

Genetic Testing for Inherited Susceptibility to Colorectal, Endometrial and Gastric Cancer

MEDICAL POLICY NUMBER: 115

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INSTRUCTIONS FOR USE: Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Company reserves the right to determine the application of medical policies and make revisions to medical policies at any time. The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement. Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

SCOPE: Providence Health Plan, Providence Health Assurance, and Providence Plan Partners as applicable (referred to individually as “Company” and collectively as “Companies”).

PLAN PRODUCT AND BENEFIT APPLICATION

☒ Commercial

☐ Medicaid/OHP*

☐ Medicare**

*Medicaid/OHP Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

Notice to Medicaid Policy Readers: For comprehensive rules and guidelines pertaining to this policy, readers are advised to consult the Oregon Health Authority. It is essential to ensure full understanding and compliance with the state's regulations and directives. Please refer to OHA's prioritized list for the following coverage guidelines:

Guideline Notes: D25, 106

**Medicare Members

This Company policy may be applied to Medicare Plan members only when directed by a separate Medicare policy. Note that investigational services are considered “**not medically necessary**” for Medicare members.

COVERAGE CRITERIA

Notes:

- Genetic tests addressed in this policy only include the following well-defined inherited cancer syndromes:
 - Hereditary Non-Polyposis Colorectal Cancer (HNPCC, also known as Lynch Syndrome);
 - Polyposis Syndromes
 - Adenomatous Polyposis (e.g. Familial Adenomatous Polyposis (FAP); Attenuated FAP (AFAP); MUTYH-associated Polyposis (MAP))
 - Colonic Adenomatous Polyposis of Unknown Etiology
 - Peutz-Jeghers Syndrome
 - Juvenile Polyposis Syndrome
 - Serrated Polyposis Syndrome
- Testing for additional, lower penetrant syndromes or genes are not addressed by this policy and may be subject to review by the policy, Genetic and Molecular Testing.
- This policy does not address immunohistochemistry (IHC) or microsatellite instability (MSI) tests, which may be considered medically necessary and standard of care in patients with colon or endometrial cancer.
- Both maternal and paternal family histories must be considered separately when identifying

families with an increased risk of colorectal cancer.

- When possible, family members with cancer associated with inherited colorectal, endometrial or gastric cancer should be tested first, prior to testing unaffected members. Testing an unaffected member has significant limitations on interpreting test results. Pre-test counseling notes should document the reason why an affected family member cannot be tested prior to testing an unaffected member.

Medically Necessary

I. Genetic testing for a single gene or any combination of the following genes - *APC, AXIN2, BMPR1A, BRCA1, BRCA2, CDH1, EPCAM, GREM1, MLH1, MLH3, MSH2, MSH3, MSH6, MUTYH, NTHL1, POLD1, POLE, PMS2, PTEN, RPS20, SMAD4, STK11 (LKB1), TP53* - may be considered **medically necessary** for the evaluation of high-risk colorectal, endometrial or gastric cancer syndromes when criteria in the medical policy "[Genetic Counseling \(Company\)](#)" have been met, as well as **any one** of the following criteria (A.-D.):

- A. Documentation indicates a first-degree relative* has a known pathogenic mutation in one of the genes listed above and testing is based on the identified mutation; **or**
- B. Patient has a personal history of **any one** of the following (1.-8.):
 1. At least 10 adenomas; **or**
 2. At least 2 hamartomatous polyps; **or**
 3. At least 5 serrated polyps/lesions proximal to the rectum; **or**
 4. Colorectal, endometrial or gastric cancer diagnosed <50 years; **or**
 5. Colorectal, endometrial or gastric cancer and another Lynch Syndrome (LS)-related cancer** (can be synchronous or metachronous); **or**
 6. Colorectal, endometrial or gastric cancer and one or more first- or second-degree relative(s) with an LS-related cancer diagnosed <50 years; **or**
 7. Colorectal, endometrial or gastric cancer and two or more first- or second-degree relatives with an LS-related cancer, regardless of age; **or**
 8. Colorectal, endometrial or gastric cancer at any age with tumor showing evidence of mismatch repair deficiency, either by microsatellite instability (MSI) or loss of MMR protein expression; **or**
- C. Patient has a family history of **any one** of the following (1.-5.):
 1. One or more relative(s) with any of the following (a.-c.):
 - a. At least 10 adenomas; **or**
 - b. At least 2 hamartomatous polyps; **or**
 - c. At least 5 serrated polyps/lesions proximal to the rectum; **or**
 2. One or more first-degree relative(s)* with colorectal, endometrial or gastric cancer diagnosed <50 years; **or**
 3. One or more first-degree relative(s)* with colorectal, endometrial or gastric cancer and another LS-related cancer**; **or**
 4. Two or more first- or second-degree relative(s)* with LS-related cancers, including one or more diagnosed <50 years; **or**
 5. Three or more first- or second-degree relative(s)* with LS-related cancers, regardless of age; **or**
- D. Either of the following are met (1.-2.):

