MEDICAL POLICY

MEDICAL POLICY DETAILS	
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Product Disclaimer	• *If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.* • *If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit.* • *If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.* • *If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.* • *If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.*

POLICY STATEMENT

I. Based upon our criteria and assessment of the peer-reviewed literature, including the recommendations of the American Cancer Society (ACS), the National Comprehensive Cancer Network (NCCN), and the United States Preventive Services Task Force (USPSTF), the following colorectal cancer screening modalities are considered **medically necessary** for individuals aged 45 years or older, who are average risk for colon cancer:
   A. Colonoscopy; or
   B. Fecal occult blood test* (e.g., guiac-based (gFOBT) or immunochemical (FIT)).

   Other screening options include:

   C. Flexible sigmoidoscopy*; or
   D. Virtual colonoscopy (CT colonography)*; or
   E. DNA analysis of stool samples using the Cologuard multi-targeted stool DNA test*.

   *If tests results are positive, then colonoscopy should be performed to complete the screening spectrum.

II. Based upon our criteria and assessment of the peer-reviewed literature, including the ACS guidelines for colorectal cancer screening and the recommendations of the NCCN, colonoscopy is considered **medically necessary** for individuals aged less than 50 years who are at an increased or high risk of colorectal cancer.

III. Based upon our criteria and assessment of the peer-reviewed literature, virtual colonoscopy is considered a **medically appropriate** option for diagnosis of patients:
   A. in whom a conventional endoscopic colonoscopy of the entire colon is incomplete due to an inability to pass the colonoscope proximally. Failure to advance the colonoscope may be secondary to an obstructing neoplasm, spasm,

redundant colon, chronic diverticular disease, extrinsic compression or aberrant anatomy/scarring from prior surgery; or

B. with concurrent medical conditions for whom conventional colonoscopy is contraindicated. Medical contraindications may include, but are not limited to, coagulopathy, intolerance to sedation, aged 80 years or older, and recent (within the last 60 days) myocardial infarction (MI).

IV. Based upon our criteria and assessment of the peer-reviewed literature, blood serum testing for colorectal cancer screening has not been medically proven to be effective and, therefore, is considered **investigational**.

V. Based upon our criteria and assessment of the peer-reviewed literature, including the recommendations of the ACS, the NCCN, and the USPSTF, colorectal cancer screening for adults aged 76 to 85 years should be individualized, taking into account the patient's overall health and prior screening history. The USPSTF does not recommend colorectal cancer screening for adults older than 85 years.

POLICY GUIDELINES

I. Individuals at increased or high risk of colorectal cancer include those with any of the following:
   A. A personal history of colorectal cancer or adenomatous polyps;
   B. A personal history of inflammatory bowel disease (e.g.,ulcerative colitis or Crohn's disease);
   C. A strong family history of colorectal cancer or polyps (*Please refer to Description section*); or
   D. A known family history of a hereditary colorectal cancer syndrome such as familial adenomatous polyposis (FAP) or Lynch syndrome (hereditary non-polyposis colon cancer or HNPCC).

II. **Contraindications** for a virtual colonoscopy include, but are not limited to:
   A. Active Crohn's disease, ulcerative colitis, inflammatory bowel disease or diverticulitis;
   B. Total hip replacement (metal in prosthesis may cause CT scan artifacts);
   C. Recent surgery;
   D. Pregnancy; or
   E. Severe pain or cramps on day of examination.

III. Recommended screening intervals for average risk individuals:

Screening Modality	**Time Interval**
Fecal occult blood test (e.g., guiac-based (gFOBT) or immunochemical (FIT))	Annually
DNA analysis of stool samples using the Cologuard multi-targeted stool DNA test (FIT-DNA)	Every 1- 3 years
Virtual colonoscopy (CT colonography)	Every 5 years
Flexible sigmoidoscopy	Every 5 years; or every 10 years plus FIT annually
Colonscopy	Every 10 years

IV. Recommended screening intervals with colonoscopy for increased or high risk of colorectal cancer:

Risk	**Time Interval**
Personal History: Individuals with 1 or 2 small (less than 1 cm) tubular adenomas with low-grade dysplasia	5 to 10 years after the polyps are removed, depending on family history and other clinical factors
Personal History: Individuals with 3 to 10 adenomas, or a large (at least 1 cm) adenoma, or any adenomas with high-grade dysplasia or villous features	3 years after the polyps are removed; then every 5 years

