

Analysis of KRAS Status

Last Review Date: August 11, 2023

Number: MG.MM.LA.19bC2

Medical Guideline Disclaimer

Property of EmblemHealth. All rights reserved. The treating physician or primary care provider must submit to EmblemHealth the clinical evidence that the patient meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request for prior authorization. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary. If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication. EmblemHealth Services Company LLC, ("EmblemHealth") has adopted the herein policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

KRAS gene	A type of oncogene that encodes the RAS protein predisposed to mutations that result in a constitutively activated protein. The activated protein is implicated in various malignancies, including colorectal carcinoma, lung adenocarcinoma, and ductal carcinoma of the pancreas, and may cause tumor resistance to epidermal growth factor receptor inhibitors.
KRAS sequence variant analysis	A tool used to predict an individual's response to anti EGFR drug therapy for conditions including metastatic colorectal cancer and anal cancer.
KRAS mutation status	A mutation at codon 12 or 13 of the KRAS gene. The presence of a KRAS mutation correlates with lack of response to anti-EGFR therapy with cetuximab or with panitumumab. Screening for KRAS mutations status may be used as a prognostic marker as patients with colorectal cancer and positive KRAS tumors have a worse prognosis.
KRAS wild-type status	The typical or non-mutated form of the KRAS gene. Tumors with this KRAS type increases the likelihood of a response to anti-EGFR therapy with cetuximab or with panitumumab.

Related Medical Guidelines

[BRAF Mutation Analysis](#)

[Erbbitux® \(cetuximab\)](#)

[Gene Expression Profiling](#)

MCG Colorectal Cancer — KRAS and NRAS Genes (A-0773)

MCG Non-Small Cell Lung Cancer — Gene Testing (A-0795)

[Vectibix® \(panitumumab\)](#)

Guideline

Analysis of KRAS status in members with non-small cell lung cancer, stage IV colon cancer, rectal cancer, colorectal cancer or anal adenocarcinoma is considered medically necessary to predict response to Lumakras (sotorasib), Erbitux (cetuximab) or Vectibix (panitumumab) prior to initiation of therapy.

Limitations/Exclusions

Analysis of KRAS status is considered investigational and not medically necessary for all other indications that do not meet the above criteria.

Revision History

9/10/2021	Lumakras (sotorasib) added to list of drugs for which KRAS analysis prior to initiation of therapy is warranted
10/14/2016	Added non-small cell lung cancer as covered indication

Applicable Procedure Codes

81275	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; variants in exon 2 (eg, codons 12 and 13)
81276	KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (eg, carcinoma) gene analysis, variants in codons 12 and 13, additional variant(s) (eg, codon 61, codon 146)
81403	Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of 10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)
88363	Examination and selection of retrieved archival (ie, previously diagnosed) tissue(s) for molecular analysis (eg, KRAS mutational analysis)

Applicable ICD-10 Diagnosis Codes

C17.0	Malignant neoplasm of duodenum
C17.1	Malignant neoplasm of jejunum
C17.2	Malignant neoplasm of ileum
C17.3	Meckel's diverticulum, malignant
C17.8	Malignant neoplasm of overlapping sites of small intestine
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction

C20	Malignant neoplasm of rectum
C21.0	Malignant neoplasm of anus, unspecified
C21.1	Malignant neoplasm of anal canal
C21.2	Malignant neoplasm of cloacogenic zone
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C77.0	Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck
C77.1	Secondary and unspecified malignant neoplasm of intrathoracic lymph nodes
C77.2	Secondary and unspecified malignant neoplasm of intra-abdominal lymph nodes
C77.3	Secondary and unspecified malignant neoplasm of axilla and upper limb lymph nodes
C77.4	Secondary and unspecified malignant neoplasm of inguinal and lower limb lymph nodes
C77.5	Secondary and unspecified malignant neoplasm of intrapelvic lymph nodes
C77.8	Secondary and unspecified malignant neoplasm of lymph nodes of multiple regions
C77.9	Secondary and unspecified malignant neoplasm of lymph node, unspecified
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.1	Secondary malignant neoplasm of mediastinum
C78.2	Secondary malignant neoplasm of pleura
C78.30	Secondary malignant neoplasm of unspecified respiratory organ
C78.39	Secondary malignant neoplasm of other respiratory organs
C78.4	Secondary malignant neoplasm of small intestine
C78.5	Secondary malignant neoplasm of large intestine and rectum
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C78.80	Secondary malignant neoplasm of unspecified digestive organ
C78.89	Secondary malignant neoplasm of other digestive organs

