GENETIC TESTING FOR COLORECTAL CANCER SUSCEPTIBILITY

The purpose of this document is to assist providers enrolled in the Connecticut Medical Assistance Program (CMAP) with the information needed to support a medical necessity determination for genetic testing for individuals who are at higher than average risk for the development of colorectal cancer. By clarifying the information needed for prior authorization of services, HUSKY Health hopes to facilitate timely review of requests so that individuals obtain the medically necessary care they need as quickly as possible.

Genetic testing provides information that can be used to diagnose genetic diseases and susceptibility to diseases or conditions that are inherited. Such testing includes studying chromosomes to the level of individual genes, biochemical testing for the possible presence of genetic diseases, and identifying mutant forms of genes associated with increased risk of developing genetic disorders. The results of a genetic test can be used to confirm or rule out a genetic condition or to help determine an individual’s chance of developing a genetic condition or passing on a genetic disorder. The results of testing can provide individuals with the information necessary to make fully informed health-care decisions. Results are often used to influence choices about health care and management of an identified genetic disorder or susceptibility to one. Several hundred genetic tests are currently available.

Genetic testing is available for those at risk for various types of hereditary colon cancer. This policy describes genetic testing for familial adenomatous polyposis (FAP), MYH-associated polyposis and Lynch syndrome (formerly known as HNPCC). Two commonly used tests are the Colaris® and Colaris AP® tests.

FAP can be clinically recognized by the presence of hundreds of colon polyps, typically apparent by age 10-20. If left untreated, affected individuals will go on to develop colorectal cancer.

Individuals with HNPCC tend to have early-onset colorectal cancer, right-sided tumors and/or multiple synchronous or metachronous lesions. Extracolonic tumors may also be present. The lifetime risk of developing colorectal cancer in HNPCC is approximately 80%.

Germline mutations have been associated with both FAP and HNPCC creating the option of genetic testing of both affected individuals (to establish the genetic basis of the tumor) and their family members (to determine whether an individual carries the same mutation as the affected relative). EPCAM mutations cause the MSH2 gene to become inactivated by a mechanism known as promoter hypermethylation. The MSH2 protein is crucial in repairing mistakes in DNA. Loss of this protein prevents proper DNA repair and may result in uncontrolled cell growth and an increased risk of cancer.

MYH-associated polyposis (MAP) is an autosomal recessive form of FAP that increases the individual’s risk of developing attenuated adenomatous polyposis and colorectal cancer. There may also be an increased risk of polyps in the duodenum, although the incidence of duodenal polyposis is reported less frequently than in FAP. The magnitude of the risk of duodenal cancer has not yet been defined.

COLARIS® is a test that detects mutations in the MLH1, MSH2, MSH6, PMS2, EPCAM and MYH genes.

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that are responsible for the majority of Lynch Syndrome and MYH-associated polyposis (MAP) cases.

COLARIS AP® is a test that detects mutations in the APC and MYH genes, which cause adenomatous polyposis colon cancer syndromes, including familial adenomatous polyposis (FAP), attenuated FAP (AFAP), and MYH-associated polyposis (MAP).

Genetic testing for hereditary colon cancers may affect individual management in a variety of ways. A positive test may lead to a decision between the individual and his or her provider to pursue additional surveillance or possibly consider a prophylactic colectomy.

CLINICAL GUIDELINE
Coverage guidelines for colorectal cancer susceptibility testing are made in accordance with the DSS definition of Medical Necessity and in line with published recommendations and guidelines disseminated by organizations including the American Gastroenterological Association, The National Cancer Institute, and the National Comprehensive Cancer Network. The following criteria are guidelines only. Coverage determinations are based on an individual assessment of the member and his or her unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail. The guidelines are as follows:

Note: Typically, genetic testing is appropriate only when offered in a setting with adequately trained health care professionals to provide appropriate pre-and post-test counseling.

