**Medica Coverage Policy**

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<th>Policy Name</th>
<th>Molecular Profiling in Colorectal Cancer to Guide Treatment</th>
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<td>Effective Date</td>
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**Important Information – Please Read Before Using This Policy**

These services may or may not be covered by all Medica plans. Please refer to the member’s plan document for specific coverage information. If there is a difference between this general information and the member’s plan document, the member’s plan document will be used to determine coverage. With respect to Medicare and Minnesota Health Care Programs, this policy will apply unless those programs require different coverage. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Medica coverage policy may call the Medica Provider Service Center toll-free at 1-800-458-5512.

Medica coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

**Coverage Policy**

Genetic testing to guide targeted pharmacogenetic treatment in colorectal cancer (CRC) is **COVERED** for the following genes/tests when ordered by a board-certified pathologist, medical geneticist, oncologist, hematologist, or advanced practitioner in these fields:

- RAS mutation testing, including KRAS and NRAS
- BRAF p.V600 mutational analysis
- Mismatch repair (MMR) analysis
- Microsatellite instability (MSI) analysis.

Multigene panels to guide targeted pharmacogenetic treatment that include any of the above genes are **COVERED** when ordered by a board-certified pathologist, medical geneticist, oncologist, hematologist, or advanced practitioner in these fields.

**Note:** See also related Medica coverage policy, *Gene Expression Profiling Assays for Predicting Colon Cancer Recurrence Risk*.

**Description**

Colorectal cancer is one of the most common malignant neoplasms and a leading cause of cancer death in the U.S. and worldwide. Molecular markers may be used to determine a diagnosis, as an indicator of disease (cancer) progression, or to document clinical response to treatment. Molecular markers that predict response to a specific therapy or treatment regimen are known as predictive biomarkers. Molecular testing to select targeted and conventional therapies for patients with CRC has been the focus of much research. As a result, a number of molecular biomarkers have been identified for use in selecting patients who can benefit from enhanced treatment with targeted therapies and the use of these markers has been integrated into the clinical setting as standard of care. The main targeted therapies in CRC, for which knowledge of mutational status is useful, are the monoclonal antibody therapies that target the epidermal growth factor receptor (EGFR) signaling pathways. In addition, DNA mismatch repair status is recommended for all patients with CRC to evaluate for possible Lynch syndrome. Finally, the presence of microsatellite instability has both prognostic and therapeutic implications in the choice of chemotherapy.
Another approach to molecular profiling is the use of multigene expression profiling assays, such as Oncotype Dx Colon, to predict the likelihood of recurrence in stage II and stage III CRC patients. These assays test tumor tissue for a number of genes that have been determined to be associated with an increased risk of recurrence. The resulting data are then analyzed using a proprietary algorithm and a Recurrence Score (RS) is calculated that quantifies the patient’s risk of CRC recurrence. This information is also purported to be useful in determining the patient’s need for adjuvant chemotherapy. However, the clinical implications of a patient’s RS are not clear nor are the actual effects on patient management.

FDA Approval
Genetic tests are regulated under the Clinical Laboratory Improvement Amendments (CLIA) Act of 1988. Premarket approval from the FDA is not required as long as the assay is performed in a laboratory facility that observes CLIA regulations and the test is not marketed for general distribution.

Prior Authorization
Prior authorization is not applicable. Claims for this service are subject to retrospective review and denial of coverage, as investigative services are not eligible for reimbursement.

Coding Considerations
Use the current applicable CPT/HCPCS code(s). The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

CPT Codes:
81525 - Oncology (colon), mRNA, gene expression profiling by real-time RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence score

Original Effective Date: 2/1/2011

Re-Review Date(s):
9/1/2012
6/17/2015
1/4/2016 – Administrative update; code update
5/17/2017
7/16/2018 – Administrative update; addition of “note”
2/20/2020 – Administrative update; format