specific therapeutic is FDA- approved and treatment eligibility is dependent upon BRCA1/2 or PALB2 testing

PALB2 mutation testing:

The Plan considers full sequence analysis molecular testing for PALB2 mutation to be medically necessary when **ALL** of the following are met:

- The member is 18 years of age or older
- Member has met criteria for BRCA1/2 analysis;
- Member tested negative for BRCA1/2

The Plan considers known familial mutation analysis for PALB2 mutation to be medically necessary when ALL of the following are met:

- The member is 18 years of age or older
- A mutation in PALB2 has been identified in 1st, 2nd, or 3rd degree relative(s)

Genetic testing is appropriate only when offered in a setting where a licensed or certified genetic counselor* or adequately trained health care professional is able to provide appropriate pre- and post-test genetic counseling, and medical necessity is supported by ALL of the following criteria:

1. The information is needed to adequately assess risk in the member; **and**
2. The information will be used in the immediate care plan of the member; **and**
3. Pedigree analysis establishes that the insured individual is in a high risk group for the disease; **or**
4. Clinical presentation of symptomology is evident and diagnosis cannot be established with conventional evaluation testing.

*A genetic counselor is considered by the Plan to be qualified if the following are met:

- M.S. or Ph.D. degree from a genetic counseling program approved/ certified by the American Board of Genetic Counseling or the American Board of Medical Genetics
- or**
- Board certified or board qualified/eligible in the orderly process of obtaining board certification by the American Board of Genetic Counseling or American Board of Medical Genetics
- and**

- Proof of current competence and demonstrated ability (minimum of two years recent and continual experience within the past three years).

EXCLUSIONS:

- Genetic testing for BRCA1 or BRCA2 mutations on those less than 18 years of age is considered **experimental, investigational, and unproven.**
- Testing of unaffected individuals with no significant family history of cancer or no known genetic mutations in the family is considered **not medically necessary**
- Genetic testing to assess the risk breast or prostate cancer in men without breast cancer is considered **experimental, investigational, and unproven.**
- The use of CHECK2 testing is considered **experimental, investigational, and unproven.**
- The use of direct-to-consumer testing for hereditary breast and/or ovarian cancer (e.g., 23 and Me) is **experimental, investigational, or unproven.** These tests have not been validated for clinical use and have a substantial error rate. They are not able to provide information that is appropriate for medical management and are therefore **NOT COVERED.**

PROCESS:

The Plan will utilize available published, peer reviewed medical literature, independent technology assessment program reports and/or review by the Geisinger Clinic Technology Assessment Committee to evaluate the following criteria when assessing the validity and efficacy of a specific genetic test:

- The analytical power of a test determined by its sensitivity and specificity is established.
- There is evidence of defined outcome measures that permits conclusions concerning the effect on health outcomes.
- The net health outcomes benefit of the test as compared to established alternatives is evaluated if applicable.
- The availability of test to membership is evaluated.
- The appropriate governmental and/or professional regulatory body approval is established.
- The test result will influence the treatment or alter the management of the insured individual medical care plan
- The test result has the capability to confirm a diagnosis when conventional medical evaluation is equivocal.

Note: A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in MP 15 - Experimental Investigational or Unproven Services or Treatment.

Medicaid Business Segment:

Any requests for services, that do not meet criteria set in the PARP, may be evaluated on a case by case basis.

CODING ASSOCIATED WITH: Genetic Testing for BRCA1 or BRCA2 for Breast or Ovarian Cancer

The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at www.cms.gov or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements.

- 81162 BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis
- 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 sequence analysis
- 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)
- 81211 BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants in BRCA1 (ie, exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-

