Clinical Policy: Panitumumab (Vectibix)

Reference Number: CP.PHAR.321
Effective Date: 03/17
Last Review Date: 03/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for panitumumab for injection (Vectibix®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Vectibix is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Colorectal Cancer (must meet all):

1. Diagnosis of colorectal cancer (CRC);
2. Disease is KRAS or NRAS wild type (i.e., not mutated);
3. Meets a or b:
   a. FDA approved use (i and ii):
      i. Prescribed for metastatic CRC as primary therapy in combination with FOLFOX*;
      ii. As subsequent therapy as a single agent after failing fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy;
   b. Off-label NCCN recommended use:
      i. Prescribed for unresectable, metastatic or inoperable CRC (a, b or c):
         a) As primary therapy;
         b) As subsequent therapy (1, 2 or 3):
            1) If not previously treated with cetuximab or panitumumab;
            2) Following primary treatment with chemoradiation or local therapy;
            3) For unresectable metastatic disease;
         c) As adjuvant therapy** (1 or 2):
            1) For unresectable metastatic disease that has converted to resectable disease;
            2) Following resection and/or local therapy for metastases if (a or b):
               a. Member has received previous chemotherapy;
               b. Positive for growth on neoadjuvant** chemotherapy;
      ii. Prescribed for rectal cancer in combination with FOLFOX* or FOLFIRI*, or as a single agent if intensive therapy is not appropriate:
         a) As primary therapy for disease characterized as:
            1) T3, N0, M0 (Stage IIA)†;
            2) Any T, N1-2, M0 (Stage III)†;
            3) T4 (Stage IIB-C, Stage IIIB-C, Stage IV)†;
            4) Locally unresectable or inoperable disease with no metastases if resection is contraindicated following neoadjuvant** therapy.

**FOLFIRI (fluorouracil, leucovorin, irinotecan); FOLFOX (fluorouracil, leucovorin, oxaliplatin).*
***Adjuvant therapy (therapy administered after the main treatment to help decrease the risk of cancer recurring); neoadjuvant therapy (therapy given as a first step to shrink a tumor before the main therapy).*
†T (primary tumor characteristics); N (regional lymph nodes); M (metastatic disease).

Approval duration: 3 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. Colorectal Cancer (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member has none of the following reasons to discontinue:
   a. Disease progression or unacceptable toxicity;
   b. Dermatologic reactions (e.g., bullous mucocutaneous disease with blisters, erosions, skin sloughing, acneiform dermatitis, pruritus, erythema, rash, skin exfoliation, paronychia, dry skin, skin fissures):
      i. Grade 3* (serious):
         a) Fourth occurrence;
         b) Any occurrence that does not recover after withholding ≥ 2 doses;
      ii. Grade 4* (life-threatening);
   c. Interstitial lung disease;
   d. Acute or worsening keratitis due to risk of corneal perforation.

**Grading is based on the Common Terminology Criteria for Adverse Events (CTCAE).*

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy**.**

Background

Description/Mechanism of Action:

The EGFR is a transmembrane glycoprotein that is a member of a subfamily of type I receptor tyrosine kinases, including EGFR, HER2, HER3, and HER4. EGFR is constitutively expressed in normal epithelial tissues, including the skin and hair follicle. EGFR is overexpressed in certain human cancers, including colon and rectum cancers. Interaction of EGFR with its normal ligands (eg, EGF, transforming growth factor-alpha) leads to phosphorylation and activation of a series of intracellular proteins, which in turn regulate transcription of genes involved with cellular growth and survival, motility, and proliferation. KRAS (Kirsten rat sarcoma 2 viral oncogene homologue) and NRAS (Neuroblastoma RAS viral oncogene homologue) are highly related members of the RAS oncogene family. Signal transduction through the EGFR can result in

activation of the wild-type KRAS and NRAS proteins; however, in cells with activating RAS somatic mutations, the RAS-mutant proteins are continuously active and appear independent of EGFR regulation.

Panitumumab binds specifically to EGFR on both normal and tumor cells, and competitively inhibits the binding of ligands for EGFR. Nonclinical studies show that binding of panitumumab to the EGFR prevents ligand-induced receptor autophosphorylation and activation of receptor-associated kinases, resulting in inhibition of cell growth, induction of apoptosis, decreased proinflammatory cytokine and vascular growth factor production, and internalization of the EGFR. In vitro assays and in vivo animal studies demonstrate that panitumumab inhibits the growth and survival of selected human tumor cell lines expressing EGFR.

Formulations:
Vectibix is supplied as a sterile, colorless, preservative-free solution containing 20 mg/mL Vectibix (panitumumab) in a single-use vial. Vectibix is provided as one vial per carton:

- Each 5 mL single-use vial contains 100 mg of panitumumab in 5 mL (20 mg/mL)
- Each 10 mL single-use vial contains 200 mg of panitumumab in 10 mL (20 mg/mL)
- Each 20 mL single-use vial contains 400 mg of panitumumab in 20 mL (20 mg/mL)

FDA Approved Indications:
Vectibix is an epidermal growth factor receptor (EGFR) antagonist/intravenous formulation indicated for:

- Metastatic colorectal cancer
  - Vectibix is indicated for the treatment of patients with wild-type KRAS (exon 2 in codons 12 or 13) metastatic colorectal cancer (mCRC) as determined by an FDA-approved test for this use:
    - As first-line therapy in combination with FOLFOX.
    - As monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy.

  Limitation of use: Vectibix is not indicated for the treatment of patients with RAS-mutant mCRC or for whom RAS mutation status is unknown.

Appendices
Appendix A: Abbreviation Key
CRC: Colorectal cancer
CTCAE: Common terminology criteria for adverse events
EGF: Epidermal growth factor
EGFR: Epidermal growth factor receptor
FOLFIRI: Fluorouracil, leucovorin, irinotecan
FOLFOX: Fluorouracil, leucovorin, oxaliplatin
HER: Human epidermal growth factor receptor
KRAS: Kirsten rat sarcoma 2 viral oncogene homologue
mCRC: Metastatic colorectal cancer
NRAS: Neuroblastoma RAS viral oncogene homologue

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9303	Injection, panitumumab, 10 mg

Reviews, Revisions, and Approvals	Date	Approval Date
Policy split from CP.PHAR.182 Excellus Oncology. NCCN off-label recommended uses added. CRC: NRAS wild type (i.e., not mutated) is added to KRAS wild type as NCCN notes recent evidence indicates that, like KRAS, NRAS mutations are predictive for a lack of benefit to panitumumab. KRAS and NRAS are members of the RAS human oncogene family. Some NCCN colon cancer off-label recommendations are collapsed and combined into a colorectal cancer section with some rectal cancer indications.	01/17	03/17

References
1. Vectibix prescribing information. Thousand Oaks, CA: Amgen, Inc.; March 2015. Available at http://pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/vectibix/vectibix_pi.ashx. Accessed January 25, 2017.
2. Panitumumab. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed January 25, 2017.
3. Colon cancer (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed January 25, 2017.
4. Rectal cancer (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed January 25, 2017.

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.