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

Reference Number: CP.MP.125 Coding Implications
Last Review Date: 07/20 Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 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 DNA analysis of stool (i.e., Cologuard) is **experimental/investigational** for any circumstances other than those specified above.

Background

Colorectal cancer has become the second leading cause of cancer-related deaths in the United States, according to the latest statistics.[3] 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.[1] The FDA approved Cologuard (Exact Sciences) based on this multi-target stool testing.[2] 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. 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.

United States Preventative Services Task Force (USPSTF)

The USPSTF recommends screening for colorectal cancer starting at age 50 years and continuing until age 75 years. 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 and associated adverse events per screening test.[3] While no longitudinal follow-up data exists, with an abnormal FIT-DNA test result followed by a negative colonoscopy, there is potential for overly intensive surveillance due to clinician and patient concerns about the implications of the genetic component of the test.[3]

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, noting 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 50-75 years of age, 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.

Coding Implications
This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2020, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

CPT® Codes	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

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	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 is 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	

References

1. Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. Multitarget stool DNA testing for colorectal-cancer screening. *N Engl J Med* 2014;370:1287-97.
2. Abramowicz, Mark, Gianna Zuccotti, and Jean-Marie Pflomm. A stool DNA test (Cologuard) for colorectal cancer screening." *JAMA.* 2014;312(23).
3. US Preventive Services Task Force. Final Recommendation Statement: Screening for Colorectal Cancer. Announcement detail. June 2016. Accessed May 29, 2019. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/colorectal-cancer-screening
4. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: Colorectal cancer screening. Version 2.2020. Accessed June 11, 2020.
5. Centers for Medicare and Medicaid Services. National Coverage Determination (NCD) for Colorectal Cancer Screening Tests (210.3). CMS.gov. Effective October 9, 2014. Accessed June 11, 2020.
6. American Cancer Society. American Cancer Society Guideline for Colorectal Cancer Screening: A Summary for Clinicians. American Cancer Society. 2018. Accessed June 11, 2020.
7. Siegel RL, Fedewa SA, Anderson WF, et al. Colorectal Cancer Incidence Patterns in the United States, 1974–2013. J Natl Cancer Inst. 2017 Aug 1;109(8). doi: 10.1093/jnci/djw322.
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. Epub 2017 Jun 6.
9. Doubeni C. Screening for colorectal cancer: Strategies in patients at average risk. In: UpToDate. Lamont JT, Elmore JG (Eds). UpToDate, Waltham, MA. Accessed June 11, 2020

10. Doubeni C. Tests for screening for colorectal cancer In: UpToDate. Lamont JT, Elmore JG (Eds). March 18, 2020. Accessed June 11, 2020

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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.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended to recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

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expressed herein through the terms of their contracts. Where no such contract exists, providers, members/enrollees and their representatives agree to be bound by such terms and conditions by providing services to members/enrollees and/or submitting claims for payment for such services.

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.