Fecal DNA Test for Colorectal Cancer

Policy Number: HS-040

Original Effective Date: 8/21/2008


APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

DISCLAIMER

The Clinical Coverage Guideline (CCG) is intended to supplement certain standard WellCare benefit plans. The terms of a member’s particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member’s benefit plan may contain specific exclusions related to the topic addressed in this CCG. When a conflict exists between the two documents, the Member’s Benefit Plan always supersedes the information contained in the CCG. Additionally, CCGs relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. The application of the CCG is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any. All links are current at time of approval by the Medical Policy Committee (MPC). Lines of business (LOB) are subject to change without notice; current LOBs can be found at www.wellcare.com – select the Provider tab, then “Tools” and “Clinical Guidelines”.

BACKGROUND

Colorectal cancer (CRC) is the second leading cause of cancer death, and accounts for approximately 9 percent of cancer deaths and 3 percent of total deaths. Approximately one in three people diagnosed with CRC die of this disease in the five years after diagnosis. Removal of premalignant adenomas can prevent the cancer and removal of localized cancer may prevent CRC-related death. Multiple test options are available for screening to detect either early-stage cancer or precancerous polyps. Test options have complementary strengths and weaknesses in the attributes of an ideal test: sensitivity and specificity, evidence of effectiveness, effect size, convenience, safety, availability, and cost. No one test is best in all these dimensions.

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Fecal deoxyribonucleic acid (DNA) screening is performed on stool samples that are submitted to a laboratory after being collected by patients at home or at an outpatient clinic. A single, entire bowel movement (minimum of 30 grams) is collected from the patient. DNA is extracted and purified from 4 to 10 grams of stool by homogenization, centrifugation to remove debris, enzymatic digestion of contaminating proteins, extraction of contaminants with organic solvent, precipitation of nucleic acids with alcohol, re-suspension, digestion of contaminating ribonucleic acid (RNA) with ribonuclease, and specific capture of target DNA sequences with complementary DNA sequences attached to magnetic beads. The purified DNA is then selectively amplified by polymerase chain reaction (PCR), an enzymatic process that requires a separate amplification reaction and two sequence-specific DNA primers for each gene being analyzed. Finally, mutations in the amplified DNA are detected by gel electrophoresis and solid-phase DNA sequencing. Patients with a positive fecal DNA test result then undergo definitive testing for colon cancer, such as colonoscopy.2

Results of feasibility studies and moderate to large clinical trials indicate that fecal DNA testing can detect precancerous and cancerous colorectal lesions with moderate to high accuracy, especially when multiple mutations and DNA abnormalities are assessed. However, the evidence is too limited to fully evaluate diagnostic performance and, to date, no clinical trials have evaluated the impact of fecal DNA testing on patient management or CRC-related mortality. Likewise, there have been no published studies that specifically evaluate fecal DNA testing as a means to monitor the development of CRC in patients with known or suspected HNPCC. No definitive patient selection criteria can be established for the detection of CRC by fecal DNA testing, and no health benefit has been proven.2

**Cologuard**

Cologuard is a noninvasive, multitarget fecal DNA test for the qualitative detection of colorectal neoplasia-associated DNA markers in addition to the presence of occult hemoglobin in stool. A clinician must prescribe the test, but the sample is collected by the patient at home and shipped to a specified laboratory via prepaid mailer. Cologuard™ is not a replacement for diagnostic colonoscopy or surveillance colonoscopy in people at high risk for CRC. It is FDA indicated for screening in adults ≥ 50 years of age, which means that it should be used only in people who have no signs or symptoms of CRC and who have no risk factors associated with development of the disease. Patients with a positive Cologuard™ result should be referred for diagnostic colonoscopy.2 Genetic mutations and epigenetic changes acquired during carcinogenesis can be detected in the stool from DNA shed by colorectal neoplasms. Cologuard combines testing stool for DNA mutations and methylation markers using a gene amplification technique and testing for hemoglobin with an FIT. Cologuard has been approved by the US Food and Drug Administration (FDA) in August 2014 as a screening test for colorectal carcinoma to be followed, when abnormal, by diagnostic colonoscopy.1

**ColoVantage**

ColoVantage® is a convenient blood test that aids in the detection of colorectal cancer in patients non-adherent to current testing approaches. This test detects methylated Septin9 DNA, a proven marker of the presence of colorectal cancer that has been validated in multiple studies. In a clinical validation study, ColoVantage achieved an overall 70% sensitivity and 89% specificity. ColoVantage has successfully detected cancer at all stages. Patients who test positive for methylated Septin9 should be further evaluated for the presence of colorectal cancer.4