Personal History: Individuals with more than 10 adenomas on a single exam	Within 3 years after the polyps are removed
Personal History: Individuals with sessile adenomas that are removed in pieces	2 to 6 months after adenoma removal
Personal History: Individuals who have had colon or rectal cancer removed by surgery	Within 1 year after cancer resection (or 1 year after colonoscopy to make sure the rest of the colon/rectum was clear); if normal, repeat in 3 years, and if normal at 3 years, repeat every 5 years thereafter
Personal History: Individuals diagnosed with colon or rectal cancer	At time of colorectal surgery, or if no metastases, 3 to 6 months after surgery
Family History: Colorectal cancer or adenomatous polyps (e.g., high-grade dysplasia, greater than or equal to 1 cm, villous or tubulovillous histology) in any first-degree relative before age 60, or in two or more first-degree relatives at any age (if not a hereditary syndrome)	Age 40, or 10 years before the youngest case in the immediate family, whichever is earlier; then every 5 to 10 years
Family History: Colorectal cancer or adenomatous polyps in any first-degree relative aged 60 or older, or in at least two second-degree relatives at any age	Age 40; intervals the same as average risk
Family history: Lynch syndrome (hereditary non-polyposis colon cancer or HNPCC), or at increased risk of Lynch syndrome based on family history without genetic testing	Age 20 to 25 years, or 10 years before the youngest case in the immediate family; repeat every 1 to 2 years
Familial adenomatous polyposis (FAP) diagnosed by genetic testing, or suspected FAP without genetic testing	Age 10 to 12 years; yearly flexible sigmoidoscopy to look for signs of FAP
Personal History of inflammatory bowel disease: -chronic ulcerative colitis -Crohn's disease	Cancer risk begins to be significant 8 years after the onset of pancolitis (involvement of entire large intestine), or 12 to 15 years after the onset of left-sided colitis; repeat every 1 to 2 years

DESCRIPTION

Screening is the process of looking for cancer or pre-cancer in people who have no symptoms of the disease. Regular colorectal cancer screening is one of the most powerful weapons against colorectal cancer. Excluding skin cancers, colorectal cancer is the third most common cancer diagnosed in both men and women in the United States. Overall, the lifetime risk for developing colorectal cancer is a little less than one in 23 (4.4%) and is slightly lower for women than for men.

Colorectal cancer (CRC) is the second leading cause of cancer death when numbers for both men and women are combined. The death rate (the number of deaths per 100,000 people per year) of colorectal cancer has been dropping for several decades. One reason for this is that, today, colorectal polyps are more often found by screening and removed before they can develop into cancers. However, cohort trends indicate that CRC incidence is decreasing only for persons 55 years or older while there is a trend of finding advanced stage colorectal cancers in an alarming number of people younger than 50.

It can take as many as 10 to 15 years for a polyp to develop into colorectal cancer. Regular screening can prevent many cases of colorectal cancer altogether, by finding and removing certain types of polyps before they have the chance to turn into cancer. Screening can also help find colorectal cancer early, when it is small, has not spread, and is easier to treat.

When colorectal cancer is found at an early stage before it has spread, the five-year relative survival rate is about 90%; however, only about four out of 10 colorectal cancers are found at this early stage. When cancer has spread outside the colon or rectum, survival rates are lower.

Colonoscopy

Colonoscopy is a screening modality that can detect colorectal polyps and cancer. A colonoscopy requires a full bowel preparation. A flexible tube with a tiny camera is inserted through the anus. The inside of the rectum and colon can be viewed for polyps, cancer, and diseases. The colonoscope is about four feet in length and allows the entire colon to be visualized. The exam takes about 30 minutes, and sedation may be necessary. Tissue samples and polyps may be removed and sent to the lab, to determine whether the specimen is cancerous. Although colonoscopy is considered to be the reference standard against which the sensitivity of other colorectal cancer screening tests is compared, complications from the procedure may occur. There may be some discomfort and bloating from the air that is used to inflate the colon during the procedure. There is also potential for the colonoscope to injure the intestinal wall, causing perforation, infection, or bleeding, although this is rare.

