Colorectal cancer screening

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Policy contains: Colonography; colonoscopy; deoxyribonucleic acid testing; fecal immunochemistry; fecal occult blood test; flexible sigmoidoscopy.

This policy is a Sandhills Center Clinical Coverage Policy adopted from AmeriHealth Caritas of North Carolina. These clinical policies are used to assist with making coverage determinations. Sandhills Center's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Sandhills Center when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Sandhills Center clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Sandhills Center's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Sandhills Center will update its clinical policies as necessary. Sandhills Center clinical policies are not guarantees of payment.

Coverage policy

The following services for colorectal cancer screening are clinically proven and, therefore, medically necessary for average-risk members (i.e., asymptomatic, with no personal history of colorectal cancer, adenomatous polyposis, inflammatory bowel disease, or family history of known genetic disorders that predispose them to a high lifetime risk of colorectal cancer) ages 45 to 75 (National Comprehensive Cancer Network, 2021; U.S. Preventive Services Task Force, 2021; Wolf, 2018):

- Colonoscopy every 10 years.
- Flexible sigmoidoscopy every five years.
- Flexible sigmoidoscopy every 10 years plus fecal immunochemical test every year.
- Fecal immunochemical test with multi-targeted stool deoxyribonucleic acid testing every three years.
- Fecal immunochemical test every year.
- High-sensitivity guaiac-based fecal occult blood test every year.

Virtual colonoscopy every five years is clinically proven and, therefore, medically necessary when any of the following criteria are met (Shaukat, 2021; U.S. Preventive Services Task Force, 2021; Wolf, 2018):

- A conventional colonoscopy is contraindicated due to presence of lower gastrointestinal bleeding, colonic stenosis, colonic obstructions, diverticulosis, or diverticulitis.
- The patient had complications with a prior colonoscopy.
- The patient is taking anti-coagulation medicine or is otherwise at risk for a bleeding disorder.

- The patient has an elevated risk from sedation during a colonoscopy, from conditions such as chronic obstructive pulmonary disease, hypotension from sedation, a recent acute myocardial infarction, recent colonic surgery, or a previous adverse reaction to anesthesia.
- The patient has obstructive colorectal cancer.

Any screening method for colorectal cancer listed above is clinically proven and, therefore, medically necessary for members with any of the following risk factors; age at initial screening and screening interval will depend on the member's risk status (National Comprehensive Care Network, 2021):

- A personal history of colorectal cancer or adenomatous polyps (as often as every year).
- A personal history of inflammatory bowel disease, e.g., ulcerative colitis or Crohn's disease (as often as every year).
- A first-degree relative (sibling, parent, child) with a history of colorectal cancer or adenomatous polyps diagnosed before age 60 (or two first-degree relatives diagnosed at any age); screening may start at age 40 or 10 years before the youngest affected relative, whichever is earlier. Colonoscopy every five years is recommended.
- A single first-degree relative diagnosed with colorectal cancer or an advanced adenoma at age 60 years or older. Tests and intervals are as per the average-risk screening recommendations.
- A known family history of a hereditary colorectal cancer syndrome, e.g., familial adenomatous polyposis or hereditary non-polyposis colon cancer; screening colonoscopy may begin 10 years before the age at diagnosis of the youngest affected relative.

The medical necessity of colorectal cancer screening between the ages of 75 and 84 is a physician-patient decision dependent on the patient's risk status (U.S. Preventive Services Task Force, 2021; Wolf, 2018).

Colorectal cancer screening over age 85 is investigational/not medically necessary, as there is insufficient evidence of a clinical benefit (U.S. Preventive Services Task Force, 2021; Wolf, 2018).

Limitations

All other tests for colorectal cancer screening are considered investigational and, therefore, not medically necessary, including, but not limited to magnetic resonance imaging, wireless colon capsule endoscopy, urine testing, and blood biomarker testing such as the circulating methylated septin 9 deoxyribonucleic acid (SEPT9 DNA) assay (Epi proColon, Epigenomics, Germantown, Maryland) (Mojtabanezhad Shariatpanahi, 2018; Nikolaou, 2018; Sun, 2018; Toiyama, 2018; U.S. Preventive Services Task Force, 2021; Wolf, 2018; Ye, 2018).

