Vectibix® (panitumumab)
(Intravenous)

-E-

Document Number: IC-0389

Last Review Date: 10/03/2023
Date of Origin: 04/03/2019
Dates Reviewed: 04/2019, 07/2019, 09/2019, 01/2020, 04/2020, 07/2020, 10/2020, 01/2021, 04/2021, 07/2021, 10/2021, 02/2022, 05/2022, 10/2022, 01/2023, 05/2023, 07/2023, 10/2023

I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Vectibix 100 mg/5 mL solution for injection single-dose vial: 3 vials every 14 days
- Vectibix 400 mg/20 mL solution for injection single-dose vial: 1 vial every 14 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 100 billable units every 14 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Colorectal Cancer † ‡ [1,2,6-8,10,11,3e,5e,8e,11e,13e-15e]

- Patient is both KRAS and NRAS mutation negative (wild-type) as determined by an FDA or CLIA-compliant test❖; **AND**
- Patient has not been previously treated with cetuximab or panitumumab; **AND**
- Will not be used as part of an adjuvant treatment regimen; **AND**
- Will not be used in combination with an anti-VEGF agent (e.g., bevacizumab, ramucirumab); **AND**
- Patient has metastatic, unresectable (or medically inoperable), or advanced disease that is BRAF mutation negative (wild-type); **AND**
  - Used as primary treatment §; **AND**

- Use of panitumumab as primary treatment will be restricted to patients with a contraindication or intolerance to cetuximab; **AND**
    - Used in combination with FOLFOX †; **OR**
    - Used in combination with CapeOX or FOLFIRI; **AND**
        - Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease; **OR**
        - Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **OR**
    - Used in combination with an irinotecan-based regimen after previous FOLFOX or CapeOX within the past 12 months; **AND**
        - Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease; **OR**
    - Used in combination with CapeOx, FOLFOX, or FOLFIRI for <u>rectal</u> cancer if resection is contraindicated following neoadjuvant therapy; **AND**
        - Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease; **OR**
        - Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **OR**
- Used as subsequent therapy; **AND**
    - Used as a single agent; **AND**
        - Use of panitumumab as subsequent therapy will be restricted to patients with a contraindication or intolerance to cetuximab; **AND**
            - Patient has fluoropyrimidine-, oxaliplatin-, and irinotecan-refractory disease †; **OR**
            - Patient has irinotecan-intolerant disease; **AND**
                - Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease; **OR**
                - Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **OR**
    - Used in combination with irinotecan for oxaliplatin-refractory disease, irinotecan-refractory disease, or oxaliplatin- and irinotecan-refractory disease §; **AND**
        - Patient has one of the following:

- Mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease
- Mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **AND**

– Use of panitumumab as subsequent therapy will be restricted to patients with a contraindication or intolerance to cetuximab; **AND**

<u>Oxaliplatin-refractory disease ONLY:</u>

– Patient must demonstrate an inadequate response to bevacizumab (*or a commercially available bevacizumab biosimilar agent*) in combination with irinotecan, unless there is a contraindication or intolerance, prior to approval of panitumumab; **OR**

- Used in combination with FOLFIRI for oxaliplatin-refractory disease **§****; **AND**
  - Patient has one of the following:
    - Mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease
    - Mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **AND**

– Use of panitumumab will be restricted to patients with a contraindication or intolerance to bevacizumab (*or a commercially available bevacizumab biosimilar agent*) in combination with FOLFIRI; **AND**

– Use of panitumumab as subsequent therapy will be restricted to patients with a contraindication or intolerance to cetuximab

§Colon cancer patients must have left-sided tumors only.

******May also be used for progression on non-intensive therapy in patients with improvement in functional status (except if received previous fluoropyrimidine). (Note: Step therapy for bevacizumab does <u>not</u> apply if patient had progression on non-intensive therapy).*

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

❖*If confirmed using an FDA approved assay – http://www.fda.gov/companiondiagnostics*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,6,11]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by a stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: dermatologic/soft-tissue toxicity, electrolyte depletion, severe infusion-related reactions, acute renal failure, pulmonary fibrosis/interstitial lung disease (ILD), photosensitivity, ocular toxicities (i.e., keratitis, corneal perforation), etc.

