

UPMC Health Plan POLICY AND PROCEDURE MANUAL

POLICY NUMBER: PAY.042
REVISION DATE: N/A
ANNUAL APPROVAL DATE: 11/09
PAGE NUMBER: 1 of 7

SUBJECT: Genetic Testing for Inherited Colorectal Cancers
INDEX TITLE: Medical Management
ORIGINAL DATE: June 2009

This policy applies to the following lines of business: (Check those that apply.)

Commercial:					
HMO ()		POS ()		PPO ()	
Fully Insured ()		Self-funded/ASO ()		HSA ()	
Medicare Select ()		Medicare Supplement ()			
DPW-MA:					
Health Choices ()			Voluntary ()		All ()
CMS-MA:					
OH ()		WV ()		PA ()	All (X)
HMO (X)	PPO (X)	Specialty Needs Plan (X)	Part D ()	PFFS (X)	All ()
PID-CHIP:					
Free ()		Sub ()		Full ()	All ()
APPLICABLE TO:					
Community Care ()			Work Partners ()		

I. POLICY

It is the policy of UPMC Health Plan to cover Genetic Testing for syndromes of inherited colorectal cancer when it is medically necessary and consistent with good medical practice for screening members with a hereditary predisposition for colorectal cancer.

UPMC Health Plan recognizes the need for genetic studies when the identification of these inherited colorectal cancers is based primarily on personal/family history and related clinical indications and according to the member's specific benefit plan.

II. DEFINITIONS

First Degree Relative – includes an individual's parents, full siblings and children.

HNPCC – is an inherited predisposition to developing colorectal cancer and cancers of the endometrium, small intestine, ovary, hepatobiliary system, kidney and ureter.

Homozygous Mismatch Repair Mutations – is defined as rare individuals who are homozygous for mutations in MLH1, MSH2 and PMS2.

Microsatellite Instability (MSI) Testing – refers to the diverse pattern of microsatellite repeats that are observed when DNA is amplified from tumors compared with DNA amplified from adjacent normal tissue.

MSI-H (high scoring) histology includes the presence of tumor-infiltrating lymphocytes, Crohn's like lymphocyte reaction, mucinous/signet-ring differentiation, or medullary growth pattern.

Muir-Torre Syndrome – is defined by the combination of sebaceous neoplasms of the skin and one or more internal malignancies, commonly seen in HNPCC.

Second Degree Relative – includes the individual's grandparents, grandchildren, aunts, uncles, nephews, nieces, and half-siblings.

Turcot Syndrome – is defined as colorectal cancer or colorectal adenomas in addition to tumors of the central nervous system.

III. PURPOSE

The purpose of this policy is to establish criteria for coverage of the COLARIS® Genetic Testing for inherited colorectal cancers.

IV. SCOPE

This policy applies to various UPMC Health Plan departments as indicated by the Benefit and Reimbursement Committee. These include but are not limited to Medical Management, Benefit Configuration and Claims departments.

V. PROCEDURE

A. Medical Description / Background

There are currently two types of hereditary colorectal cancer- familial adenomatous polyposis (FAP) and hereditary nonpolyposis colorectal cancer (HNPCC). While FAP can be identified by the appearance of characteristic polyps, the identification of HNPCC is based primarily on family history and related criteria.

HNPCC also known as Lynch syndrome is an autosomal dominant disease characterized by an increased risk for cancer of the colon and rectum as well as other extracolonic cancers such as endometrium, small bowel, ureter or renal pelvis. Individuals with HNPCC have a risk of colorectal cancer of up to 80% by age 70 and females with HNPCC mutations have a risk of cancer of the endometrium of up to 71% by the same age. This is a large risk compared to the general population's risk. Additionally individuals with HNPCC mutations may have more than one type of cancer. Tumors often develop at a young age (average age at diagnosis is 44- 45 years) in affected individuals.

