

# ONCOLOGY: CANCER SCREENING

## OVERVIEW

This policy relates to genetic and biomarker tests that aim to screen for specific cancers in individuals who are at risk to develop them. These screening tests can be designed for asymptomatic individuals that are at an average risk level for cancer, or for individuals that are known to be at a higher risk to develop a specific cancer. Genetic and biomarker cancer screening tests aim to identify the presence of cancer before symptoms appear and when treatment is often most effective. These tests are not currently diagnostic for cancer, but typically determine if an individual has an increased chance that cancer is present.

Screening tests for colorectal cancer may be performed by analyzing specific DNA present in fecal matter or peripheral blood. Cancer screening tests may also be performed on urine samples to screen for bladder cancer and colon polyps. These methods offer a noninvasive alternative to currently available screening approaches such as colonoscopy.

Screening tests for lung cancer are potentially useful adjuncts to the low-dose CT (LDCT), a recommended lung cancer screening tool in high-risk populations. Biomarkers such as autoantibodies, metabolites, proteins, and microRNA may be sampled from many different bodily sources, including whole blood, serum, plasma, bronchial brushings, and sputum. Circulating blood-based and serum based biomarkers are a convenient compartment to sample as they are relatively easy and inexpensive to collect.

## POLICY REFERENCE TABLE

Below are a list of higher volume tests and the associated laboratories for each coverage criteria section. This list is not all inclusive.

<a href="#">Coverage Criteria Sections</a>	Example Tests (Labs)	Common CPT Codes	Common ICD Codes	<a href="#">Ref</a>
<a href="#">Colorectal Cancer Screening Tests</a>				
<a href="#">FIT-DNA Testing (Stool DNA Testing)</a>	Cologuard (Exact Sciences Corporation)	81528	Z12.10-Z12.13	1, 2, 3
<a href="#">Urinary Biomarker Tests for</a>	PolypDx, Metabolomic Technologies	0002U	Z12.10-Z12.13	1, 2

<a href="#">Pre-cancerous Colon Polyps</a>				
<a href="#">Blood-based Biomarker Tests</a>	BeScreened (Beacon Biomedical)	0163U	Z12.10-Z12.13	1, 2, 4, 9
	FirstSightCRC (CellMax Life)	0091U		
	ColonSentry (StageZero Life Sciences)	81599		
	Epi proColon (Epigenomics)	81327, G0327		
	ColoVantage (Quest Diagnostics)			
<b><a href="#">Lung Cancer Screening Tests</a></b>				
<a href="#">Blood-based Biomarker Tests</a>	EarlyCDT-Lung (Oncimmune)	83520	Z12.2	5, 6, 7, 8

## OTHER RELATED POLICIES

This policy document provides coverage criteria for cancer screening tests. Please refer to:

- **Oncology: Molecular Analysis of Solid Tumors and Hematologic Malignancies** for criteria related to DNA testing of a solid tumor or a blood cancer.
- **Genetic Testing: Hereditary Cancer Susceptibility Syndromes** for criteria related to genetic testing to determine if an individual has an inherited cancer susceptibility syndrome.
- **Oncology: Algorithmic Testing** for criteria related to gene expression profiling and tumor multianalyte assays with algorithmic analyses.
- **Oncology: Circulating Tumor DNA and Circulating Tumor Cells (Liquid Biopsy)** for criteria related to circulating tumor DNA (ctDNA) or circulating tumor cell testing performed on peripheral blood for cancer diagnosis, management and surveillance.
- **Genetic Testing: General Approach to Genetic Testing** for coverage criteria related to cancer screening that is not specifically discussed in this or another non-general policy.

## COVERAGE CRITERIA

### COLORECTAL CANCER SCREENING TESTS

#### FIT-DNA Testing (Stool DNA Testing)

- I. The use of FIT-DNA Testing (stool DNA testing) (81528) to screen for colorectal cancer may be considered **medically necessary** when:
  - A. The member is 45 years of age or older, **AND**
  - B. The member is an individual who is at average risk for colorectal cancer, because the member does not have any of the following:
    1. A personal history of colorectal cancer or adenoma or sessile serrated polyp
    2. A family history of colorectal cancer
    3. A personal history of inflammatory bowel disease (ulcerative colitis or Crohn's disease)
    4. A confirmed or suspected hereditary colorectal cancer syndrome, such as familial adenomatous polyposis (FAP) or Lynch syndrome (hereditary non-polyposis colon cancer or HNPCC)
    5. A personal history of receiving radiation to the abdomen (belly) or pelvic area to treat a prior cancer
- II. The use of FIT-DNA Testing (stool DNA testing) (81528) to screen for colorectal cancer is considered **investigational** for all other indications.

**Note:** Fecal immunochemical testing (FIT) alone is not in the scope of this policy (see definitions)

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#### Urinary Biomarker Tests for Pre-cancerous Polyps

- I. The use of urinary biomarker tests for pre-cancerous polyps (0002U) is considered **investigational**.

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## Blood-based Biomarkers

- I. The use of blood-based biomarkers to screen for colorectal cancer (0091U, 0163U, 81327, 81599, G0327) is considered **investigational**.

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## LUNG CANCER SCREENING TESTS

### Blood-based Biomarkers

- I. The use of blood-based biomarker tests (83520) for lung cancer screening are considered **investigational**.

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## NOTES AND DEFINITIONS

**Fecal immunohistochemical testing (FIT)** is a screening test for colon cancer that detects human blood in the lower intestines. (FIT testing alone does not involve any genetic test and is outside of the scope of this policy).

