Panitumumab: Drug information

(For additional information see "Panitumumab: Patient drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

ALERT: US Boxed Warning

Dermatologic toxicity:

Dermatologic toxicities occurred in 90% of patients and were severe (National Cancer Institute Common Toxicity Criteria [NCI-CTC] grade 3 and higher) in 15% of patients receiving panitumumab monotherapy.

Brand Names: US

Vectibix

Brand Names: Canada

Vectibix

Pharmacologic Category

Antineoplastic Agent, Epidermal Growth Factor Receptor (EGFR) Inhibitor; Antineoplastic Agent, Monoclonal Antibody

Dosing: Adult

Colorectal cancer, metastatic, *KRAS* wild-type: IV: 6 mg/kg every 14 days as a single agent (Van Cutsem, 2007) or in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin) (Douillard, 2010; Douillard, 2013); continue until disease progression or unacceptable toxicity (Douillard, 2010; Van Cutsem, 2007)

Colorectal cancer, metastatic, *KRAS* wild-type in combination with FOLFIRI (fluorouracil, leucovorin, and irinotecan; off-label combination): IV: 6 mg/kg every 14 days; continue until disease progression or unacceptable toxicity (Peeters, 2010)

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Hepatic Impairment

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Adjustment for Toxicity

Infusion reactions, mild-to-moderate (grade 1 or 2): Reduce the infusion rate by 50% for the duration of infusion.

Infusion reactions, severe (grade 3 or 4): Stop infusion; consider permanent discontinuation (depending on severity or persistence of reaction).

Dermatologic toxicity:

Grade 3 toxicity (first occurrence): Withhold 1 to 2 doses; if reaction improves to <grade 3, resume therapy at initial dose.

Grade 3 toxicity (second occurrence): Withhold 1 to 2 doses; if reaction improves to <grade 3, resume therapy at 80% of initial dose.

Grade 3 toxicity (third occurrence): Withhold 1 to 2 doses; if reaction improves to <grade 3, resume therapy at 60% of initial dose.

Grade 3 toxicity (fourth occurrence), grade 3 toxicity that does not recover to <grade 3 after withholding 1 or 2 doses, or grade 4 toxicity: Permanently discontinue.

Ocular toxicity (acute or worsening keratitis): Interrupt or discontinue treatment.

Pulmonary toxicity:

Acute onset or worsening pulmonary symptoms: Interrupt treatment.

Interstitial lung disease: Permanently discontinue treatment.

Dosage Forms

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Intravenous [preservative free]:

Vectibix: 100 mg/5 mL (5 mL); 400 mg/20 mL (20 mL)

Generic Equivalent Available (US)

No

Administration

IV: Administer via infusion pump; do not administer IV push or as a bolus. Doses ≤1000 mg, infuse over 1 hour; if first infusion is tolerated, subsequent doses may be administered over 30 to 60 minutes. Doses >1000 mg, infuse over 90 minutes. Administer through a low protein-binding 0.2 or 0.22 micrometer in-line filter. Flush line with NS before and after infusion; do not mix or administer with other medications. Reduce infusion rate by 50% for mild-to-moderate infusion reactions (grades 1 and 2); stop infusion for severe infusion reactions (grades 3 and 4) and consider permanent discontinuation. Appropriate medical support for the management of infusion reactions should be readily available.

Use

Colorectal cancer, metastatic: Treatment of patients with wild-type *KRAS* (exon 2 in codons 12 or 13) metastatic colorectal cancer (mCRC), either as first-line therapy in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or as a single agent following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens

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

Use: Off-Label

Colorectal cancer, metastatic, KRAS wild-type (in combination with other chemotherapy agents)

Medication Safety Issues

Sound-alike/look-alike issues:

Panitumumab may be confused with pertuzumab

Adverse Reactions

Monotherapy:

>10%:

Central nervous system: Fatigue (26%)

