Medical Coverage Policy | Serologic Genetic and Molecular Screening for Colorectal Cancer

EFFECTIVE DATE: 09|01|2023
POLICY LAST UPDATED: 05|03|2023

OVERVIEW

It is well established that early detection of colorectal cancer (CRC) reduces disease-related mortality. For patients at average risk for CRC, organizations such as the U.S. Preventive Services Task Force have recommended several options for colon cancer screening. Currently accepted screening options for CRC include colonoscopy or sigmoidoscopy, fecal occult blood testing, and fecal immunochemical testing. However, many individuals do not undergo recommended screening with fecal tests or colonoscopy. A simpler screening blood test for genetic alterations associated with non-familial CRC may have the potential to encourage screening and decrease mortality if associated with increased screening compliance. Genetic testing is also being investigated to guide therapy.

The following tests are addressed in this policy:

- BeScreened™–CRC test (Beacon Biomedical, Inc., CPT code 0163U)
- Colorectal cancer screening; blood-based biomarker (HCPCS code G0327)
- Gene expression profiling (eg, ColonSentry® by StageZero Life Sciences. Ltd.) (Unlisted CPT code)
- SEPT9 methylated DNA testing (eg, ColoVantage® by Enterix, Epi proColon® by Epigenomics) (CPT code 81327)

MEDICAL CRITERIA

Medicare Advantage Plans and Commercial Products

Unless otherwise noted, for any test filed with an Unlisted CPT code, the medical necessity criteria in the Genetic Testing Services policy would be used. Please see the Related Policies section.

PRIOR AUTHORIZATION

Medicare Advantage Plans and Commercial Products

There is no specific CPT coding for some of the services referenced in this policy. Therefore, an Unlisted CPT code should be used (see Coding Section for details). All Unlisted genetic testing CPT codes require prior authorization to determine what service is being rendered and if the service is covered or not medically necessary. See the Related Policies section.

Prior authorization is required for Medicare Advantage Plans and recommended for Commercial Products and is obtained via the online tool for participating providers. See the Related Policies section.

Note: Laboratories are not allowed to obtain clinical authorization or participate in the authorization process on behalf of the ordering physician. Only the ordering physician shall be involved in the authorization, appeal or other administrative processes related to prior authorization/medical necessity.

In no circumstance shall a laboratory or a physician/provider use a representative of a laboratory or anyone with a relationship to a laboratory and/or a third party to obtain authorization on behalf of the ordering physician, to facilitate any portion of the authorization process or any subsequent appeal of a claim where the authorization process was not followed and/or a denial for clinical appropriateness was issued, including any element of the preparation of necessary documentation of clinical appropriateness. If a laboratory or a third party is found to be supporting any portion of the authorization process, BCBSRI (Blue Cross & Blue Shield of Rhode Island) will deem the action a violation of this policy and severe action will be taken up to and including termination from the BCBSRI provider network. If a laboratory provides a laboratory service that

has not been authorized, the service will be denied as the financial liability of the participating laboratory and may not be billed to the member.

POLICY STATEMENT

Medicare Advantage Plans

The following test(s) are covered without an authorization requirement:

- Colorectal cancer screening; blood-based biomarker (HCPCS G0327)

The following test(s) are not covered as the evidence is insufficient to determine that the technology results in an improvement in the net health outcomes:

- BeScreened™–CRC test (CPT code 0163U)
- Gene expression profiling (eg, ColonSentry®) (Unlisted CPT code)
- SEPT9 methylated DNA testing (eg, ColoVantage,® Epi proColon®) (CPT code 81327)

Note: Blue Cross & Blue Shield of Rhode Island (BCBSRI) must follow Centers for Medicare and Medicaid Services (CMS) guidelines, such as national coverage determinations or local coverage determinations for all Medicare Advantage Plans policies. Therefore, Medicare Advantage Plans policies may differ from Commercial products. In some instances, benefits for Medicare Advantage Plans may be greater than what is allowed by the CMS.

Commercial Products

The following test(s) are not medically necessary as the evidence is insufficient to determine that the technology results in an improvement in the net health outcomes:

- BeScreened™–CRC test (CPT code 0163U)
- Colorectal cancer screening; blood-based biomarker (HCPCS code G0327)
- Gene expression profiling (eg, ColonSentry®) (Unlisted CPT code)
- SEPT9 methylated DNA testing (eg, ColoVantage,® Epi proColon®) (CPT code 81327)

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for applicable not medically necessary/not covered benefits/coverage.