1. An individual with a LS-related cancer or an unaffected individual with a $\geq 5\%$ risk for having an MMR gene mutation based on one of the following prediction models: MMRpro, PREMM5, or MMRpredict. *** (See [Policy Guidelines](#) for links to tools.); **or**
 2. An individual without a personal history of colorectal or endometrial cancer with a $\geq 2.5\%$ for having an MMR gene mutation based on one of the following prediction models: MMRpro, PREMM5, or MMRpredict. *** (See Policy Guidelines for links to tools).
 - E. Individuals with colorectal or endometrial cancer aged ≥ 50 years who do not meet other testing criteria and have no known mismatch repair deficiency in tumor testing; **or**
 - F. A pathogenic or likely pathogenic variant is identified on tumor genomic testing that has clinical implications.
- II. Genetic testing for *BRAF* V600E or *MLH1* promoter methylation testing is considered **medically necessary** to rule out a diagnosis of Lynch syndrome in patients with a loss of DNA protein expression of *MLH1* on IHC tumor testing or an MSI-H test result.

Not Medically Necessary

- III. Genetic testing for a single gene or any combination of the following genes - *APC*, *AXIN2*, *BMPR1A*, *BRCA1*, *BRCA2*, *CDH1*, *EPCAM*, *GREM1*, *MLH1*, *MLH3*, *MSH2*, *MSH3*, *MSH6*, *MUTYH*, *NTHL1*, *POLD1*, *POLE*, *PMS2*, *PTEN*, *RPS20*, *SMAD4*, *STK11* (*LKB1*), *TP53* - is considered **not medically necessary** when criteria I., II., or III., are not met, including but not limited to the following:
- A. Cancer risk assessment in the general population.
 - B. When the genetic variant reported in a family member is a variant of unknown significance (VUS) (also known as unclassified variant, variant of uncertain significance).
 - C. When testing in criteria II. above results in a positive test for the *BRAF* V600E mutation and/or *MLH1* promoter hypermethylation.
- IV. Repeat testing of the same germline genetic content, for the same genetic information, is considered **not medically necessary**.
- V. Genetic panel testing which includes genes other than *APC*, *AXIN2*, *BMPR1A*, *BRCA1*, *BRCA2*, *CDH1*, *EPCAM*, *GREM1*, *MLH1*, *MLH3*, *MSH2*, *MSH3*, *MSH6*, *MUTYH*, *NTHL1*, *POLD1*, *POLE*, *PMS2*, *PTEN*, *RPS20*, *SMAD4*, *STK11* (*LKB1*), *TP53* is considered **not medically necessary**, unless requested as part of a multi-gene panel that meets criteria per the Medical Policy, "[Next Generation Sequencing for Cancer \(Company\)](#)". Examples of not medically necessary panels include, but are not limited to, the following:
- A. +RNAinsight for ColoNext test (Ambry Genetics)
 - B. Myriad myRisk® panel test
 - C. Ambry ColoNext® panel test
 - D. GeneDx Colorectal Cancer Panel test

Link to [Evidence Summary](#)

POLICY CROSS REFERENCES

- [Genetic Counseling](#), MP316
- [Next Generation Sequencing for Cancer \(Company\)](#), MP352

The full Company portfolio of current Medical Policies is available online and can be [accessed here](#).

POLICY GUIDELINES

Genetic Panel Testing

The clinical utility of testing has been established for all six of the genes listed above in the policy criteria. Therefore, when medical necessity criteria are met, genetic panel testing for Lynch and well-defined polyposis syndromes may include one or more of **any combination** of the genes listed in this section above. For example, genetic panels, such as the Myriad's COLARIS® panel test, which includes only the genes, or a subset of the genes, addressed in the medical necessity criteria (II.) above, may be considered medically necessary when criteria are met.