**FIT-DNA test** combines fecal immunochemical (FIT), which uses antibodies to detect blood in the stool, with a test that detects abnormal DNA from cancer or polyp cells in the stool.

**Low-dose computed tomography (LDCT)** has been proposed as a method of screening asymptomatic, high risk individuals for lung cancer; it refers to a non contrast study with a multi-detector CT scanner during a single maximal inspiratory breath-hold with a scanning time of under 25 seconds. It has been suggested that LDCT may be an improved early lung cancer detection tool based on the advantages it appears to have over CXR and sputum cytology to detect lung cancer at an earlier stage.

**MicroRNAs (miRNAs)** are tissue specific, small, non-coding RNAs regulating gene expression which may identify candidates for early detection of lung cancer.

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## CLINICAL CONSIDERATIONS

Screening tests are not diagnostic tests. The results from a screening test put an individual into a lower risk or higher risk status. For an individual that is put into the higher risk status, following up with an appropriate diagnostic test would be necessary to make a definitive diagnosis of cancer.

For lung cancer in particular, approaches in which a biomarker based initial screen is followed by low-dose computed tomography (LDCT) or in which a biomarker test is combined with LDCT show promise for use in early detection. However, at this time more high quality evidence is needed to support and guide the implementation of these tests.

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## BACKGROUND AND RATIONALE

### Practice Guidelines and Position Statements

#### National Comprehensive Cancer Network (NCCN):

##### *Colorectal Cancer Screening:*

Current NCCN guidelines on colorectal cancer screening (v2.2021) support the use of FIT-DNA in average-risk individuals aged 45-75 who might have a life expectancy  $\geq 10$  years, and notes that the decision to screen individuals aged 76-85 should be individualized.

Current NCCN guidelines (v2.2021) do not include a recommendation for colorectal cancer screening via blood-based or urine-based screening.

##### *Lung Cancer Screening:*

Current NCCN guidelines on lung cancer screening (v1.2021) does not recommend lung cancer screening via blood-based or micro-RNA based screening. Current NCCN guidelines support lung cancer screening using LDCT for individuals with high risk factors.

#### US Preventive Services Task Force (USPSTF):

The USPSTF published an updated recommendation statement (2021) on screening for colorectal cancer that included the following:

“The USPSTF recommends screening for colorectal cancer in all adults aged 50 to 75 years. (A recommendation) The USPSTF recommends screening for colorectal cancer in adults aged 45 to 49 years. (B recommendation) The USPSTF recommends that clinicians selectively offer screening for colorectal cancer in adults aged 76 to 85 years. Evidence indicates that the net benefit of screening all persons in this age group is small. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the patient’s overall health, prior screening history, and preferences. (C recommendation)”

The USPSTF published a recommendation statement (2021) on screening for lung cancer that included the following:

“The USPSTF recommends annual screening for lung cancer with low dose computed tomography (LCDT) in adults aged 50 to 80 years who have a 20 pack year smoking history and currently smoke or have quit within the past 15 years.

“Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.”

“A rating of A and B from the USPSTF applies to the Affordable Care Act (ACA) preventative services. This recommendation is Grade B.”

### U.S. Food and Drug Administration (FDA)

Cologuard (Exact Sciences):

On August 12, 2014, Cologuard (Exact Sciences) was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process as an automated fecal DNA testing product (P130017). Cologuard is intended for the qualitative detection of colorectal neoplasia associated with DNA markers and occult hemoglobin in human stool. A positive result may indicate the presence of CRC or advanced adenoma and should be followed by diagnostic colonoscopy.

On September 20, 2019, the FDA approved the expansion of the Cologuard label to include adults ages  $\geq 45$  years. Cologuard was previously indicated for those  $\geq 50$  years. Cologuard is not a replacement for diagnostic colonoscopy or surveillance colonoscopy in high-risk individuals.

### Epi ProColon (Epigenomics):

On April 12, 2014, Epi ProColon (Epigenomics) was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process as a qualitative in vitro diagnostic test for the detection of methylated Septin 9 DNA in EDTA plasma derived from patient whole blood specimens (P130001). The FDA approval notes that, “the Epi proColon test is indicated to screen adults of either sex, 50 years or older, defined as average risk for CRC, who have been offered and have a history of not completing CRC screening. Tests that are available and recommended in the USPSTF 2008 CRC screening guidelines should be offered and declined prior to offering the Epi proColon test. Patients with a positive Epi proColon test result should be referred for diagnostic colonoscopy. The Epi proColon test results should be used in combination with physician's assessment and individual risk factors in guiding patient management.”

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### Concert Genetics Technical Assessment 2021

#### Blood-based Biomarker Colon Cancer Screening Tests

This review focused on peer-reviewed, published evidence of the clinical utility of BeScreened, FirstSight CRC, ColonSentry, Epi ProColon, and Colovantage through October 2021. PubMed and ECRI Guidelines Trust searches were performed. Search terms included BeScreened, FirstSight CRC, ColonSentry, Epi ProColon, Colovantage, colon cancer screen, circulating tumor cells, Cripto, ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6, VNN1, SEPT9. References were also identified from the performing laboratory's website. A total of 60 abstracts from these sources were reviewed, and 17 full text publications were evaluated. At the present time, BeScreened, FirstSight CRC, ColonSentry, Epi ProColon, and Colovantage have not been adequately shown in peer-reviewed publications to effectively result in improved health outcomes compared to the current standard of care.

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