C79.00	Secondary malignant neoplasm of unspecified kidney and renal pelvis
C79.01	Secondary malignant neoplasm of right kidney and renal pelvis
C79.02	Secondary malignant neoplasm of left kidney and renal pelvis
C79.10	Secondary malignant neoplasm of unspecified urinary organs
C79.11	Secondary malignant neoplasm of bladder
C79.19	Secondary malignant neoplasm of other urinary organs
C79.2	Secondary malignant neoplasm of skin
C79.31	Secondary malignant neoplasm of brain
C79.32	Secondary malignant neoplasm of cerebral meninges
C79.40	Secondary malignant neoplasm of unspecified part of nervous system
C79.49	Secondary malignant neoplasm of other parts of nervous system
C79.51	Secondary malignant neoplasm of bone
C79.52	Secondary malignant neoplasm of bone marrow
C79.60	Secondary malignant neoplasm of unspecified ovary
C79.61	Secondary malignant neoplasm of right ovary
C79.62	Secondary malignant neoplasm of left ovary
C79.70	Secondary malignant neoplasm of unspecified adrenal gland
C79.71	Secondary malignant neoplasm of right adrenal gland
C79.72	Secondary malignant neoplasm of left adrenal gland
C79.81	Secondary malignant neoplasm of breast
C79.82	Secondary malignant neoplasm of genital organs
C79.89	Secondary malignant neoplasm of other specified sites
C79.9	Secondary malignant neoplasm of unspecified site
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.048	Personal history of other malignant neoplasm of rectum, rectosigmoid junction, and anus

References

1. Allegra CJ, Jessup JM, Somerfield MR, et al. American Society of Clinical Oncology provisional clinical opinion: testing for KRAS gene mutations in patients with metastatic colorectal carcinoma to predict response to anti-epidermal growth factor receptor monoclonal antibody therapy. *J Clin Oncol*. 2009. <http://jco.ascopubs.org/content/27/12/2091.long>. Accessed August 18, 2023.
2. Amado RG, Wolf M, Peters M et al. Wild-type KRAS is required for panitumumab efficacy in patients with metastatic colorectal cancer. *J Clin Oncol* 2008; 26(10):1626-1634.
3. Cervantes A, Macarulla T, Martinelli E, et al. Correlation of KRAS status (wild type [wt] vs. mutant [mt]) with efficacy to first-line cetuximab in a study of cetuximab single agent followed by cetuximab + FOLFIRI in patients (pts) with metastatic colorectal cancer (mCRC). *J Clin Oncol* 26: 2008 (May 20 suppl; abstr 4129).
4. College of American Pathologists (CAP). Perspectives on Emerging Technology Report (POET). KRAS Mutation Testing for Colorectal Cancer (CRC). September 2009 (Rev 3). <http://www.cap.org/apps/docs/committees/technology/KRAS.pdf>. Accessed August 18, 2023.
5. Freeman D, Juan T, Meropol NJ, et al: Association of somatic KRAS gene and clinical outcome in patients (pts) with metastatic colorectal cancer (mCRC) receiving panitumumab monotherapy. *Eur J Cancer Suppl* 5: 239, 2007 (abstr O3014)
6. Lumakras (sotorasib) [Product Information], Thousand Oaks, CA. Amgen. Revised May 2021. May 2021. https://www.pi.amgen.com/~media/amgen/repositorysites/pi-amgen-com/lumakras/lumakras_pi_hcp_english.ashx. Accessed August 18, 2023.

7. Mao C, Qiu LX, Liao RY et al. KRAS mutations and resistance to EGFR-TKIs treatment in patients with non-small cell lung cancer: a meta-analysis of 22 studies. *Lung Cancer* 2010; 69(3):272-278.
8. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Colon cancer V2.2023. http://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed August 18, 2023.
9. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Rectal cancer V4.2023. http://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed August 18, 2023.
10. National Comprehensive Cancer Network (NCCN). NCCN Drugs & Biologics Compendium. Cetuximab. 2010a. <https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia>. Accessed August 18, 2023.
11. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer V3.2023. http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. August 18, 2023.
12. Tanaka M, Chari S, Adsay V, et al. International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. *Pancreatology*. 2006; 6(1-2):17-32.
13. Van Cutsem E, Cervantes A, Nordlinger B, et al. Metastatic colorectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2014; 25 Suppl 3:iii1-9.
14. Varras MN, Sourvinos G, Diakomanolis E, et al. Detection and clinical correlations of ras gene mutations in human ovarian tumors. *Oncology*. 1999; 56(2):89-96.
15. Vectibix (Panitumumab) [Product Information], Thousand Oaks, CA. Amgen. Revised August 2021. http://pi.amgen.com/united_states/vectibix/vectibix_pi.pdf. Accessed August 18, 2023.