Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Panitumumab (Vectibix®)	MP-RX-FP-99-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Other TYPE B DRUG

Service Description

This document addresses the use of *Panitumumab (Vectibix®),* an epidermal growth factor receptor (EGFR) antagonist approved by the Food and Drug Administration (FDA) 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).

Background Information

Vectibix is a human monoclonal antibody that targets and inhibits the biologic activity of the human epidermal growth factor receptor (EGFR) that is primarily used to treat colorectal cancer.

Colorectal cancer is the third most common cancer worldwide, accounting for approximately 10% of all cancer cases and is the second leading cause of cancer-related deaths worldwide. Approximately 70 to 80% of all colorectal carcinomas demonstrated an over-expression of the epidermal growth factor receptor (EGFR), a known participant in cancer-related processes such as cell proliferation, apoptosis, angiogenesis, and metastasis.

Monoclonal antibodies that target EGFR have shown anti-tumor activity and enhanced the efficacy of chemotherapy. Among these antibodies, Panitumumab (Vectibix) is a human monoclonal antibody that inhibits the extracellular domain of EGFR and has not been linked to the development of antibodies against it. EGFR is a transmembrane glycoprotein that is naturally expressed in various normal epithelial tissues, such as the skin and hair follicles. Additionally, EGFR is found to be overexpressed in many human cancers, including those affecting the colon and rectum. Interaction between EGFR and its normal ligands leads to phosphorylation and activation of intracellular tyrosine kinases, subsequently regulating the transcription of molecules involved in cellular growth, survival, motility, proliferation, and transformation.

The FDA approved indications for Vectibix include as first line therapy in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or as monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy. The National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for the use of Vectibix. NCCN recommends appendiceal adenocarcinoma be treated with chemotherapy according to colon cancer guidelines. Similarly, it is recommended that anal adenocarcinoma, a rare histologic form of anal cancer, may be treated according to guidelines for rectal cancer.

Policy Name	Policy Number	Scope
Panitumumab (Vectibix®)	MP-RX-FP-99-23	☒ MMM MA ☒ MMM Multihealth

The FDA label includes the requirement for confirmed RAS wild-type histology and that Vectibix is not indicated for those with somatic RAS mutations in either KRAS or NRAS or for whom RAS mutation status is unknown. NCCN also notes that research has demonstrated that mutations in the KRAS, and more recently NRAS genes, are a predictive factor for a lack of response to Vectibix therapy for colorectal cancer. Mutations in the BRAF gene cause a cancer signal downstream of the EGFR/RAS pathway. In the presence of BRAF mutations, NCCN notes that response to EGFR inhibitors is very unlikely unless given with a BRAF inhibitor. NCCN recommends the combination use of Vectibix and encorafenib for BRAF mutation positive colorectal cancer after prior therapy.

Vectibix and Erbitux (cetuximab) are two EGFR antagonists approved by the FDA. There is currently no evidence to support switching to either Erbitux or Vectibix after failure of the other drug and NCCN recommends against this practice. In addition, studies have shown that combination with more than one biologic agent is not associated with improved outcomes and can cause increased toxicity, specifically regarding the addition of Erbitux or Vectibix to a bevacizumab-containing regimen (Tol 2009, Hecht 2009). NCCN strongly recommends against the use of therapy involving concurrent combination of an anti-EGFR agent and an anti-VEGF agent.

Vectibix has a black box warning for dermatologic toxicity. Dermatologic toxicities occurred in 90% of patients and were severe (NCI-CTC grade 3 and higher) in 15% of patients receiving Vectibix monotherapy.

Definitions and Measures

- Adenocarcinoma: Cancer originating in cells that line specific internal organs and that have gland-like (secretory) properties.
- Anal cancer: Cancer originating in the tissues of the anus; the anus is the opening of the rectum (last part of the large intestine) to the outside of the body.
- BRAF: The oncogene which directions production of a protein in the regulating MAP kinase/ERKs signaling pathway, which affects cell division, differentiation, and secretion.
- Colon cancer: Cancer originating in the tissues of the colon (the longest part of the large intestine). Most colon cancers are adenocarcinomas that begin in cells that make and release mucus and other fluids.
- Colorectal cancer: Cancer originating in the colon (the longest part of the large intestine) or the rectum (the last several inches of the large intestine before the anus).
- KRAS wild-type: The normal or typical form of the KRAS gene, as distinguished from any mutant forms of KRAS; KRAS lacking mutation.
- Mutation: A permanent, transmissible change in genetic material. One line of therapy: Single line of therapy.
- One line of therapy: Single line of therapy.
- Rectal cancer: Cancer originating in tissues of the rectum (the last several inches of the large intestine closest to the anus).
- Vascular endothelial growth factor (VEGF): A substance made by cells that stimulates new blood vessel formation.

