

# Premier Health Insuring Corporation

## POLICY AND PROCEDURE MANUAL

Policy Number: MP.088.PC  
Last Review Date: 11/12/2015  
Effective Date: 01/01/2016  
Renewal Date: 01/01/2017

### MP.088.PH - Colorectal Cancer, Mutation Testing for Treatment

This policy applies to the following line(s) of business:

- ✓ Premier Health Insuring Corporation MA – DSNP

Premier Health Insuring Corporation considers Mutation Testing for Treatment of Colorectal Cancer (CRC) medically necessary for the following indications:

KRAS mutation testing is considered medically necessary for a diagnosis of CRC 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 from either primary tumor or metastatic tumor tissue.

#### Limitations

KRAS mutation testing for CRC not listed above is considered not medically necessary.

#### 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) and panitumumab (Vectibix; Amigen Inc.) are anti-EGFR monoclonal antibodies used for treatment in patients with metastatic disease. To determine benefit from this treatment, biomarkers are needed to select the potential patient population. The KRAS (v-Ki-ras2 Kirsten rat sarcoma) mutation test is to identify those individuals who are unlikely to respond to treatment with anti-EGFR monoclonal antibodies. The KRAS mutation assay detects mutations at codons 12 and 13 of the KRAS gene and these mutations have been associated with lack of response to EGFR targeted therapies.

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.

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### Codes:

CPT Codes / HCPCS Codes / ICD-10 Codes	
Code	Description
<b>CPT Codes</b>	
81275	KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene)( e.g. carcinoma) gene analysis, variants in codons 12 and 13
<b>CPT Codes (Medicare Only)</b>	
81210	BRAF (v-raf murine sarcoma viral oncogene homolog B1) (eg, colon cancer), gene analysis, V600E variant
81479	Unlisted molecular pathology
<b>ICD-9 codes covered if selection criteria are met:</b>	
152.0-152.9	Malignant neoplasm of small intestine including duodenum
153.0-154.8	Malignant neoplasm of colon, rectum, and anus
197.5	Secondary malignant neoplasm of large intestine and rectum
230.3-230.6	Carcinoma in situ anus, colon, or rectum
<b>ICD-10 codes covered if selection criteria are met:</b>	
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

### Variations

#### Medicare (see LCD L35396):

The following testing will be covered for Medicare members for the condition of Colorectal Cancer:

- KRAS (12/13) – PRED of resistance to anti-EGFR agent
- KRAS codon 61 – PRED of resistance to anti-EGFR agent
- KRAS codon 146 – PRED of resistance to anti-EGFR agent
- NRAS – PRED of resistance to anti-EGFR agent

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- BRAF – PRED of resistance to an anti-EGFR agent + DX (sporadic + Lynch syndrome)
- PIK3CA – PRED of resistance to an anti-EGFR agent + PROG for local recurrence
- MSI by PCR – PRED of 5-FU resistance + DX
- MLHI promoter hypermethylation – PRED of 5-FU resistance + DX

DX = Diagnosis; PROG = prognostic; and/or PRED = predictive

### 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 Apr; 27(12): 2091-2096.  
<http://jco.ascopubs.org/content/27/12/2091.full.pdf+html>
2. American College of Pathologists. The Pathologist's Message. KRAS Mutation Testing for Colorectal Cancer (CRC). Last updated: Dec. 17, 2010.  
[http://www.cap.org/apps/cap.portal?\\_nfpb=true&cntvwrPtlActionOverride=%2Fportlets%2FcontentViewer%2Fshow&\\_windowLabel=cntvwrPtl&cntvwrPtl%7BactionForm.contentReference%7D=committees%2Ftechnology%2FKRAS\\_Mutation.html&\\_state=maximized&\\_pageLabel=cntvwr](http://www.cap.org/apps/cap.portal?_nfpb=true&cntvwrPtlActionOverride=%2Fportlets%2FcontentViewer%2Fshow&_windowLabel=cntvwrPtl&cntvwrPtl%7BactionForm.contentReference%7D=committees%2Ftechnology%2FKRAS_Mutation.html&_state=maximized&_pageLabel=cntvwr)
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 17. [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: 10/01/2015.  
<https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=35396&ContrlId=324&ver=27&ContrVer=1&Date=&DocID=L35396&bc=iAAAAAgAAAAAA%3d%3d&>
5. Centers for Medicare and Medicaid Services (CMS). Local Coverage Article: Biomarkers for Oncology (A52986). (Contractor: Novitas Solutions, Inc.). Revision Effective Date: 10/01/2015. [https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=52986&ver=26&ContrlId=324&ContrVer=1&CtrctrSelecte d=324\\*1&Date=&DocID=A52986&bc=hAAAAAgAAAAAA%3d%3d&](https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=52986&ver=26&ContrlId=324&ContrVer=1&CtrctrSelecte d=324*1&Date=&DocID=A52986&bc=hAAAAAgAAAAAA%3d%3d&)
6. General Electric Healthcare: Clariant Diagnostic Services, Inc., *Colorectal Cancer Testing* ©2015, Clariant Diagnostic Services, Inc.  
<http://clariant.gehealthcare.com/Diagnostic-Services/Colorectal-Cancer-Testing>

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7. Hayes Genetic Testing Evaluation. KRAS Sequence Variant Analysis for Predicting Response to Colorectal Cancer Drug Therapy. Annual Review May 27, 2015.
8. National Comprehensive Cancer Network (NCCN): NCCN Clinical Practice Guidelines in Oncology- Colon Cancer Version 3.2014. J Natl Compr Canc Netw 2014; 12: 1028-1059. <http://www.jnccn.org/content/12/7/1028.abstract>
9. Plesec TP, Hunt JL. KRAS mutation testing in colorectal cancer. Adv Anat Pathol. 2009 Jul; 16(4): 196-203. <http://www.ncbi.nlm.nih.gov/pubmed/19546608>
10. Quest Diagnostics®. Test Center: KRAS Mutation Analysis. Content reviewed: 03.2014 . ©2000-2014, Quest Diagnostics, Inc. [http://www.questdiagnostics.com/testcenter/testguide.action?dc=TS\\_KRAS](http://www.questdiagnostics.com/testcenter/testguide.action?dc=TS_KRAS)
11. United States Food and Drug Administration: Cetuximab (Erbix) and Panitumumab (Vectibix). Page Last Updated: 01/11/2010. <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm172905.htm>

### Disclaimer:

Premier Health Insuring Corporation medical payment and prior authorization policies do not constitute medical advice and are not intended to govern or otherwise influence the practice of medicine. The policies constitute only the reimbursement and coverage guidelines of Premier Health Insuring Corporation and its affiliated managed care entities. Coverage for services varies for individual members in accordance with the terms and conditions of applicable Certificates of Coverage, Summary Plan Descriptions, or contracts with governing regulatory agencies.

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