Indication
Vectibix® is indicated for the treatment of patients with 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 first-line therapy in combination with FOLFOX.
• 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.

Important Safety Information
BOXED WARNING: DERMATOLOGIC TOXICITY
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.

*Defined as wild type in both KRAS and NRAS.
†OS with updated information based on events in 82% of patients.
CI = confidence interval; HR = hazard ratio; mCRC = metastatic colorectal cancer; OS = overall survival; PFS = progression-free survival; PRIME = Panitumumab Randomized Trial in Combination With Chemotherapy for Metastatic Colorectal Cancer to Determine Efficacy; WT = wild type.

Please see full Important Safety Information, including Boxed WARNING, on pages 4 and 5.
Dosing and administration

**Dosing & administration**

- **6 mg/kg** every 14 days
- No loading dose.
- The recommended dose of Vectibix® is 6 mg/kg every 14 days.

**Dosing & administration**

- **60 min**
- **30–60 min**
- **90 min**

Vectibix® is given by IV infusion over 60 minutes.

- If the first infusion is tolerated, subsequent infusions may be administered over 30 to 60 minutes.
- Doses of > 1,000 mg should be administered over 90 minutes.

**Dose Modifications for Infusion Reactions**

- Reduce infusion rate by 50% in patients experiencing a mild or moderate (grade 1 or 2) infusion reaction for the duration of that infusion.
- Terminate the infusion in patients experiencing severe infusion reactions. Depending on the severity and/or persistence of the reaction, permanently discontinue Vectibix®.

**Patient biomarker status and safety**

**Patient selection**

- Prior to initiation of treatment with Vectibix®, assess RAS mutational status in colorectal tumors and confirm the absence of a RAS mutation in exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146) of both KRAS and NRAS.
- Information about FDA-approved tests for the detection of RAS mutations in patients with metastatic colorectal cancer is available at [http://www.fda.gov/](http://www.fda.gov/CompanionDiagnostics)

**Dermatologic toxicities**

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**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.

**Dose Modifications for Dermatologic Toxicity**

- Upon first occurrence of a grade 3 dermatologic reaction, withhold 1 to 2 doses of Vectibix®. If the reaction improves to < grade 3, reinitiate Vectibix® at the original dose.
- Upon the second occurrence of a grade 3 dermatologic reaction, withhold 1 to 2 doses of Vectibix®. If the reaction improves to < grade 3, reinitiate Vectibix® at 80% of the original dose.
- Upon the third occurrence of a grade 3 dermatologic reaction, withhold 1 to 2 doses of Vectibix®. If the reaction improves to < grade 3, reinitiate Vectibix® at 60% of the original dose.
- Upon the fourth occurrence of a grade 3 dermatologic reaction, permanently discontinue Vectibix®.
- Permanently discontinue Vectibix® following the occurrence of a grade 4 dermatologic reaction or for a grade 3 dermatologic reaction that does not recover after withholding 1 or 2 doses.

Please see full Important Safety Information, including Boxed WARNING, on pages 4 and 5.
Do not administer Vectibix® as an intravenous push or bolus.¹

Visually inspect parenteral drug products for particulate matter and discoloration prior to administration. Vectibix® solution is colorless and may contain a small amount of visible translucent-to-white, amorphous, proteinaceous particles. Do not use if the solution is discolored or cloudy, or if foreign matter is present.¹

Use a 21-gauge or larger gauge (small bore) hypodermic needle to withdraw the necessary amount of Vectibix® for a dose of 6 mg/kg. Do not use needle-free devices (e.g., vial adapters) to withdraw vial contents.¹

Dilute to a total volume of 100 mL with 0.9% sodium chloride injection, USP. Doses of higher than 1,000 mg should be diluted to 150 mL with 0.9% sodium chloride injection, USP. Do not exceed a final concentration of 10 mg/mL.¹

Mix diluted solution by gentle inversion. Discard any unused portion of the vial.¹

Prepare the solution for infusion, using aseptic technique, as follows¹:

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Flush line before and after Vectibix® administration with 0.9% sodium chloride injection, USP, to avoid mixing with other drug products or intravenous solutions. Do not mix Vectibix® with, or administer as an infusion with, other medicinal products. Do not add other medications to solutions containing panitumumab.¹