HNPCC is caused by a germline mutation in any of the DNA mismatch repair (MMR) genes or associated with tumors exhibiting microsatellite insensitivity (MSI-H). The definitive test for detection of these MMR mutations is expensive

and involves gene sequence analysis. The COLARIS® test offered by Myriad Genetic Laboratories detects HNPCC associated mutations in 3 genes which are responsible for the majority of HNPCC (i.e. MLH1, MSH2 and MSH6). MSH6 testing should only be performed after MLH1 and MSH2 testing is determined to be negative for HNPCC mutations. It is important to remember that although cancer risks are increased in HNPCC they are not 100% so not all people with HNPCC will develop cancer. However, once a person has been found to be a HNPCC carrier via genetic testing, surveillance programs can be put in place to help detect tumors at an earlier stage or prevent their development

Microsatellite instability (MSI-H) testing or immunohistochemical analysis of the tumor may be covered as an initial screening in individuals with colorectal cancer who meet the revised Bethesda criteria in order to identify those individuals who should then proceed with the HNPCC mutation analysis. If the MSI-H result is positive, then one should proceed to genetic testing.

The hereditary colorectal cancer syndromes associated with multiple adenomatous polyps are FAP, attenuated FAP and MYH associated polyposis (MAP). Classic FAP is caused by germline mutations in the APC gene and is also inherited in an autosomal dominant fashion- which means that each child has a 50% chance of inheriting the predisposition. MAP has been described in individuals with varying degrees of colonic polyposis and is caused by mutation in the MYH gene. Most affected persons have >100 colorectal adenomas and persons with more than 100 colorectal adenomas have FAP by definition.

A variant of FAP called the attenuated APC (AAPC) is associated with usually 20-100 adenomas, with a tendency toward right-sided colonic adenomas and an earlier age onset than for FAP.

Individuals with a family history of colorectal cancer should therefore be considered to be at higher than average risk, and should receive appropriately stringent screenings than the average risk patient. However, only individuals who meet criteria for defined genetic syndromes (e.g. HNPCC, FAP) should consider genetic testing.

The Comprehensive COLARIS AP test includes testing for the Adenosis Polyposis Coli (APC) gene to determine carrier status for familial adenomatous polyposis (FAP), attenuated FAP (AFAP) and MYH associated polyposis (MAP).

Genetic counseling prior to genetic testing is prudent, considering the impact of positive results on the member and the family. Colonoscopy is the recommended screening surveillance every 1-2 years beginning at age 20-25 years or 10 years earlier than the youngest age of colon cancer diagnosis in the family- whichever comes first.

B. Indications

- 1. HNPCC testing:** Two approaches for genetic testing for HNPCC mutation have been developed to direct when testing may be considered medically necessary to assess a person's risk of developing colorectal cancer among high risk families. One approach is based on family history using the Amsterdam II criteria and the other approach is based upon the modified Bethesda criteria. The approach adopted in this policy is based on the modified Bethesda criteria.

MSI-H testing: An alternative indication for who should have genetic testing is to perform the MSI-H testing on colon cancer tissue of patients meeting any of the Bethesda modified criteria. If MSI-H is positive, then one could proceed with genetic testing for HNPCC.

Bethesda (modified) criteria (2003) for identification of patients with colorectal tumors who should undergo testing. Individual must meet one of the following:

- Diagnosed with colorectal cancer before the age of 50 years
- Presence of synchronous or metachronous colorectal or other HNPCC related tumors regardless of the age
- Colorectal cancer with the MSI-H histology diagnosed in individual before the age of 60 years
- Individuals with colorectal cancer with one or more first-degree relatives with an HNPCC related tumor, with one of the cancers diagnosed before age 50 years
- Colorectal cancer diagnosed in two or more first or second degree relatives with an HNPCC related tumor, regardless of age

Note: Genetic testing to determine the carrier status of the HNPCC gene may be considered medically necessary in patients without a history of colorectal cancer but who have a first- or second-degree relative with a known HNPCC mutation.