Dermatologic: Skin toxicity (90%; grades 3/4: 15%), erythema (66%; grades 3/4: 6%), pruritus (58%; grades 3/4: 3%), acneiform eruption (57%; grades 3/4: 7%), paronychia (25%; grades 3/4: 2%), rash (22%; grades 3/4: 1%), skin fissure (20%; grades 3/4: 1%), exfoliative dermatitis (18%; grades 3/4: 2%), acne vulgaris (14%; grades 3/4: 1%)

Endocrine & metabolic: Hypomagnesemia (grades 3/4: 7%)

Gastrointestinal: Nausea (23%), diarrhea (21%; grades 3/4: 2%), vomiting (19%)

Ophthalmic: Ocular toxicity (16%)

Respiratory: Dyspnea (18%), cough (15%)

Miscellaneous: Fever (17%)

1% to 10%:

Cardiovascular: Pulmonary embolism (1%)

Central nervous system: Chills (3%)

Dermatologic: Nail toxicity (10%), xeroderma (10%), desquamation (9%; grades 3/4: <1%), dermal ulcer (6%; grades 3/4: <1%), pustular rash (4%), papular rash (2%)

Endocrine & metabolic: Dehydration (3%)

Gastrointestinal: Mucositis (7%), stomatitis (7%), xerostomia (5%)

Immunologic: Antibody formation (≤5%)

Ophthalmic: Abnormal eyelash growth (6%), conjunctivitis (5%)

Respiratory: Epistaxis (4%), interstitial pulmonary disease (1%)

Miscellaneous: Infusion related reaction (3%; grades 3/4: <1%)

<1%: Hypersensitivity reaction, pulmonary fibrosis

Combination therapy with FOLFOX:

>10%:

Dermatologic: Skin rash (56%; grades 3/4: 17% to 26%), acneiform eruption (32%; grades 3/4: 10%), pruritus (23%; grades 3/4: <1%), paronychia (21%; grades 3/4: 3%), xeroderma (21%; grades 3/4: 2%), erythema (16%; grades 3/4: 2%), skin fissure (16%; grades 3/4: <1%), alopecia (15%), acne vulgaris (14%; grades 3/4: 3%)

Endocrine & metabolic: Hypomagnesemia (30%), hypokalemia (21%), weight loss (18%)

Gastrointestinal: Diarrhea (62%), anorexia (36%), abdominal pain (28%), stomatitis (27%), mucosal inflammation (25%)

Neuromuscular & skeletal: Weakness (25%)

Ophthalmic: Conjunctivitis (18%)

Respiratory: Epistaxis (14%)

1% to 10%:

Cardiovascular: Deep vein thrombosis (5%)

Central nervous system: Fatigue (≥1%), paresthesia (≥1%)

Dermatologic: Nail disorder (10%; grades 3/4: 1%), palmar-plantar erythrodysesthesia (9%; grades 3/4: 1%), cellulitis (3%)

Endocrine & metabolic: Dehydration (8%), hypocalcemia (6%)

Hypersensitivity: Hypersensitivity (≥1%)

Local: Localized infection (4%)

<1%: Antibody development

Postmarketing and/or case reports (mono- and combination therapy): Abscess, angioedema, bullous skin disease (mucocutaneous), corneal ulcer, keratitis, necrotizing fasciitis, sepsis, skin necrosis, Stevens-Johnson syndrome, toxic epidermal necrolysis

Contraindications

There are no contraindications listed in the manufacturer's US labeling.

Canadian labeling: History of severe or life-threatening hypersensitivity reactions to panitumumab or any component of the formulation.

Warnings/Precautions

Concerns related to adverse effects:

• Dermatologic toxicity: **[US Boxed Warning]: Dermatologic toxicities have been reported in**

