



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Subject **Panitumumab (Vectibix™)**

Effective Date 2/15/2011
Next Review Date..... 2/15/2012
Coverage Position Number..... 1101

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INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2011 CIGNA

Coverage Policy

CIGNA covers panitumumab (Vectibix™) as medically necessary for EITHER of the following indications:

- advanced or metastatic colorectal cancer expressing the wild type Kirsten rat sarcoma (KRAS) gene
- advanced or metastatic small bowel adenocarcinoma expressing the wild type Kirsten rat sarcoma (KRAS) gene

When coverage is available and medically necessary, the dosage, frequency, site of administration, and duration of therapy should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to panitumumab (Vectibix™).

FDA Approved Indications

Vectibix is indicated as a single agent for the treatment of epidermal growth factor receptor (EGFR)-expressing, metastatic colorectal carcinoma (mCRC) with disease progression on or following fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens. The effectiveness of Vectibix as a single agent for the treatment of EGFR-expressing, metastatic colorectal carcinoma is based on progression-free survival. Currently, no data demonstrate an improvement in disease-related symptoms or increased survival with Vectibix. Retrospective subset analyses of metastatic colorectal cancer trials have not

shown a treatment benefit for Vectibix in patients whose tumors had *KRAS* mutations in codon 12 or 13. Use of Vectibix is not recommended for the treatment of colorectal cancer with these mutations.

FDA Recommended Dosing

The recommended dose of Vectibix is 6 mg/kg, administered as an intravenous infusion over 60 minutes, every 14 days. Doses higher than 1000 mg should be administered over 90 minutes. Appropriate medical resources for the treatment of severe infusion reactions should be available during Vectibix infusions.

Black Box Warnings

WARNING: DERMATOLOGIC TOXICITY and INFUSION REACTIONS

Dermatologic toxicities occurred in 89% of patients and were severe (NCI-CTC grade 3 and higher) in 12% of patients receiving Vectibix monotherapy. Severe infusion reactions occurred in approximately 1% of patients. Although not reported with Vectibix, fatal infusion reactions have occurred with other monoclonal antibody products.

Drug Availability

Vectibix is supplied as a sterile, colorless, preservative-free solution containing 20 mg/mL Vectibix (panitumumab) in a single-use vial. Vectibix is provided as one vial per carton. Each 5 mL single-use vial contains 100 mg of panitumumab in 5 mL (20 mg/mL). Each 10 mL single-use vial contains 200 mg of panitumumab in 10 mL (20 mg/mL). Each 20 mL single-use vial contains 400 mg of panitumumab in 20 mL (20 mg/mL).

General Background

Pharmacology

Panitumumab is a recombinant, fully human monoclonal antibody for the extracellular domain of the human EGFR. Panitumumab competitively inhibits the binding of endogenous ligands to the EGFR, preventing activation of intracellular tyrosine kinases, which inhibits cell growth, decreases production of vascular endothelial growth factor, induces apoptosis, and decreases further expression of EGFR. Current data indicate that EGFR testing has no predictive value and routine testing is not recommended. However, all patients should be screened for the presence of mutant *KRAS*. Do not use panitumumab or cetuximab if mutations are present. Panitumumab is administered intravenously and exhibits nonlinear pharmacokinetics. Steady state is achieved by the third infusion, when given every 14 days. Distribution and metabolism have yet to be studied. Elimination half-life is about 7.5 days.

Guidelines

The National Comprehensive Cancer Network (NCCN) recommends Vectibix for colon cancer for the following:

Grade 2A

Used in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen for tumors expressing *KRAS* wild-type gene as neoadjuvant therapy for patients with synchronous liver and/or lung metastases or with resectable metachronous metastases; adjuvant therapy for patients with resected synchronous liver and/or lung metastases or with metachronous metastases; primary therapy for patients with unresectable synchronous liver and/or lung metastases, with synchronous abdominal/peritoneal metastases, or with unresectable metachronous metastases.

Initial therapy for patients with tumors expressing *KRAS* wild-type gene who have unresectable advanced or metastatic disease in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen for those who can tolerate intensive therapy; as a single agent for patients who cannot tolerate intensive therapy.

Used in combination with FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen for tumors expressing *KRAS* wild-type gene as therapy after first progression following FOLFOX (fluorouracil, leucovorin, oxaliplatin, and irinotecan) or CapeOX (capecitabine and oxaliplatin) regimen with or without bevacizumab for patients who can tolerate intensive therapy

Therapy as a single agent for patients with tumors expressing *KRAS* wild-type gene who have unresectable advanced or metastatic disease and are not able to tolerate cetuximab plus irinotecan after first progression

following FOLFIRI (fluorouracil, leucovorin, and irinotecan) with or without bevacizumab or FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen; after second or third progression except in patients receiving cetuximab or panitumumab for first progression.

Clinical Efficacy

No trials have compared panitumumab with other monoclonal antibodies used in colorectal cancer. The efficacy of panitumumab for EGFR-expressing metastatic colorectal carcinomas was evaluated in one randomized comparative trial (Van Cutsem, et.al., 2007) and two descriptive studies (Berlin, et.al., 2007, Hecht, et.al., 2007, and Muro, et.al., 2009). In pretreated patients randomized to panitumumab plus best supportive care (BSC), progression free survival at 8 weeks was 49% compared to the BSC only group at 30%, $p < 0.001$. Partial response at 12 months in the panitumumab plus BSC group was 10% compared to BSC only at zero, $p < 0.001$. Overall, in the experimental and descriptive trials, panitumumab stabilized disease in 27% to 33% of patients and partial response occurred in 9% to 13.5% of patients. Median progression-free survival ranged from 8 weeks to 14 weeks.

KRAS (Kirsten rat sarcoma) testing is recommended in patients with metastatic colorectal carcinoma from either a primary tumor or metastatic tumor tissue and in the work-up of patients with stage IV rectal cancer. KRAS has also been proposed for use in the management of non-small cell lung cancer and potentially other cancers, but its clinical utility has not been established (Okudela, 2010; Mao, 2009).

Adverse Drug Reactions / Drug Interactions

The most common adverse effect is dermatologic toxicity (up to 90%) with severe skin reactions occurring in up to 14% of patients. Infusion reactions occur infrequently (4%) and are severe in 1% of patients. Panitumumab carries a black box warning for dermatologic toxicity and severe infusion reactions. Other common adverse effects include hypomagnesemia (may be delayed), fatigue, abdominal pain, and nausea. Panitumumab should not be used in combination with chemotherapy. Decreased overall survival was noted in patients receiving panitumumab, bevacizumab, and oxaliplatin- or irinotecan-based chemotherapy.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

HCPCS Codes	Description
J9303	Injection, panitumumab, 10 mg

ICD-9-CM Diagnosis Codes	Description
153.0-153.9	Malignant neoplasm of colon
154.0-154.8	Malignant neoplasm of rectum, rectosigmoid junction, and anus

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