Policy Name	Policy Number	Scope
Panitumumab (Vectibix®)	MP-RX-FP-99-23	☒ MMM MA ☒ MMM Multihealth

Approved Indications

A. Vectibix is indicated by the FDA 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):

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

Vectibix is **not** indicated for the treatment of patients with *RAS*-mutant mCRC or for whom *RAS* mutation status is unknown.

Other Uses

i. NCCN no longer recommends the off-label use of Vectibix as second-line palliative therapy in penile cancer. FDA label and compendia do not support this indication either. Though anal adenocarcinoma is an acceptable use for Vectibix, NCCN guidelines for squamous cell anal cancer, the most common type of anal cancer, do not currently include Vectibix among recommended treatments.

ii. NCCN guideline for small bowel adenocarcinoma (SBA) notes that cetuximab and panitumumab should not be used to treat SBA due to inconclusive evidence.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J9303	Injection, panitumumab, 10 mg [Vectibix]

ICD-10	Description
C17.0-C17.8	Malignant neoplasm of small intestine
C18.0-C18.9	Malignant neoplasm of colon
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.0-C21.8	Malignant neoplasm of colon, rectum, rectosigmoid junction, anus
C78.5	Secondary malignant neoplasm of large intestine and rectum

Policy Name	Policy Number	Scope
Panitumumab (Vectibix®)	MP-RX-FP-99-23	☒ MMM MA ☒ MMM Multihealth

Z51.11-Z51.12	Encounter for antineoplastic chemotherapy and immunotherapy
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.048	Personal history of other malignant neoplasm of rectum, rectosigmoid junction, and anus

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Panitumumab (Vectibix®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

i. Individual has a diagnosis of unresectable of metastatic colon, rectal, colorectal, appendiceal, or anal adenocarcinoma and the following are met: (Label, NCCN 2A)

A. Panitumumab is used as a single agent or as part of combination therapy; **AND**

B. *One* of the following is met:

1. Extended RAS gene mutation testing determines the tumor is RAS wild-type (RAS wildtype means that the KRAS and NRAS genes are normal or lacking mutations) and individual is using in combination with irinotecan or oxaliplatin;

OR

2. Tumor is determined to be BRAF wild-type and individual is using in combination with irinotecan or oxaliplatin;

OR

3. Gene mutation testing has determined the tumor to be BRAF V600E positive and panitumumab is used in combination with encorafenib;

OR

4. Gene mutation testing has determined the tumor to be KRAS G12C positive and panitumumab is used in combination with sotorasib or adagrasib.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Panitumumab (Vectibix®), therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of an unacceptable toxicity or disease progression while on the current regimen. The following information should be submitted for reauthorization:

Policy Name	Policy Number	Scope
Panitumumab (Vectibix®)	MP-RX-FP-99-23	☒ MMM MA ☒ MMM Multihealth

A. A current oncology note documenting the patient's response to treatment showing no progression of disease.

B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. All other indications not included above (Section A: Criteria for Initial Approval); **OR**
ii. Treatment of RAS-mutant metastatic colorectal cancer, small bowel or anal adenocarcinoma, (that is, when an FDA approved test has confirmed the presence of genetic mutations in any of the RAS genes) or when RAS mutation status is unknown; **OR**
iii. In combination with other monoclonal antibodies or anti-VEGF agents; **OR**
iv. Treatment of penile cancer; **OR**
v. Treatment of squamous cell anal carcinoma; **OR**
vi. Individual has received prior treatment with cetuximab (cetuximab discontinuation due to adverse reaction is not considered prior treatment).

Limits or Restrictions

1. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

2. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Policy Name	Policy Number	Scope
Panitumumab (Vectibix®)	MP-RX-FP-99-23	☒ MMM MA ☒ MMM Multihealth

Drug	Recommended Dosing Schedule
Panitumumab (Vectibix®) 100 mg/5ml; 400mg/20ml	6 mg/kg I.V. every 14 days until disease progression or unacceptable toxicity.
Exceptions	
None	

Reference Information

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2023. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: March 13, 2023.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
5. NCCN Clinical Practice Guidelines in Oncology™. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on March 16, 2023.
    a. Colon Cancer. V1.2023. Revised March 29, 2023.
    b. Rectal Cancer. V1.2023. Revised March 29, 2023.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy Name	Policy Number	Scope
Panitumumab (Vectibix®)	MP-RX-FP-99-23	☒ MMM MA ☒ MMM Multihealth

Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review 11/15/2024	Update background information. Update colon, rectal, colorectal, appendiceal, anal adenocarcinoma criteria for unresectable or metastatic disease, update criteria to add BRAF V600E and KRAS G12C combination use, wording changes. Coding Reviewed: No changes.	3/14/2025	4/2/2025
Select Review 2/15/2024	Update statement for criteria for initial approval: Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met all approval criteria.	3/25/2024	5/9/2024
Policy Inception 11/15/2023	Elevance Health's Medical Policy adoption.	N/A	11/30/2023