For Medicare members only

Colorectal cancer screening is clinically proven and, therefore, medically necessary when administered in accordance with the conditions for and limitations on coverage set forth in 42 CFR 410.37 and National Coverage Determination 210.3 (Centers for Medicare & Medicaid Services, 2021). Virtual colonoscopy is considered not medically necessary for this purpose.

Alternative covered services

No alternative covered services were identified during the writing of this policy.

Background

Colorectal cancer is one of the most commonly diagnosed cancers in the United States, with 149,500 new cases estimated in 2021 (American Cancer Society, 2021). The five-year survival rate for colorectal cancer following diagnosis is 64%. Survival for those cancers considered localized is 90%, and declines to 71% with regional metastasis and 14% for those with distant metastases, illustrating the importance of early detection. The risk of

colorectal cancer rises sharply at middle age, but since the mid-1980s, the overall age-adjusted incidence and mortality rates have declined. These encouraging results are attributed to greater numbers of pre-cancerous polyps being detected and removed after screening, although racial, gender, and geographic disparities persist.

Because blood in the stool is often the only symptom of colorectal cancer, screening can play a useful role in early detection and treatment. According to the Centers for Disease Control and Prevention, colorectal cancer screening rates increased from 2000 to 2015, but still fall short of Healthy People 2020 targets (White, 2017). Since the goals of screening are to maximize the total number of persons who are screened and reduce colorectal cancer deaths, offering choice in colorectal cancer screening strategies may increase screening uptake.

The U.S. Food and Drug Administration (2016) approved the PillCam COLON 2 Capsule Endoscopy System (Given Imaging Ltd, Yoqneam, Illinois) to provide visualization of the colon in patients with previously incomplete colonoscopy or in patients with lower gastrointestinal bleeding. The PillCam 2 is intended for patients who are at high risk for colonoscopy or sedation but who could tolerate colonoscopy and moderate sedation in the event of a positive result on capsule endoscopy. Contraindications include patients with: known or suspected gastrointestinal obstructions, strictures, or fistulas; cardiac pacemakers or other implanted electromedical devices; or swallowing disorders.

Findings

This policy relies heavily on U.S. Preventive Services Task Force screening recommendations. Several U.S. professional societies have developed guidelines for colorectal cancer screening, some by themselves and some as part of a joint effort; they generally align with U.S. Preventive Services Task Force recommendations but may offer preferences for testing based on sensitivity and risk stratification. These organizations include: the American Cancer Society (2018); American College of Physicians (Qaseem, 2012); National Comprehensive Cancer Network (2017); and the U.S. Multi-Society Task Force on Colorectal Cancer, which consists of the American College of Gastroenterology, American Gastroenterological Association, and American Society for Gastrointestinal Endoscopy (Rex, 2017).

There is consensus that screening reduces the incidence and mortality of colorectal cancer. Because the risk of colorectal cancer increases sharply in middle age, guidelines agree that screening should occur between the ages of 50 and 74 for persons at average risk, which is defined as asymptomatic individuals who have no personal or family history of colorectal cancer. Screening between the ages of 75 and 84 is a physician-patient decision dependent on the patient's risk status, and screening over age 85 is not recommended. Screening is considered appropriate starting at an earlier age if the patient has a risk factor such as personal or family history of colorectal cancer, and screening should begin at age 45 for African Americans, who have an elevated risk for the disease compared to other racial and ethnic groups.

Colonoscopy is considered the most efficacious means of diagnosing colorectal cancer, pre-cancerous polyps, or adenomas. A 5% sample of Medicare beneficiaries found that 2.3% were diagnosed with colorectal cancer within 10 years of a negative colonoscopy, resulting in 97.7% specificity (Singh, 2011). The colonoscopy "miss rate" (false negatives) for other disorders of the colon and rectum include polyps of all sizes (28%), adenomas (20%), polyps greater than five millimeters in diameter (9%), and advanced adenomas (11%) (Heresbah, 2008).

