

The Department of Vermont Health Access Clinical Criteria

Subject: Hereditary Colorectal Cancer Genetic Testing – Lynch Syndrome, Familial Adenomatous Polyposis (FAP), Attenuated FAP and MUTYH-associated Polyposis

Last Review: August 30, 2024*

Past Revisions: July 26, 2023, December 21, 2021, February 18, 2020, June 6, 2016, and August 26, 2015

***Please note: Most current content changes will be highlighted in yellow.**

Description of Service or Procedure

Hereditary colorectal cancer (HCRC) is comprised of a group of diseases or syndromes with a mutational genetic component. Classification of HCRCs is complex based upon emerging advances in genetics and clinical criteria utilized to describe these cancers. They have been categorized broadly into two large groups in some literature as Hereditary Non-Polyposis Colorectal Cancer (HNPCC) and Hereditary Polyposis Colorectal Cancer (HPCC). However, some literature has replaced the use of the term HNPCC with Lynch Syndrome as this is the commonest of this group of cancers. Per Hall et al. in UpToDate (2024):

Hereditary nonpolyposis colorectal cancer refers to patients and/or families who fulfill the Amsterdam criteria. A portion of these patients will have Lynch syndrome on germline molecular testing.

Lynch syndrome refers to patients and families with a germline mutation in one of the DNA mismatch repair genes (MLH1, MSH2, MSH6, PMS2) or the EPCAM gene.

Lynch Syndrome is the most common cause of inherited colorectal cancer (CRC). It has an autosomal dominant inheritance pattern, which means a child with a parent with a mutated gene has a 50% chance of inheriting the mutated gene and being affected by the condition. HNPCC is characterized by a significantly increased risk for CRC, endometrial, ovary, stomach, glioblastoma, and small bowel cancers. Mutations of genes including MLH1, MSH2, MSH6, PMS2 and EPCAM have been associated with HNPCC. Unlike familial adenomatous polyposis, individuals with HNPCC do not have an unusual number of colonic polyps.

Familial adenomatous polyposis (FAP) and attenuated FAP (AFAP) are related germline mutations of the APC gene. FAP carriers are very at high risk of colorectal cancer and increased risk of gastric, small bowel, pancreas, and thyroid carcinomas, as well as medulloblastoma and pediatric hepatoblastoma. Individuals may have multiple (>100) precancerous polyps in the colon and rectum developing after the first decade of life and may also have polyps in the upper GI tract, dental abnormalities (especially supernumerary teeth and/or odontomas) and



extraintestinal manifestations such as osteomas, epidermoid cysts and fibromas, desmoid tumors, congenital hypertrophy of retinal pigment epithelium (CHRPE), and other malignant changes such as papillary thyroid cancer, gastric and pancreatic cancers, hepatoblastoma and medulloblastoma. FAP may be associated with central nervous system (CNS) tumors, referred to as Turcot syndrome.

MUTYH-associated polyposis (MAP) is related to mutations in the Mut Y Homolog gene. Clinical features of individuals with MAP include multiple colorectal adenomas with or without cancer. This condition may account for a portion of individuals that present with multiple adenomas like FAP but are negative for APC gene mutations.

Disclaimer

Coverage is limited to that outlined in Medicaid Rule or Health Care Administrative Rules that pertain to the member's aid category. Prior Authorization (PA) is only valid if the member is eligible for the applicable item or service on the date of service.

Medicaid Rule

Medicaid and Health Care Administrative Rules can be found at <https://humanservices.vermont.gov/rules-policies/health-care-rules/health-care-administrative-rules-hcar/adopted-rules>

- 7102.2 Prior Authorization Determination
- 7405 Laboratory and Radiology Services
- 4.101 Medical Necessity for Covered Services
- 4.104 Medicaid Non-Covered Services
- 4.106 Early and Periodic Screening, Diagnostic and Treatment (EPSDT) Services

Coverage Position

Colon cancer genetic testing may be covered for members:

- When the service is prescribed by a licensed medical provider, enrolled in the Vermont Medicaid program, operating within their scope of practice as described on the Vermont's Office of Professional Regulation's website*, Statute, or rule who is knowledgeable regarding colon cancer genetic testing, and who provides medical care to the member AND
- When the clinical criteria below are met.

* Vermont's Office of Professional Regulation's website: <https://sos.vermont.gov/opr/>

Coverage Criteria

The Department of Vermont Health Access (DVHA) considers genetic testing for Lynch Syndrome (HNPCC) and FAP medically necessary to establish a molecular diagnosis of an inheritable disease in accordance with current [National Comprehensive Cancer Network \(NCCN\) guidelines on genetic/familial high-risk colorectal cancer syndromes.](#)

The NCCN endorses universal immunohistochemical (IHC) and microsatellite instability (MSI) testing on all newly diagnosed colorectal and rectal cancers regardless of family history to determine which patients should have genetic testing for Lynch Syndrome.

Considerations: Providers requesting this test should provide pre- and post-test genetic counseling for the member and family, if applicable.

