Clinical Policy: Panitumumab (Vectibix)

Reference Number: PA.CP.PHAR.321
Effective Date: 01/18
Last Review Date: 10/30/2019

Coding Implications
Revision Log

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

FDA Approved Indication(s)
Vectibix is indicated for the treatment of patients with wild-type *RAS* (defined as wild-type in both *KRAS* and *NRAS* as determined by an FDA-approved test for this use) metastatic colorectal cancer (CRC):

- In combination with FOLFOX for first-line treatment
- As monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy

Limitation(s) of use: Vectibix is not indicated for the treatment of patients with *RAS*-mutant metastatic CRC or for whom *RAS* mutation status is unknown.

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness ® 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. Prescribed by or in consultation with an oncologist;
3. Disease is wild-type *RAS* (defined as wild-type in both *KRAS* and *NRAS*);
4. One of the following (a, b, c, or d):
   a. Request is for first-line treatment: Prescribed in combination with FOLFOX or FOLFIRI (off-label);
   b. Previous treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy (e.g., FOLFOXIRI);
   c. Previous treatment with an oxaliplatin containing regimen (e.g., FOLFOX, CapeOx): Prescribed in combination with FOLFIRI, irinotecan, or irinotecan with Zelboraf® if BRAF V600E mutation positive (off-label);
   d. Previous treatment with FOLFIRI: Prescribed in combination with irinotecan, or irinotecan with Zelboraf if BRAF V600E mutation positive (off-label);
5. Request meets one of the following (a or b):
   e. Dose does not exceed 6 mg/kg every 14 days;
   f. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
    a. New dose does not exceed 6 mg/kg every 14 days;
    b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 12 months

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

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)

Appendices

Appendix A: Abbreviation/Acronym Key

CRC: colorectal cancer
EGFR: epidermal growth factor receptor
FDA: Food and Drug Administration
FOLFIRI: fluorouracil, leucovorin, irinotecan
FOLFOX: fluorouracil, leucovorin, oxaliplatin
KRAS: Kirsten rat sarcoma 2 viral oncogene homologue
CRC: colorectal cancer
FOLFOXIRI: fluorouracil, leucovorin, oxaliplatin, irinotecan
NRAS: neuroblastoma RAS viral oncogene homologue

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Modified FOLFOX 6	Day 1: oxaliplatin 85 mg/m^2 IV Day 1: Folinic acid 400 mg/m^2 IV Days 1–3: 5-FU 400 mg/m^2 IV bolus on day 1, then 1,200 mg/m^2/day × 2 days (total 2,400 mg/m^2 over 46–48 hours) IV continuous infusion Repeat cycle every 2 weeks.	See dosing regimen
CapeOX	Day 1: Oxaliplatin 130 mg/m^2 IV Days 1–14: Capecitabine 1,000 mg/m^2 PO BID Repeat cycle every 3 weeks.	See dosing regimen
FOLFIRI	Day 1: Irinotecan 180 mg/m^2 IV Day 1: Leucovorin 400 mg/m^2 IV Day 1: Flurouracil 400 mg/m^2 IV followed by 2,400 mg/m^2 continuous IV over 46 hours Repeat cycle every 14 days.	See dosing regimen
FOLFOXIRI	Day 1: Irinotecan 165 mg/m^2 IV, oxaliplatin 85 mg/m^2 IV, leucovorin 400 mg/m^2 IV, flurouracil 1,600 mg/m^2 continuous IV for 2 days (total 3,200 mg/m^2)	See dosing regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Repeat cycle every 2 weeks.	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): None reported
- Boxed warning(s): dermatologic toxicity

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
4Q 2018 annual review: no significant changes; summarized NCCN and FDA-approved uses for improved clarity; added specialist involvement in care; references reviewed and updated.	07/18	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/30/19	

References

1. Vectibix Prescribing Information. Thousand Oaks, CA: Amgen, Inc.; June 2017. Available at https://www.vectibix.com/. Accessed July 24, 2018.
2. Panitumumab. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed July 24, 2018.
3. Colon cancer (Version 2.2018). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed July 24, 2018.
4. Rectal cancer (Version 2.2018). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed July 24, 2018.