Hereditary Non-Polyposis Colorectal Cancer (HNPCC [Lynch Syndrome])

Genetic testing to detect mutations in the HNPCC genes, associated with genetic counseling may be considered medically necessary when any of the following criteria are met:

Personal History of:
- The individual has 2 or more HNPCC-related tumors, (colorectal, endometrial, biliary tract, thyroid, pancreas, ureter or renal pelvis, ovarian, brain, gastric, or small intestinal cancers, sebaceous gland adenomas or keratoconanthomas), including synchronous and metachronous tumors; OR
- The individual has a history of colorectal cancer and a first-degree relative with colorectal cancer diagnosed prior to age 50 ; OR
- The individual has a history of colorectal cancer and a first-degree relative with an HNPCC-related cancer diagnosed prior to age 50; OR
- The individual has a history of colorectal cancer and a first-degree relative with colorectal adenoma diagnosed prior to age 40; OR
- The individual has colorectal cancer or endometrial cancer diagnosed prior to age 50; OR
- The individual has a colorectal adenoma diagnosed prior to age 40; OR
- The individual has a first- or second-degree relative with a known HNPCC mutation (Lynch syndrome in family); OR
- The individual has a personal history of colorectal or endometrial cancer and tumor shows high micro-satellite instability (MSI).

Family History of:
- The individual has a first-or second-degree relative with a known HNPCC mutation (Lynch Syndrome in family); or
- For individuals with a family history of potentially HNPCC related cancer, genetic testing to detect
mutations in the HNPCC genes, associated with genetic counseling, may be considered medically necessary when an individual has a relative who would meet any of the following criteria, but that relative is not available for testing:

- The individual for whom the test is requested, has a first- or second-degree relative with 2 or more HNPCC-related tumors (colorectal, endometrial, biliary tract, pancreas, ureter or renal pelvis, ovarian, brain, gastric, or small intestinal cancers, or sebaceous gland adenomas or keratoacanthomas), including synchronous and metachronous tumors; OR
- The individual for whom the test is requested, has a history of colorectal cancer and that relative has a first-degree relative with colorectal cancer diagnosed prior to age 50; OR
- The individual for whom the test is requested, has a first- or second-degree relative with a history of colorectal cancer and that relative has a first-degree relative with an HNPCC-related cancer diagnosed prior to age 50; OR
- The individual for whom the test is requested, has a first- or second-degree relative with colorectal cancer or endometrial cancer diagnosed prior to age 50; OR
- The individual for whom the test is requested, has a first- or second-degree relative with colorectal cancer and that relative has an HNPCC-related cancer diagnosed prior to age 40; OR
- The individual for whom the test is requested, has a first- or second-degree relative with a history of colorectal cancer and that relative has a first-degree relative with colorectal adenoma diagnosed prior to age 40.

Genetic testing for EPCAM mutations may be considered medically necessary to make a diagnosis of Lynch Syndrome in an individual with colorectal or endometrial cancer when both a) the tumor is negative for MSH2 and MSH6 expression as demonstrated by immunohistochemistry (IHC) and b) the individual tested negative for a MSH2 germline mutation.

**Familial Adenomatous Polyposis (FAP)**

Genetic testing to detect mutations in the FAP genes, associated with genetic counseling, may be considered medically necessary in individuals who meet any of the following criteria:

- Individuals with greater than 20 adenomatous colonic polyps during their lifetime; OR
- First- or second-degree relatives of individuals diagnosed with Familial Adenomatous Polyposis (FAP); OR
- First- or second-degree relatives of individuals with a known FAP gene mutation.

**MYH (Human MutY homolog)-associated Polyposis (MAP)**

Genetic testing for MYH (also known as MUTYH)–associated polyposis (MAP), associated with genetic counseling, may be considered medically necessary when any of the following criteria are met:

- The individual has greater than 10 adenomatous colonic polyps and a recessive inheritance (family history positive only for siblings); OR
- The individual has greater than 10 adenomatous colonic polyps and had adenomatous polyposis coli (APC) testing with negative results; OR
- The individual has greater than 15 cumulative adenomas in 10 years and a recessive inheritance (family history positive only for siblings); OR
- The individual had greater than 15 cumulative adenomas in 10 years and had adenomatous polyposis coli (APC) testing with negative results; OR
• The individual is asymptomatic and has a sibling with known MYH-associated polyposis (MAP).

Note: Genetic testing for colon or rectal cancer susceptibility is considered investigational and typically not considered medically necessary in individuals not meeting the above criteria; however this testing may be considered medically necessary based on an assessment of the individual and his or her unique clinical needs.

NOTE: EPSDT Special Provision
Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) is a federal Medicaid requirement that requires the Connecticut Medical Assistance Program (CMAP) to cover services, products, or procedures for Medicaid enrollees under 21 years of age where the service or good is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition identified through a screening examination. The applicable definition of medical necessity is set forth in Conn. Gen. Stat. Section 17b-259b (2011) [ref. CMAP Provider Bulletin PB 2011-36].

