Geisinger

# Geisinger Health Plan Policies and Procedure Manual

**Policy: MP328**

**Section: Medical Benefit Policy**

**Subject: Genetic Susceptibility Cancer Panels (Multi-Gene Panel Testing)**

**Applicable line of business:**

| | | | |
|---|---|---|---|
| **Commercial** | **x** | **Medicaid** | **x** |
| **Medicare** | **x** | **ACA** | **x** |
| **CHIP** | **x** | | |

**I. Policy:** Genetic Susceptibility Cancer Panels (Multi-Gene Panel Testing)

**II. Purpose/Objective:**

To provide a policy of coverage regarding Genetic Susceptibility Cancer Panels (Multi-Gene Panel Testing)

**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.

Commercial

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.

Medicare

Geisinger Gold Medicare Advantage HMO, PPO, and HMO D-SNP plans are offered by Geisinger Health Plan/Geisinger Indemnity Insurance Company, health plans with a Medicare contract. Continued enrollment in Geisinger Gold depends on contract renewal. Geisinger Health Plan/Geisinger Indemnity Insurance Company are part of Geisinger, an integrated health care delivery and coverage organization.

CHIP

Geisinger Health Plan Kids (GHP Kids) is a Children's Health Insurance Program (CHIP) offered by Geisinger Health Plan in conjunction with the Pennsylvania Department of Human Services (DHS). Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Medicaid

Geisinger Health Plan Family (GHP Family) is a Medical Assistance (Medicaid) insurance program offered by Geisinger Health Plan in conjunction with the Pennsylvania Department of Human Services (DHS). Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization

**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

**DESCRIPTION:**
Hereditary cancer syndromes,also called family cancer syndrome and inherited cancer syndromes, are a group of disorders in which the presence of one or a combination of gene variants have been shown to increase the risk for the development of specific cancers. In a hereditary cancer syndrome, certain patterns of cancer may be seen within families. These patterns include having several close family members (such as a mother, daughter, and sister) with the same type of cancer, developing cancer at an early age, or having two or more types of cancer develop in the same person.

While the majority of cancer is not hereditary, 5-10% of all malignancies are estimated to be related to an inherited risk factor. Testing for this group of syndromes via multi-gene panel has demonstrated clinical utility and can lead to meaningful changes to a member's medical management through prevention, early detection, specialized, or more frequent cancer screening tests.

**INDICATIONS: <u>REQUIRES PRIOR AUTHORIZATION BY A PLAN MEDICAL DIRECTOR OR DESIGNEE</u>**

For members presenting with a personal or family history of cancer suggestive of hereditary breast and ovarian cancer syndrome please refer to **MP097 Genetic Testing for BRCA1 or BRCA2 for Breast or Ovarian Cancer**

- HBOC related cancers include: breast, ovary, pancreas, and prostate

For members presenting with a personal or family history of cancer suggestive of Lynch syndrome (LS), Familial Adenomatous Polyposis (FAP), MUTYH-associated polyposis (MAP), and rare polyposis syndrome such as Peutz-Jeghers or Juvenile Polyposis please refer to **MP098 Genetic Testing Related to Colorectal Cancer.**

- LS-related cancers include: brain, colorectal, endometrial, gastric, ovarian, pancreatic, renal, small intestine, prostate, or ureter cancers, sebaceous adenomas, and sebaceous carcinomas.
- FAP, MAP, and rare polyposis syndromes are described in the above policy.