Early and Periodic Screening, Diagnostic and Treatment (EPSDT): Vermont Medicaid will provide comprehensive services and furnish all Medicaid coverable, appropriate, and medically necessary services needed to correct and ameliorate health conditions for Medicaid members under age 21.

Please note, Vermont Medicaid Clinical Criteria is reviewed based on available literature, evidence-based guidelines/standards, Medicaid rule and policy, and Medicare coverage determinations that may be appropriate to incorporate when applicable.

Coding guidelines

The following table outlines procedure codes covered by Vermont Medicaid for HNPCC and HPCC genetic testing. See the VT Medicaid fee schedules at <http://vtmedicaid.com/#!/feeSchedule> for the most up to date information.

Procedure Code	Prior Auth Required?	Procedure Code Description
81288	No	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; promoter methylation analysis
81292	No	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; full sequence analysis
81293	No	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; known familial variants
81294	No	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; duplication/deletion variants
81295	No	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; full sequence analysis
81296	No	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; known familial variants
81297	No	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; duplication/deletion variants

81298	No	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; full sequence analysis
81299	No	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; known familial variants
81300	No	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; duplication/deletion variants
81317	No	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; full sequence analysis
81318	No	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; known familial variants
81319	No	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; duplication/deletion variants
81403	Yes	Molecular pathology procedure, Level 4 (e.g., 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): EPCAM (epithelial cell adhesion molecule) (e.g., Lynch Syndrome), duplication/deletion

FAP

Procedure Code	Prior Auth Required?	Procedure Code Description
81201	No	APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; full gene sequence
81202	No	APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; known familial variants
81203	No	APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; duplication/deletion variants
81401	Yes	Molecular pathology procedure, Level 2 (e.g., 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 specified as the following]: <ul style="list-style-type: none"> MUTYH (mutY homolog [E.coli]) (e.g., MYH-associated polyposis), common variants (e.g., Y165C, G382D)
81406	Yes	Molecular pathology procedure, Level 7 (e.g., 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 specified as the following]: <ul style="list-style-type: none"> • MUTYH (mutY homolog [E.coli]) (e.g., MYH-associated polyposis), full gene sequence
--	--	---

Clinical criteria for repeat service or procedure

Once per lifetime.

Type of service or procedure not covered (this list may not be all inclusive)

Colon cancer genetic testing does not cover:

- Genetic testing for all other gene mutations for Lynch Syndrome or colorectal cancer
- In general, genetic testing for HNPCC is not recommended for at-risk individuals younger than age 18 years. Guidelines established jointly by the American Society of Human Genetics (ASHG) and the American College of Medical Genetics and Genomics as well as another done collaboratively by the American Academy of Pediatrics and the American College of Medical Genetics and Genomics state that predictive genetic testing should only be performed in individuals younger than age 18 years when it will affect their medical management
- Testing of genetic carriers who are unaffected with a Lynch related cancer is not a covered benefit.
- Universal testing

References

American Academy of Pediatrics. (2013 reaffirmed 2018). Ethical and policy issues in genetic testing and screening of children. *Pediatrics*, 131(3), 620–622. <https://doi.org/10.1542/peds.2012-3680>

Boardman, L.A., Vilar, E., You, N.A., & Samadder, J. (2020). AGA clinical practice update on young adult–onset colorectal cancer diagnosis and management: Expert review. *AGA*, 18(11), 2415-2424. <https://doi.org/10.1016/j.cgh.2020.05.058>

Botkin, Jeffrey R., Belmont, John W., Berg, Jonathan S., Berkman, Benjamin E., Bombard, Y., Holm, Ingrid A., Levy, Howard P., Ormond, Kelly E., Saal, Howard M., Spinner, Nancy B., Wilfond, Benjamin S., & McInerney, Joseph D. (2015). Points to consider: Ethical, legal, and psychosocial implications of genetic testing in children and adolescents. *The American Journal of Human Genetics*, 97(1), 6–21. <https://doi.org/10.1016/j.ajhg.2015.05.022>

Capasso, I., Santoro, A., Lucci, E., Perrone, E., Tronconi, F., Catena, U., Zannoni, G. F., Scambia, G., Fanfani, F., Lorusso, D., & Duranti, S. (2023). Lynch syndrome and gynecologic tumors: Incidence, prophylaxis, and management of patients with cancer. *Cancers*, 15(5), 1400–1400. <https://doi.org/10.3390/cancers15051400>