V. Dosage/Administration [1,6,11]

Indication	Dose
Colorectal Cancer	Administer 6 mg/kg intravenously every 14 days until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS Code:

- J9303 – Injection, panitumumab, 10 mg; 1 billable unit = 10 mg

NDC(s):

- Vectibix 100 mg/5 mL single-dose vial; solution for injection: 55513-0954-xx
- Vectibix 400 mg/20 mL single-dose vial; solution for injection: 55513-0956-xx

VII. References (STANDARD)

1. Vectibix [package insert]. Thousand Oaks, CA; Amgen, Inc; August 2021. Accessed September 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) panitumumab. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed September 2023.

3. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. J Oncol Pract. 2018 Mar;14(3):e130-e136.
4. Hematology/Oncology Pharmacy Association (2019). *Intravenous Cancer Drug Waste Issue Brief*. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf
5. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. BMJ. 2016 Feb 29;352:i788.
6. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Colon Cancer Version 2.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. Accessed September 2023.
7. Van Cutsem E, Peeters M, Siena S, et al. Open-label phase III trial of panitumumab plus best supportive care compared with best supportive care alone in patients with chemotherapy-refractory metastatic colorectal cancer. J Clin Oncol. 2007 May 1;25(13):1658-64.
8. Price TJ, Peeters M, Kim TW, et al. Panitumumab versus cetuximab in patients with chemotherapy-refractory wild-type KRAS exon 2 metastatic colorectal cancer (ASPECCT): a randomised, multicentre, open-label, non-inferiority phase 3 study. Lancet Oncol. 2014 May;15(6):569-79. doi: 10.1016/S1470-2045(14)70118-4. Epub 2014 Apr 14.
9. Kim TW, Elme A, Kusic Z, et al. A phase 3 trial evaluating panitumumab plus best supportive care vs best supportive care in chemorefractory wild-type KRAS or RAS metastatic colorectal cancer. Br J Cancer. 2016 Nov 8;115(10):1206-1214. doi: 10.1038/bjc.2016.309. Epub 2016 Oct 13.
10. Douillard JY, Siena S, Cassidy J, et al. Final results from PRIME: randomized phase III study of panitumumab with FOLFOX4 for first-line treatment of metastatic colorectal cancer. Ann Oncol. 2014 Jul;25(7):1346-55. doi: 10.1093/annonc/mdu141. Epub 2014 Apr 8.
11. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Rectal Cancer. Version 4.2023. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed September 2023.

VIII. References (ENHANCED)

1e. Douillard JY, Oliner KS, Siena S, et al. Panitumumab–FOLFOX4 Treatment and RAS Mutations in Colorectal Cancer. N Engl J Med 2013; 369:1023-1034.

2e. Hurwitz H, Fehrenbacher L, Novotny W, et al. Bevacizumab plus Irinotecan, Fluorouracil, and Leucovorin for Metastatic Colorectal Cancer. N Engl J Med 2004; 350:2335-2342.

3e. Van Cutsem E, Kohne CH, Hitre E, et al. Cetuximab and Chemotherapy as Initial Treatment for Metastatic Colorectal Cancer. N Engl J Med 2009; 360:1408-1417.

4e. Van Cutsem E, Köhne CH, Láng I, et al. Cetuximab Plus Irinotecan, Fluorouracil, and Leucovorin As First-Line Treatment for Metastatic Colorectal Cancer: Updated Analysis of Overall Survival According to Tumor KRAS and BRAF Mutation Status. Journal of Clinical Oncology 2011 29:15, 2011-2019.

5e. Qin S, Li J, Wang L, et al. Efficacy and Tolerability of First-Line Cetuximab Plus Leucovorin, Fluorouracil, and Oxaliplatin (FOLFOX-4) Versus FOLFOX-4 in Patients With RAS Wild-Type Metastatic Colorectal Cancer: The Open-Label, Randomized, Phase III TAILOR Trial[published online ahead of print, 2018 Sep 10]. J Clin Oncol. 2018;36(30):JCO2018783183. doi:10.1200/JCO.2018.78.3183

6e. Schwartzberg LS, Rivera F, Karthaus M, et al. PEAK: A Randomized, Multicenter Phase II Study of Panitumumab Plus Modified Fluorouracil, Leucovorin, and Oxaliplatin (mFOLFOX6) or Bevacizumab Plus mFOLFOX6 in Patients With Previously Untreated, Unresectable, Wild-Type KRAS Exon 2 Metastatic Colorectal Cancer. Journal of Clinical Oncology 2014 32:21, 2240-2247.

