Protocol

Analysis of Human DNA in Stool Samples as a Technique for Colorectal Cancer Screening

(20429)

Medical Benefit		**Effective Date**: 03/01/06	**Next Review Date**: 01/15
Preauthorization	No	**Review Dates**: 01/07, 01/08, 01/09, 01/10, 01/11, 01/12, 01/13, 01/14	

The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. ***Preauthorization is not required but is recommended if, despite this Protocol position, you feel this service is medically necessary; supporting documentation must be submitted to Utilization Management.*** *Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

Description

Detection of genetic abnormalities associated with colorectal cancer in stool samples has been proposed as a screening test for colorectal cancer. This technology is another potential alternative to currently available screening approaches such as fecal occult blood testing or colonoscopy.

Background

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 Lynch syndrome (formerly known as hereditary nonpolyposis colorectal cancer or HNPCC) and in a subgroup of patients with sporadic colon carcinoma. Tumor-associated gene mutations and epigenetic markers can be detected in exfoliated intestinal cells in stool specimens. 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 Lynch syndrome 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 could 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.

2. 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.

Several types of tests have been evaluated in studies and some have been marketed. One of these, PreGen-Plus™, tests for 21 different mutations in the *p53*, *APC*, and K-*ras* genes; the BAT-26 MSI marker; and incorporates the DNA Integrity Assay (DIA®). PreGen-Plus™ has not been cleared by the U.S. Food and Drug Administration (FDA). Although the scientific studies that are the basis of the PreGen-Plus™ test were conducted

or funded by EXACT Sciences, LabCorp is identified as the test developer. LabCorp is regulated under the Clinical Laboratory Improvement Amendments (CLIA) of 1988 and is certified as qualified to perform high-complexity testing. As a result, LabCorp may develop tests in-house and offer them as laboratory services (i.e., laboratory-developed tests). Historically, the FDA has not regulated laboratory-developed tests. However, on January 13, 2006, the FDA sent correspondence to LabCorp indicating that PreGen-Plus™ may be subject to FDA regulation as a medical device. As a consequence, and as a result of studies showing better performance of other tests, this test is no longer offered. Exact Sciences is currently seeking FDA premarket approval for its latest automated fecal DNA testing product, Cologuard™.

The currently available test is called ColoSure™, developed by OncoMethylome, which detects aberrant methylation of the vimentin (hV) gene. This test is offered as a laboratory-developed test, not subject to FDA regulation.

Policy (Formerly Corporate Medical Guideline)

DNA analysis of stool samples is considered **investigational** as a screening technique for colorectal cancer in both patients with average to moderate risk, and in patients considered at high risk for colorectal cancer.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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