Colorectal cancer treated in localized, early stages has a five-year survival rate of 90 percent.2 Yet, only 40 percent of cases3 are diagnosed in early stages, due to low screening rates. Colonoscopy, the "gold standard" for colorectal cancer screening, has >95% sensitivity and 90% specificity4 and should be offered first when medically possible. However, approximately half of all Americans aged 50 and over do not have any colorectal cancer screening. Patients resist or delay colonoscopy most often because of unpleasant preparation, economic challenges, fear of pain, procedural risk, embarrassment and concerns about anesthesia. Fecal tests are an option for patients unable or unwilling to do colonoscopy and are recommended yearly for screening eligible patients. These tests have a sensitivity range of 56% to 91% and specificity of 83% to 98%.6 Patients also resist these tests due to unpleasant specimen collection. ColoVantage does not require any dietary restrictions or special patient preparation and can be added to routine blood work. The blood can be drawn at any time of day.4
Centers for Medicare and Medicaid Services and the FDA. As of October 2014, the Centers for Medicare and Medicaid Services (CMS) include coverage for this test once every three years for asymptomatic Medicare beneficiaries age 50 to 84 years at average risk for CRC. This marked the first time that the Food and Drug Administration (FDA) and CMS concurrently reviewed a medical device under the FDA-CMS Parallel Review joint pilot program. The FDA granted approval for Colorguard™ in August 2014.

United States Preventive Services Task Force (USPSTF). In 2016, the USPSTF updated their previous recommendation to include screening for colorectal cancer starting at age 50 years and continuing until age 75 years. The decision to screen for colorectal cancer in adults aged 76 to 85 years should be an individual one, taking into account the patient’s overall health and prior screening history. Adults in this age group who have never been screened for colorectal cancer are more likely to benefit. Screening would be most appropriate among adults who 1) are healthy enough to undergo treatment if colorectal cancer is detected and 2) do not have comorbid conditions that would significantly limit their life expectancy.

Additional Professional Organizations. The statement is further supported by the National Cancer Institute and the American Society for Gastrointestinal Endoscopy. According to the American College of Gastroenterology, fecal DNA testing should not be used as the primary source of colorectal cancer detection due to cost factors. When testing is done, it should be done no more than every three years. The ACG and Burt et al. also state the need for more research on how to treat patients testing positive using a fecal DNA test and have a negative colonoscopy. Burt et al. explain that “stool tests are less likely to detect adenomatous polyps for cancer prevention…[and] sensitivity can be limited by inadequate specimen collection or suboptimal processing and interpretation, and is significantly lower than for structural tests”. However, this type of screening offers individuals a noninvasive method to test for colorectal cancer for those who refuse or cannot undergo a traditional colonoscopy. There are currently no position statements or guidelines by any of the national medical organizations.

POSITION STATEMENT

Applicable To:

☑ Medicaid – Hawaii
☑ Medicare – California (Easy Choice Health Plan), Hawaii

NOTE: For other lines of business, please defer to applicable vendor criteria for authorizations.

Exclusions

Fecal DNA testing for colorectal cancer using tests other than Cologuard™ (e.g., PreGen-Plus™) or ColoVantage is considered experimental and investigational and not a covered benefit.

Coverage

Fecal DNA testing using Cologuard™ or ColoVantage is considered medically necessary when the following are met:

- Member is age 50 to 85 years; AND,
- Member is asymptomatic (no signs or symptoms of colorectal disease including but not limited to lower gastrointestinal pain, blood in stool, positive guaiac fecal occult blood test or fecal immunochemical test); AND,
- Member is at average risk of developing colorectal cancer (no personal history of adenomatous polyps, colorectal cancer, or inflammatory bowel disease, including Crohn’s Disease and ulcerative colitis; no family history of colorectal cancers or an adenomatous polyp, familial adenomatous polyposis, or hereditary nonpolyposis colorectal cancer).

NOTE: Testing is limited to once every three years.
FECAL DNA TEST FOR COLORECTAL CANCER
HS-040

CODING

Covered CPT® Code
81401 Molecular Pathology Procedure Level 2
81327 SEPT9 (Septin9) (eg, colorectal cancer) methylation analysis
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

Covered HCPCS Code
S3890* DNA Analysis, fecal for colorectal cancer screening
*S- Codes are NON COVERED FOR MEDICARE Deleted 1/1/2016

Non-Covered CPT® Code
81479 Unlisted molecular pathology procedure when specified as stool DNA analysis for colorectal cancer screening other than Cologuard

Covered ICD-10-CM Diagnosis Code
Z12.11 Encounter for screening for malignant neoplasm of colon
Z12.12 Encounter for screening for malignant neoplasm of rectum


REFERENCES


MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

<table>
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<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>3/2/2017</td>
<td>Approved by MPC. Inclusion of coverage of screening tests (CPT 81387 ColoVantage).</td>
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<tr>
<td>3/5/2015</td>
<td>Approved by MPC. Inclusion of CMS NDC stating coverage for Cologuard under Medicare Part B.</td>
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<td>10/2/2014, 9/5/2013, 9/6/2012</td>
<td>Approved by MPC. No changes.</td>
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<tr>
<td>12/1/2011</td>
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