

## Clinical Policy: DNA Analysis of Stool to Screen for Colorectal Cancer

Reference Number: CP.MP.125

Date of Last Revision: 06/21

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### Description

Cologuard is a noninvasive screening test for colon cancer. This test comprises a multi-target screen for several aberrant DNA markers of colon cancer, as well as a hemoglobin immunoassay. This policy describes the medical necessity requirements for DNA analysis of stool with Cologuard.

### Policy/Criteria

- I. It is the policy of health plans affiliated with Centene Corporation® that screening for colorectal cancer by DNA analysis of stool (i.e., Cologuard) is **medically necessary** every one to three years when meeting the following:
  - A. Age 45-85 years;
  - B. Asymptomatic and at average risk for colon cancer;
  - C. Is not within the standard interval of another screening test for colon cancer.
- II. It is the policy of health plans affiliated with Centene Corporation that current research does not support the use of DNA analysis of stool (i.e., Cologuard) for any circumstances other than those specified above.

### Background

Colorectal cancer is the third leading cause of cancer death for both men and women.<sup>3</sup> Multi-target stool testing for colorectal cancer is a noninvasive DNA test that screens for multiple lesions, including those related to *Kras* mutations, *NDRG4* and *BMP3* methylations, *β-actin*, and hemoglobin immunoassay.<sup>1</sup> The FDA approved Cologuard (Exact Sciences) based on this multi-target stool testing.<sup>2</sup> The sensitivity for detecting colorectal cancer from the multi-target DNA testing was 92.3% (60 of 65) and 73.8% (48 of 65) with fecal immunohistochemical tests (FIT), which look for intact human hemoglobin. Multi-target DNA testing is not a replacement for diagnostic colonoscopy testing in patients at high risk for colorectal cancer.

#### *American Cancer Society*

2018 Guidelines by the ACS give a qualified recommendation for screening for colorectal cancer starting at age 45 in average risk adults. A qualified recommendation “indicates there is clear evidence of benefit of screening but less certainty about the balance of benefits and harms, or about patients’ values and preferences, which could lead to different decisions about screening.” The ACS gives a strong recommendation that colorectal cancer screening be performed in adults aged 50-75, and a qualified recommendation for adults aged 76-85.<sup>6</sup>

#### *United States Preventative Services Task Force (USPSTF)*

The USPSTF recommends screening all adults age 45-75 years for colorectal cancer. According to this recommendation, the specificity of FIT-DNA is lower than that of FIT alone, and has a higher number of false-positive results, as well as a higher likelihood of follow-up colonoscopy

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and associated adverse events per screening test.<sup>3</sup> In addition, there is insufficient evidence about appropriate longitudinal follow-up of abnormal findings after a negative follow-up colonoscopy.<sup>3</sup>

*National Comprehensive Cancer Network (NCCN)*

NCCN recommends the inclusion of multitarget stool DNA testing as a potential screening modality in average-risk individuals, but data to help determine an appropriate interval between screening, adherence to/participation rates of screening, and how multitarget stool DNA testing may fit into an overall screening program are limited. NCCN notes also that there are “no or limited data in high-risk individuals and the use of stool DNA should be individualized.” NCCN recommends colorectal cancer screening for average-risk individuals ≥ 45-75 years who might have a life expectancy of ≥ 10 years and on an individualized basis for those 76-85 years of age.

*Multi-Society Task Force for Colorectal Cancer*

The American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy issued a joint statement recommending FIT-fecal DNA tests every 3 years, as a second-tier screening tool for colorectal cancer. They offer a strong recommendation, based on high-quality evidence, for colorectal cancer screening beginning at age 50. Based on limited evidence and the high incidence of colorectal cancer in African-Americans, they recommend screening for this population starting at age 45.

*American College of Gastroenterology (ACG)*

The ACG offer a strong recommendation, based on moderate-quality evidence, for colorectal cancer screening in average-risk individuals between ages 50 and 75 years to reduce incidence of advanced adenoma, CRC, and mortality from CRC. They also suggest CRC screening in average-risk individuals between ages 45 and 49 years as a conditional recommendation; based on very low-quality evidence. The ACG recommends colonoscopy and FIT as the primary screening modalities for CRC screening, further noting that the following screening tests for individuals unable or unwilling to undergo colonoscopy or FIT can be considered: flexible sigmoidoscopy, multitarget stool DNA test, CT colonography or colon capsule.<sup>11</sup>

**Coding Implications**

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| CPT®<br>Codes | Description  |
|---------------|--|
| 81528         | Oncology (colorectal) screening, quantitative real time target and signal amplification of 10 DNA markers (KRAS mutations, promoter methylation of |

| CPT® Codes | Description  |
|------------|--|
|            | NDRG4 and BMP3) and fecal hemoglobin, utilizing stool, algorithm reported as a positive or negative result |

| HCPCS Codes | Description |
|-------------|-------------|
| N/A         |             |

**ICD-10-CM Diagnosis Codes that Support Coverage Criteria**

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

| Reviews, Revisions, and Approvals   | Revision Date | Approval Date |
|---|---------------|---------------|
| Policy converted from Health Net policy   | 08/16         | 09/16         |
| Added that request is not within the standard interval of another normal screen for colon cancer.   | 10/16         |               |
| Removed parenthetical example of appropriate intervals for colon cancer screening in I.C.   | 06/17         |               |
| References reviewed and updated.  | 09/17         | 09/17         |
| Background updated. References reviewed and updated. HCPCS code G0464 removed from the policy as the code was deleted in 2018.  | 07/18         | 07/18         |
| References reviewed and updated   | 05/19         | 07/19         |
| Changed age supporting medical necessity from 50-85 to 45-85.   | 11/19         | 11/19         |
| Updated background with no impact on criteria. Added ICD-10 code Z12.12. References reviewed and updated. Specialist reviewed.  | 06/20         | 07/20         |
| Replaced “members” with “members/enrollees” in all instances.   | 11/20         |               |
| Changed policy statement in I. to note DNA analysis of stool is allowed every 1-3 years. Replaced investigational language in policy statement II. with “current research does not support the use of ....” Background updated with no impact on criteria. References reviewed, updated and reformatted. Changed “review date” in the header to “date of last revision” and “date” in the revision log header to “revision date.” | 06/21         | 06/21         |

**References**

1. Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. Multitarget stool DNA testing for colorectal-cancer screening. *N Engl J Med* 2014;370:1287-1297. doi:10.1056/NEJMoa1311194
2. A stool DNA test (Cologuard) for colorectal cancer screening. *JAMA*. 2014;312(23):2566. doi:10.1001/jama.2014.15746

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3. US Preventive Services Task Force. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA* 2021;325(19):1965–1977. doi:10.1001/jama.2021.6238
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6. Wolf AMD, Fontham ETH, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin*. 2018;68(4):250-281. doi:10.3322/caac.21457.
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8. Rex DK, Boland CR, Dominitz JA, et al. Colorectal Cancer Screening: Recommendations for Physicians and Patients from the U.S. Multi-Society Task Force on Colorectal Cancer. *Am J Gastroenterol*. 2017;112(7):1016-1030. doi:10.1038/ajg.2017.174
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### **Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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**Note: For Medicaid members/enrollees**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**Note: For Medicare members/enrollees**, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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