

# MedStar Health, Inc.

## POLICY AND PROCEDURE MANUAL

Policy Number: MP.042.MH  
Last Review Date: 05/27/2021  
Effective Date: 08/01/2021

### MP.042.MH - Genetic Testing- Inherited Colorectal Cancers

This policy applies to the following lines of business:

- ✓ MedStar Employee (Select)
- ✓ MedStar CareFirst PPO

MedStar Health 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

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- History of FAP in first degree relatives; or
- Individuals with 10-100 adenomas may be considered for APC testing.

**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.

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

### 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

### References

1. Ahnen DJ, Axell L. Clinical manifestations and diagnosis of familial adenomatous polyposis. UpToDate®. Topic 2593. Version 14.0. Last Updated: Nov 28, 2017. Available at: <https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-familial-adenomatous-polyposis>
2. Ahnen DJ, Axell L. Lynch syndrome (hereditary nonpolyposis colorectal cancer): Clinical manifestations and diagnosis. UpToDate®. Topic 2605. Version 25.0. Last Updated: November 20, 2020. Available at: <http://www.uptodate.com/contents/lynch-syndrome-hereditary-nonpolyposis-colorectal-cancer-clinical-manifestations-and-diagnosis?source=machineLearning&search=premm&selectedTitle=1%7E1&sectionRank=1&anchor=H28#H28>

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3. American Cancer Society recommendations for colorectal cancer early detection. Last revised: November 17, 2020. Available at:  
<http://www.cancer.org/cancer/colonandrectumcancer/moreinformation/colonandrectumcancerearlydetection/colorectal-cancer-early-detection-ac-recommendations>
4. Balmaña J, Stockwell DH, Steyerberg SW, et al. Prediction of MLH1 and MSH2 mutations in Lynch syndrome. JAMA. 2006 Sep 27;296(12):1469-1478.  
<http://jama.jamanetwork.com/article.aspx?articleid=203427>
5. Bapat B, Lindor NM, Baron J, et al. The association of tumor microsatellite instability phenotype with family history of colorectal cancer. Cancer Epidemiol Biomarkers Prev. 2009 Mar; 18(3):967-975. doi:10.1158/1055-9965.EPI-08-0878.  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2763617/pdf/nihms139549.pdf>
6. Centers for Medicare and Medicaid Services (CMS). Medicare Learning Network (MLN). MLN Matters - Colorectal Cancer: Preventable, Treatable, and Beatable: Medicare Coverage and Billing for Colorectal Cancer Screening. SE0613. Updated: Oct. 12, 2012. <https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/JA0613.pdf>
7. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD): Molecular Diagnostic Tests (MDT). Revision Effective Date: 10/01/2018. LCD ID: L36021. <https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?lcdid=36021&ver=43&bc=CAAAAAAAAAAAAA>
8. Chen S, Wang W, Lee S, et al. Prediction of germline mutations and cancer risk in the Lynch syndrome. JAMA. 2006 Sep 27;296(12):1479-1487.  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2538673/pdf/nihms41829.pdf>
9. Department of Health and Human Services. Agency for Healthcare Research and Quality. (AHRQ). National Guideline Clearinghouse (NGC). Identification of individuals at risk for Lynch syndrome using targeted evaluations and genetic testing: National Society of Genetic Counselors and the Collaborative Group of the Americas on Inherited Colorectal Cancer joint practice guideline. NGC #9003. Last Updated: July 16, 2012. <http://www.ncbi.nlm.nih.gov/pubmed/22167527>
10. Giardiello FM, Allen JI, Axilbund JE, et al. [American Society for Gastrointestinal Endoscopy]. Guidelines on genetic evaluation and management of Lynch syndrome: a consensus statement by the U.S. Multi-Society Task Force on Colorectal Cancer. Gastrointest Endosc. 2014 Aug;80(2):197-220. doi: 10.1016/j.gie.2014.06.006. <http://www.ncbi.nlm.nih.gov/pubmed/25003300>
11. Gruber SB. New Concepts in Gastroenterology. New developments in Lynch Syndrome (Hereditary Nonpolyposis Colorectal Cancer) and mismatch repair gene testing. Gastroenterology. 2006 Feb; 130(2):577-587.  
<http://www.ncbi.nlm.nih.gov/pubmed/16472609>