Colonoscopy offers the most thorough means of examining the lower intestine; allows the provider to remove any polyps during the same procedure; and, in persons testing negative who show no subsequent symptoms, needs only to be repeated every 10 years. Limits of colonoscopy include the extensive preparation required, the chance of a puncture, sedation risk, disqualification of some patients for medical reasons, surgical risk (including perforation of the colon) for four to eight per 10,000 colonoscopy patients, and patient unwillingness factor (Lin, 2016).

Colonoscopy is also recommended three to six months after colon cancer surgery, for endoscopically resected Stage I, surgically resected Stages II and III, and Stage IV cancers. If this examination is normal, another colonoscopy should be performed in one year to detect metachronous lesions, based on reports of a high incidence of these second cancers. If this examination is normal, the interval before the next examination should be three years (Kahi, 2016).

Flexible sigmoidoscopy has demonstrated effectiveness in detecting colorectal cancer and polyps and reducing mortality. Screening with the procedure every five to 10 years resulted in one fewer colorectal cancer death per 5,000 persons screened in 4.3 years (Tang, 2015), and reduced colorectal cancer mortality by 27% (Lin, 2016), compared to no screening. Screening every five years lowered colorectal cancer incidence by 22% and mortality by 28% (Shroff, 2014). The procedure also reduced distal colorectal cancer incidence by 64% and mortality by 66%, with no reduction in proximal colorectal cancer incidence (Brenner, 2014).

Sigmoidoscopy is able to detect 81.0% to 84.4% of the colorectal cancer cases that colonoscopy does (Schoen, 2012), and when combined with fecal immunochemical test, has reduced colorectal cancer mortality more than sigmoidoscopy alone (Holme, 2014). Colonoscopy reduced colorectal cancer-related mortality 29% more than sigmoidoscopy, but reduction from sigmoidoscopy was 26% greater than fecal occult blood test (Elmunzer, 2015).

Endoscopic approaches like colonoscopy and sigmoidoscopy show a higher detection rate of advanced colorectal neoplasia than do fecal tests (relative risk = 3.21) and are useful in reducing colorectal cancer (Hassan, 2012). They also have a lower rate of participation (relative risk = 0.67), require extensive preparation, and have associated surgical and anesthetic risks, although surgical risk for sigmoidoscopy is lower than that of colonoscopy preparation (flexible sigmoidoscopy and virtual colonoscopy require similar preparation).

Non-endoscopic types of colorectal cancer screening offer certain benefits. Except for virtual colonoscopy, all tests require less extensive preparation, pose no surgical or anesthetic risk, do not disqualify patients due to medical conditions, do not create unwillingness among patients, and cost less. Conversely, non-endoscopic procedures must be performed more frequently, fail to detect as many polyps and cancers as colonoscopy, may involve radiation exposure (virtual colonoscopy), and require a separate colonoscopy if polyps are detected.

Sensitivity and specificity estimates of various non-endoscopic screening methods for detecting colorectal cancer are:

- Fecal immunochemical test alone (Lin, 2016; Imperiale, 2014) — sensitivity 74% (P = .002).
- Fecal immunochemical test-deoxyribonucleic acid (Cologuard®, Exact Sciences, Madison, Wisconsin) (Lin, 2016; Imperiale, 2014) — sensitivity 92% (P = .002); specificity 84%.
- Computed tomography colonography (Pickhardt, 2011) — sensitivity 96%.
- High-sensitivity guaiac-based fecal occult blood test (Lin, 2016) — sensitivity 62 to 79%; specificity 87 to 96%.
- Screening stool deoxyribonucleic acid testing (Yang, 2013) — sensitivity 76%; specificity 88%.
- Wireless colon capsule endoscopy for detecting polyps > 10 mm in diameter (Spada, 2016):
    - First generation — sensitivity 95%; specificity 97%;
    - Second generation — sensitivity 87%; specificity 54%.

The ability of these screening modalities to detect non-cancerous lesions varies significantly. Fecal immunochemical test appears to be effective in detecting colorectal cancer, with a diagnostic accuracy of 95% (Lee, 2014), but is less efficacious for identifying adenomas (Niedermaier, 2016). Fecal immunochemical test is able to detect adenomas greater than six mm in diameter 73% to 88% of the time; adding multi-target deoxyribonucleic acid screening to fecal immunochemical test raises this figure to 92% (Lin, 2016) and a lower proportion of false positives (Imperiale, 2014).