DOCUMENTATION REQUIREMENTS

In order to determine the clinical utility of a genetic test, the following documentation must be provided at the time of the request. Failure to submit complete documentation may affect the outcome of the review.

- Specific gene, trade or proprietary name of the test, or if a custom built test, include every gene(s) and/or component of the test
- Name of laboratory where the testing is being conducted or was conducted
- Clinical notes to include the following:
 - Documentation of genetic counseling as required in the Genetic Counseling policy which includes how test results will impact clinical decision making
 - If relevant, pre-test counseling notes should document the reason why an affected family member cannot be tested prior to testing an unaffected member
 - Reason (indication) for performing test, including the suspected condition
 - Existing signs and/or symptoms related to reason for current test request
 - Prior test/laboratory results related to reason for current test request
 - Family history, if applicable
 - How results from current test request will impact clinical decision making
 - All relevant CPT/HCPCS codes billed

DEFINITIONS

*Close Blood Relatives

The National Comprehensive Cancer Network (NCCN) defines close 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.

****Lynch Syndrome-Related Cancers**

Lynch syndrome-related cancers include: colorectal, endometrial, gastric, ovarian, pancreatic, ureter or renal pelvis, brain (usually glioblastoma), small intestinal cancers, sebaceous adenomas and carcinomas, and keratoacanthomas as seen in Muir–Torre syndrome.

*****MMR Gene Mutation Risk Prediction Models**

- MMRpro: <http://www4.utsouthwestern.edu/breasthealth/cagene/>
- PREMM5: <http://premm.dfc.harvard.edu/>
- MMRpredict: <http://hnpccpredict.hgu.mrc.ac.uk/>

BACKGROUND

Clinical Utility of Genetic Testing

Establishing the clinical utility of any test is a key component in determining its ultimate usefulness. Clinical utility may be established when published evidence demonstrates test results can be used to:

1. Guide treatment, management, or preventive decisions; **and**
2. Those decisions lead to improved primary health outcomes.

Genetic Panel Testing

Numerous genetic panels are available which test for various combinations of genes associated with hereditary colorectal cancers. Some well-designed genetic panel tests include only the genes that have demonstrated clinical utility and high penetrance for Lynch and well-defined polyposis syndromes. However, other panel tests include a broader range of genes for these and other related cancer syndromes for which penetrance levels are intermediate and low and the clinical utility of testing is not yet established. It is not recommended that patients undergo testing for gene mutations with unknown clinical significance as test results may lead to unnecessary interventions and additional testing which is not supported by current evidence or practice standards.

CLINICAL EVIDENCE AND LITERATURE REVIEW

CLINICAL PRACTICE GUIDELINES

The medical necessity criteria within this policy are primarily supported and guided by the National Comprehensive Cancer Network (NCCN) Genetic/Familial High-Risk Assessment: Colorectal, Endometrial and Gastric Cancer.

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines (v.1.2025) addressing genetic/familial high-risk assessment for colorectal, endometrial and gastric cancer recommend genetic testing in the following scenarios:¹

- Individuals with any blood relative with a P/LP variant in a cancer susceptibility gene.
- Individuals meeting criteria below but who tested negative with previous limited testing (eg, single gene or absent deletion duplication analysis) and are interested in pursuing multigene testing.
- A P/LP variant identified on tumor genomic testing that has clinical implications if also identified in the germline.
- Individual who meets Lynch syndrome (LS) testing criteria based on:
 - Family history of an LS-associated pathogenic variant.
 - Personal or family history of LS-related cancer.
 - Personal history of a mismatch repair deficient (dMMR) tumor.
- Individuals who meet adenomatous polyposis testing criteria.
- Individuals who meet clinical criteria for:
 - Juvenile Polyposis Syndrome (JPS).
 - Peutz-Jeghers Syndrome (PJS).
- Individual who meets hereditary diffuse gastric cancer (HDGC) testing criteria.
- Individual who meets testing criteria for Li-Fraumeni syndrome (LFS) or Cowden syndrome (CS)/PTEN hamartoma tumor syndrome (PHTS) testing criteria.

