PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Vectibix® (panitumumab solution for intravenous infusion – Amgem Inc)

APPROVAL DATE: 07/24/2019

OVERVIEW

Vectibix is indicated for the treatment of 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) as follows: as first-line therapy in combination with FOLFOX (5-fluorouracil [5-FU], leucovorin, oxaliplatin) and 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.

Vectibix is a fully human monoclonal antibody that binds specifically to the epidermal growth factor receptor (EGFR).[1] *KRAS* and *NRAS* are related members of the *RAS* oncogene family. Signal transduction through the EGFR can result in activation of wild-type *RAS* proteins. However, in cells with activating *RAS* somatic mutations, the resulting mutant *RAS* proteins are continuously active regardless of EGFR regulation. The EGFR plays a key role in activation of the signaling pathways involved in the pathogenesis of colorectal cancer (CRC) and is often overexpressed in mCRC.[2] Vectibix blocks EGFR action and is not effective if downstream signaling pathways are activated independent of EGFR. Detecting mutations that lead to activation of signaling pathways downstream from EGFR can predict resistance to therapy with Vectibix in CRC.

Guidelines

Colon Cancer:

The National Comprehensive Cancer Network (NCCN) colon cancer guidelines (version 2.2019 – May 15, 2019) recommend Vectibix as primary therapy for unresectable, advanced, or metastatic *KRAS/NRAS/BRAF* wild-type gene and left-sided tumors only in combination with irinotecan, FOLFOX, FOLFIRI (5-FU, leucovorin, irinotecan), or FOLFOXIRI (5-FU, leucovorin, oxaliplatin, irinotecan) regimens in patients who can tolerate intensive therapy or as a single agent in patients who cannot tolerate intensive therapy.[2,4] Reference to left-sided only disease refers to a primary tumor that originated in the left side of the colon and only refers to use of Vectibix as first-line therapy for metastatic disease. Therapies recommended after first progression vary depending on the initial treatment regimen (i.e., 5-FU/leucovorin-based or capecitabine-based therapy) that was used. The NCCN guidelines also recommend Erbitux, in combination with irinotecan and Zelboraf (vemurafenib tablets), Tafinlar (dabrafenib capsules) and Mekinist (trametinib tablets), or Braftovi (encorafenib capsules) and Mektovi (binimetinib tablets), for the subsequent treatment of *BRAF V600E* positive disease.

Rectal Cancer:

The NCCN rectal cancer guidelines (version 2.2019 – May 15, 2019) recommend Vectibix as primary therapy for unresectable advanced or metastatic, *KRAS/NRAS/BRAF* wild-type tumors in combination with irinotecan, FOLFOX, FOLFIRI, or FOLFOXIRI regimens in patients who can tolerate intensive therapy or as a single agent in patients who cannot tolerate intensive therapy.[3,4] Therapies recommended after first progression vary depending on the initial treatment regimen (i.e., 5-FU/leucovorin-based or capecitabine-based therapy) that was used. The NCCN guidelines also recommend Vectibix, in combination with irinotecan and Zelboraf, Tafinlar and Mekinist, or Braftovi and Mektovi, for the subsequent treatment of *BRAF V600E* positive disease.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Vectibix. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Vectibix as well as the monitoring required for adverse events and long-term efficacy, approval requires Vectibix to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Vectibix is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Colon and Rectal Cancer.** Approve for 1 year if the patient meets the following criteria (A, B, C, D, and E):
   - **A)** Vectibix is prescribed by or in consultation with an oncologist; AND
   - **B)** Patient has advanced or metastatic disease; AND
   - **C)** The patient's tumor or metastases are wild-type *RAS* (*KRAS* wild-type and/or *NRAS* wild-type) [that is, the tumor or metastases are *KRAS* and/or *NRAS* mutation negative]; AND
   - **D)** If Vectibix is being used for first-line treatment, the primary tumor originated on the left side of the colon (from splenic flexure to rectum); AND
   - **E)** Patient meets ONE of the following criteria (i or ii):
     - **i.** The patient's tumor or metastases are wild-type *BRAF* (that is, the tumor or metastases are *BRAF V600E* mutation negative); OR
     - **ii.** The patient's tumor or metastases are *BRAF V600E* mutation-positive and the patient meets the following (a and b):
       a) The patient has previously received a chemotherapy regimen for colon or rectal cancer. NOTE: Examples of chemotherapy regimens include a fluoropyrimidine such as 5-fluorouracil (5-FU), capecitabine, oxaliplatin, irinotecan, or an adjunctive chemotherapy regimen such as FOLFOX (5-FU, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin); AND
       b) Vectibix is prescribed as part of a combination regimen for colon or rectal cancer. NOTE: Examples of combination regimens include: Vectibix/irinotecan/Zelboraf (vemurafenib tablets), or Vectibix/Tafinlar (dabrafenib capsules)/Mekinist (trametinib tablets), or Vectibix/ Braftovi (encorafenib capsules)/Mektovi (binimetinib tablets).[2-4]

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Vectibix has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Vectibix® injection for intravenous infusion [prescribing information]. Thousand Oaks, CA: Amgen Inc; June 2017.
2. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (Version 2.2019 – May 15, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 3, 2019.
3. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (Version 2.2019 – May 3, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 3, 2019.
4. The NCCN Drugs and Biologics Compendium. © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 3, 2019. Search term: panitumumab.

OTHER REFERENCES UTILIZED

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- 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;15:569-579.
- 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;15:1065-1075.
- Douillard JY, Siena S, Cassidy J, et al. Final results from PRIME: randomized phase 3 study of panitumumab with FOLFOX4 for first-line treatment of metastatic colorectal cancer. *Ann Oncol.* 2014;25:1346-1355.
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- Allegra CJ, Rumble RB, Hamilton SR, et al. Extended RAS gene mutation testing in metastatic colorectal carcinoma to predict response to anti-epidermal growth factor receptor monoclonal antibody therapy: American Society of Clinical Oncology Provisional Clinical Opinion Update 2015. *J Clin Oncol*. 2016;34:179-185.