PROCEDURE
Prior authorization of genetic testing is required. Requests for coverage of colorectal cancer susceptibility testing will be reviewed in accordance with procedures in place for reviewing requests for genetic testing. Coverage determinations will be based upon a review of requested and/or submitted case-specific information.

The following information is needed to review requests for colorectal cancer susceptibility testing:
1. Fully completed State of Connecticut, Department of Social Services Outpatient Prior Authorization Request form or fully completed authorization request via on-line web portal;
2. Clinical information supporting the need for requested services to include pertinent clinical and family history; and
3. Other information as requested by CHNCT.

EFFECTIVE DATE
This Policy is effective for prior authorization requests for genetic testing for individuals covered under the HUSKY Health Program on or after August 1, 2014.

LIMITATIONS
Not Applicable

CODES:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>81201</td>
<td>APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; full gene sequence</td>
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<tr>
<td>81202</td>
<td>APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; known familial variants</td>
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<tr>
<td>81203</td>
<td>APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; duplication/deletion variants</td>
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<tr>
<td>81288</td>
<td>MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis</td>
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<tr>
<td>81292</td>
<td>MLH1 (mutL homolog 1, colon cancer, nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis</td>
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<tr>
<td>81293</td>
<td>MLH1 (mutL homolog 1, colon cancer, nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis</td>
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<tr>
<td>81294</td>
<td>MLH1 (mutL homolog 1, colon cancer, nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants</td>
</tr>
<tr>
<td>81295</td>
<td>MSH2 (mutS homolog 2, colon cancer, nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants</td>
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<tr>
<td>81296</td>
<td>MSH2 (mutS homolog 2, colon cancer, nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis</td>
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<tr>
<td>81297</td>
<td>MSH2 (mutS homolog 2, colon cancer, nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants</td>
</tr>
<tr>
<td>81298</td>
<td>MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis</td>
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<tr>
<td>81299</td>
<td>MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants</td>
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<td>81300</td>
<td>MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants</td>
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<tr>
<td>81301</td>
<td>Microsatellite instability analysis (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) markers for mismatch repair deficiency (e.g., BAT25, BAT26), includes comparison of neoplastic and normal tissue if performed</td>
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<td>81317</td>
<td>PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; full sequence analysis</td>
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<td>81318</td>
<td>PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; known familial variants</td>
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<tr>
<td>81319</td>
<td>PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch Syndrome) gene analysis; duplication/deletion variants</td>
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<tr>
<td>81401</td>
<td>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., Y1 G382D)</td>
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<tr>
<td>81403</td>
<td>Molecular pathology procedure, Level 4 (e.g., analysis of single exon by DNA sequence analysis, analysis of &gt;10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons) [when specified as the following]: EPCAM (epithelial cell adhesion molecule) (e.g., Lynch syndrome), duplication/deletion analysis</td>
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<td>81406</td>
<td>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</td>
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**DEFINITIONS**

1. **Current Procedural Terminology (CPT):** The most recent edition of a listing, published by the American Medical Association, of descriptive terms and identifying codes for reporting medical services performed by providers.
2. **Familial adenomatous polyposis (FAP):** An inherited disorder characterized by the presence of adenomatous polyps throughout the colon that commonly progress to develop colon cancer.

3. **First-degree relative:** Any relative who is a parent, sibling, or offspring to another.

4. **Genetic counseling:** A process involving the guidance of a specially trained professional in the evaluation of family history, medical records, and genetic test results, in assessing the risk of genetic diseases, understanding the ramifications of diagnosis, and explanation of available treatment options.

5. **Genetic testing:** A type of test that is used to determine the presence or absence of a specific gene or set of genes to help diagnose a disease, screen for specific health conditions, and for other purposes.

6. **Hereditary nonpolyposis colorectal cancer (HNPPC [Lynch Syndrome]):** An inherited colorectal cancer syndrome that accounts for 5% to 8% of all colorectal cancers.

7. **HUSKY A:** Connecticut children and their parents or a relative caregiver; and pregnant women may qualify for HUSKY A (also known as Medicaid). Income limits apply.

8. **HUSKY B:** Uninsured children under the age of 19 in higher income households may be eligible for HUSKY B (also known as the Children's Health Insurance Program) depending on their family income level. Family cost-sharing may apply.