Flexible sigmoidoscopy

Flexible sigmoidoscopy is another screening modality that can detect colorectal polyps and cancer. A lighted endoscope with a tiny camera is passed through the rectum and lower part of the colon, allowing the operator to visualize the sigmoid and descending colon on a small monitor screen. The sigmoidoscope is approximately two feet long; consequently, only the lower colon can be visualized. Bowel preparation is necessary prior to the test, which usually takes about 10 to 20 minutes and can be performed without sedation. Small polyps or tissue samples may be removed and sent to the lab to determine whether the specimen is cancerous.

Virtual colonoscopy

Virtual colonoscopy, also known as CT colonography, is a non-invasive imaging technique for examination of the colonic lumen. The test involves the generation of both two-dimensional and three-dimensional views of the colon and rectum using data derived from helical computed tomography, involving thin-section helical computed tomography (CT) to generate high-resolution two-dimensional axial images of the colon. Two- or three-dimensional images, which resemble the endoluminal images obtained with conventional endoscopic colonoscopy, are then reconstructed offline. Virtual colonoscopy has been investigated as an alternative to conventional endoscopic colonoscopy specifically as an alternative screening technique for colon cancer.

While virtual colonoscopy requires a full bowel preparation similar to conventional colonoscopy, no sedation is required, and the examination is less time-consuming. Gas insufflation of the intestine, which may be uncomfortable to the patient, is required, and interpretation of the images is a separate process. When polyps are detected with virtual colonoscopy, treatment requires that the patients undergo a subsequent endoscopic colonoscopy, which may require another bowel preparation.

Multi-targeted stool DNA test

Gene mutations that characterize colorectal neoplasia are detectable in exfoliated epithelial cells in the stool. Whereas neoplastic bleeding is intermittent, epithelial shedding is continual, potentially making fecal DNA testing more sensitive than other methods for screening.

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 KRAS 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 hereditary nonpolyposis colorectal cancer (HNPCC) and in a subgroup of patients with sporadic colon carcinoma. 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.

Fecal occult blood tests (FOBT)

Two types of FOBT are approved by the Food and Drug Administration (FDA) to screen for colorectal cancer: guaiac FOBT (gFOBT) and the fecal immunochemical (or immunohistochemical) test (FIT, also known as iFOBT). With both types of FOBT, stool samples are collected by the patient using a kit, and the samples are returned to the doctor. Guaiac FOBT uses a chemical to detect heme, a component of the blood protein hemoglobin. Because the guaiac FOBT can also detect heme in some foods (e.g., red meat), people have to avoid certain foods before having this test. FIT uses antibodies to detect human hemoglobin protein specifically. Dietary restriction are typically not required for FIT.

Blood serum tests

- Blood serum testing for colorectal cancer screening is currently available. Two examples of blood serum testing include: (1) the Methylated Septin9 DNA plasma assay test (ColoVantage); and (2) the BeScreened-CRC, which tests for three cancer-related, blood-based proteins. The Septin9 assay test has received FDA approval. Although BeScreened-CRC was created in accordance with federal standards for laboratory testing, it is currently not approved by the FDA. As a laboratory developed test (LDT) under the Centers for Medicare and Medicaid Services' (CMS') Clinical Laboratory Improvement Amendments (CLIA), BeScreened-CRC is available for the clinical use and it does not require FDA clearance or approval. This test is intended as a CRC screening test and is not to be regarded as being investigational or for research. There is insufficient clinical evidence to determine the effects of these technologies on health outcomes, and, therefore, the USPSTF does not currently identify blood serum testing as a means for CRC screening. The 2021 American College of Gastroenterology recommendations suggests against the use of Sepint9 for CRC screening; Conditional recommendation, very low-quality of evidence.

