



KRAS SEQUENCE VARIANT ANALYSIS FOR METASTATIC COLORECTAL CANCER HS-137



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KRAS Sequence Variant Analysis for Metastatic Colorectal Cancer

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DISCLAIMER

The Clinical Coverage Guideline is intended to supplement certain standard WellCare benefit plans. The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this Clinical Coverage Guideline. When a conflict exists between the two documents, the Member's Benefit Plan always supersedes the information contained in the Clinical Coverage Guideline. Additionally, Clinical Coverage Guidelines relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

BACKGROUND

Genetic testing for *KRAS* sequence variants is generally performed using polymerase chain reaction (PCR) amplification followed by confirmation using sequencing of variants. Most assays detect the presence of sequence variants in codons 12 and 13 of the *KRAS* gene, where the majority of variants are found. The potential patient population is all patients under consideration for treatment with anti-EGFR monoclonal antibodies (cetuximab and panitumumab) for CRC.

Colon and rectal cancer are collectively known as colorectal cancer (CRC). It is the third most common cancer in the United States. The morbidity and mortality associated with CRC are significant, with an estimated 49,960 deaths caused by CRC in 2008. The 5-year survival rate for those diagnosed with CRC is 64% over all stages; however, this drops to 11% in those with metastatic disease. Treatment of CRC through surgery is the usual approach for cancers that have not metastasized, and is often curative. Before or following surgery, chemotherapy, sometimes with radiotherapy, is given to patients with stage III or IV cancer. Cetuximab (Erbix®; Imclone Systems/Bristol-Myers Squibb) and panitumumab (Vectibix®; Amgen Inc.) are anti-epidermal growth factor receptor (EGFR) monoclonal antibodies that are generally used for second- or third-line treatment in patients with metastatic disease following failure of first-line chemotherapy. Clinical evidence suggests that the benefit from these drugs is limited to a subgroup of 10% to 30% of CRC patients. Accordingly, biomarkers are needed to help select those patients who will benefit from treatment with EGFR inhibitors. One of the biomarkers that has been investigated as a negative prognostic indicator is the presence of sequence variants in the Kirsten rat sarcoma viral oncogene homolog (*KRAS*) gene. *KRAS* sequence variants are found in 27% to 42% of patients with CRC and are generally absent in normal controls (from Hayes, 2008).

National Comprehensive Cancer Network (NCCN)

In November 2008, the NCCN updated their guidelines for both colon and rectal cancer to recommend that *KRAS* sequence variant testing of either the primary tumor or a site of metastasis should be part of the pretreatment work-up for all patients diagnosed with metastatic CRC. In addition, the NCCN Guidelines state that the EGFR inhibitors cetuximab and panitumumab are now recommended only for patients with tumors that do not have sequence variants in the *KRAS* gene.

Cost Information

The cost of genetic testing for *KRAS* sequence variants is reported to be \$500 to \$1000. In contrast the monthly costs of cetuximab and panitumumab are \$10,000 and \$8,000, respectively.

POSITION STATEMENT

KRAS (Kirsten Rat Sarcoma) sequence variant analysis is considered medically necessary if ALL of the following criteria are met:

- Member has metastatic colorectal cancer; **AND,**
- Member has failed or is refractory to first-or second-line chemotherapy; **AND,**
- The test is used to predict response to treatment with anti-EGFR monoclonal antibodies (cetuximab and panitumumab monotherapy, and for combination therapy of cetuximab with irinotecan or oxaliplatin)

KRAS (Kirsten Rat Sarcoma) sequence variant analysis is considered experimental and investigational for all other indications other than metastatic colorectal cancer.

CODING

CPT® Codes This list may not be all inclusive.

83891	Molecular diagnostics; isolation or extraction of highly purified nucleic acid
83892	Molecular diagnostics; enzymatic digestion
83894	Molecular diagnostics; separation by gel electrophoresis (e.g., agarose, polyacrylamide)
83898	Molecular diagnostics; amplification, target, each nucleic acid sequence
83904	Molecular diagnostics; mutation identification by sequencing, single segment, each segment
83907	Molecular diagnostics; lysis of cells prior to nucleic acid extraction (eg, stool specimens, paraffin embedded tissue)
83909	Molecular diagnostics; separation and identification by high resolution technique (eg, capillary electrophoresis)
83912	Molecular diagnostics; interpretation and report

ICD-9-CM Procedure Codes - No applicable codes

HCPCS Level II © Code

S3713 Kras mutation analysis testing

**S- Codes are NON COVERED FOR MEDICARE. For Medicare, bill the appropriate CPT Code.*

Covered ICD-9-CM Diagnosis Codes

The following primary cancer codes are covered when the above criteria has been met:

153.0 – 153.9	Malignant Neoplasm of Colon
154.0 – 154.1	Malignant Neoplasm of Rectosigmoid Junction and Rectum

The following Metastatic Sites Secondary to Colorectal Cancer must be documented and billed:

196.2	Lymph nodes - Intra-abdominal; Secondary malignant neoplasm originating in digestive system.
196.6	Lymph nodes - Intra-pelvic; Secondary malignant neoplasm originating in digestive system
197.0	Lung; Secondary malignant neoplasm originating in digestive system
197.6	Peritoneum; Secondary malignant neoplasm originating in digestive system
197.7	Liver; Secondary malignant neoplasm originating in digestive system
198.3	Brain; Secondary malignant neoplasm originating in digestive system
198.5	Bone; Secondary malignant neoplasm originating in digestive system
198.6	Ovary; Secondary malignant neoplasm originating in digestive system

*Current Procedural Terminology (CPT®) ©2011 American Medical Association: Chicago, IL.

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Peer Reviewed

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Government Agencies, Professional and Medical Organizations

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HISTORY AND REVISIONS

Date	Action
12/1/2011	<ul style="list-style-type: none">• New template design approved by MPC.
9/15/2011	<ul style="list-style-type: none">• Approved by MPC. No changes.