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Corporate Medical Policy

Multigene Expression Assay for Predicting Colon Cancer Recurrence AHS-M2111

File Name:	multigene_expression_assay_for_predicting_colon_cancer_recurrence
Origination:	1/1/2019
Last CAP Review:	4/2020
Next CAP Review:	4/2020
Last Review:	7/2020

Description of Procedure or Service

Colorectal cancer (CRC) involves the accumulation of genetic and epigenetic modifications within pathways that regulate proliferation, apoptosis, and angiogenesis resulting in carcinoma of the colon and rectum (Fearon & Vogelstein, 1990). Tumors originate in adenomas or flat dysplasia, and evolve into different morphologic patterns with invasion and expansion (Compton, 2017).

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

Multigene expression assay for predicting colon cancer recurrence is considered investigational for all applications. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Multigene Expression Assay For Colon Cancer Recurrence is covered

Not applicable.

When Multigene Expression Assay For Colon Cancer Recurrence is not covered

Gene expression assays for determining the prognosis of stage II colon cancer following surgery are **investigational.**

Policy Guidelines

Literature Review

Colorectal cancer (CRC) is the second leading cause of cancer-related deaths in the United States following lung cancer. 20% of patients with colorectal cancer will present with metastatic colorectal cancer (mCRC) at diagnosis and a significantly poorer prognosis. The 5-year survival is 13.1% in patients with distant metastases from CRC, as compared to 64.9% for all CRC patients (El-Deiry et al., 2015).

Approximately one-quarter of the patients with colon cancer present with stage II disease (Lee, Lee, Chuang, & Lee, 2013). The current National Comprehensive Cancer Network guidelines include adjuvant chemotherapy as a treatment option in this setting, particularly for high-risk stage II patients, as determined by clinical and pathological parameters(NCCN, 2017). Although some of the routinely used parameters for estimating recurrence risk such as T-stage and mismatch repair (MMR) status are well established, they may not be reliable predictors of recurrence risk in this population(Gray et al., 2011; Gunderson, Jessup, Sargent, Greene, & Stewart, 2010; Harris et al., 2008; Ribic et al., 2003; Sargent et al., 2010; Venook et al., 2013). These patients could therefore benefit from a tool that would further refine their risk of recurrence and facilitate individualized adjuvant treatment decisions(Brenner et al., 2016).

The 12-gene Onco*type* DX Colon Cancer Assay (Genomic Health, Inc., Redwood City, CA) is a reverse transcriptase polymerase chain reaction–based assay that provides a Recurrence Score (RS) result (O'Connell et al., 2010). The assay has been clinically validated as a predictor of recurrence risk following surgical resection in patients with both stage II and III colon cancer(Brenner et al., 2016; Gray et al., 2011; Simon, Paik, & Hayes, 2009).

Two additional colon cancer genomic assays have become available, ColoPrint (Agendia NV, Amsterdam, The Netherlands) and ColDx assay (Almac Diagnostics, Craigavon, Northern Ireland) use microarray technology for assessing the gene expression of 18 and 634 genes, respectively, to stratify patients into low and high recurrence risk groups (Kennedy et al., 2011; Maak et al., 2013; Salazar et al., 2011). Both assays have been clinically validated using retrospective cohort studies (Brenner et al., 2016; Simon et al., 2009).

Several studies have evaluated the impact of the gene expression profiling on clinical decision making in certain colon cancer subgroups. Brenner et al (Brenner et al., 2016) assessed the clinical impact of the 12-gene Colon Cancer Recurrence Score Assay in treatment of T3 mismatch repair proficient (MMR-P) stage II colon cancer. The authors concluded that testing significantly impacted adjuvant treatment decisions in clinical practice. Cartwright et al (Cartwright et al., 2014) performed a web-based survey evaluating the impact of the 12-gene Colon Cancer Recurrence Score Assay in stage II colon cancer patients. The authors found that 29% of treatment recommendations were changed for patients receiving Recurrence Score testing, and use of the assay led to reductions in treatment intensity. Srivastava et al (Srivastava et al., 2014) conducted a prospective study assessing the impact of recurrence score results on physician recommendations regarding adjuvant chemotherapy in T3 MMR-P stage II colon cancer patients. The study concluded that treatment recommendation changes were made for 45% of patients. However, none of these studies gauged the impact of testing on patient survival or recurrence outcomes. Further research is required to study the clinical utility gene expression profiling assays in colon cancer patients (Sepulveda et al., 2017).

Applicable Federal Regulations

To date, no gene expression test for evaluation of prognosis in stage II colon cancer has been cleared for marketing by the U.S. Food and Drug Administration (FDA). These tests are offered as laboratory-developed developed, validated and performed by individual laboratories.

LDTs are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA'88).

As an LDT, the U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network (NCCN)
Current clinical practice guidelines from NCCN state that "there are insufficient data to recommend the use of multi-gene assays to determine adjuvant therapy" in patients with stage 2 colon cancer (NCCN, 2018).

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 81479, 81525, 81599, 84999, 88299

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

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Medical Director review 8/2019

Specialty Matched Consultant Advisory Panel 4/2020

Medical Director review 4/2020

Medical Director review 7/2020

Policy Implementation/Update Information

1/1/2019 New policy developed. Multigene expression assay for predicting colon cancer recurrence/ prognosis of stage II colon cancer following surgery are **investigational.** Medical Director review 1/1/2019. Policy noticed 1/1/2019 for effective date 4/1/2019. (lpr)

9/10/19 Reviewed by Avalon 2nd Quarter 2019 CAB. Deleted coding table from Billing/Coding section. Deleted CPT code 81504. Medical Director review 8/2019. (lpr)

5/26/20 Specialty Matched Consultant Advisory Panel review 4/15/2020. No change to policy statement. (lpr)

7/28/20 Reviewed by Avalon 2nd Quarter 2020 CAB. Updated references. (lpr)