RATIONALE

Colonoscopy

In the Updated Evidence Report and Systematic Review for the USPSTF (2016), the diagnostic accuracy of colonoscopy was evaluated by four prospective studies with fair- to good-quality evidence. Comparing colonoscopy with CTC or CTC plus colonoscopy, per-person (or per-lesion) sensitivity for adenomas ≥ 10 mm was 89% to 98%, and per-person sensitivity for adenomas ≥ 6 mm was 75% to 93%. Studies were not designed to assess diagnostic accuracy to detect cancers. There were limited studies with large number of endoscopists that were applicable to community practice. Harms from screening colonoscopy or colonoscopy in asymptomatic persons was estimated at four perforations/10,000 procedures (95% CI, 2-5/10 000) (number of studies = 26) and eight major bleeds/10,000 procedures (95% CI,5-14/10,000) (number of studies = 22). Risk of perforations, bleeding, and other serious harms from colonoscopy increased with age.

In the 2021 USPSTF's Updated Evidence Report and Systematic Review, two large prospective observational studies evaluated the association of obtaining a screening colonoscopy with CRC incidence or mortality. After 24 years of follow up, the one study amongst health professionals (88,902) found that CRC specific mortality rate was lower when one self-reported colonoscopy was reported versus those who had never had a screening colonoscopy (adjusted hazard ratio 0.32 [95% CI, 0.24-0.45]). This study found that screening colonoscopies were associated with lower CRC mortality from both distal and proximal cancers. The other study, which was completed with Medicare beneficiaries (348,025), with shorter follow up found that people age 70-74 years who underwent a screening colonoscopy had a lower 8-year standardized risk of CRC versus those who did not test. There is also more data on colonoscopy harms demonstrating higher estimates of major bleeding than previously described in 2016.

The National Comprehensive Cancer Network (NCCN) notes that colonoscopy is the most commonly employed CRC screening test and the gold standard for average and high risk individuals. There are numerous case controls and cohort studies that support that a colonoscopy has the potential ability to prevent CRC associated morbidity and cancer deaths.

Flexible sigmoidoscopy

In the Updated Evidence Report and Systematic Review prepared for the USPSTF (2016), the effectiveness of screening for flexible sigmoidoscopy (SIG) was evaluated in four randomized, controlled trials. SIG consistently decreased CRC-specific mortality, compared with no screening at 11 to 12 years of follow-up (IRR, 0.73; 95% CI, 0.66-0.82). The

mortality benefit was limited to distal CRC. Only one trial evaluated more than a single round of screening. Variation in referral criteria led to differing rates of follow-up colonoscopy. Applicability to US practice is fair to poor. Flexible sigmoidoscopy is no longer widely used in the United States. Harms from screening flexible sigmoidoscopy were estimated at one perforation/10,000 procedures (95% CI,0.4-1.4/10 000) (number of studies = 16) and two major bleeds/10,000 procedures (95% CI,0.7-4/10 000) (number of studies = 10).

In the 2021 USPSTF's Updated Evidence Report and Systematic Review, the same four randomized control trials from the 2016 review were used. While three of the four trials have published longer term follow up, the conclusion drawn from the new data did not change the conclusions related to screening effectiveness. There were 22 studies (n=5.4 million) that reported serious bleeding complications in people receiving screening colonoscopies, the pooled estimate was 14.6 bleeds per 10,000 procedures (95% CI, 9.4 to 19.9; I^2=99.5%, range of estimates from individual studies 0 to 68.7 bleeds per 10,000).

Virtual colonoscopy

Reformatted software systems for interpretation of virtual colonoscopy have been approved by the FDA. One example is the Viatronix V3D-colon virtual colonoscopy system (Viatronix, Inc., Stonybrook, NY), which was cleared for marketing by the FDA via the Section 510(k) process on April 19, 2004 for use as a screening tool in detecting colon cancer.

Computer-aided detection (CAD) for virtual colonoscopy has not yet received FDA approval.