BACKGROUND

Colorectal Cancer

For patients at average risk for colorectal cancer (CRC), organizations such as the U.S. Preventive Services Task Force have recommended several options for colon cancer screening. The diagnostic performance characteristics of the currently accepted screening options (ie, colonoscopy, sigmoidoscopy, fecal tests) have been established using colonoscopy as the criterion standard. Modeling studies and clinical trial evidence on some of the screening modalities have allowed some confidence in the effectiveness of several cancer screening modalities. The efficacy of these tests is supported by numerous studies evaluating the diagnostic characteristics of the test for detecting cancer and cancer precursors along with a well-developed body of knowledge on the natural history of the progression of cancer precursors to cancer. Early detection of CRC reduces disease-related mortality, yet many individuals do not undergo recommended screening with fecal occult blood test or colonoscopy. A simpler screening blood test may have the potential to encourage screening and decrease mortality if associated with increased screening compliance.

SEPT9 Methylated DNA

ColoVantage (various manufacturers) blood tests for serum Septin9 (*SEPT9)* methylated DNA are offered by several laboratories (ARUP Laboratories, Quest Diagnostics, Clinical Genomics). Epi proColon (Epigenomics) received U.S. Food and Drug Administration (FDA) approval in April 2016. Epigenomics has licensed its Septin 9 DNA biomarker technology to Polymedco and LabCorp. ColoVantage and Epi proColon are both polymerase chain reaction (PCR) assays; however, performance characteristics vary across tests, presumably due to differences in methodology (eg, DNA preparation, PCR primers, probes).

Gene Expression Profiling
ColonSentry (Stage Zero Life Sciences) is a PCR assay that uses a blood sample to detect the expression of 7 genes found to be differentially expressed in CRC patients compared with controls: *ANXA3*, *CLEC4D*, *TNFAIP6*, *LMNB1*, *PRRG4*, *VNN1*, and *IL2RB*. The test is intended to stratify average-risk adults who are non-compliant with colonoscopy and/or fecal occult blood testing. Because of its narrow focus, the test is not expected to alter clinical practice for patients who comply with recommended screening schedules. BeScreened-CRC (Beacon Biomedical) is a PCR assay that uses a blood sample to detect the expression of 3 protein biomarkers: teratocarcinoma derived growth factor-1 (TDGF-1, Cripto-1); carcinoembryonic antigen, a well-established biomarker associated with CRC; and an extracellular matrix protein involved in early-stage tumor stroma changes.

For individuals who are being screened for CRC who receive serologic molecular or genetic screening for CRC, the evidence includes case-control, cross-sectional, and prospective diagnostic accuracy studies along with systematic reviews of those studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, change in disease status, and morbid events. The evaluation of SEPT9 Biomarker Performance for Colorectal Cancer Screening (PRESEPT) prospective study estimated the sensitivity and specificity of Epi proColon detection of invasive adenocarcinoma at 48% and 92%, respectively. Other studies were generally low to fair quality. In systematic reviews, sensitivity ranged from 62% to 71% and pooled specificity ranged from 91% to 93%. Based on results from these studies, the clinical validity of Septin9 (SEPT9) methylated DNA screening is limited by the low sensitivity of the test. Optimal intervals for retesting are not known. Sensitivity in the 2 cross-sectional studies of ColonSentry ranged from 61% to 72% and specificity for detecting CRC were 70% to 77% Based on results from these studies, the clinical validity of gene expression screening is limited by low sensitivity and low specificity. No published peer-reviewed evidence was identified for BeScreened-CRC. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Medicare Advantage Plans
Blood-based Biomarker Tests
Blood-based DNA testing detects molecular markers of altered DNA that are contained in the cells shed into the blood by colorectal cancer and pre-malignant colorectal epithelial neoplasia. A blood-based biomarker test is covered as an appropriate colorectal cancer screening test. Please refer to the Preventive Services for Medicare Advantage Plans.

CODING

Medicare Advantage Plans and Commercial Products
The following code(s) is covered for Medicare Advantage Plans and not medically necessary for Commercial Products:

G0327 Colorectal cancer screening; blood-based biomarker

The following CPT code(s) are not covered for Medicare Advantage Plans and are not medically necessary for Commercial Products:

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

This code can be used for BeScreened™–CRC test

0163U Oncology (colorectal) screening, biochemical enzyme-linked immunosorbent assay (ELISA) of 3 plasma or serum proteins (teratocarcinoma derived growth factor-1 [TDGF-1, Cripto-1], carcinoembryonic antigen [CEA], extracellular matrix protein [ECM]), with demographic data (age, gender, CRC-screening compliance) using a proprietary algorithm and reported as likelihood of CRC or advanced adenomas

CPT codes have not been assigned to all of the tests addressed in this policy. Therefore, an Unlisted code(s) should be used.

RELATED POLICIES

Genetic Testing Services Policy
Medicare Advantage Plans National and Local Coverage Determinations
Preventive Services for Medicare Advantage Plans
Proprietary Laboratory Analyses (PLA)

PUBLISHED

Provider Update, July 2023
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