05-82000-27

Original Effective Date: 08/15/03

Reviewed: 01/24/19

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Subject: Analysis of Human DNA as a Technique for Colorectal Cancer Screening

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DESCRIPTION:

Several genetic alterations have been associated with colorectal cancer (CRC). In the proposed multistep model of carcinogenesis, the tumor suppressor gene p53 and the proto-oncogene KRAS are most frequently altered. Variants in adenomatous polyposis coli genes and epigenetic markers (e.g., hypermethylation of specific genes) have also been detected. CRC is also associated with DNA replication errors in microsatellite sequences (termed microsatellite instability) in patients with Lynch Syndrome (formerly known as hereditary nonpolyposis CRC) and in subgroups of patients with sporadic colon carcinoma. Tumor-associated gene variants and epigenetic markers can be detected in exfoliated intestinal cells in stool specimens. Since cancer cells are shed into stool, tests have been developed to detect these genetic alterations in the DNA from shed CRC cells isolated from stool samples.

Assays that detect circulating methylated SEPT9 DNA have been proposed as a screening test for CRC. The Septin 9 protein is involved in cell division, migration, and apoptosis and acts as a tumor suppressor; when hypermethylated, expression of SEPT9 is reduced. There are various tests available however, performance characteristics vary across tests, presumably due to differences in methodology (eg, DNA preparation, PCR primers, probes).

POSITION STATEMENT:

The use of an FDA approved fecal DNA test (e.g. Cologuard™) **meets the definition of medical necessity** once every three years as a screening technique for members 50 - 75 years of age in whom colorectal cancer preventive screening is indicated.

The use of an FDA approved fecal DNA test is considered **experimental or investigational** for all other indications including post colorectal cancer diagnosis surveillance. The evidence is insufficient to determine the effects of the technology on health outcomes.

The use of non-FDA approved fecal DNA test and all other methods for the analysis of DNA in stool samples are considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes.

Septin 9 (SEPT9) DNA methylation assays (e.g. ColoVantage®, Epi proColon®) are considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes.

BILLING/CODING INFORMATION:

CPT Coding:

81327	SEPT9 (Septin9) (eg, colorectal cancer) promoter methylation analysis **(Investigational)**
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

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage products: The following National Coverage Determination (NCD) was reviewed on the last guideline reviewed date: Colorectal Cancer Screening Tests (210.3) located at cms.gov.

The following Local Coverage Determinations (LCDs), located at fcso.com, were reviewed on the last guideline reviewed date: Colorectal Cancer Screening (L36355) and Molecular Pathology Procedures (L34519).

DEFINITIONS:

None.

RELATED GUIDELINES:

01-99385-03, Preventive Services

OTHER:

None Applicable.

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Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology, CA Cancer j Clin 2008, accessed at amcancersoc.org 02/20/12.

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy & Coverage Committee on 01/24/19.

GUIDELINE UPDATE INFORMATION:

08/15/03	New Medical Coverage Guideline.
07/15/04	Scheduled review. No change in policy statement.
01/01/05	HCPCS update. Added S3890.
08/15/05	Scheduled review. No change in policy statement. Updated references and related Internet links.
08/15/06	Annual review; continue investigational.
07/15/07	Scheduled review; investigational status maintained, guideline reformatted, references updated.
09/15/08	Annual review: position statement maintained, description section and references updated.
07/15/09	Annual review: position statement maintained, description section and references updated.
05/15/10	Annual review: position statement maintained, description section and references updated.
04/15/12	Annual review; position statement maintained and references updated.
04/15/13	Annual review; position statement maintained and references updated.
04/15/14	Annual review; investigational position statement maintained, Medicare program exception and references updated.
01/01/15	Annual HCPCS/CPT update. Added code G0464.
04/15/15	Annual review; position statement maintained; program exception and references updated.
01/01/16	Annual HCPCS/CPT update; code 81528 added, codes G0464 and S3890 deleted.
05/15/16	Annual review; position statement section, description, program exception, and references

	updated.
08/12/16	Revisions to Position Statement.
12/15/16	Revision; position statement section and references updated.
01/01/17	Annual CPT/HCPCS update. Added 81327.
01/11/17	Revision; position statement section updated.
01/01/19	Annual CPT/HCPCS coding update. Revised code 81327.
02/15/19	Review: Position statements, title, description, program exception, and references updated.