Genetic evaluation using a multi-gene cancer panel is considered medically necessary when the following criteria are met:

*1.* The member has a personal **or** family history where current NCCN criteria for evaluation of a well-described inherited cancer syndrome have been satisfied.
*Please refer to the following NCCN guidelines:*
   a. Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic and Prostate
   b. Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric
   c. Acute Myeloid Leukemia
   d. Biliary Tract Cancers
   e. Central Nervous System Cancers
   f. Kidney Cancer
   g. Thyroid Carcinoma
   h. Melanoma: Cutaneous, Melanoma: Uveal
   i. Myelodysplastic Neoplasms

2. A personal or family history that is consistent with Hereditary Breast & Ovarian Cancer Syndrome (HBOC) *or* Lynch syndrome (LS), **AND**
   a) prior testing was limited (e.g. BRCA1 and BRCA2 sequencing only), or included high-penetrance genes only (e.g. *BRCA1, BRCA2, MLH1, MSH2, MSH6, PMS2, EPCAM, PTEN, STK11, TP53,*) and the result was negative or indeterminate; **AND**
   b) update testing is available with genes that have medical management recommendations per NCCN.

**OR**

3. A personal history of *any* solid tumor type, where:

a) Testing will impact the member's medical management, **AND**
b) The personal and family history is suggestive of more than one hereditary cancer syndromes; **AND**
c) more than one gene may be associated with the inherited cancer syndrome being evaluated
   i. (eg.PTEN-Hamartoma Tumor Syndrome, Lynch syndrome, Hereditary Leukemia and Hematologic Malignancies Syndromes, Li-Fraumeni Syndrome, DICER1 Tumor Predisposition Syndrome, BAP1 Tumor Predisposition Syndrome, Hereditary, Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC) syndrome, Von Hippel-Lindau, Multiple endocrine neoplasias, etc.);

**OR**

4. If a member's history does not meet the above guidelines (or NCCN guidelines) for evaluation, **ALL of the following** criteria are met:
   - A personal history of two or more different primary solid tumors at any age, **or**
   - A first degree relative with two or more different primary solid tumors at any age, or
   - A personal history of a solid tumor with at least one somatic finding suggestive of potential germline etiology due to variant type, location, concordance with tumor type, or allele frequence, **or**
   - At least three people on the same side of the family with the same type of malignancy within three generations.
     - (e.g., solid tumor or hematologic malignancies of the same origin (e.g. myeloid vs lymphoid).

**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 or 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:**
Multi-gene hereditary cancer panels (including, but not limited to MI CancerSeek, etc) are unproven and not medically necessary for general population screening, and all other indications not meeting the criteria outlined in this policy.

## Medicare Business Segment:

Germline testing for inherited cancer syndromes are covered per MolDx L38972

## 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

**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.**

**CODING ASSOCIATED WITH: Genetic Susceptibility Cancer Panel**

***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.***

0101U Hereditary colon cancer disorders (e.g., Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis), 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 (15 genes [sequencing and deletion/duplication], EPCAM and GREM1 [deletion/duplication only]) [hereditary®, Ambry Genetics®, Ambry Genetics]

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]) [BreastNext®, Ambry Genetics®, Ambry Genetics]

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]) [OvaNext®, Ambry Genetics®, Ambry Genetics]

0129U hereditary breast cancer related disorders (eg, 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)

0130U Hereditary colon cancer disorders (e.g., Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis), targeted mRNA sequence analysis panel (APC, CDH1, CHEK2, MLH1, MSH2, MSH6, MUTYH, PMS2, PTEN, and TP53)

0131U Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), targeted mRNA sequence analysis panel (13 genes)

0132U Hereditary ovarian cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), targeted mRNA sequence analysis panel (17 genes)

0133U Hereditary prostate cancer-related disorders, targeted mRNA sequence analysis panel (11 genes)

0134U Hereditary pan cancer (e.g., hereditary breast and ovarian cancer, hereditary endometrial cancer, hereditary colorectal cancer), targeted mRNA sequence analysis panel (18 genes)

0135U Hereditary gynecological cancer (e.g., hereditary breast and ovarian cancer, hereditary endometrial cancer, hereditary colorectal cancer), targeted mRNA sequence analysis panel (12 genes)

0160U MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis

0161U PMS2 (PMS1 homolog 2, mismatch repair system component) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis

0162U Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2)

