MedStar Health, Inc.
POLICY AND PROCEDURE MANUAL

Policy Number: MP.042.MH
Last Review Date: 11/12/2015
Effective Date: 01/01/2016
Renewal Date: 01/01/2017

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

This policy applies to the following lines of business:

- ✓ MedStar Employee (Select)
- ✓ MedStar MA – DSNP – CSNP
- ✓ 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 ≥ 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.

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.

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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.

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
CPT codes:	
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
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

Variation
For Medicare Members in Maryland

Local Medicare coverage of such biomarkers must be predicated upon four fundamental principles
First, the biomarkers must have proven clinical validity/utility (CVU).
Second, to support the medical necessity of the service, there must be acceptance/uptake of specific testing into patient management. **It is essential that physicians be familiar enough with all specific biomarkers, which they order, such that all test results may become clinically actionable.**

Note: Off-label chemotherapeutic agents, corresponding genotypic testing, which is designed to better help guide therapy, is also coverable.
Third, providers managing oncological conditions must demonstrate that the use of biomarkers will be used to assist in the management/treatment of the beneficiary.
Finally, it is quite useful to categorize oncology biomarkers into functional clusters which reflect both (1) The predominant intent of testing (with the caveat that individual assays may cross over into more than one category) and (2) The relative evidentiary expectations:

APC *adaenomatous polyposis coli* full gene sequence	Covered
APC *adaenomatous polyposis coli* known familial variants	Covered
APC *adaenomatous polyposis coli* duplication deletion	Covered
Mcoln1 gene	Covered less than 40
Mlh 1 gene dup/delete variant	Covered
Msh2 gene full seq	Covered if age less than 65
Msh2 gene known variants	Covered if age less than 65
Msh2 gene dup/delete variants	Covered if age less than 65
Prms2 gene full seq analysis	Covered if age less than 65
Prms2 known familial variants	
Prms2 gene dup/delete variants	

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