MASSACHUSETTS

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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 (For Plan internal use only)

Related Policies

None

Policy[1]

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

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

- Age 45 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 individuals with average to moderate risk and individuals considered at high risk for colorectal cancer, is **INVESTIGATIONAL**.

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**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **not required**.
Commercial PPO and Indemnity	Prior authorization is **not required**.

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:

CPT Codes

CPT codes:	Code Description
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

The following CPT code is considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
0464U	Oncology (colorectal) screening, quantitative real-time target and signal amplification, methylated DNA markers, including LASS4, LRRC4 and PPP2R5C, a reference marker ZDHHC1, and a protein marker (fecal hemoglobin), utilizing stool, algorithm reported as a positive or negative result
0501U	Oncology (colorectal), blood, quantitative measurement of cell- free DNA (cfDNA)

The following HCPCS code is considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

HCPCS Codes

HCPCS codes:	Code Description
G0327	Colorectal cancer screening; blood-based biomarker

DESCRIPTION

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 the stool, tests have been developed to detect these genetic alterations in the DNA from shed CRC cells isolated from stool samples.

Summary

Description

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, though other publications also use the terms stool DNA (sDNA)-FIT and multitarget stool DNA (mt-sDNA).

Summary of Evidence

For individuals who are asymptomatic and at average risk of colorectal cancer (CRC) who receive fecal immunochemical testing (FIT) -DNA, the evidence includes a number of small studies comparing FIT-DNA (in early stages of development) with colonoscopy, screening studies comparing the final version of the FIT-DNA (using colonoscopy as the reference standard), 2 systematic reviews of screening studies, 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 an improvement in the net health outcome.

Policy History

Date	Action
10/2024	Clarified coding information.
7/2024	Clarified coding information.
1/2024	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
1/2023	Annual policy review. Minor editorial refinements to policy statements; intent unchanged.
1/2022	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
7/2021	Clarified coding information
1/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
1/2021	Medicare information removed. See MP #132 Medicare Advantage Management for local coverage determination and national coverage determination reference.
1/2020	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
1/2019	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
1/2018	Annual policy review. New references added.
12/2016	Annual policy review. New references added.
1/2016	Clarified coding information.
10/2015	New medically necessary statement added for commercial plans. Effective 10/1/2015.
1/2015	CMS decision memo for screening for colorectal cancer - stool DNA testing (CAG-00440N) added. Clarified coding information. Effective 10/9/2014.

12/2014	Annual policy review. New references added.
2/2014	Annual policy review. New references added.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
7/2011	Reviewed - Medical Policy Group – Hematology and Oncology. No changes to policy statements.
3/21/2011	New policy describing ongoing non-coverage.

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

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Endnotes

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