90% of patients receiving single agent panitumumab and were severe (grade 3 or higher) in 15% of patients; may include dermatitis acneiform, pruritus, erythema, rash, skin exfoliation, paronychia, dry skin, and skin fissures. Severe skin toxicities may be complicated by infection, sepsis, necrotizing fasciitis, or abscesses. The median time to development of skin (or ocular) toxicity was 2 weeks, with resolution ~12 weeks after discontinuation. The severity of dermatologic toxicity is predictive for response; grades 2 to 4 skin toxicity correlates with improved progression free survival and overall survival, compared to grade 1 skin toxicity (Peeters, 2009; Van Cutsem, 2007). Monitor all dermatologic toxicities for development of inflammation or infection. Rare cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported; bullous mucocutaneous disease (life-threatening/fatal) have been observed. Withhold treatment for severe or life-threatening dermatologic or soft tissue toxicities associated with severe/life-threatening inflammatory or infectious complications; dermatologic toxicity may require dose reduction or permanent discontinuation. Patients should minimize sunlight exposure and wear sunscreen and protective clothing/hat; sunlight may exacerbate skin reactions. Nail toxicity has also been reported.

• Diarrhea: May cause diarrhea; the incidence and severity of chemotherapy-induced diarrhea is increased with combination chemotherapy. Severe diarrhea and dehydration (which may lead to acute renal failure) has been observed with panitumumab in combination with chemotherapy. Gastric mucosal toxicity has also been reported.

• Electrolyte depletion: Magnesium and/or calcium depletion may occur during treatment (may be delayed; hypomagnesemia occurred ≥8 weeks after completion of panitumumab) and after treatment is discontinued; electrolyte repletion may be necessary. Monitor for hypomagnesemia and hypocalcemia during treatment and for at least 8 weeks after completion. Hypokalemia has also been reported.

• Infusion reactions: Severe infusion reactions (bronchospasm, dyspnea, fever, chills, and hypotension) have been reported in ~1% of patients; fatal infusion reactions have been reported with postmarketing surveillance. Discontinue infusion for severe reactions; permanently discontinue in patients with persistent severe infusion reactions. Appropriate medical support for the management of infusion reactions should be readily available. Mild-to-moderate infusion reactions are managed by slowing the infusion rate.

• Ocular toxicity: Keratitis and ulcerative keratitis (known risk factors for corneal perforation) have occurred. Monitor for evidence of ocular toxicity; interrupt or discontinue treatment for acute or worsening keratitis.

• Pulmonary toxicity: Pulmonary fibrosis and interstitial lung disease have been observed (rarely) in clinical trials; fatalities have been reported. Interrupt treatment for acute onset or worsening of pulmonary symptoms; permanently discontinue treatment if interstitial lung disease is confirmed. Patients with a history of or evidence of interstitial pneumonitis or pulmonary fibrosis were excluded from most clinical trials; consider the benefits of therapy versus the risk of pulmonary complications in such patients.

Disease-related concerns:

• Colorectal cancer and *RAS* (*KRAS* and *NRAS*) mutation status: Patients with codons 12 and 13 (exon 2), codons 59 and 61 (exon 3), or codons 117 and 146 (exon 4) *RAS* (*KRAS* or *NRAS*) mutations are unlikely to benefit from EGFR inhibitor therapy. Panitumumab is not indicated in patients with *RAS* mutation-positive metastatic colorectal cancer or patients in which *RAS* mutation

status is unknown. Utilizing an anti-EGFR-directed antibody in patients whose tumors contain *RAS* mutations resulted in increased toxicity without clinical benefit. In a study of FOLFOX4 (fluorouracil, leucovorin and oxaliplatin) ± panitumumab, patients with a *KRAS* mutation who received panitumumab with FOLFOX4 experienced a significantly shortened progression-free survival (Douillard, 2010). In addition, a subset analysis of patients with wild-type *KRAS* identified additional *RAS* (*KRAS* [exons 3 and 4] or *NRAS* [exons 2, 3, 4]) mutations; progression-free survival and overall survival were significantly shortened in patients with *RAS* mutations who received FOLFOX4 in combination with panitumumab (Douillard, 2013). The American Society of Clinical Oncology (ASCO) provisional clinical opinion (Allegra, 2009) recommends genotyping tumor tissue for *KRAS* mutation in all patients with metastatic colorectal cancer (genotyping may be done on archived specimens). An updated ASCO provisional clinical opinion recommends that all patients with metastatic colorectal cancer who are candidates for anti-EGFR therapy should be tested (in a certified lab) for mutations in both *KRAS* and *NRAS* exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146); anti-EGFR monoclonal antibody therapy should only be considered in patients whose tumors lack mutations after extended *RAS* testing (Allegra, 2015). Panitumumab is also reported to be ineffective in patients with BRAF V600E mutation (Di Nicolantonio, 2008).

