

## MP.042.MPC – Genetic Testing – Inherited Colorectal Cancers

Maryland Physicians Care considers **Genetic Testing for Inherited Colorectal Cancers** medically necessary for the following indications:

1. **Hereditary nonpolyposis colorectal cancer (HNPCC) testing is covered if the member meets one of the following:**
  - A. Member meets Amsterdam II criteria or revised Bethesda guidelines; or
  - B. Member is diagnosed with endometrial cancer before age 50 years; or
  - C. Member has a 1st- or 2nd-degree relative with a disease confirmed to be caused by a HNPCC mutation upon testing of the 1st- or 2nd-degree relative
  - D. Individuals with >5 percent chance of a MMR gene mutation by prediction models
2. **Microsatellite instability (MSI) testing or immunohistochemical (IHC) analysis of the tumor (colorectal and/or endometrial)** is considered medically necessary if the member meets the following:
  - MSI is used as an initial test in persons with colorectal cancer who meet the revised Bethesda criteria in order to identify those persons who should proceed with HNPCC mutation analysis.
3. **APC testing** is considered medically necessary if the member meets the following:
  - Personal history of  $\geq 20$  adenomas
  - Known deleterious APC mutation in family
  - Consider testing if a personal history of a desmoid tumor, hepatoblastoma, cribriform-morular variant of papillary thyroid cancer, or between 10-20 adenomas
4. **Familial Adenomatous Polyposis (FAP) testing:** Genetic Testing to determine the carrier status of the APC gene in individuals with existing polyps is considered medically necessary in any of the following:
  - Members with greater than 100 colonic polyps identified by colonoscopy; or
  - History of FAP in first degree relatives; or
  - Individuals with 10-100 adenomas may be considered for APC testing.

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**5. MYH Associated Polyposis (MAP) testing** is considered medically necessary when the member meets one of the following:

- Individuals with personal history of adenomatous polyposis (>10 adenomas) and negative APC test and a negative family history for adenomatous polyposis; or
- Individual with a personal history of APC and family history for recessive inheritance where only siblings are affected; or
- Asymptomatic siblings of individuals with known MYH polyposis.

### Limitations

1. Not indicated for mass screening of the general population.
2. In general – not recommended for individuals under the age of 18 years.
3. The test is considered experimental/investigational for all other indications
4. A member with a negative MSI-H test would not need genetic testing for HNPCC.
5. MSH6 mutations are not considered medically necessary in persons who have mutations in the MLH1 or MLH2 genes.
6. Single site MSH6 testing may be done for testing family members or persons with HNPCC from an identified MSH6 mutation.
7. All other genetic tests for inherited predisposition to colorectal cancers, other than the ones listed in this policy, are considered experimental/investigational.

### Background

Up to one third of colorectal cancer cases are inherited. Inherited syndromes of colon cancer include:

- Familial Adenomatous Polyposis (FAP)
- MYH associated polyposis (MAP)
- Hereditary Nonpolyposis Colorectal Cancer (HNPCC) or Lynch Syndrome

FAP is an autosomal dominant syndrome caused by a germ-line mutation of the APC gene and CRC is inevitable in patients with FAP if colectomy is not performed. FAP can be identified by the appearance of characteristic polyps, the identification of HNPCC is based primarily on family history and related criteria.

Centers for Medicare and Medicaid Services (CMS) reports that HNPCC or Lynch Syndrome is an autosomal dominant syndrome that accounts for about 3-5% of colorectal cancer cases. HNPCC syndrome mutations occur in the following genes: hMLH1, hMSH2, hMSH6, PMS2 and EPCAM.

MAP arises from mutations of the MYH gene and is an autosomal recessive disease.

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### Amsterdam Criteria II

There should be at least three relatives with an HNPCC-associated cancer (cancer of the colorectum, endometrium, small bowel, ureter, or renal pelvis) and:

- One should be a first-degree relative to the other two;
- At least two successive generations should be affected;
- At least one should be diagnosed before age 50;
- Familial adenomatous polyposis should be excluded;
- Tumors should be verified by pathological examination

### Revised Bethesda Guidelines:

- Individual with CRC diagnosed by age 50
- Individual with synchronous or metachronous CRC, or other HNPCC-associated tumors regardless of age
- Individual with CRC and MSI-H histology diagnosed by age 60
- Individual with CRC and more than 1 FDR with an HNPCC-associated tumor, with one cancer diagnosed by age 50
- Individual with CRC and more than 2 FDRs or SDRs with an HNPCC-associated tumor, regardless of age

### Codes:

CPT Codes / HCPCS Codes / ICD-10 Codes	
Code	Description
<b>CPT codes:</b>	
81292	MLH1 (mutl homolog 1, colon cancer, nonpolyposis type 2) (e.g, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis: full sequence analysis
81293	MLH1 (mutl 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

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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, nonpolyposis type 1) (e.g, hereditary non-polyposis colorectal 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; full sequence analysis
81299	MSH6 (mutS homolog 6 [E coli]) (e.g, hereditary non-polyposis 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
81301	Microsatellite instability analysis (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) of markers for mismatch repair deficiency (e.g., BAT25, BAT26), includes comparison of neoplastic and normal tissue, if performed
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

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