For a range of adenomas and sessile polyps, adding multi-targeted fecal deoxyribonucleic acid to fecal immunochemical test significantly improved detection rates over fecal immunochemical test alone (Imperiale, 2014):

- Advanced precancerous lesions, 42.4% versus 23.8% ($P < .001$), respectively.
- Polyps with high-grade dysplasia, 69.2% versus 46.2% ($P = .004$).
- Serrated sessile polyps measuring at least one centimeter, 42.4% and 5.1% ($P < .001$).

Among participants with nonadvanced or negative findings, specificities with deoxyribonucleic acid testing and fecal immunochemical test were 86.6% and 94.9%, respectively, ($P < .001$), and among those with negative results on colonoscopy, specificities were 89.8% and 96.4%, respectively, ($P < .001$). The numbers of persons who would need to be screened to detect one cancer were 154 with colonoscopy, 166 with deoxyribonucleic acid testing, and 208 with fecal immunochemical test (Imperiale, 2014). For advanced adenocarcinoma in high-risk groups, the sensitivity and specificity of screening stool deoxyribonucleic acid testing were 68% and 92%, respectively; corresponding numbers were lower for average-risk persons (Yang, 2013).

Fecal immunochemical test is superior to fecal occult blood test for screening colorectal cancer (Rabeneck, 2012). A meta-analysis of average-risk patients in 11 randomized and cohort trials found that fecal immunochemical test detected two to three times more advanced colorectal neoplasms than fecal occult blood test (Zhu, 2010). Fecal immunochemical test had a 16% greater adherence to screening, and approximately double the rate of detection of advanced neoplasia (relative risk = 2.28) and cancer (relative risk = 1.96) than did fecal occult blood test (Hassan, 2012).

Biennial fecal occult blood test tests have been associated with a 22% reduced risk of colorectal cancer 30-year mortality (Lin, 2016). Compared to controls, fecal occult blood test reduced colorectal cancer mortality 18%, less than the 26% reduction for those undergoing sigmoidoscopy (Fitzpatrick-Lewis, 2016). Among types of fecal occult blood test products, OC-Sensor® (Somagen™ Diagnostics, Edmonton, Alberta, Canada) has greater sensitivity and specificity (87% and 93%, respectively) than does hemoccult (47% and 93%, respectively) (Launois, 2014).

In a review of 20 studies, screening stool deoxyribonucleic acid sensitivity and specificity were 76% and 88% for colorectal cancer, and 68% and 92% for advanced adenocarcinoma in high-risk groups, respectively; corresponding numbers were lower for non-risk persons screened (Yang, 2013). Fecal deoxyribonucleic acid testing alone has proven cost effective versus no screening, but not cost-effective versus all other screening alternatives (Skally, 2013). However, the cost-effectiveness may be more favorable if fecal deoxyribonucleic acid testing can capture more of the eligible population and improve adherence to colorectal cancer screening.

In persons over age 55 with symptoms suggestive of colorectal cancer, barium enema detected colorectal cancer in 5.6% of persons screened, significantly lower than the 7.3% mark for computed tomography colonography. The 2.2% detection rate of barium enema to detect large polyps was also lower than the 3.6% figure for virtual colonoscopy (Halligan, 2015).

Each approach to colorectal cancer screening has demonstrated a benefit. The table below lists model-estimated life-years gained per 1,000 persons screened, based on screening individuals between ages 50 and 75, plus appropriate follow-up for the remainder of the patient's life span (U.S. Preventive Services Task Force, 2017):

Screening method and frequency	**Life-years gained per 1,000**
Colonoscopy every 10 years	270
Fecal immunochemical test-deoxyribonucleic acid every year	261
Flexible sigmoidoscopy every 10 years plus	256

fecal immunochemical test every year

Virtual colonoscopy every five years	248
High-sensitivity guaiac-based fecal occult blood test every year	247
Fecal immunochemical test every year	244
Fecal immunochemical test-deoxyribonucleic acid every three years	226
Flexible sigmoidoscopy every five years	221

The U.S. Preventive Services Task Force (2017) recommends any of the above tests without preference, acknowledging there is no “one size fits all” approach to colorectal cancer screening. Each testing strategy has varying levels of evidence supporting their effectiveness, and different strengths and limitations. The U.S. Preventive Services Task Force seeks to provide clinicians and patients with the best possible evidence about all screening methods to enable informed, individual decision making. In their 2017 update, they added fecal immunochemical test-deoxyribonucleic acid testing to their list of recommended screening strategies at a testing interval of every one to three years, with follow-up colonoscopy for positive results.