- 2. FAP testing:** Genetic Testing to determine the carrier status of the APC gene in individuals with existing polyps is considered medically necessary in the following:
 - Members with greater than 100 colonic polyps identified by colonoscopy**OR**
 - History of FAP in first degree relatives.
 - Individuals with 10-100 adenomas may be considered for APC testing

3. MYH Associated Polyposis (MAP) testing:

- Individuals with personal history of adenomatous polyposis and negative APC test and a negative family history for adenomatous polyposis.
- Individual with a personal history of AP and family history for recessive inheritance where only siblings are affected
OR
- Asymptomatic individuals with known MYH polyposis.

C. Limitations

- Not indicated for mass screening of the general population
- In general – not recommended for individuals under the age of 18 years
- The test is considered experimental/investigational for all other indications
- A negative MSI-H test would not need genetic testing for HNPCC
- MSH6 mutations are not considered medically necessary in persons who have mutations in the MLH1 or MLH2 genes.
- Single site MSH6 testing may be done for testing family members or persons with HNPCC from an identified MSH6 mutation

D. Variations

N/A

E. Quality Audit

Quality Audit may monitor policy compliance or billing accuracy at the request of the UPMC Health Plan's Technology Assessment Committee or the Benefits Reimbursement Committee.

F. Records Retention

Records Retention for UPMC Health Plan documents, regardless of medium are provided within the UPMC Health System Policy and as indicated in the UPMC Insurance Services Division Policy and Procedure.

G. References

1. National Guideline Clearinghouse, *ASGE Guideline: colorectal cancer screening and surveillance*, 2006, www.guideline.gov
2. ECRI Institute, *Genetic Testing for Hereditary Nonpolyposis Colorectal Cancer Syndrome*, 09/30/08
3. AHRQ, *Hereditary Nonpolyposis Colorectal Cancer*, May 2007,

- www.ahrq.gov/clinic/tp/hnpcctp.htm
4. Myriad Genetics, Inc., *COLARIS is a genetic test for HNPCC*, 2009, www.myriad.com/products/COLARIS.php
 5. NIH, Gene Reviews – *Hereditary Non-polyposis Colon Cancer*, Last update 11/29/2006, www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=hnpcc
 6. American Gastroenterological Association (AGA), *Colorectal Cancer Screening and Surveillance: Clinical Guidelines and Rationale – Update Based on New Evidence*, *Gastroenterology* 2003; 124:544-560
 7. American College of Gastroenterology- *ACG Guidelines for Colorectal Cancer Screening 2008*, Revised 10/21/2008, www.acg.gi.org/media/releases/ACG2009CRCCGuidelines
 8. *Gastroenterology, New Developments in Lynch (HNPCC) and Mismatch Repair Gene Testing*, Volumes 130, Issue 2, Pages 577-587 (February 2006)
 9. ECRI Institute, *Guidelines for Genetic Testing to Identify Persons at Risk for Colorectal Cancer*, 03/14/2006
 10. ECRI Institute, *Microsatellite Instability testing for Hereditary Nonpolyposis Colorectal Cancer*, 01/28/2002
 11. Medscape, *Testing Guidelines for Hereditary Non-polyposis Colorectal Cancer*, *Nat Rev Cancer* 4(2):153-158, 2004, Posted 02/09/2004

Disclaimer:

UPMC Health Plan medical payment and prior authorization policies do not constitute medical advice and are not intended to govern or otherwise influence the practice of medicine. The policies constitute only the reimbursement and coverage guidelines of UPMC Health Plan and its affiliated managed care entities. Coverage for services varies for individual members in accordance with the terms and conditions of applicable Certificates of Coverage, Summary Plan Descriptions, or contracts with governing regulatory agencies.

UPMC Health Plan reserves the right to review and update the medical payment and prior authorization guidelines in its sole discretion. Notice of such changes, if necessary, shall be provided in accordance with the terms and conditions of provider agreements and any applicable laws or regulations.

These policies are the proprietary information of UPMC Health Plan. Any sale, copying, or dissemination of said policies is prohibited.