Results of available studies indicate that CT colonography (CTC) (virtual colonoscopy) can have relatively high sensitivity and specificity for detection of cancerous colorectal lesions that are at least 6-10 mm in diameter, with lower sensitivity for precancerous, smaller, and flat lesions. The sensitivity of CTC in published studies is heterogeneous, varying widely, but improving as polyp size increases. CTC specificity in published studies is homogeneous, also improving as polyp size increases. CTC does not allow for removal of lesions during the procedure, as can be done during conventional colonoscopy. Results from the National CT Colonography Trial, ACRIN-6664 (NCT00084929), which is-an interventional, screening, open-label trial of 2,600 participants who had a CTC followed by their scheduled colonoscopy, showed that, for large adenomas and cancers, the mean (±SE) per-patient estimated sensitivity, specificity, positive and negative predictive values, and area under the receiver-operating-characteristic curve for CT colonography were 0.90±0.03, 0.86±0.02, 0.23±0.02, 0.99±<0.01, and 0.89±0.02, respectively. The sensitivity of 0.90 (i.e., 90%) indicated that CT colonography failed to detect a lesion measuring 10 mm or more in diameter in 10% of patients. The per-polyp sensitivity for large adenomas or cancers was 0.84±0.04. The per-patient sensitivity for detecting adenomas that were 6 mm or more in diameter was 0.78. These findings support and extend previously published data regarding the role of CT colonography in screening patients with an average risk of colorectal cancer.

As CTC requires bowel preparation and bowel insufflation, it is unclear if patient acceptance will be much higher than for conventional colonoscopy. Preliminary evidence suggests that CTC can detect colorectal polyps and tumors in sections of the colon that cannot be evaluated by conventional colonoscopy due to poor bowel preparation, an unsuitable colon configuration, an obstructing neoplasm, or poor patient tolerance. CTC can also detect some extracolonic abdominal disorders that cannot be detected using conventional colonoscopy; however, clinical evidence does not indicate the impact of CTC extracolonic findings on patient management and disease outcomes.

There is no direct evidence as to whether CTC improves health outcomes; nor does the current evidence allow conclusions as to the comparative efficacy of CT colonography and other colon cancer screening techniques.

The USPSTF Final Recommendation Statement: Colorectal Cancer Screening (2016) states the evidence for assessing the effectiveness of computed tomography (CT) colonography is limited to studies of its test characteristics. Computed tomography colonography can result in unnecessary diagnostic testing or treatment of incidental extracolonic findings that are of no importance or would never have threatened the patient's health or become apparent without screening (i.e., overdiagnosis and overtreatment). Extracolonic findings are common, occurring in about 40% to 70% of screening examinations. The USPSTF's Updated Evidence Report and Systematic Review reports that approximately 1.3 to 11.4 percent of examinations have extracolonic findings that necessitate diagnostic follow-up. From empirical evidence to date, it remains unclear whether detection of extracolonic findings represents an overall true benefit (from detection and treatment of clinically significant disease) or harm (from unnecessary diagnostic workup or identification of disease

without clinical intervention). As with other screening strategies, indirect harms from CT colonography can also occur from follow-up colonoscopy for positive findings. Radiation-induced cancer is a potential long-term concern with repeated use of CT colonography. No studies directly measured this risk, but radiation exposure during the procedure seems to be low, with a maximum exposure of about 7 mSv per examination.

Multi-targeted stool DNA test

Cologuard (Exact Sciences, Madison, WI) was approved by the FDA on August 11, 2014. The test includes molecular assays for aberrantly methylated BMP3 and NDRG4 promoter regions, mutant KRAS, β-actin, and an immunochemical assay for human hemoglobin.

The USPSTF Final Recommendation Statement: Colorectal Cancer Screening (2016) stated that multi-targeted stool DNA testing (FIT-DNA) is an emerging screening strategy that combines a FIT with testing for altered DNA biomarkers in cells shed into the stool. Multi-targeted stool DNA testing has increased single-test sensitivity for detecting colorectal cancer, compared with FIT alone. The harm of stool-based testing primarily result from adverse events associated with follow-up colonoscopy of positive findings. The specificity of FIT-DNA is lower than that of FIT alone, which means that it has a higher number of false-positive results and higher likelihood of follow-up colonoscopy, thereby increasing the likelihood of experiencing an associated adverse event per screening test. There are no empirical data on the appropriate longitudinal follow-up for an abnormal FIT-DNA test result followed by a negative colonoscopy; however, there is potential for overly intensive surveillance due to clinician and patient concerns about the implications of the genetic component of the test.