Several professional organizations have revised their guidance for colorectal cancer screening to improve screening rates, particularly where access to screening colonoscopy is limited (American Cancer Society, 2018; National Comprehensive Cancer Network, 2017; Rex, 2017). All agree that offering multiple screening options may improve screening rates and detection. There is no consensus on whether presenting all options at once or sequentially with colonoscopy as the first choice, or using a risk-stratified approach that further stratifies the average-risk population, should be used (Rex, 2017). Several organizations now include fecal immunochemical test-deoxyribonucleic acid testing every three years as an option for persons of average risk.

In 2018, the National Cancer Comprehensive Network updated its guideline on colorectal cancer screening. The use of the fecal immunochemical test is increasing because of its superior test performance relative to the well-established fecal occult blood test, patient preference for a less invasive procedure, and availability of testing alternatives; the higher participation rate associated with fecal immunochemical testing complements the higher advanced neoplasia detection rate of endoscopic strategies (Robertson, 2017). Both the National Cancer Comprehensive Network (2018) and the U.S. Preventive Services Task Force (2017) offer a combined screening strategy of flexible sigmoidoscopy every 10 years plus fecal immunochemical test every year based on an improved colorectal cancer–specific mortality benefit with combined testing than with flexible sigmoidoscopy alone. The policy was modified with this addition.

Epidemiological trends showing a marked increase in colorectal cancer incidence—particularly rectal cancer—and subsequent premature mortality among individuals below age 50, the age at which screening is typically offered, has prompted the American Cancer Society to update recommendations for screening of average risk individuals (Wolf, 2018). Their analyses included an evidence synthesis and three simulation modeling studies commissioned for the U.S. Preventive Services Task Force guideline (2017) and another simulation modeling study of the potential benefit (life-years gained and colorectal cancer deaths averted) and burden of different screening strategies for black and white women and men.

The new analyses demonstrated a favorable benefit-to-burden balance for initiating screening earlier with an expected reduction in colorectal cancer mortality and incidence (Meester, 2018; Peterse, 2018). Based on these findings, the American Cancer Society recommends that all adults at average risk start colorectal cancer screening at age 45 years using either a high-sensitivity stool based test or a structural (visual) examination, depending on patient preference and test availability (Wolf, 2018). Lowering the starting age is expected to benefit the segments of the population who suffer disproportionately from the disease—blacks, Alaska Natives,

and American Indians—as well as those individuals otherwise considered to be at average risk. The policy was modified to reflect this change. The policy ID was changed from CP# 08.01.09 to CCP.1319.

In 2019, we added four meta-analyses that found insufficient evidence supporting the value of fecal deoxyribonucleic acid methylation (Mojtabanezhad Shariatpanahi, 2018), magnetic resonance imaging (Sun, 2018), micro-ribonucleic acid biomarkers (Toiyama, 2018), or fecal calprotectin (Ye, 2018) as screening tools for colorectal cancer. Two systematic reviews and meta-analyses ((de Klerk, 2018; Imperiale, 2018) examined the diagnostic performance of fecal immunochemical testing and the factors affecting screening performance. Accurate screening detection depended on the threshold for a positive result (10 microg/g versus 20 microg/g) and disease state (detection of colorectal cancer versus advanced adenomas), with the highest sensitivity demonstrated at lower positivity thresholds for detection of colorectal cancer; accurate detection of adenomas was low, regardless of threshold (Imperiale, 2019).