9. **HUSKY C:** Connecticut residents who are age 65 or older or residents who are ages 18-64 and who are blind, or have another disability, may qualify for Medicaid coverage under HUSKY C (this includes Medicaid for Employees with Disabilities (MED-Connect), if working). Income and asset limits apply.

10. **HUSKY D:** Connecticut residents who are ages 19-64 without dependent children and who: (1) do not qualify for HUSKY A; (2) do not receive Medicare; and (3) are not pregnant, may qualify for HUSKY D (also known as Medicaid for the Lowest-Income populations).

11. **HUSKY Health Program:** The HUSKY A, HUSKY B, HUSKY C, HUSKY D and HUSKY Limited Benefit programs, collectively.

12. **HUSKY Limited Benefit Program or HUSKY, LBP:** Connecticut's implementation of limited health insurance coverage under Medicaid for individuals with tuberculosis or for family planning purposes and such coverage is substantially less than the full Medicaid coverage.

13. **HUSKY Plus Physical Program (or HUSKY Plus Program):** A supplemental physical health program pursuant to Conn. Gen. Stat. § 17b-294, for medically eligible members of HUSKY B in Income Bands 1 and 2, whose intensive physical health needs cannot be accommodated within the HUSKY Plan, Part B.

14. **Medically Necessary or Medical Necessity:** (as defined in Connecticut General Statutes § 17b-259b) Those health services required to prevent, identify, diagnose, treat, rehabilitate or ameliorate an individual's medical condition, including mental illness, or its effects, in order to attain or maintain the individual's achievable health and independent functioning provided such services are: (1) Consistent with generally-accepted standards of medical practice that are defined as standards that are based on (A) credible scientific evidence published in peer-reviewed medical literature that is generally recognized by the relevant medical community, (B) recommendations of a physician-specialty society, (C) the views of physicians practicing in relevant clinical areas, and (D) any other relevant factors; (2) clinically appropriate in terms of type, frequency, timing, site, extent and duration and considered effective for the individual's illness, injury or disease; (3) not primarily for the convenience of the individual, the individual's health care provider or other health care providers; (4) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the individual's illness, injury or disease; and (5) based on an assessment of the individual and his or her medical condition.

15. **Mutation:** A change in DNA sequence.

16. **Next-generation sequencing:** Any of the technologies that allow rapid sequencing of large
numbers of segments of DNA, up to and including entire genomes. This technology includes but is not limited to massively parallel sequencing and microarray analysis.

17. **Prior authorization:** A process for approving covered services prior to the delivery of the service or initiation of the plan of care based on a determination by CHNCT as to whether the requested service is medically necessary.

18. **Second-degree relative:** Any relative who is a grandparent, grandchild, uncle, aunt, niece, nephew, or half-sibling to another.

**CLINICAL MEDICAL POLICY CROSS REFERENCE:** Genetic Testing

**ADDITIONAL RESOURCES AND REFERENCES:**

**Peer Reviewed Publications:**

**Government Agency, Medical Society, and Other Authoritative Publications:**
4. DSS Provider Bulletin 2012-26: Consolidated Laboratory Fee Schedule Update, dated June 2012


Web Sites for Additional Information:

PUBLICATION HISTORY

<table>
<thead>
<tr>
<th>Status</th>
<th>Date</th>
<th>Action Taken</th>
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<tr>
<td>Original publication</td>
<td>July 2014</td>
<td>Policy approved at the September 15, 2014 Clinical Quality Subcommittee meeting.</td>
</tr>
<tr>
<td>Updated</td>
<td>August 2015</td>
<td>Updated definitions of HUSKY A, B, C and D programs at request of DSS.</td>
</tr>
<tr>
<td>Updated</td>
<td>March 2016</td>
<td>Updates to language in introductory paragraph pertaining to purpose of policy. Updates to Clinical Guideline section pertaining to definition of Medical Necessity. Updates throughout policy to reflect importance of person-centeredness when reviewing requests for this service. Changes approved at the March 21, 2016 Clinical Quality Subcommittee meeting. Changes approved by DSS on June 14, 2016.</td>
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<tr>
<td>Updated</td>
<td>September 2016</td>
<td>Reviewed at the September 2016 Medical Policy Review Committee Meeting. Updates to Clinical Guideline section. Under HNPCC (Lynch Syndrome) added thyroid cancers to list of HNPCC-Related tumors. Re-formatted HNPCC section to separate family history from individual history. Changes approved at the December 20, 2016</td>
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