Fecal occult blood test (FOBT)

In the Updated Evidence Report and Systematic Review for the USPSTF (2016), the effectiveness of screening for gFOBT, Hemoccult II was evaluated in five randomized, controlled trials. Biennial screening with Hemoccult II compared with no screening consistently resulted in reduction of CRC-specific mortality, ranging from 9% to 22% after two to nine rounds of screening with 11 to 30 years of follow-up. There was variation in the number of screening rounds, use of rehydrated samples, definition of “test positive,” and recommended diagnostic follow-up.

The prospective diagnostic accuracy of FIT was evaluated by six qualitative and seven quantitative studies. In studies with colonoscopy follow-up for all, FIT sensitivity varied considerably across assays for each outcome. OC-Light had the highest sensitivity and specificity for CRC, from 88% and 91%, respectively, to 79% and 93%, respectively. OC FIT-CHEK had the best sensitivity and specificity for CRC, from 73% and 96%, respectively, to 92% and 87%, respectively. Variation in test performance resulted from the use of 18 different FITs (FIT families), different numbers of stool samples, and, to some extent, different assay cut-off values. Sparse data on most individual tests limited comparisons.

In the 2021 USPSTF’s Updated Evidence Report and Systematic Review, there were six well-conducted trials (n = 780 458) of biennial or annual gFOBT screening that demonstrated a reduction in CRC incidence and mortality. Based on 5 RCTs (n = 419 966) that used intention-to-screen analyses, biennial screening with Hemoccult II (Beckman Coulter) was associated with a reduction of CRC-specific mortality compared with no screening after 2 to 9 rounds of screening at 11 to 30 years of follow-up (relative risk [RR], 0.91 [95% CI, 0.84-0.98] at 19.5 years; RR, 0.78 [95% CI, 0.65-0.93] at 30 years). One additional trial of screening with Hemoccult II in Finland (n = 360 492) reported only interim findings, with a follow-up of 4.5 years.

The NCCN V.2. 2021 guidelines note that there is direct evidence from randomized control trials that low sensitivity guaiac FOBT testing reduces mortality from CRC.

Blood serum test

The first FDA-approved blood serum test for CRC screening is the Sept9 assay (Epigenomics, Seattle, Wash). Methylated Sept9 DNA plasma assay is a blood-based biomarker for CRC screening. In a large screening colonoscopy study, this test had a sensitivity of 48% for detection of CRC and 0% sensitivity for detection of precancerous polyps. The Sept9 assay has markedly inferior performance characteristics compared with FIT, including lower sensitivity for cancer, inability to detect advanced adenomas, and low cost-effectiveness relative to other screening tests. The test appears to have higher sensitivity for late-stage cancer, compared with early-stage cancer. Therefore, the U.S. Multi-Society Task Force of

Colorectal Cancer (MSTF) suggests that Sept9 not be used for colorectal cancer screening. The USPSTF's colorectal cancer screening recommendations included a search for studies to include methylated *SEPT9* DNA blood tests, but the task force concluded that there is limited evidence evaluating use of the test.

The NCCN V.2. 2021 guidelines note that the sensitivity of the Sept9 DNA test for the detection of CRC has been reported to be 68% with a specificity of 80%. Based on current data, the NCCN panel concludes that the interval for repeat testing is unclear. The NCCN will continue to review this strategy and monitor any new emerging data.

The 2021 American College of Gastroenterology recommendations suggests against the use of Sepint9 for CRC screening; Conditional recommendation, very low-quality of evidence.

BeScreened-CRC is a simple, blood-based, CLIA laboratory-developed test for colorectal cancer screening. It is intended only for people aged 50 to 85 years who are at average risk for colorectal cancer or who are unable or unwilling to be screened by colonoscopy or fecal-based tests (with or without DNA). The panel tests three cancer-related, blood-based proteins that are combined into a single positive or negative result that indicates the potential presence of colorectal cancer or precancerous polyps. BeScreened-CRC was created in accordance with federal standards for laboratory testing, but currently does not have FDA approval.

The Epi proColon (EPT9 methylated DNA testing) test has emerged as another potential non-invasive option for the early detection of colorectal cancer. While the Epi proColon test is the only FDA-approved blood-based biomarker test for colorectal cancer screening, there are other blood-based tests in development using different biomarkers. The evidence is insufficient to determine the effects of the technologies on health outcomes.