7e. Holch JW, Ricard I, Stintzing S, et al. The relevance of primary tumour location in patients with metastatic colorectal cancer: A meta-analysis of first-line clinical trials. Eur J Cancer. 2017 Jan;70:87-98.

8e. Hecht JR, Mitchell E, Chidiac T, et al. A Randomized Phase IIIB Trial of Chemotherapy, Bevacizumab, and Panitumumab Compared With Chemotherapy and Bevacizumab Alone for Metastatic Colorectal Cancer. Journal of Clinical Oncology 2009 27:5, 672-680. N Engl J Med 2009; 360:563-572.

9e. Tol J, Koopman M, Cats A, et al. Chemotherapy, Bevacizumab, and Cetuximab in Metastatic Colorectal Cancer. N Engl J Med 2009; 360:563-572.

10e. Amado RG, Wolf M, Peeters M, et al. Wild-Type KRAS Is Required for Panitumumab Efficacy in Patients With Metastatic Colorectal Cancer. Journal of Clinical Oncology 2008 26:10, 1626-1634.

11e. Peeters M, Price TJ, Cervantes A, et al. Randomized Phase III Study of Panitumumab With Fluorouracil, Leucovorin, and Irinotecan (FOLFIRI) Compared With FOLFIRI Alone As Second-Line Treatment in Patients With Metastatic Colorectal Cancer. Journal of Clinical Oncology 2010 28:31, 4706-4713.

12e. Hochster HS, Catalano PJ, O'Dwyer PJ, et al. Randomized trial of irinotecan and cetuximab (IC) versus irinotecan, cetuximab and ramucirumab (ICR) as 2nd line therapy of advanced colorectal cancer (CRC) following oxaliplatin and bevacizumb based therapy: Result of E7208. Journal of Clinical Oncology 2018 36:15_suppl, 3504-3504.

13e. Heinemann V, von Weikersthal LF, Decker T, et al. FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal

cancer (FIRE-3): a randomised, open-label, phase 3 trial. Lancet Oncol. 2014 Sep;15(10):1065-75. doi: 10.1016/S1470-2045(14)70330-4.

14e. Venook AP, Niedzwiecki D, Innocenti F, et al. Impact of primary (1º) tumor location on overall survival (OS) and progression-free survival (PFS) in patients (pts) with metastatic colorectal cancer (mCRC): Analysis of CALGB/SWOG 80405 (Alliance). J Clin Oncol 34, 2016 (suppl; abstr 3504).

15e. Carrato A, Abad A, Massuti B, et al. First-line panitumumab plus FOLFOX4 or FOLFIRI in colorectal cancer with multiple or unresectable liver metastases: A randomised, phase II trial (PLANET-TTD). Eur J Cancer. 2017 Aug;81:191-202. doi: 10.1016/j.ejca.2017.04.024.

16e. Corcoran RB, André T, Atreya CE, et al. Combined BRAF, EGFR, and MEK Inhibition in Patients with BRAFV600E-Mutant Colorectal Cancer. Cancer Discov. 2018;8(4):428–443. doi:10.1158/2159-8290.CD-17-1226.

17e. Hecht JR, Cohn A, Dakhil S, et al. SPIRITT: A Randomized, Multicenter, Phase II Study of Panitumumab with FOLFIRI and Bevacizumab with FOLFIRI as Second-Line Treatment in Patients with Unresectable Wild Type KRAS Metastatic Colorectal Cancer. Clin Colorectal Cancer. 2015 Jun;14(2):72-80.

18e. Magellan Rx Management. Vectibix Clinical Literature Review Analysis. Last updated September 2023. Accessed September 2023.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C18.0	Malignant neoplasm of cecum
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of large intestines
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum

C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
Z85.038	Personal history of other malignant neoplasm of large intestine

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC