Medical Drug Clinical Criteria

Subject:	Vectibix (panitumumab)		
Document #:	CC-0105	**Publish Date:**	~~06/20/2023~~07/01/2024
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Overview

This document addresses the use of Vectibix (panitumumab). Vectibix is a human monoclonal antibody that targets and inhibits the biologic activity of the human epidermal growth factor receptor (EGFR) that is primarily used to treat colorectal cancer

The FDA approved indications for Vectibix include as first line therapy in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or as monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy. The National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for the use of Vectibix. NCCN recommends appendiceal adenocarcinoma be treated with chemotherapy according to colon cancer guidelines. Similarly, it is recommended that anal adenocarcinoma, a rare histologic form of anal cancer, may be treated according to guidelines for rectal cancer.

The FDA label includes the requirement for confirmed RAS wild-type histology and that Vectibix is not indicated for those with somatic RAS mutations in either KRAS or NRAS or for whom RAS mutation status is unknown. NCCN also notes that research has demonstrated that mutations in the KRAS, and more recently NRAS genes, are a predictive factor for a lack of response to Vectibix therapy for colorectal cancer. Mutations in the BRAF gene cause a cancer signal downstream of the EGFR/RAS pathway. In the presence of BRAF mutations, NCCN notes that response to EGFR inhibitors is very unlikely unless given with a BRAF inhibitor. NCCN recommends the combination use of Vectibix and encorafenib for BRAF mutation positive colorectal cancer after prior therapy.

Vectibix and Erbitux (cetuximab) are two EGFR antagonists approved by the FDA. There is currently no evidence to support switching to either Erbitux or Vectibix after failure of the other drug and NCCN recommends against this practice. In addition, studies have shown that combination with more than one biologic agent is not associated with improved outcomes and can cause increased toxicity, specifically regarding the addition of Erbitux or Vectibix to a bevacizumab-containing regimen (Tol 2009, Hecht 2009). NCCN strongly recommends against the use of therapy involving concurrent combination of an anti-EGFR agent and an anti-VEGF agent.

Other Uses

NCCN no longer recommends the off-label use of Vectibix as second-line palliative therapy in penile cancer. FDA label and compendia do not support this indication either. Though anal adenocarcinoma is an acceptable use for Vectibix, NCCN guidelines for squamous cell anal cancer, the most common type of anal cancer, do not currently include Vectibix among recommended treatments. NCCN guideline for small bowel adenocarcinoma (SBA) notes that cetuximab and panitumumab should not be used to treat SBA due to inconclusive evidence.

Vectibix has a black box warning for dermatologic toxicity. Dermatologic toxicities occurred in 90% of patients and were severe (NCI-CTC grade 3 and higher) in 15% of patients receiving Vectibix monotherapy.

Definitions and Measures

Adenocarcinoma: Cancer originating in cells that line specific internal organs and that have gland-like (secretory) properties.

Anal cancer: Cancer originating in the tissues of the anus; the anus is the opening of the rectum (last part of the large intestine) to the outside of the body.

BRAF: The oncogene which directions production of a protein in the regulating MAP kinase/ERKs signaling pathway, which affects cell division, differentiation, and secretion.

Colon cancer: Cancer originating in the tissues of the colon (the longest part of the large intestine). Most colon cancers are adenocarcinomas that begin in cells that make and release mucus and other fluids.

Colorectal cancer: Cancer originating in the colon (the longest part of the large intestine) or the rectum (the last several inches of the large intestine before the anus).
KRAS wild-type: The normal or typical form of the KRAS gene, as distinguished from any mutant forms of KRAS; KRAS lacking mutation.

Mutation: A permanent, transmissible change in genetic material.

One line of therapy: Single line of therapy.

Rectal cancer: Cancer originating in tissues of the rectum (the last several inches of the large intestine closest to the anus).