Urine test:

The 2021 USPSTF's Updated Evidence Report and Systematic Review notes that only one urine based test, testing for various metabolites in the urine, is available for use by CLIA-certified laboratories. There is limited evidence on test accuracy.

The USPSTF (May 2021) updated their guidelines for colorectal cancer screening (Grade B recommendation). The USPSTF recommends screening for colorectal cancer in adults aged 45 to 49 years. This recommendation applies to asymptomatic adults, 45 years or older, who are at average risk of colorectal cancer (i.e., no prior diagnosis of colorectal cancer, adenomatous polyps, or inflammatory bowel disease; no personal diagnosis or family history of known genetic disorders that predispose them to a high lifetime risk of colorectal cancer [such as Lynch syndrome or familial adenomatous polyposis]).

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

- *CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.*
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*

CPT Codes

Code	Description
45346	Sigmoidoscopy, flexible; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed)
45378	Colonoscopy, flexible; diagnostic, including collection of specimens(s) by brushing or washing, when performed (separate procedure)
74261	Computed tomographic (CT) colonography, diagnostic, including image postprocessing; without contrast material
74262	Computed tomographic (CT) colonography, diagnostic, including image postprocessing; with contrast material(s) including non-contrast images, if performed

Code	Description
74263	Computed tomographic (CT) colonography, screening, including image postprocessing
81327 **(E/I)**	SEPT9 (Septin9) (e.g., colorectal cancer) promoter 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
82270	Blood, occult, by peroxidase activity (e.g., guaiac), qualitative; feces, consecutive collected specimens with single determination, for colorectal neoplasm screening (i.e., patient was provided 3 cards or single triple card for consecutive collection)
82274	Blood, occult, by fecal hemoglobin determination by immunoassay, qualitative, feces, 1-3 simultaneous determinations
0163U **(E/I)**	Oncology (colorectal) screening, biochemical enzyme-linked immunosorbent assay (ELISA) of three plasma or serum proteins (teratocarcinoma-derived growth factor-1 [TDGF-1, Cripto-1], carcinoembryonic antigen [CEA], extracellular matrix protein [ECM]), with demographic data (age, gender, CRC-screening compliance) using a proprietary algorithm and reported as likelihood of CRC or advanced adenomas (BeScreened-CRC, Beacon Biomedical)

HCPCS Codes

Code	Description
G0104	Colorectal cancer screening; flexible sigmoidoscopy
G0105	Colorectal cancer screening; colonoscopy on individual at high risk
G0121	Colorectal cancer screening; colonoscopy on individual not meeting criteria for high risk
G0327 **(E/I)**	Colorectal cancer screening; blood-based biomarker *(effective 07/01/2021)*
G0328	Colorectal cancer screening; fecal occult blood test, immunoassay, one to three simultaneous determinations
G9936	Surveillance colonoscopy - personal history of colonic polyps, colon cancer, or other malignant neoplasm of rectum, rectosigmoid junction, and anus
G9937	Diagnostic colonoscopy

ICD10 Codes

Code	Description
C26.0-C26.9	Malignant neoplasm of other and ill-defined digestive organs (code range)
Z12.11	Encounter for screening for malignant neoplasm of colon

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*Key Article

KEY WORDS

Cologuard, CT Colonography, FIT, gFOBT, virtual colonoscopy, fecal DNA, fecal occult blood test, Septin9, ColoVantage, BeScreened-CRC

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a National Coverage Determination (NCD) for Colorectal Cancer Screening Tests. Screening computed tomographic colonography (CTC) is considered non-covered, effective May 12, 2009. Please refer to the following NCD website for Medicare Members: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=281&ncdver=5&bc=AgAAgAAAAQAAAA%3d%3d&

There is currently a Local Coverage Determination (LCD)for CT Colonography for Diagnostic Uses. Please refer to the following LCD website for Medicare Members: https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=33562&ver=26&CntrctrSelected=298*1&Cntrctr=298&s=41&DocType=Active&bc=AggAAAIAgAAA&

There is currently a Proposed Decision Memo for Screening for Colorectal Cancer - Blood-Based Biomarker Tests. Please refer to the following website for Medicare members: www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=Y&NCAId=299 accessed 07/07/22