Authors also wrote that genetic evaluation is clinically indicated in patients who meet clinical criteria for serrated polyposis syndrome or to aid in surgical decision-making and medical management (e.g. planning extent of colon resection and type and timing of risk-reducing surgeries), as well as patients with personal or family history of any of the following:

- Colorectal cancer
- Endometrial cancer
- Gastric cancer
- At least 10 adenomatous polyps
- At least 2 hamartomatous polyps
- At least 5 serrated polyps/lesions proximal to the rectum.

In addition, NCCN states that there are many clinical scenarios in which multi-gene testing may be considered, with some examples including:

- When multiple genes could potentially explain a hereditary cancer syndrome.
- In cases where single gene testing returns negative or inconclusive results, yet family history strongly indicates an inherited cancer risk.
- For families with complex patterns of cancer types that might involve mutations in different genes.
- To identify potential risks from moderate-penetrance genes, even though specific management guidelines might be limited.
- As a cost-effective and efficient method by examining multiple genes simultaneously.
- When conducted under the guidance of genetic counselors or clinicians with expertise in hereditary syndromes.

- Though it increases the likelihood of identifying Variants of Uncertain Significance (VUS), which require careful analysis.
- When considering the clinical actionability of findings, particularly concerning moderate-risk genes, within multigene panels.

The NCCN guideline stated that multi-gene testing should be done in the context of pre- and post-test genetic counseling by certified genetic counselors or clinicians with extensive training in cancer genetics.

Medically Necessary Testing

There is sufficient evidence to support that genetic testing for the following genes – APC, AXIN2, BMPR1A, BRCA1, BRCA2, CDH1, EPCAM, GREM1, MLH1, MLH3, MSH2, MSH3, MSH6, MUTYH, NTHL1, POLD1, POLE, PMS2, PTEN, RPS20, SMAD4, STK11 (LKB1), and TP53 – may improve health outcomes in individuals at risk for hereditary colorectal, endometrial, or gastric cancer syndromes, including Lynch syndrome and various polyposis syndromes (e.g., FAP, AFAP, MAP, JPS, PJS, SPS). These genes are supported by current NCCN clinical practice guidelines for individuals with a personal or family history suggestive of inherited cancer risk. Therefore, genetic testing for these genes is considered medically necessary when policy criteria are met.

Additionally, there is strong evidence that testing for the BRAF V600E mutation or MLH1 promoter methylation can help distinguish sporadic colorectal or endometrial cancers from Lynch syndrome. This testing can guide appropriate use of germline testing and inform clinical management. NCCN guidelines recommend these tests in patients with tumors showing loss of MLH1 protein expression or MSI-H status. Therefore, BRAF V600E or MLH1 promoter methylation testing is considered medically necessary when policy criteria are met.

Not Medically Necessary Testing

Genetic testing for Lynch syndrome and polyposis syndromes is not considered medically necessary when individuals do not meet specific clinical or family history criteria. Testing in low-risk populations may lead to unnecessary interventions, over-surveillance, and uncertain clinical management, particularly when variants of uncertain significance (VUS) are identified. Current NCCN guidelines do not support testing in these scenarios.

Furthermore, multigene panel testing that includes genes outside of the NCCN-recommended list (i.e., genes other than APC, AXIN2, BMPR1A, BRCA1, BRCA2, CDH1, EPCAM, GREM1, MLH1, MLH3, MSH2, MSH3, MSH6, MUTYH, NTHL1, POLD1, POLE, PMS2, PTEN, RPS20, SMAD4, STK11, and TP53) has not been shown to improve health outcomes and is not supported by current clinical guidelines. Therefore, such testing is considered not medically necessary.

HEALTH EQUITY CONSIDERATIONS

The Centers for Disease Control and Prevention (CDC) defines health equity as the state in which everyone has a fair and just opportunity to attain their highest level of health. Achieving health equity requires addressing health disparities and social determinants of health. A health disparity is the occurrence of diseases at greater levels among certain population groups more than among others. Health disparities are linked to social determinants of health which are non-medical factors that

influence health outcomes such as the conditions in which people are born, grow, work, live, age, and the wider set of forces and systems shaping the conditions of daily life. Social determinants of health include unequal access to health care, lack of education, poverty, stigma, and racism.

