Corporate Medical Policy

Colorectal Cancer Screening AHS-B0001

File Name: colorectal_cancer_screening
Origination: 3/2019
Last Review: 3/2022

Description of Procedure or Service

Colorectal Cancer

Several cellular genetic alterations have been associated with colorectal cancer (CRC). In the proposed multistep model of carcinogenesis, the tumor suppressor gene *p53* and the proto-oncogene *KRAS* are most frequently altered. Variants in adenomatous polyposis coli genes and epigenetic markers (eg, hypermethylation of specific genes) have also been detected. CRC is also associated with DNA replication errors in microsatellite sequences (termed microsatellite instability) in patients with Lynch syndrome (formerly known as hereditary nonpolyposis CRC) and in subgroups of patients with sporadic colon carcinoma. Tumor-associated gene variants and epigenetic markers can be detected in exfoliated intestinal cells in stool specimens. Because cancer cells are shed into stool, tests have been developed to detect these genetic alterations in the DNA from shed CRC cells isolated from stool samples.

In 2021, the United States Preventive Services Task Force (USPSTF) recommended universal screening for asymptomatic average risk adults aged 45 years or older (B recommendation). Average risk is defined by USPSTF as no prior diagnosis of colorectal cancer, adenomatous polyps, or inflammatory bowel disease; no personal diagnosis or family history of know genetic disorders that predispose them to a high lifetime risk of colorectal cancer such as Lynch syndrome or familial adenomatous polyposis.

Regulatory Status

In 2014, Cologuard™ (Exact Sciences) was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process as an automated fecal DNA testing product (P130017). Cologuard™ is intended for the qualitative detection of colorectal neoplasia associated DNA markers and of occult hemoglobin in human stool. A positive result may indicate the presence of CRC or advanced adenoma and should be followed by diagnostic colonoscopy. Cologuard™ is not a replacement for diagnostic colonoscopy or surveillance colonoscopy in high-risk individuals.

Over the past several years, different stool DNA tests have been evaluated in studies, and some have been marketed. One previously marketed test, PreGen-Plus™ (LabCorp), tests for 21 different variants in the *p53*, adenomatous polyposis coli, and *KRAS* genes; the BAT-26 microsatellite instability marker; and incorporates the DNA Integrity Assay (DIA®). PreGen-Plus™ has not been cleared by FDA. In January 2006, FDA informed LabCorp 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. Another previously marketed test is called ColoSure™ (OncoMethylome Sciences; now MDxHealth), which detects aberrant methylation of the vimentin (*hV*) gene. This test was offered as a laboratory-developed test and is not subject to FDA regulation.

Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

BCBSNC will provide coverage for colorectal cancer screening when it is determined the medical criteria or reimbursement guidelines below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Colorectal Cancer Screening is covered

Reimbursement of colorectal cancer screening with DNA analysis of stool samples is allowed every 3 years as a screening technique in patients at average risk of colorectal cancer.

When Colorectal Cancer Screening is not covered

Reimbursement is not allowed for colorectal cancer screening with DNA analysis of stool samples for all other indications.

Reimbursement is not allowed for screening with DNA analysis of stool samples at an interval of less than 3 years.

Policy Guidelines

There is a specific CPT code for the Cologuard test:

81528 Oncology (colorectal) screening, quantitative real-time target and signal amplification of 10 DNA markers (KRAS mutations, promoter methylation of *NDRG4* and *BMP3*) and fecal hemoglobin, utilizing stool, algorithm reported as a positive or negative result.

Detection of DNA abnormalities associated with colorectal cancer (CRC) in stool samples has been proposed as a screening test for CRC. This technology is another potential alternative to currently available screening approaches such as fecal occult blood testing, fecal immunochemical testing (FIT), and colonoscopy. The currently available stool DNA test combines FIT and DNA analysis and is referred to as FIT-DNA in this review.

For individuals who are asymptomatic and at average risk of CRC who receive FIT-DNA, the evidence includes a number of small studies comparing FIT-DNA (in early stages of development) with colonoscopy, 2 screening studies comparing the final version of the FIT-DNA (using colonoscopy as the reference standard), and modeling studies. Relevant outcomes are overall survival and disease-specific survival. The screening studies have reported that FIT-DNA has higher sensitivity and lower specificity than FIT. There are no studies directly assessing health outcomes such as overall survival or disease-specific survival. The test characteristics of FIT-DNA show the potential of the test to be an effective CRC screening test, but there is uncertainty about other aspects of it. The screening interval for the test has not been firmly established nor is there evidence on the adherence of the test at a recommended screening interval. Effective screening for CRC requires a screening program with established screening intervals and appropriate follow-up for positive tests. Clinical utility of FIT-DNA is based on modeling studies. These studies have demonstrated that the diagnostic characteristics of FIT-DNA are consistent with decreases in CRC mortality that are in the range of other accepted modalities. FIT-DNA every 3 years is less effective than most other accepted screening strategies, while FIT-DNA every year is close to the efficacy of colonoscopy every 10 years. The evidence is

sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 81528

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.29, 11/9/17

Specialty Matched Consultant Advisory Panel 8/2018

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.29, 11/8/18

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.29, 11/8/18

United States Preventive Services Task Force (USPSTF). Colorectal Cancer Screening. 2017. https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/colorectalcancer-screening2
Accessed December 11, 2018.

Medical Director review 2/2019

Specialty Matched Consultant Advisory Panel 8/2019

Specialty Matched Consultant Advisory Panel 8/2020

Specialty Matched Consultant Advisory Panel 8/2021

United States Preventive Services Task Force (USPSTF). Colorectal Cancer Screening. 2021. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/colorectal-cancer-screening

Policy Implementation/Update Information

4/1/19 New policy developed. DNA analysis of stool samples can be considered **medically necessary** as a screening technique for colorectal cancer in patients at average risk of colorectal cancer. Medical Director review 2/2019. Reference added. (lpr)

10/29/19 Wording in the Policy, When Covered, and/or Not Covered section(s) changed from Medical Necessity to Reimbursement language, where needed. (gn)

3/31/20 Specialty Matched Consultant Advisory Panel review 8/21/19. Consultant agreed with the policy. No change to policy intent. Reference added. Medical Director review 8/2019 with CAP. (lpr)

9/8/20 Specialty Matched Consultant Advisory Panel review 8/19/2020. No change to policy statement. (lpr)

9/7/21 Specialty Matched Consultant Advisory Panel review 8/18/2021. No changes to policy statement. (lpr)

3/4/22 Description section updated with USPSTF reference for screening average risk adults aged 45 or older. Reference added. (lpr)