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

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Policy Number: 557
BCBSA Reference Number: 2.04.29
NCD/LCD: Decision Memo for Screening for Colorectal Cancer - Stool DNA Testing (CAG-00440N)

Related Policies
None

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Cologuard, a multitarget stool DNA test, is considered MEDICALLY NECESSARY as a colorectal cancer screening test for asymptomatic, average risk patients who meet all of the following criteria:

- Age 50 to 85 years, AND
- 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
- 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 adenomatous polyps, familial adenomatous polyposis, or hereditary nonpolyposis colorectal cancer).

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

Decision Memo for Screening for Colorectal Cancer - Stool DNA Testing (CAG-00440N)
Prior Authorization Information

Inpatient
- For services described in this policy, precertification/preauthorization is required for all products if the procedure is performed inpatient.

Outpatient
- For services described in this policy, see below for products where prior authorization might be required if the procedure is performed outpatient.

<table>
<thead>
<tr>
<th>Outpatient</th>
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<tbody>
<tr>
<td><strong>Commercial Managed Care (HMO and POS)</strong></td>
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<tr>
<td>Prior authorization is not required.</td>
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<tr>
<td><strong>Commercial PPO and Indemnity</strong></td>
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<td>Prior authorization is not required.</td>
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<tr>
<td><strong>Medicare HMO Blue℠</strong></td>
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<td>Prior authorization is not required.</td>
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<tr>
<td><strong>Medicare PPO Blue℠</strong></td>
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<td>Prior authorization is not required.</td>
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CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The above medical necessity criteria must be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

<table>
<thead>
<tr>
<th>CPT Codes</th>
<th>Code Description</th>
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<tr>
<td><strong>81528</strong></td>
<td>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</td>
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DESCRIPTION

Colorectal Cancer
Several cellular genetic alterations have been associated with 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 the stool, tests have been developed to detect these genetic alterations in the DNA from shed CRC cells isolated from stool samples.

Summary
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, two screening studies comparing the final version of the FIT-DNA (using colonoscopy as the reference standard), and modeling studies. The 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 three years is less effective than most other accepted screening strategies, while FIT-DNA every year is close to the efficacy of colonoscopy every ten years. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

**Policy History**

<table>
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<th>Date</th>
<th>Action</th>
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<tr>
<td>1/2018</td>
<td>New references added from BCBSA National medical policy.</td>
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<td>12/2016</td>
<td>New references added from BCBSA National medical policy.</td>
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<td>1/2016</td>
<td>Clarified coding information.</td>
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<tr>
<td>12/2014</td>
<td>New references added from BCBSA National medical policy.</td>
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<td>2/2014</td>
<td>New references added from BCBSA National medical policy.</td>
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**Information Pertaining to All Blue Cross Blue Shield Medical Policies**

Click on any of the following terms to access the relevant information:
- Medical Policy Terms of Use
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines

**References**


Endnotes

1 Based on Medicare Decision Memo for Screening for Colorectal Cancer - Stool DNA Testing (CAG-00440N)