Utilization Review Policy

Policy: Oncology – Vectibix® (panitumumab solution for intravenous infusion – Amgen 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 medical benefit coverage of Vectibix. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (e.g., Medical Director or Pharmacist). All approvals are provided for the duration noted below.

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.

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

FDA-Approved Indication
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

   Dosing. Approve the following dosing regimen: Each individual dose must not exceed 6 mg/kg administered by intravenous infusion given no more frequently than once every 14 days.1

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Erbitux 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

OTHER REFERENCES UTILIZED

HISTORY

<table>
<thead>
<tr>
<th>Type of Revision</th>
<th>Summary of Changes</th>
<th>Approval Date</th>
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</thead>
<tbody>
<tr>
<td>Annual</td>
<td>No changes to criteria.</td>
<td>08/17/2016</td>
</tr>
<tr>
<td>Annual</td>
<td>Colorectal cancer criteria revised to add RAS. Previously criteria stated KRAS and/or NRAS that are the components of RAS. Wild-type refers to both KRAS and NRAS. A criterion was added requiring that if Vectibix is being used for first-line treatment of metastatic colorectal cancer, the primary tumor originated on the left side of the colon.</td>
<td>08/23/2017</td>
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<tr>
<td>Annual</td>
<td>Colorectal cancer criteria updated to include: Vectibix in combination with irinotecan, or irinotecan plus vemurafenib (BRAF V600E mutation positive). Removed Patient has been Started on Vectibix criteria.</td>
<td>08/08/2018</td>
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<tr>
<td>Annual</td>
<td>Removed Initial Approval/Extended Approval, Duration of Therapy and Labs/Diagnostics sections. Increased approval duration to 1 year. Revised colon and rectal cancer criteria E to include the management of patients with BRAF V600E mutation-positive and mutation-negative disease. Removed Other Cancer Indications section. Removed Waste Management section. Revised Conditions not Recommended for Approval section.</td>
<td>07/24/2019</td>
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