MEDICAL POLICY

Excellus

SUBJECT: FECAL DNA ANALYSIS FOR COLORECTAL CANCER	EFFECTIVE DATE: 07/21/05
	REVISED DATE: 04/20/06, 02/15/07, 01/17/08, 01/15/09, 01/21/10, 01/20/11, 01/19/12, 01/17/13, 01/16/14
POLICY NUMBER: 2.02.28	
CATEGORY: Laboratory Test	PAGE: 1 OF: 4

- ***If the member's subscriber contract excludes coverage for a specific service it is not covered under that contract. In such cases, medical policy criteria are not applied.***
- ***Medical policies apply to commercial and Medicaid products only when a contract benefit for the specific service exists.***
- ***Medical policies only apply to Medicare products when a contract benefit exists and where there are no National or Local Medicare coverage decisions for the specific service.***

POLICY STATEMENT:

Based upon our criteria and review of peer-reviewed literature, DNA analysis of stool samples has not been medically proven to be effective and is considered **investigational** as a screening or monitoring technique for colorectal cancer.

Refer to Corporate Medical Policy #2.02.11 regarding Genetic Testing for Inherited Susceptibility to Colorectal Cancer: Familial Adenomatous Polyposis and Hereditary Nonpolyposis Colorectal Cancer.

Refer to Corporate Medical Policy #11.01.03 Experimental and Investigational Services.

Refer to Corporate Medical Policy #11.01.12 regarding Screening Tests.

POLICY GUIDELINES:

It is important to note that because the FDA does not regulate diagnostic tests unless they are sold as kits, companies can market these so-called "home-brew" tests without FDA approval. Laboratories involved in fecal DNA testing are regulated by the Clinical Laboratory Improvement Act (CLIA) regulations of the FDA.

DESCRIPTION:

Colorectal cancer is the third most frequently diagnosed caner in the USA. Screening for colorectal cancer lowers both the mortality and incidence of the disease and is recommended for people age 50 or older. Interest in screening has increased in recent years but compliance remains low. Colonoscopy, sigmoidoscopy, and double-contrast barium enema are standard tests for neoplasia but are limited by their invasive nature, requirements for trained personnel, cost and acceptance by patients. Tests for fecal occult blood are noninvasive and useful however, the relatively high false-positivity rates and other problems have led to a search for more specific non-invasive tests. In this regard, assays for mutations in fecal DNA are seen as promising. Gene mutations that characterize colorectal neoplasia are detectable in exfoliated epithelial cells in the stool. Whereas neoplastic bleeding is intermittent, epithelial shedding is continual, potentially making fecal DNA testing more sensitive than other methods for screening.

Several genetic alterations have been associated with colorectal cancer. In the proposed multistep model of carcinogenesis, the tumor suppressor gene *p53* and the proto-oncogene K- *ras* are most frequently altered. Mutations in APC (Adenomatous polyposis coli) genes and epigenetic markers (e.g., hypermethylation of specific genes) have also been detected. Colorectal cancer is also associated with DNA replication errors in microsatellite sequences (termed microsatellite instability or MSI) in patients with hereditary nonpolyposis colorectal cancer (HNPCC) and in a subgroup of patients with sporadic colon carcinoma. Since cancer cells are shed into stool, tests have been developed that detect these genetic alterations in the DNA from shed colorectal cancer cells isolated from stool samples. This has been proposed for use in screening two populations of patients for colon cancer:

1. *Known or suspected carriers of HNPCC mutations, considered at high risk of developing colorectal cancer.* In this setting, testing of fecal samples could be used to monitor patients over time for development of colorectal cancer. The test may be used either in lieu of routinely scheduled surveillance colonoscopies or during intervals between scheduled colonoscopies. Those patients testing positive for cancer-related genetic alterations could be further evaluated with colonoscopy.

II. *In patients at average risk of colorectal cancer*. In this setting, testing of fecal samples could be offered in lieu of, or as an adjunct to, other recommended colorectal cancer screening tests, including fecal occult blood testing, flexible sigmoidoscopy, colonoscopy, or double contrast barium enema.

In addition, investigators are beginning to study changes in this assay following surgery for colon cancer.

RATIONALE:

As of June 5, 2008, EXACT Sciences has stopped offering the PreGen-Plus™ test. The ColoSure™ (DNA Direct, Inc., San Francisco, CA), a new version of the fecal DNA testing has been developed which is based on the Vimentin gene, a methylated DNA marker that in published studies was shown to be associated with colorectal cancer. The new test is currently available.

The BCBS Association TEC Special Report (2006) noted that fecal DNA testing is a noninvasive colorectal cancer screening technology that may eventually offer sensitivity for cancer closer to that of colonoscopy than that of conventional, guaiac-based FOBTs. The report commented about a newer version of the PreGen-Plus™ test that had been developed and indicated that information is needed about the performance characteristics of this new configuration. The report noted that several important questions remain before fecal DNA screening can be widely recommended. These questions include the following:

I. Can sensitivity for large adenoma be significantly increased compared to FOBT?
II. Can false-positive rates be maintained appropriately low for a screening program?
III. What is the final configuration of the PreGen-Plus test and what are its published performance characteristics in an average-risk screening population?
IV. What is the optimal screening interval?
V. Which patients should not be screened with fecal DNA testing?
VI. Does the test improve compliance with colorectal cancer screening?

Screening and Surveillance for the Early Detection of Colorectal Cancer and Adenomatous Polyps, 2008: A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology (Levin et al.) have noted the benefits of fecal analysis of DNA for colorectal cancer screening and surveillance include the fact that the test is noninvasive, causes no physical harm to the patient, appears to be accepted by both patients and providers, is not dependent upon the detection of occult bleeding and requires only a single stool sample. The limitations of the test include, but are not limited to the following: (1) Test sensitivity is based on a panel of markers that appear to identify some, but not all colorectal cancers; (2) The cost of the test is significantly higher than the cost of other stool tests; (3) The interval at which the test should be performed is unclear; and (4) The uncertainty around how positive results without evidence of cancer or advanced lesions on follow-up should be interpreted and whether or not these patients require an alternate plan for ongoing surveillance.

A summary of recommendations of colorectal cancer screening by the US Preventative Services Task Force concluded that the evidence is insufficient to assess the benefits and harms of computed tomographic colonography and fecal DNA testing as screening modalities for colorectal cancer.

The National Cancer Institute (NCI) (10/17/08) reports that genetic testing of stool samples is being studied as a possible way to screen for colorectal cancer. The lining of the colon is constantly shedding cells into the stool. Testing stool samples for genetic alterations that occur in colorectal cancer cells may help doctors find evidence of cancer or precancerous growths. Research conducted thus far has shown that this kind of test can detect colorectal cancer in people already diagnosed with this disease by other means. However, more studies are needed to determine whether this type of test can accurately detect colorectal cancer or precancerous polyps in people who do not have symptoms.

CODES: Number Description

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).

CPT: The CPT coding for DNA analysis of stool samples consists of a number of CPT codes describing the individual steps in the DNA analysis and are not specific to fecal DNA analysis.

HCPCS: S3890 **(E/I)** DNA analysis, fecal, for colorectal cancer screening

ICD9: Multiple codes

ICD10: Multiple codes

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KEY WORDS:

Colorectal cancer screening, DNA Analysis, Fecal DNA, Pre-Gen tests.

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a National Coverage Determination (NCD) for Colorectal Cancer Screening Tests. Please refer to the following NCD website for Medicare Members: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=281&ncdver=3&bc=AgAAgAAAAAAA&