Infuse doses of 1,000 mg or lower over 60 minutes through a peripheral intravenous line or indwelling intravenous catheter. If the first infusion is tolerated, administer subsequent infusions over 30 to 60 minutes.¹

• Administer doses of > 1,000 mg over 90 minutes¹

Use the diluted infusion solution of Vectibix® within 6 hours of preparation if stored at room temperature, or within 24 hours of dilution if stored at 2°C to 8°C (36°F to 46°F). DO NOT FREEZE.¹

Prepare the solution for infusion, using aseptic technique, as follows¹:

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Important Safety Information

• In Study 20020408, dermatologic toxicities occurred in 90% of patients and were severe (NCI-CTC grade 3 and higher) in 15% of patients with mCRC receiving Vectibix®. The clinical manifestations included, but were not limited to, acneiform dermatitis, pruritus, erythema, rash, skin exfoliation, paronychia, dry skin, and skin fissures.

• Monitor patients who develop dermatologic or soft tissue toxicities while receiving Vectibix® for the development of inflammatory or infectious sequelae. Life-threatening and fatal infectious complications including necrotizing fasciitis, abscesses, and sepsis have been observed in patients treated with Vectibix®. Life-threatening and fatal bullous mucocutaneous disease with blisters, erosions, and skin sloughing has also been observed in patients treated with Vectibix®. It could not be determined whether these mucocutaneous adverse reactions were directly related to EGFR inhibition or to idiosyncratic immune-related effects (eg, Stevens Johnson syndrome or toxic epidermal necrolysis). Withhold or discontinue Vectibix® for dermatologic or soft tissue toxicity associated with severe or life-threatening inflammatory or infectious complications. Dose modifications for Vectibix® concerning dermatologic toxicity are provided in the product labeling.

• Vectibix® must be administered via infusion pump using a low-protein-binding 0.2 μm or 0.22 μm in-line filter¹

• Vectibix® is not indicated for the treatment of patients with colorectal cancer that harbor somatic RAS mutations in exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146) of either KRAS or NRAS and hereafter is referred to as “RAS.”

• Retrospective subset analyses across several randomized clinical trials were conducted to investigate the role of RAS mutations on the clinical effects of anti-EGFR-directed monoclonal antibodies (panitumumab or cetuximab). Anti-EGFR antibodies in patients with tumors containing RAS mutations resulted in exposing those patients to anti-EGFR related adverse reactions without clinical benefit from these agents. Additionally, in Study 20050203, 272 patients with RAS-mutant mCRC tumors received Vectibix® in combination with FOLFOX and 276 patients received FOLFOX alone. In an exploratory subgroup analysis, OS was shorter (HR = 1.21, 95% CI: 1.01-1.45) in patients with RAS-mutant mCRC who received Vectibix® and FOLFOX versus FOLFOX alone.

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BOXED WARNING: DERMATOLOGIC TOXICITY

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 [see Dosage and Administration (2.3), Warnings and Precautions (5.1), and Adverse Reactions (6.1)].

- In Study 20020408, dermatologic toxicities occurred in 90% of patients and were severe (NCI-CTC grade 3 and higher) in 15% of patients with mCRC receiving Vectibix®. The clinical manifestations included, but were not limited to, acneiform dermatitis, pruritus, erythema, rash, skin exfoliation, paronychia, dry skin, and skin fissures.

- Monitor patients who develop dermatologic or soft tissue toxicities while receiving Vectibix® for the development of inflammatory or infectious sequelae. Life-threatening and fatal infectious complications including necrotizing fasciitis, abscesses, and sepsis have been observed in patients treated with Vectibix®. Life-threatening and fatal bullous mucocutaneous disease with blisters, erosions, and skin sloughing has also been observed in patients treated with Vectibix®. It could not be determined whether these mucocutaneous adverse reactions were directly related to EGFR inhibition or to idiiosyncratic immune-related effects (eg, Stevens Johnson syndrome or toxic epidermal necrolysis). Withhold or discontinue Vectibix® for dermatologic or soft tissue toxicity associated with severe or life-threatening inflammatory or infectious complications. Dose modifications for Vectibix® concerning dermatologic toxicity are provided in the product labeling.