- 20 del 26kb, exon 22 del 510bp, exon
- 81212 BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants
- 81213 BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; uncommon duplication/deletion variants
- 81214 BRCA1 (breast cancer 1) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants (ie, exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)
- 81215 BRCA1 (breast cancer 1) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant
- 81216 BRCA2 (breast cancer 2) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
- 81217 BRCA2 (breast cancer 2) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant
- 81307 PALB2 (PARTNER AND LOCALIZER OF BRCA2) (EG, BREAST AND PANCREATIC CANCER) GENE ANALYSIS; FULL GENE SEQUENCE
- 81308 PALB2 (PARTNER AND LOCALIZER OF BRCA2) (EG, BREAST AND PANCREATIC CANCER) GENE ANALYSIS; KNOWN FAMILIAL VARIANT
- 81432 Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 14 genes, including ATM, BRCA1, BRCA2, BRIP1, CDH1, MLH1, MSH2, MSH6, NBN, PALB2, PTEN, RAD51C, STK11, and TP53 **(Requires PE for Medicaid)**
- 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 **(Requires PE for Medicaid)**
- 81403 PALB2 known familial mutation analysis
- 81406 PALB2 sequencing
- 81308 PALB2 (Partner and Localizer of BRCA2)(eg, breast and pancreatic cancer) gene analysis, known family variant
- 0102U Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA, and array CGH, with mRNA analytics to resolve variants of unknown significance when indicated (17 genes [sequencing and deletion/duplication])
- 0103U Hereditary ovarian cancer (e.g., hereditary ovarian cancer, hereditary endometrial cancer), genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA, and array CGH, with mRNA analytics to resolve variants of unknown significance when indicated (24 genes [sequencing and deletion/duplication], EPCAM [deletion/duplication only])
- 0129U Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), genomic sequence analysis and deletion/duplication analysis panel (ATM, BRCA1, BRCA2, CDH1, CHEK2, PALB2, PTEN, and TP53)
- 0138U BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) mRNA sequence analysis
- 0172U Oncology (solid tumor as indicated by the label), somatic mutation analysis of BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) and analysis of homologous recombination deficiency pathways, DNA, formalin-fixed paraffin-embedded tissue, algorithm quantifying tumor genomic instability score

Current Procedural Terminology (CPT®) © American Medical Association: Chicago, IL

LINE OF BUSINESS:

Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD's and NCD's will supercede this policy. For PA Medicaid Business segment, this policy applies as written.

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This policy will be revised as necessary and reviewed no less than annually.

Devised: 9/25/98

Revised: 6/17/99; 6/27/03, 7/23/04; 6/20/05;6/06 (removed prior auth); 6/07 (revised criteria); 7/08; 7/09 (add'l exclusion); 12/09 (revised criteria); 12/10 (revised criteria); 6/11 (clarified criteria for males); 1/13 (added triple negative criteria); 7/13(removed BART testing indications) , 4/14(updated criteria); 4/16 (revised criteria); 3/17(revised criteria); 5/18 (added criteria related to known variants) 3/19 (revised pancreatic and prostate cancer criteria); 2/20 (add PALB2 criteria); 3/23 (revise criteria based on NCCN updates), 3/24 (revise Indications)

Reviewed: 4/15, 3/18, 3/21, 3/22

CMS UM Oversight Committee Approval: 12/23, 5/24

Geisinger Health Plan may refer collectively to health care coverage sponsors Geisinger Health Plan, Geisinger Quality Options, Inc., and Geisinger Indemnity Insurance Company, unless otherwise noted. Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Coverage for experimental or investigational treatments, services and procedures is specifically excluded under the member's certificate with Geisinger Health Plan. Unproven services outside of an approved clinical trial are also specifically excluded under the member's certificate with Geisinger Health Plan. This policy does not expand coverage to services or items specifically excluded from coverage in the member's certificate with Geisinger Health Plan. Additional information can be found in MP015 Experimental, Investigational or Unproven Services.

Prior authorization and/or pre-certification requirements for services or items may apply. Pre-certification lists may be found in the member's contract specific benefit document. Prior authorization requirements can be found at <https://www.geisinger.org/health-plan/providers/ghp-clinical-policies>

Please be advised that the use of the logos, service marks or names of Geisinger Health Plan, Geisinger Quality Options, Inc. and Geisinger Indemnity Insurance Company on a marketing, press releases or any communication piece regarding the contents of this medical policy is strictly prohibited without the prior written consent of Geisinger Health Plan. Additionally, the above medical policy does not confer any endorsement by Geisinger Health Plan, Geisinger Quality Options, Inc. and Geisinger Indemnity Insurance Company regarding the medical service, medical device or medical lab test described under this medical policy.