Vascular endothelial growth factor (VEGF): A substance made by cells that stimulates new blood vessel formation.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Vectibix (panitumumab)

Requests for Vectibix (panitumumab) may be approved if the following criteria are met:

I. Individual has a diagnosis of ~~stage IV~~ unresectable of metastatic colon, rectal, colorectal, appendiceal, or anal adenocarcinoma and the following are met: (Label, NCCN 2A)
   A. Panitumumab is used as a single agent or as part of combination therapy; **AND**
   B. One of the following is met:
      1. Extended RAS gene mutation testing ~~with an FDA-approved test is confirmed and~~determines the tumor is ~~determined to be~~ RAS wild-type (RAS wild-type means that the KRAS and NRAS genes are normal or lacking mu~~t~~tations) and individual is using in combination with irinotecan or oxaliplatin; ~~**AND**~~**OR**
      2. Tumor is determined to be BRAF wild-type and individual is using in combination with irinotecan or oxaliplatin; **OR**
      3. Gene mutation testing has determined the tumor to be BRAF V600E positive and panitumumab is used in combination with encorafenib; **OR**
      ~~B.~~4. Gene mutation testing has determined the tumor to be KRAS G12C positive and panitumumab is used in combination with sotorasib or adagrasib.
   ~~C. Panitumumab is used in a single line of therapy; **AND**~~
   ~~D. Panitumumab is not used in combination with anti-VEGF agents (bevacizumab, ziv-aflibercept, or ramucirumab) (NCCN 2A);~~

~~**OR**~~

~~II. Individual has a diagnosis of unresectable, advanced, or metastatic colorectal cancer and the following are met (Label, NCCN 2A):~~
   ~~A. Individual has BRAF V600E mutation with test results confirmed; **AND**~~
   ~~B. Individual has demonstrated disease progression after one or more prior lines of systemic therapy; **AND**~~
   ~~C. Panitumumab is not used in combination with anti-VEGF agents (bevacizumab, ziv-aflibercept, or ramucirumab); **AND**~~
   ~~D.~~A. ~~Panitumumab is used in a single line of therapy~~

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Requests for Vectibix (panitumumab) may not be approved for the following:

I. All other indications not included above; **OR**
II. Treatment of RAS-mutant metastatic colorectal cancer, small bowel or anal adenocarcinoma, ~~(that is, when an FDA approved test has confirmed the presence of genetic mutations in any of the RAS genes)~~ or when RAS mutation status is unknown; **OR**
III. In combination with other monoclonal antibodies or anti-VEGF agents (NCCN 2A); **OR**
IV. Treatment of penile cancer; **OR**
V. Treatment of squamous cell anal carcinoma; **OR**
VI. Individual has received prior treatment with cetuximab (cetuximab discontinuation due to adverse reaction is not considered prior treatment).

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9303	Injection, panitumumab, 10 mg [Vectibix]

ICD-10 Diagnosis

C17.0-C17.8	Malignant neoplasm of small intestine
C18.0-C18.9	Malignant neoplasm of colon
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.0-C21.8	Malignant neoplasm of colon, rectum, rectosigmoid junction, anus
C78.5	Secondary malignant neoplasm of large intestine and rectum
Z51.11-Z51.12	Encounter for antineoplastic chemotherapy and immunotherapy
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

Document History

Revised: 05/17/2024
Document History:

- 05/17/2024 – Annual Review: Update colon, rectal, colorectal, appendiceal, anal adenocarcinoma criteria for unresectable or metastatic disease, update criteria to add BRAF V600E and KRAS G12C combination use, wording changes. Coding Reviewed: No changes.
- 05/19/2023 – Annual Review: update colorectal criteria remove encorafenib requirement per NCCN, update may not approve criteria. Coding Reviewed: No changes.
- 05/20/2022 – Annual Review: No changes. Coding Reviewed: No changes.
- 11/19/2021 – Select Review: Update criteria to include combination with encorafenib per NCCN. Coding Changes. No changes.
- 05/21/2021 – Annual Review: No changes. Coding Changes: No changes.
- 05/15/2020 – Annual Review: Remove small bowel adenocarcinoma from criteria as NCCN no longer recommends this use. Coding Review: Remove ICD-10-dx C17.9
- 08/16/2019 – Annual Review: Update RAS testing requirements to not include BRAF mutation testing per FDA label. Coding reviewed: No changes
- 05/17/2019 – Annual Review: First review of Vectibix clinical criteria. Wording and formatting updates for clarity and consistency. Coding Reviewed: No changes.

References

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2024 URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.
5. NCCN Clinical Practice Guidelines in Oncology™. © 2024 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on March 4, 2024.
    a. Colon Cancer. V1.2024. Revised January 29, 2024.
    b. Rectal Cancer. V1.2024. Revised January 29, 2024.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.