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12. Katrinos F, Steyerberg SW, Balmaña J, et al. Comparison of the clinical prediction model PREMM(1,2,6) and molecular testing for the systematic identification of Lynch syndrome in colorectal cancer. *Gut*. 2013 Feb;62(2):272-279. doi: 10.1136/gutjnl-2011-301265. Epub 2012 Feb 16.  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3470824/pdf/nihms384438.pdf>
13. Kohlmann W, Gruber SB. Lynch Syndrome. Last update: February 4, 2021. In: Pagon RA, Adam MP, Bird TD, et al. editors. *Gene Reviews®* [Internet]. Available at: <http://www.ncbi.nlm.nih.gov/books/NBK1211/>
14. Levin B, Liberman D, Mcfarland B, et al. Screening and surveillance for early detection of colorectal cancer adenomatous polyps, 2008: a joint guideline from the American Cancer society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *CA Cancer J Clin*. 2008 May – Jun; 58(3):130-160. Doi: 10.3322/CA.2007.0018. Epub 2008 Mar 5.  
<http://www.ncbi.nlm.nih.gov/pubmed/18322143>
15. Mosby's Medical Dictionary: Definition of adenomatous polyposis coli (APC). Mosby's Medical Dictionary, 8th edition.© 2009, Elsevier. Available at: <http://medical-dictionary.thefreedictionary.com/adenomatous+polyposis+coli>
16. Myriad Genetics, Inc. *myRisk™*: Hereditary Cancer Testing for Colorectal Cancer, Uterine Cancer. © 2019, Myriad Genetics. Available at: <https://www.myriad.com/patients-families/disease-info/colon-cancer/>
17. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Genetic/Familial High-Risk Assessment: Colorectal. Version: 1.2015. Issued: 05/04/2015.  
[http://www.nccn.org/professionals/physician\\_gls/pdf/genetics\\_colon.pdf](http://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf)
18. National Library of Medicine. Genetics Home Reference (GHR): APC Gene. Reviewed: March 2013. Published: April 16, 2019. Last Updated: August 18, 2020. Available at: <http://ghr.nlm.nih.gov/gene/APC>
19. Rex DK, Johnson DA, Anderson JC, et al. American College of Gastroenterology- American College of Gastroenterology guidelines for colorectal cancer screening 2008. *Am J Gastroenterol* 2009; 104:739 – 750; doi: 10.1038/ajg.2009.104; published online 24 February 2009.  
<https://gi.org/guideline/colorectal-cancer-screening/>
20. Umar A, Boland CR, Terdiman JP, et al. Revised Bethesda Guidelines for hereditary nonpolyposis colorectal cancer (Lynch Syndrome) and microsatellite instability. *J Natl Cancer Inst*. 2004; 96: 261-268.  
<https://pubmed.ncbi.nlm.nih.gov/14970275/>
21. Vasen HF, Watson P, Mecklin JP, Lynch HT. New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch Syndrome) proposed by the International Collaborative Group on HNPCC. *Gastroenterology*. 1999;116:1453-1456. <https://pubmed.ncbi.nlm.nih.gov/10348829/>

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22. Winawer S, Fletcher R, Rex D, et al. American Gastroenterological Association (AGA). Colorectal cancer screening and surveillance: clinical guidelines and rationale – Update based on new evidence. Gastroenterology 2017; 124:544-560 <https://gi.org/guideline/colorectal-cancer-screening-recommendations-for-physicians-and-patients-from-the-u-s-multi-society-task-force-on-colorectal-cancer/>
23. Woods MO, Younghusband HB, Parfrey PS, et al. The genetic basis of colorectal cancer in a population-based incident cohort with a high rate of familial disease. Gut. 2010 Oct;59(10):1369-1377. doi: 10.1136/gut.2010.208462. Epub 2010 Aug 3. <http://www.ncbi.nlm.nih.gov/pubmed/20682701>

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