

Policy #: 104

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Page: 1 of 3

Title

KRAS Mutation Analysis in Metastatic Colorectal Cancer

Description

The purpose of KRAS mutation analysis is to identify those individuals with metastatic colorectal cancer who are unlikely to respond to treatment with the monoclonal antibodies cetuximab and panitumumab. The term KRAS refers to a set of genes and proteins (manufactured from these genes) that regulate the growth, division, and proliferation of cells. In normal tissue, the proliferation of cells is tightly controlled by several genes. At times, cells do need to grow, divide, and proliferate. The cell can receive a chemical signal that binds to a receptor on the surface of the cell membrane known as epidermal growth factor receptor (EGFR). This signal to grow is transmitted to the nucleus of the cell by proteins produced by the KRAS genes.

There are a number of mechanisms by which cells can divide and proliferate abnormally and turn into a cancer. One mechanism can be over-stimulation of receptors such as EGFR, often due to a mutation in the DNA of the gene that codes for EGFR which produces too many receptors or receptors with too much activity. This mutated gene is known as an oncogene. It has been found that the monoclonal antibodies cetuximab and panitumumab, which specifically bind to the EGFR, prevent other chemical signals from binding to this receptor, thereby reducing the signal to the cell to proliferate.

Another mutation that can cause unregulated growth and proliferation occurs in the KRAS genes. There are three common mutations in these genes, found in up to 50% of patients with colorectal metastases, which allows these proteins to signal the cell nucleus to direct the cell to grow and divide, independently of any messages from the epidermal growth factor receptor. Since the KRAS proteins are no longer influenced by the EGFR, inhibiting the EGFR with the monoclonal antibodies will not prevent the cell from proliferating, and therefore be of no benefit to as many as half of the patients with colorectal cancer. The KRAS mutation analysis therefore enables clinicians to determine which patients are not likely to respond to monoclonal antibody therapy, so this expensive treatment can be appropriately avoided in these patients.

When services are covered for all Products (including Medicare HMOB, Medicare PPO Blue and Blue Medicare PFFS PlusRx Products)

We **cover KRAS mutation analysis** to predict non response to anti-EGFR monoclonal antibodies (Cetuximab and Panitumumab) in the treatment of metastatic colorectal cancer.

When services are not covered for all Products (including Medicare HMOB, Medicare PPO Blue and Blue Medicare PFFS PlusRx Products)

We **do not cover KRAS mutation analysis** for other than testing metastatic colorectal cancer because it does not meet the Blue Cross Blue Shield of Massachusetts Medical Technology Assessment Guidelines, #350.

Individual consideration

All our medical policies are written for the majority of people with a given condition. Each policy is based on medical science. For many of our medical policies, each individual's unique clinical circumstances may be

considered in light of current scientific literature. For consideration of an individual patient, physicians may send relevant clinical information to:

For services already billed

Blue Cross Blue Shield of Massachusetts
Provider Appeals
P. O. Box 986065
Boston, MA 02298

Prior to performance of service

Blue Cross Blue Shield of Massachusetts,
Case Creation/Medical Policy
One Enterprise Drive
Quincy, MA 02171
Tel: 1-800-327-6716
Fax: 1-888-641-5330

Managed care guidelines

- Authorizations are not required.
- All specialist visits require a referral.

Indemnity and PPO guidelines

- Authorizations are not required if performed in an outpatient setting.

Coding information

Procedure codes are from current CPT, HCPCS Level II, Revenue Code, and/or ICD-9-CM manuals, as recommended by the American Medical Association, Centers for Medicare and Medicaid Services and American Hospital Associations. Blue Cross Blue Shield Association national codes may be developed when appropriate.

The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

HCPCS code:

- **S3713:** KRAS mutation analysis testing

Policy update history

New medical policy document, effective 6/2009. Updated 8/09 to include new specific HCPCS Level II code, effective 10/1/2009, and editing of the Code Information section to align with new formatting. Reviewed 9/2009 MPG-Hematology and Oncology, no changes in coverage were made.

Footnotes

¹ Based on the Blue Cross Blue Shield Association medical policy *KRAS Mutation Analysis in Metastatic Colorectal Cancer*, #2.04.53.

References

References for Footnote 1

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13. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Colon Cancer. Version 3.2008. http://www.nccn.org/professionals/physician_gls/PDF/colon.pdf

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