Multiple risk factors known at the time of screening can increase the risk of false results (de Klerk, 2018). Use of non-steroidal anti-inflammatory drugs was associated with a higher risk for false positive results, while male gender, family history of colorectal cancer, hyperglycemia, hypertension, obesity, and positive smoking history were associated with a higher risk for false negative results. Age had no effect on either false-positivity or false-negativity. This information can inform the choice of optimal screening method and surveillance in populations at risk of false fecal immunochemical test results, but these new findings warrant no policy changes.

In 2020, there is continued interest in identifying noninvasive tests suitable for screening. We updated the National Comprehensive Cancer Network (2019) guideline on colorectal cancer screening and added a comprehensive systematic review (Nikolaou, 2018; n = 51 included studies) of blood biomarkers for colorectal cancer screening. The review noted a lack of well-designed studies and follow-up studies for many candidate markers comprising nucleic acids, cytokines, antibodies, and proteins in asymptomatic populations. The best studied blood biomarker was methylated SEPT9 DNA, which showed highly variable sensitivities ranging from 48.2% to 95.6% and specificities from 80% to 98.9%. The new information is consistent with the current policy and no policy changes are warranted.

In 2021, we updated the guidelines from the U.S. Preventive Services Task Force (2021, update of Rex, 2017), American Cancer Society (2020, update of 2018), the National Comprehensive Cancer Network (2021, update of 2020), and the American College of Gastroenterology (Shaukat, 2021). We consolidated the coverage statements listing medically necessary screening tests and modified the coverage statement for members at increased risk for colorectal cancer, based on recommendations of the National Comprehensive Care Network (2021) and the U.S. Preventive Services Task Force (2021).

We added a separate coverage statement for Medicare members based on 42 CFR § 410.37 and National Coverage Determination 210.3 (Centers for Medicare & Medicaid Services, 2021) to reflect the differences in coverage between the Medicaid and Medicare populations. Three main differences that apply to the Medicare population are: the initial age for screening average risk populations (still age 50); noncoverage of virtual colonoscopy; and coverage for blood-based biomarker testing when specific criteria are met.

The American College of Gastroenterology issued a conditional recommendation for wireless colon capsule endoscopy as a screening modality every five years for individuals unable or unwilling to undergo the other recommended screening tools (Shaukat, 2021). The recommendation is based on very low-quality evidence, their rationale being that as a screening modality, colon capsule endoscopy could guide the decision to perform a colonoscopy in high-risk populations or in patients who refuse colonoscopy, assuming no contraindications to the procedure.

Two systematic reviews analyzed the screen detection rate of capsule endoscopy compared to colonoscopy in fecal immunochemical test-screened populations and as a primary screening modality. In 1,898 fecal immunochemical test-positive patients, the sensitivity and specificity of second-generation capsule endoscopy

were 83% to 90% and 75% to 95%, respectively, for polyps at least six millimeters in size (Kjølhede, 2020). In another systematic review (Vuik, 2021) of five studies, the sensitivity and specificity of capsule endoscopy as a primary screening modality was 79 % to 96 % and 66 % to 97 %, respectively, for polyps larger than six millimeters. In both analyses, no capsule endoscopy-related adverse events occurred, but inadequate bowel preparation and a high rate of incomplete investigations limited the findings.

The advantages of colon capsule endoscopy is its minimal invasiveness, no sedation requirement, and the ability of the newer generation tests to be done at home. However, it still requires bowel preparation, and the optimal repeat interval has not been determined. As with the other noncolonoscopic screening options, a positive test would require colonoscopic confirmation and a robust quality assurance program to ensure that follow-up colonoscopy is performed. Additional research is needed to determine the effectiveness and relative cost-effectiveness of screening capsule endoscopy on important outcomes such as disease-specific mortality, especially in high-risk populations. No other policy changes are warranted.

References

On April 15, 2021, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “Colorectal Neoplasms” (MeSH), “Early Detection of Cancer” (MeSH), “colorectal cancer screening,” “fecal DNA,” “fecal occult blood test,” “fecal immunochemical test,” and “double contrast barium enema.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

3/2017: initial review date and clinical policy effective date: 4/2017

6/2018: Policy references updated. Policy changed per guideline recommendations, and policy ID changed.

6/2019: Policy references updated.

6/2020: Policy references updated.

7/2021: Policy references updated. Coverage modified. Medicare coverage added.