Clinical Policy: Panitumumab (Vectibix)

Reference Number: PA.CP.PHAR.321
Effective Date: 01/2018
Last Review Date: 10/2024

Description
Panitumumab (Vectibix®) is an epidermal growth factor receptor (EGFR) antagonist.

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 (mCRC):

- 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 PA Health & 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 advanced, recurrent, or metastatic colorectal cancer (CRC);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is one of the following (a, b, c, d or e):
   a. KRAS/NRAS/BRAF wild-type (i.e., no mutations in KRAS, NRAS, or BRAF genes);
   b. BRAF V600E mutation positive;
   c. KRAS G12C mutation positive;
   d. Deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H);
   e. Polymerase epsilon/delta (POLE/POLD1) mutation positive;
5. Prescribed in one of the following (a, b, c, d or e)*:
   a. As a single agent;
   b. In combination with FOLFIRI, FOLFOX, CapeOX;
   c. In combination with irinotecan in the initial or subsequent line setting;
   d. If BRAF V600E mutation positive: In combination with Braftovi® following prior therapy;
   e. If KRAS G12C mutation positive: In combination with Lumakras or Krazati following prior therapy;

   **Prior authorization may be required.*
6. For colon cancer that is KRAS/NRAS/BRAF wild-type with unresectable synchronous metastases: Colon cancer is left-sided only (*see Appendix D*);

7. For dMMR/MSI-H or POLE/POLD1 mutation positive cancer: Member is ineligible for or has progressed on checkpoint inhibitor immunotherapy (*see Appendix B*);*
   **Prior authorization may be required.*
8. Request meets one of the following (a or b):
   a. Dose does not exceed 6 mg/kg every 14 days;
   b. 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 PA Health & Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.PHARM.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 PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.PHARM.01) applies; or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CapeOX: capecitabine and oxaliplatin
CRC: colorectal cancer
dMMR/MSI-H: deficient mismatch repair/microsatellite instability-high
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
POLE/POLD1: polymerase epsilon/delta

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 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) Repeat cycle every 2 weeks.	See dosing regimen
Braftovi (Encorafenib)	300 mg PO once daily in combination with panitumumab (6 mg/kg IV every 14 days) until disease progression or unacceptable toxicity.	450 mg/day.
Checkpoint inhibitor therapies: Opdivo® (nivolumab) ± Yervoy® (ipilimumab) or Keytruda® (pembrolizumab)	Varies	Varies

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

Appendix D: KRAS/NRAS/BRAF Wild-Type Colon Cancer with Unresectable, Synchronous Liver and/or Lung Metastases

- The NCCN Colon Cancer Guidelines recommend that panitumumab should only be used for left-sided tumors in KRAS/NRAS/BRAF wild-type colon cancer with

unresectable, synchronous liver and/or lung metastases. The NCCN defines the left side of the colon as splenic flexure to rectum. Evidence suggests that patients with tumors originating on the right side of the colon (hepatic flexure through cecum) are unlikely to respond to panitumumab. Data on the response to panitumumab in patients with primary tumors originating in the transverse colon (hepatic flexure to splenic flexure) are lacking.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CRC	6 mg/kg IV over 60 minutes (≤ 1000 mg) or 90 minutes (> 1000 mg) every 14 days	6 mg/kg

V. Product Availability

Single-dose vial for injection: 100 mg/5 mL, 400 mg/20 mL

VI. References

1. Vectibix Prescribing Information. Thousand Oaks, CA: Amgen, Inc.; August 2021. Available at https://www.vectibix.com/. Accessed August 17, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 8, 2024.
3. National Comprehensive Cancer Network. Colon Cancer Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed August 8, 2024.

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
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.	07/2018
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
4Q 2020 annual review: added BRAF disease wild-type and for treatment in combination with Braftovi if BRAF V600E mutation position to colorectal indication as per NCCN 2A off label indication; references reviewed and updated.	08/2020
4Q 2021 annual review: added that combination treatment with Vectibix and Braftovi is for advanced or metastatic disease per NCCN Compendium; for	10/2021

Reviews, Revisions, and Approvals	Date
Vectibix prescribed as a single agent or in combination with irinotecan, added the option of previous oxaliplatin-based therapy without irinotecan or irinotecan-based therapy without oxaliplatin per NCCN Compendium; references reviewed and updated.	
4Q 2022 annual review: added qualifiers that CRC is advanced, recurrent, or metastatic per NCCN; added BRAF V600E mutation positive criterion option to wild-type options as this mutation also allows for Vectibix administration per NCCN category 2A rating; updated combination regimens per NCCN; references reviewed and updated.	10/2022
4Q 2023 annual review: simplified criteria by removing criterion qualifier "first-line treatment" as it overlaps with subsequent-line treatment regimens and to align with NCH criteria; added CapeOx as potential combination regimen per NCCN; added criterion that disease is left-sided only for colon cancer that is *KRAS/NRAS/BRAF* wild-type per NCCN & NCH, along with rationale in Appendix D; references reviewed and updated.	10/2023
4Q 2024 annual review: per NCCN – added pathways for dMMR/MSI-H, and POLE/POLD1 mutations with corresponding requirements related to combination use and/or prior therapy; removed prior therapy requirement when requested for use as a single agent; modified requirement for left-sided colon cancer to only apply to unresectable synchronous metastases; added Appendix D; references reviewed and updated.	10/2024