- Centers for Disease Control and Prevention. (2023, May 2). *About hereditary colorectal (colon) cancer*. Hereditary Colorectal (Colon) Cancer. Retrieved July 12, 2024, from <https://www.cdc.gov/colorectal-cancer-hereditary/about/index.html>
- Centers for Medicare & Medicaid Services. (2017). *Early and Periodic Screening, Diagnostic, and Treatment | Medicaid*. Medicaid.gov; Centers for Medicare & Medicaid Services. <https://www.medicare.gov/medicaid/benefits/early-and-periodic-screening-diagnostic-and-treatment/index.html>
- Chen, E., Xu, X., & Liu, T. (2018). Hereditary nonpolyposis colorectal cancer and cancer syndromes: Recent basic and clinical discoveries. *Journal of Oncology*, 2018. <https://doi.org/10.1155/2018/3979135>
- Coughlin, S. E., Heald, B., Clark, D. F., Nielsen, S. M., Hatchell, K. E., Esplin, E. D., & Katona, B. W. (2022). Multigene panel testing yields high rates of clinically actionable variants among patients with colorectal cancer. *JCO Precision Oncology*, 6. <https://doi.org/10.1200/po.22.00517>
- Haimov, D., Lieberman, S., Sergi Castellví-Bel, Nielsen, M., & Goldberg, Y. (2022). Nonmalignant features associated with inherited colorectal cancer syndromes: Clues for diagnosis. *Cancers*, 14(3), 628–628. <https://doi.org/10.3390/cancers14030628>
- Hall, M. J., & Neumann, C. C. (2022, August 10). Lynch syndrome (hereditary nonpolyposis colorectal cancer): Clinical manifestations and diagnosis. *UpToDate*. Retrieved April 2, 2024 from <https://www.uptodate.com/contents/lynch-syndrome-hereditary-nonpolyposis-colorectal-cancer-clinical-manifestations-and-diagnosis>
- Idos, G., & Valle, L. (2021). Lynch Syndrome. In *GeneReviews*. University of Washington. <https://www.ncbi.nlm.nih.gov/books/NBK1211>
- Jass, J.R. (2006). Hereditary non-polyposis colorectal cancer: The rise and fall of a confusing term. *World Journal of Gastroenterology*, 12(31), 4943–4950. <https://doi.org/10.3748%2Fwjg.v12.i31.4943>
- Leclerc, J., Vermaut, C., & Buisine, M.-P. (2021). Diagnosis of Lynch syndrome and strategies to distinguish Lynch-related tumors from sporadic MSI/dMMR tumors. *Cancers*, 13(3), 467. <https://doi.org/10.3390/cancers13030467>
- Medina Pabón, M. A., & Babiker, H. M. (2022). *A review of hereditary colorectal cancers*. PubMed; StatPearls Publishing. <https://www.ncbi.nlm.nih.gov/books/NBK538195/>
- Muller, C., Nielsen, S. M., Hatchell, K. E., Yang, S., Michalski, S. T., Hamlington, B., Nussbaum, R. L., Esplin, E. D., & Kupfer, S. S. (2021). Underdiagnosis of hereditary colorectal cancers among Medicare patients: Genetic testing criteria for Lynch syndrome miss the mark. *JCO precision oncology*, 5, PO.21.00132. <https://doi.org/10.1200/PO.21.00132>
- National Comprehensive Cancer Network (NCCN). (2023). NCCN clinical practice guidelines in oncology. Genetic/familial high-risk assessment: Colorectal version 2.2023. Retrieved July 12, 2024, from https://www.nccn.org/guidelines/category_2
- Nolano, A., Medugno, A., Trombetti, S., Liccardo, R., De Rosa, M., Izzo, P., & Duraturo, F. (2022). Hereditary colorectal cancer: State of the art in Lynch syndrome. *Cancers*, 15(1), 75. <https://doi.org/10.3390/cancers15010075>
- Pantaleo, A., Forte, G., Cariola, F., Valentini, A. M., Fasano, C., Sanese, P., Grossi, V., Buonadonna, A. L., De Marco, K., Lepore Signorile, M., Guglielmi, A. F., Manghisi, A.,

Gigante, G., Armentano, R., Disciglio, V., & Simone, C. (2023). Tumor testing and genetic analysis to identify lynch syndrome patients in an Italian colorectal cancer cohort. *Cancers*, 15(20), 5061. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10605602/>

Rebuzzi F, Ulivi P, Tedaldi G. (2023). Genetic predisposition to colorectal cancer: How many and which genes to test? *International Journal of Molecular Sciences*, 24(3), 2137. <https://doi.org/10.3390/ijms24032137>

Shaukat, A., Kahi, C.J., Burke, C.A., Rabeneck, L., Sauer, B.G., & Rex, D.K. (2021). ACG clinical guidelines: Colorectal cancer screening 2021. *The American Journal of Gastroenterology*, 116(3), 458-479. <https://doi.org/10.14309/ajg.0000000000001122>

Sorscher, S. (2023). Primary care implications of the expanded national guidelines for germline testing of patients previously diagnosed with colorectal cancer. *The Journal of the American Board of Family Medicine*, 36(2), 360–365. <https://doi.org/10.3122/jabfm.2022.220288r1>

Storandt, M. H., Rogen, K. R., Iyyangar, A., Schnell, R. R., Mitchell, J. L., Hubbard, J. M., Sinicrope, F. A., Jatoi, A., Mahipal, A., Shi, Q., & Jin, Z. (2023). Completion of genetic testing and incidence of pathogenic germline mutation among patients with early-onset colorectal cancer: A single institution analysis. *Cancers*, 15(14), 3570. <https://doi.org/10.3390/cancers15143570>

This document has been classified as public information.