The U.S. Department of Health and Human Services Office of Minority Health calls out unique areas where health disparities are noted based on race and ethnicity. Providence Health Plan (PHP) regularly reviews these areas of opportunity to see if any changes can be made to our medical or pharmacy policies to support our members obtaining their highest level of health. Upon review, PHP creates a Coverage Recommendation (CORE) form detailing which groups are impacted by the disparity, the research surrounding the disparity, and recommendations from professional organizations. PHP Health Equity COREs are updated regularly and can be found online [here](#).

BILLING GUIDELINES AND CODING

CODES*		
CPT	0101U	Hereditary colon cancer disorders (eg, 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])
	0130U	Hereditary colon cancer disorders (eg, 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) (List separately in addition to code for primary procedure)
	0157U	APC (APC regulator of WNT signaling pathway) (eg, familial adenomatosis polyposis [FAP]) mRNA sequence analysis (List separately in addition to code for primary procedure)
	0158U	MLH1 (mutL homolog 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
	0159U	MSH2 (mutS homolog 2) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
	0160U	MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
	0161U	PMS2 (PMS1 homolog 2, mismatch repair system component) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
	0162U	Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2) (List separately in addition to code for primary procedure)
	0238U	Oncology (Lynch syndrome), genomic DNA sequence analysis of MLH1, MSH2, MSH6, PMS2, and EPCAM, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions

81201	APC (adenomatous polyposis coli)(e.g. familial adenomatosis polyposis[FAP] gene analysis, full gene sequence
81202	APC (adenomatous polyposis coli)(e.g. familial adenomatosis polyposis [FAP] gene analysis, known familial variants
81203	APC (adenomatous polyposis coli)(e.g. familial adenomatosis polyposis [FAP] gene analysis; duplication/deletion variants
81210	BRAF (v-raf murine sarcoma viral oncogene homolog B1) (e.g. Colon Cancer) gene analysis, V600E variant
81288	MLH1 (mutl. Homolog1, colon cancer, non-polyposis type 2 (e.g. hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis
81292	MLH1 (mutl. Homolog1, colon cancer, non-polyposis type 2 (e.g. hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81293	MLH1 (homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81294	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-Polyposis colorectal cancer, Lynch Syndrome) gene analysis; duplication/deletion variants
81295	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81296	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81297	MSH2 (mutS homolog 2, colon cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81298	MSH6 (mutS homolog 6 [E.coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81299	MSH6 (mutS homolog 6 [E.coli])(e.g. hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81300	MSH6 (mutS homolog 6 [E.coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81317	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81318	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81319	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81401	Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat) – when used for MUTYH (mutY homolog [E. coli]) (eg, MYH-associated polyposis), common variants (eg, Y165C, G382D)
81403	Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons) – when used for EPCAM (epithelial cell adhesion molecule) (eg, Lynch syndrome), duplication/deletion analysis

	81406	Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia) – when used for MUTYH (mutY homolog [E. coli]) (eg, MYH-associated polyposis), full gene sequence
	81435	Hereditary colon cancer-related disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis), genomic sequence analysis panel, 5 or more genes, interrogation for sequence variants and copy number variants
	81445	Solid organ neoplasm, genomic sequence analysis panel, 5-50 genes, interrogation for sequence variants and copy number variants or rearrangements, if performed; DNA analysis or combined DNA and RNA analysis
	81455	Solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes, genomic sequence analysis panel, interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; DNA analysis or combined DNA and RNA analysis
	81479	Unlisted molecular pathology procedure
HCPCS	None	

***Coding Notes:**

- The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- See the non-covered and prior authorization lists on the Company [Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website](#) for additional information.
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as “medically unlikely edits” (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCES

1. National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric - Version 1.2025.
https://www.nccn.org/professionals/physician_gls/pdf/genetics_ceg.pdf. Published 2025.
Accessed 5/5/2026.

POLICY REVISION HISTORY

DATE	REVISION SUMMARY
2/2023	Converted to new policy template.
7/2023	Annual review. Inclusion of genes <i>NTHL1</i> , <i>POLE</i> , <i>POLD1</i> . Added criteria V. that repeat testing is not medically necessary. Updated investigational criteria to not medically necessary.

1/2024	Q1 2024 code set update. Revised code description.
5/2024	Annual update. No changes to criteria or coding. Policy name change.
1/2025	Q1 2025 code set update. Expired and revised codes.
7/2025	Annual update. Changes to policy scope and medical necessity criteria.
7/2026	Annual update. No changes.