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- Progressively decreasing serum magnesium levels leading to severe (grade 3-4) hypomagnesemia occurred in up to 7% (in Study 20080763) of patients across clinical trials. Monitor patients for hypomagnesemia and hypocalcemia prior to initiating Vectibix® treatment, periodically during Vectibix® treatment, and for up to 8 weeks after the completion of treatment.

- Other electrolyte disturbances, including hypokalemia, have also been observed. Replete magnesium and other electrolytes as appropriate.

- In Study 20020408, 4% of patients experienced infusion reactions and 1% of patients experienced severe infusion reactions (NCI-CTC grade 3-4). Infusion reactions, manifesting as fever, chills, dyspnea, bronchospasm, and hypotension, can occur following Vectibix® administration. Fatal infusion reactions occurred in postmarketing experience. Terminate the infusion for severe infusion reactions.

- Severe diarrhea and dehydration, leading to acute renal failure and other complications, have been observed in patients treated with Vectibix® in combination with chemotherapy.

- Fatal and nonfatal cases of interstitial lung disease (ILD) (1%) and pulmonary fibrosis have been observed in patients treated with Vectibix®. Pulmonary fibrosis occurred in less than 1% (2/1467) of patients enrolled in clinical studies of Vectibix®. In the event of acute onset or worsening of pulmonary symptoms interrupt Vectibix® therapy. Discontinue Vectibix® therapy if ILD is confirmed.

- In patients with a history of interstitial pneumonitis or pulmonary fibrosis, or evidence of interstitial pneumonitis or pulmonary fibrosis, the benefits of therapy with Vectibix® versus the risk of pulmonary complications must be carefully considered.

- Exposure to sunlight can exacerbate dermatologic toxicity. Advise patients to wear sunscreen and hats and limit sun exposure while receiving Vectibix®.

- Keratitis and ulcerative keratitis, known risk factors for corneal perforation, have been reported with Vectibix® use. Monitor for evidence of keratitis or ulcerative keratitis. Interrupt or discontinue Vectibix® for acute or worsening keratitis.

- In an interim analysis of an open-label, multicenter, randomized clinical trial in the first-line setting in patients with mCRC, the addition of Vectibix® to the combination of bevacizumab and chemotherapy resulted in decreased OS and increased incidence of NCI-CTC grade 3-5 (87% vs 72%) adverse reactions. NCI-CTC grade 3-4 adverse reactions occurring at a higher rate in Vectibix®-treated patients included rash/acneiform dermatitis (26% vs 1%), diarrhea (23% vs 12%), dehydration (16% vs 5%), primarily occurring in patients with diarrhea, hypokalemia (10% vs 4%), stomatitis/mucositis (4% vs < 1%), and hypomagnesemia (4% vs 0).

- NCI-CTC grade 3-5 pulmonary embolism occurred at a higher rate in Vectibix®-treated patients (7% vs 3%) and included fatal events in three (< 1%) Vectibix®-treated patients. As a result of the toxicities experienced, patients randomized to Vectibix®, bevacizumab, and chemotherapy received a lower mean relative dose intensity of each chemotherapeutic agent (oxaliplatin, irinotecan, bolus 5-FU, and/or infusional 5-FU) over the first 24 weeks on study compared with those randomized to bevacizumab and chemotherapy.
Important Safety Information (cont’d)

• Vectibix® can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment, and for at least 2 months after the last dose of Vectibix®.

• In monotherapy, the most commonly reported adverse reactions (≥ 20%) in patients with Vectibix® were skin rash with variable presentations, paronychia, fatigue, nausea, and diarrhea.

• The most commonly reported adverse reactions (≥ 20%) with Vectibix® + FOLFOX were diarrhea, stomatitis, mucosal inflammation, asthenia, paronychia, anorexia, hypomagnesemia, hypokalemia, rash, acneiform dermatitis, pruritus, and dry skin. The most common serious adverse reactions (≥ 2% difference between treatment arms) were diarrhea and dehydration.

Please see Vectibix® full Prescribing Information, including Boxed WARNING.