VERMONT

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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: July 26, 2023
Past Revisions: 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 HPNCC with Lynch Syndrome as this is the commonest of this group of cancers. Per Hall et al. in Up To Date (2023):

> 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. HPNCC 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 pertains to the beneficiary's aid category. Prior Authorization (PA) is only valid if the beneficiary 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

Coverage Position

Colon cancer genetic screening may be covered for beneficiaries:

- 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 screening, and who provides medical care to the beneficiary 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 HNPCC and FAP medically necessary to establish a molecular diagnosis of an inheritable disease in accordance with current National Comprehensive Cancer Network (NCCN) guidelines. These can be found at https://www.nccn.org/guidelines/category_2.

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]: • 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]: • MUTYH (mutY homolog [E.coli]) (e.g., MYH-associated polyposis), full gene sequence

See the Centers for Medicare and Medicaid Services (CMS) Local Coverage Article at https://www.cms.gov/medicare-coverage-database/search.aspx

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 screening 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.

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