

MP.088.MPC Colorectal Cancer, Mutation Testing for Treatment

Maryland Physicians Care considers **Mutation Testing for Treatment of Metastatic Colorectal Cancer (mCRC) – KRAS, NRAS and BRAF Mutation testing** medically necessary for a diagnosis of mCRC when it is used in predicting nonresponse to anti-epidermal growth factor receptor (EGFR) monoclonal antibodies (cetuximab and panitumumab) in the treatment of metastatic colorectal carcinoma. Testing for *KRAS* mutation (exon 2, 3, 4), *NRAS* (exon 2, 3, 4) and *BRAF* V600 mutations is considered **MEDICALLY NECESSARY** prior to deciding treatment with cetuximab or panitumumab

Testing can be performed from either the primary tumor and/or metastatic tumor tissue and can be done individually or as part of a next-generation sequencing (NGS) panel.

Limitations

Testing for *KRAS*, *NRAS* and *BRAF* V600 mutations in all other situations not described above is investigational/unproven and therefore considered **NOT MEDICALLY NECESSARY** due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of a patient's illness.

Background

Over 108,000 cases of colon and 40,700 cases of rectal cancer are expected to occur annually in the United States. CRC is the third leading cause of cancer-related deaths in the United States. The American Cancer Society (ACS) states that the risk of CRC increases with age, with over 90% of the diagnoses in patients over 50 years of age. The 5-year survival rate for those diagnosed with CRC is 67% over all stages; however, this drops to 12% in those with metastatic disease.

Cetuximab (Erbix; Imclone Systems/Bristol-Myers Squibb) Erbitux (cetuximab) package insert (FDA, 2012) indicates that the drug is to be used for "K-Ras mutation-negative (wild-type), *EGFR*-expressing, metastatic colorectal cancer as determined by FDA-approved tests and panitumumab (Vectibix; Amigen Inc.) are anti-EGFR monoclonal antibodies used for treatment in patients with metastatic disease. Use of Vectibix is not recommended for the treatment of colorectal cancer with these (*KRAS*) mutations per FDA. To determine benefit from this treatment, biomarkers are needed to select the potential patient population. The *KRAS* (v-Ki-ras2 Kirsten rat sarcoma), *NRAS* and *BRAF* mutation testing is to identify those individuals who are unlikely to respond to treatment with anti-EGFR monoclonal antibodies.

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On July 17, 2009, the Food and Drug Administration (FDA) made class labeling changes to the product labels of cetuximab (Erbix) and panitumumab (Vectibix) to indicate the drugs are now not recommended for the treatment of colorectal cancer for patients with KRAS mutation. BRAF V600E mutation makes response to cetuximab or panitumumab highly unlikely unless given with a BRAF inhibitor.

Codes:

CPT Codes / HCPCS Codes / ICD-10 Codes	
Code	Description
CPT Codes	
81210	BRAF (v-raf murine sarcoma viral oncogene homolog B1) (eg, colon cancer), gene analysis, V600E variant
81275	KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene)(e.g. carcinoma) gene analysis, variants in codons 12 and 13
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; additional variant(s) (e.g., codon 61, codon 146)
81311	NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (eg, colorectal carcinoma), gene analysis, variants in exon 2 (eg, codons 12 and 13) and exon 3 (eg, codon 61)
81479	Unlisted molecular pathology
ICD-10 codes covered if selection criteria are met:	
C17.0-C17.9	Malignant neoplasm of small intestine
C18.0-C18.9	Malignant neoplasm of colon
C19-C21.8	Malignant neoplasm of rectum and anus
C78.5	Secondary malignant neoplasm of large intestine and rectum
D01.0-D01.3	Carcinoma in situ of colon, rectum, and anus

References

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3. Carethers JM. DNA testing and molecular screening for colon cancer. *Clin Gastroenterol Hepatol.* 2014 Mar;12(3):377-381. doi: 10.1016/j.cgh.2013.12.007. Epub 2013 Dec 18. [http://www.cghjournal.org/article/S1542-3565\(13\)01933-2/abstract](http://www.cghjournal.org/article/S1542-3565(13)01933-2/abstract)
4. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD) No. L35396 - Biomarkers for Oncology. (Contractor: Novitas Solutions, Inc.). Revision Effective Date: 06/13/2019. <https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=35396&ver=187&Date=&DocID=L35396&bc=iAAAABAAAAAA&>
5. Centers for Medicare and Medicaid Services (CMS). Local Coverage Article: Biomarkers for Oncology (A52986). Revision Effective Date: 04/01/2021. <https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=52986>
6. National Comprehensive Cancer Network (NCCN): NCCN Clinical Practice Guidelines in Oncology- Colon Cancer NCCN Quick Guide <https://www.nccn.org/patients/guidelines/content/PDF/colon-patient.pdf>
7. Quest Diagnostics®. Test Center: KRAS Mutation Analysis. Content reviewed: 03.2014 . ©2000-2019, Quest Diagnostics, Inc. <https://testdirectory.questdiagnostics.com/test/test-detail/16510/kras-mutation-analysis?cc=MASTER>

Archived References

1. Hayes Genetic Testing Evaluation. KRAS Sequence Variant Analysis for Predicting Response to Colorectal Cancer Drug Therapy. Annual Review May 27, 2015. Archived: January 25, 2017.

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