Concurrent drug therapy issues:

• Bevacizumab and combination chemotherapy: In a study of bevacizumab with combination chemotherapy ± panitumumab, the use of panitumumab resulted in decreased progression-free and overall survival and significantly increased toxicity compared to regimens without panitumumab (Hecht, 2009). Toxicities included rash/acneiform dermatitis, diarrhea/dehydration, electrolyte disturbances, mucositis/stomatitis, and an increased incidence of pulmonary embolism.

Special populations:

• Elderly: Patients >65 years of age receiving panitumumab plus FOLFOX experienced a higher incidence of serious adverse events including severe diarrhea.

Metabolism/Transport Effects

None known.

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Aminolevulinic Acid: Photosensitizing Agents may enhance the photosensitizing effect of Aminolevulinic Acid. *Risk C: Monitor therapy*

Porfimer: Photosensitizing Agents may enhance the photosensitizing effect of Porfimer. *Risk C: Monitor therapy*

Verteporfin: Photosensitizing Agents may enhance the photosensitizing effect of Verteporfin. *Risk C: Monitor therapy*

Pregnancy Risk Factor

C (show table)

Pregnancy Implications

Animal reproduction studies have demonstrated adverse fetal effects. Based on animal studies, panitumumab may disrupt normal menstrual cycles. IgG is known to cross the

placenta; therefore, it is possible the developing fetus may be exposed to panitumumab. Because panitumumab inhibits epidermal growth factor (EGF), a component of fetal development, adverse effects on pregnancy would be expected. Men and women of childbearing potential should use effective contraception during and for 6 months after treatment. In the US and Canada, women who become pregnant during panitumumab treatment are encouraged to enroll in Amgen's Pregnancy Surveillance Program (US: 1-800-772-6436; Canada: 1-866-512-6436).

Breast-Feeding Considerations It is not known if panitumumab is excreted in breast milk. The decision to discontinue panitumumab or discontinue breast-feeding should take into account the benefits of treatment to the mother. If breast-feeding is interrupted for panitumumab treatment, based on the half-life, breast-feeding should not be resumed for at least 2 months following the last dose. In the US and Canada, women who nurse during panitumumab treatment are encouraged to enroll in Amgen's Lactation Surveillance Program (US: 1-800-772-6436; Canada: 1-866-512-6436).

Monitoring Parameters *KRAS* genotyping of tumor tissue. Monitor serum electrolytes, including magnesium and calcium (periodically during and for at least 8 weeks after therapy), and potassium. Monitor vital signs and temperature before, during, and after infusion. Monitor for skin toxicity, for evidence of ocular toxicity, and for acute onset or worsening pulmonary symptoms.

Mechanism of Action Recombinant human IgG2 monoclonal antibody which binds specifically to the epidermal growth factor receptor (EGFR, HER1, c-ErbB-1) and competitively inhibits the binding of epidermal growth factor (EGF) and other ligands. Binding to the EGFR blocks phosphorylation and activation of intracellular tyrosine kinases, resulting in inhibition of cell survival, growth, proliferation and transformation. EGFR signal transduction may result in *KRAS* and *NRAS* wild-type activation; cells with *RAS* mutations appear to be unaffected by EGFR inhibition.