0171U Targeted genomic sequence analysis panel, acute myeloid leukemia, myelodysplastic syndrome, and myeloproliferative neoplasms, DNA analysis, 23 genes, interrogation for sequence variants, rearrangements and minimal residual disease, reported as presence/absence MyMRD® NGS Panel RNAinsight™ for GYNPlus®, Ambry Genetics

0211U Oncology (pan-tumor), DNA and RNA by next-generation sequencing, utilizing formalin-fixed paraffin-embedded tissue, interpretative report for single nucleotide variants, copy number alterations, tumor mutational burden, and microsatellite instability, with therapy association (CARIS MI CancerSeek)

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 10 genes, always including BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, and 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

81435 Hereditary colon cancer disorders (e.g., Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include sequencing of at least 10 genes, including APC, BMPR1A, CDH1, MLH1, MSH2, MSH6, MUTYH, PTEN, SMAD4, and STK11

81436 Hereditary colon cancer disorders (e.g., Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); duplication/deletion analysis panel, must include analysis of at least 5 genes, including MLH1, MSH2, EPCAM, SMAD4, and STK11

81437 Hereditary neuroendocrine tumor disorders (e.g., medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); genomic sequence analysis panel, must include sequencing of at least 6 genes, including MAX, SDHB, SDHC, SDHD, TMEM127, and VHL

81438 Hereditary neuroendocrine tumor disorders (e.g., medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); duplication/deletion analysis panel, must include analyses for SDHB, SDHC, SDHD, and VHL



**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.**

**REFERENCES:**
Crawford B, Adams SB, Sittler T, et al. Multi-gene panel testing for hereditary cancer predisposition in unsolved high-risk breast and ovarian cancer patients. Breast Cancer Research and Treatment. 2017;163(2):383-390.

Lincoln SE, Kobayashi Y, Anderson MJ, et al. A Systematic Comparison of Traditional and Multigene Panel Testing for Hereditary Breast and Ovarian Cancer Genes in More Than 1000 Patients. J Mol Diagn. 2015 Sep;17(5):533-44.

Gardner SA, Weymouth KS, Kelly WS, et al. Evaluation of a 27-gene inherited cancer panel across 630 consecutive patients referred for testing in a clinical diagnostic laboratory. Hereditary Cancer in Clinical Practice. 2018;16:1. doi:10.1186/s13053-017-0083-8.

Babic B, Patel D, Aufforth R, et al. Pediatric patients with pheochromocytoma and paraganglioma should have routine preoperative genetic testing for common susceptibility genes in addition to imaging to detect extra-adrenal and metastatic tumors. Surgery. 2017 Jan;161(1):220-227.

Parsons DW, Roy A, Yang Y, et al. Diagnostic Yield of Clinical Tumor and Germline Whole-Exome Sequencing for Children With Solid Tumors. JAMA Oncol. 2016;2(5):616–624.

Zhang, J. et al. Germline Mutations in Predisposition Genes in Pediatric Cancer. N Engl J Med. 2015 Dec 10;373(24):2336-2346.

Achatz MI, Porter CC, Brugières L, et al. Cancer Screening Recommendations and Clinical Management of Inherited Gastrointestinal Cancer Syndromes in Childhood. Clin Cancer Res. 2017 Jul 1;23(13):e107-e114.

Nguyen KA, Syed JS, Espenschied CR, et al. Advances in the diagnosis of hereditary kidney cancer: Initial results of a multigene panel test. Cancer. 2017 Nov 15;123(22):4363-4371.

Pilié PG, Johnson AM, Hanson KL, et al. Germline genetic variants in men with prostate cancer and one or more additional cancers. Cancer. 2017 Oct 15;123(20):3925-3932.

Druker H, Zelley K, McGee RB, et al. Genetic counselor recommendations for cancer predisposition evaluation and surveillance in the pediatric oncology patient. Clin Cancer Res 2017;23.