Pharmacodynamics/Kinetics Half-life elimination: ~7.5 days (range: 4 to 11 days)

Pricing: US

Solution (Vectibix Intravenous)

100 mg/5 mL (5 mL): $1345.74

400 mg/20 mL (20 mL): $5382.96

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names Vectibix (AE, AR, AT, AU, BE, BR, CH, CL, CR, CY, CZ, DE, DK, DO, EC, EE, ES, FR, GB, GR, GT, HK, HN, HR, IE, IL, IS, IT, JO, JP, KR, KW, LB, LT, LU, LV, MT, MX, MY, NI, NL, NO, PA, PH, PL, PT, QA, RO, RU, SA, SE, SG, SI, SK, SV, TR)

REFERENCES

1. *Allegra CJ, Jessup JM, Somerfield MR, et al. American Society of Clinical Oncology Provisional Clinical Opinion: Testing*

for KRAS Gene Mutations in Patients With Metastatic Colorectal Carcinoma to Predict Response to Anti-Epidermal Growth Factor Receptor Monoclonal Antibody Therapy. J Clin Oncol. 2009;27(12):2091-2096. [PubMed 19188670]

2. *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 [published online ahead of print October 5, 2015. J Clin Oncol. 2015. [PubMed 26438111]*
3. *Amado RG, Wolf M, Peeters M, et al. Wild-Type KRAS is Required for Panitumumab Efficacy in Patients With Metastatic Colorectal Cancer. J Clin Oncol. 2008;26(10):1626-34. [PubMed 18316791]*
4. *Di Nicolantonio F, Martini M, Molinari F, et al. Wild-type BRAF is Required for Response to Panitumumab or Cetuximab in Metastatic Colorectal Cancer. J Clin Oncol. 2008;26(35):5705-5712. [PubMed 19001320]*
5. *Douillard JY, Oliner KS, Siena S, et al. Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer. N Engl J Med. 2013;369(11):1023-1034. [PubMed 24024839]*
6. *Douillard JY, Siena S, Cassidy J, et al. Randomized, Phase III Trial of Panitumumab With Infusional Fluorouracil, Leucovorin, and Oxaliplatin (FOLFOX4) Versus FOLFOX4 Alone as First-Line Treatment in Patients With Previously Untreated Metastatic Colorectal Cancer: The PRIME Study. J Clin Oncol. 2010;28(31):4697-4705. [PubMed 20921465]*
7. *Dupuis LL, Boodhan S, Sung L. Guideline for the Classification of the Acute Emetogenic Potential of Antineoplastic Medication in Pediatric Cancer Patients. Pediatr Blood Cancer. 2011;57(2):191-198. [PubMed 21465637]*
8. *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. J Clin Oncol. 2009;27(5):672-680. [PubMed 19114685]*
9. *Lynch DH and Yang XD. Therapeutic Potential of ABX-EGF: A Fully Human Anti-Epidermal Growth Factor Receptor Monoclonal Antibody for Cancer Treatment. Sem Oncol. 2002;29(1 Suppl 4):47-50.*
10. *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. J Clin Oncol. 2010; 28(31):4706-4713. [PubMed 20921462]*
11. *Peeters M, Siena S, Van Cutsem E, et al. Association of Progression-Free Survival, Overall Survival, and Patient-Reported Outcomes by Skin Toxicity and KRAS Status in Patients Receiving Panitumumab Monotherapy. Cancer. 2009, 115(7):1544-1554. [PubMed 19189371]*
12. *Rowinsky EK, Schwartz GH, Gollob JA, et al. Safety, Pharmacokinetics, and Activity of ABX-EGF, a Fully Human Anti-Epidermal Growth Factor Receptor Monoclonal Antibody in Patients with Metastatic Renal Cell Cancer. J Clin Oncol. 2004;22(15):3003-3015. [PubMed 15210739]*
13. *Segaert S and Van Cutsem E. Clinical Signs, Pathophysiology and Management of Skin Toxicity During Therapy with Epidermal Growth Factor Receptor Inhibitors. Ann Oncol. 2005;16(9):1425-33. [PubMed 16012181]*
14. *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;25(13):1658-1664. [PubMed 17470858]*
15. *Vectibix (panitumumab) [prescribing information]. Thousand Oaks, CA: Amgen; February 2015.*
16. *Vectibix (panitumumab) [prescribing information]. Mississauga, Ontario, Canada: Amgen Canada Inc; March 2017.*

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