Rosenthal ET, Bernhisel R, Brown K, et al. Clinical testing with a panel of 25 genes associated with increased cancer risk results in a significant increase in clinically significant findings across a broad range of cancer histories. Cancer Genet. 2017 Dec;218-219:58-68.

Hermel DJ, McKinnon WC, Wood ME, et al. Multi-gene panel testing for hereditary cancer susceptibility in a rural Familial Cancer Program. Fam Cancer. 2017 Jan;16(1):159-166.

Cohen JD, Lu L, et al. Detection and localization of surgically resectable cancers with a multi-analyte blood test. Science 2018:359(6378):926-993

Du S, Zhao Y, et al. Applying Serum Proteins and MicroRNA as Novel Biomarkers for Early-Stage Cervical Cancer Detection. Sci Rep 2020; 10, 9033

Marcuello M, Vymetalkova V, et al. Circulating biomarkers for early detection and clinical management of colorectal cancer. Molecular Aspects of Medicine 2019;(69):107-122

Corredor J, Woodson AH, Gutierrez Barrera A, et al. Multigene panel testing results in patients with multiple breast cancer primaries. Breast J. 2020 Jul;26(7):1337-1342.

LaDuca H, Polley EC, Yussuf A, et al. A clinical guide to hereditary cancer panel testing: evaluation of gene-specific cancer associations and sensitivity of genetic testing criteria in a cohort of 165,000 high-risk patients. Genet Med. 2020 Feb;22(2):407-415

Uson PLS Jr, Riegert-Johnson D, Boardman L, et al. Germline cancer susceptibility gene testing in in selected patients with colorectal adenocarcinoma: A multicenter prospective study. Clin Gastroenterol Hepatol. 2021 Apr 20:S1542-3565(21)00447-X.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology Genetic/familial high-risk assessment: Breast, Ovarian, Pancreatic and Prostate. v2.2025

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology on genetic/familial high-risk assessment: Colorectal Cancer v2.2023

Klein AP, Hruban RH, Brune KA, et al. Familial pancreatic cancer. Cancer J. 2001 Jul-Aug;7(4):266-73.

Hu C, et al. A Population-Based Study of Genes Previously Implicated in Breast Cancer. N Engl J Med. 2021 Feb 4;384(5):440-451.

Uson PLS Jr, Kunze KL, Golafshar MA, et al. Germline Cancer Testing in Unselected Patients with Gastric and Esophageal Cancers: A Multi-center Prospective Study. Dig Dis Sci. 2022;67(11):5107-5115.
Maccaroni E, Giampieri R, Lenci E, et al. BRCA mutations and gastrointestinal cancers: When to expect the unexpected?. World J Clin Oncol. 2021;12(7):565-580.

Esplin ED, Nielsen SM, Bristow SL, et al. Universal Germline Genetic Testing for Hereditary Cancer Syndromes in Patients With Solid Tumor Cancer. JCO Precis Oncol. 2022 Sep;6:e2100516. PMID: 36108258.

Samadder NJ, Riegert-Johnson D, Boardman L, et al. Comparison of Universal Genetic Testing vs Guideline-Directed Targeted Testing for Patients With Hereditary Cancer Syndrome. JAMA Oncol. 2021;7(2):230–237.

Hoffman TL, Kershberg H, Goff J, et al. Next-generation universal hereditary cancer screening: implementation of an automated hereditary cancer screening program for patients with advanced cancer undergoing tumor sequencing in a large HMO. Fam Cancer. 2023 Apr;22(2):225-235. PMID: 36261688.

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

**Devised:** 8/19

**Revised:** 8/20, 1/21 (add PA and genetic counselor requirement); 1/23 (update criteria and Medicare coverage) 2/24 (revise criteria); 2/25 (revise criteria)

**Reviewed:** 1/22

**CMS UM Oversight Committee Approval:** 12/23, 5/24, 4/25

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.