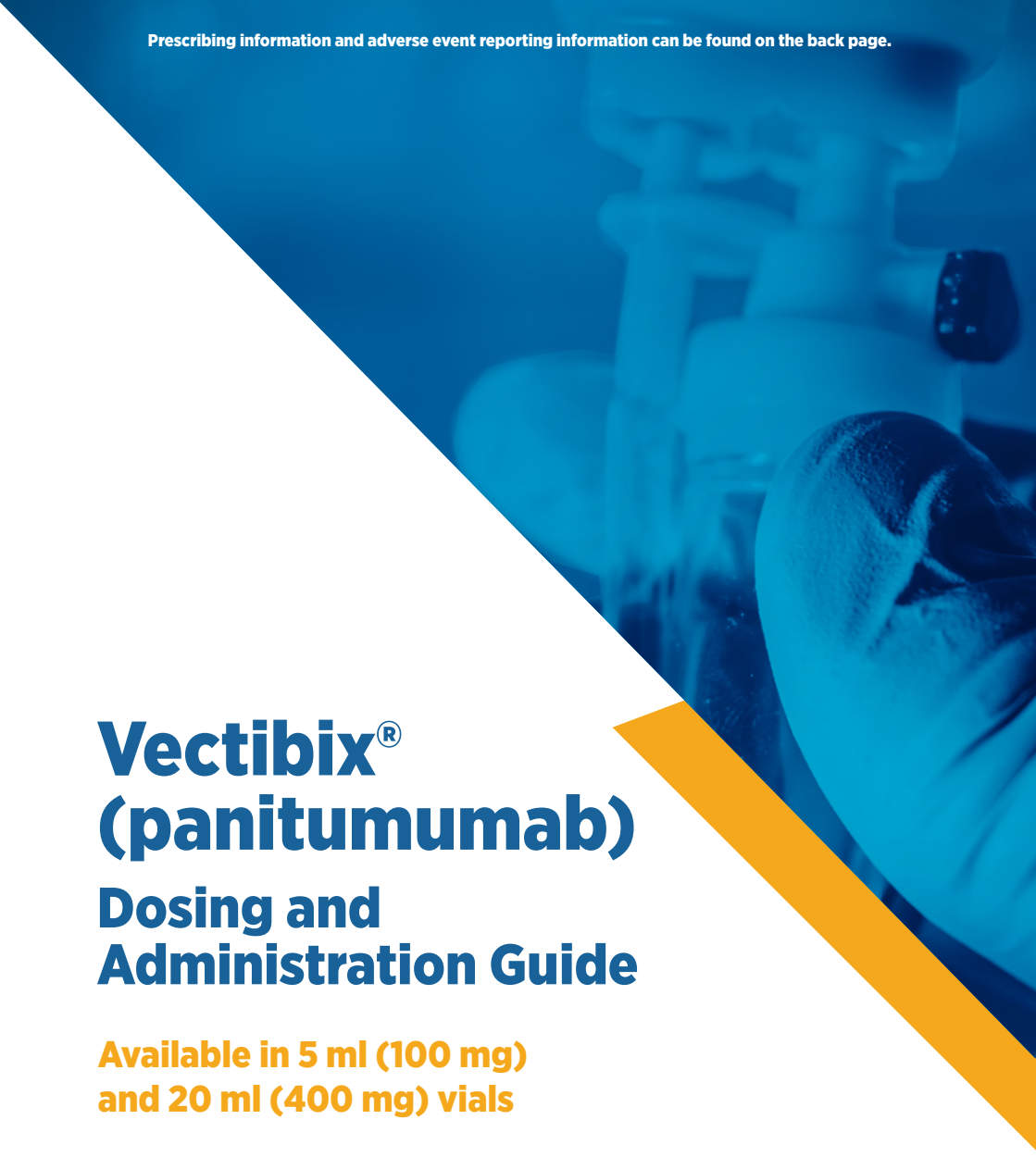
Prescribing information and adverse event reporting information can be found on the back page.



Vectibix® (panitumumab)

Dosing and Administration Guide

Available in 5 ml (100 mg) and 20 ml (400 mg) vials

AMGEN®

Vectibix® (panitumumab)

GBR-954-1023-80005. November 2023.

Vectibix® Features[1,2]

100 mg = 5 ml
400 mg = 20 ml

Monoclonal antibody structure:
100% human protein (0% mouse protein)

Frequency of administration:
Once every two weeks

Loading dose:
Not required

Pre-medication:
Not required*

Dosage/infusion time:
<1,000 mg: 6 mg/kg (30-60 minutes)
>1,000 mg: 6 mg/kg (90 minutes)

Dose calculation example:

For a 72.6 kg patient:
Dose = 435.6 mg
(6 mg/kg x 72.6 kg)
435.6 mg/20 mg/ml = 21.78 ml

Full contents from a 20 ml vial (400 mg) + 1.78 ml from a 5 ml vial (35.6 mg)

Vial sizes and contents as supplied:

Estimated administration time

	Vectibix*†**		
	Initial Dose	**Subsequent Dose**	**Frequency of Dosing**
Pre-medications	-	Not routinely required	-
Infusion chair time	1 hour	Between 30/60 mins†	Once every two weeks

* The use of pre-medication was not required in the phase II, single-arm Study 314[2]
** Doses higher than 1,000 mg should be infused over approximately 90 minutes
† If first infusion is well-tolerated, administer over 30 to 60 minutes

Dosing Example: 14.7 ml
Weight: **49 kg**
Requires: **294 mg of Vectibix®**

Administered as:
- 2 whole 5 ml vials (2x100 mg)
- 4.7 ml from a third 5 ml vial (94 mg)

Dosing Example: 25.5 ml
Weight: **85 kg**
Requires: **510 mg of Vectibix®**

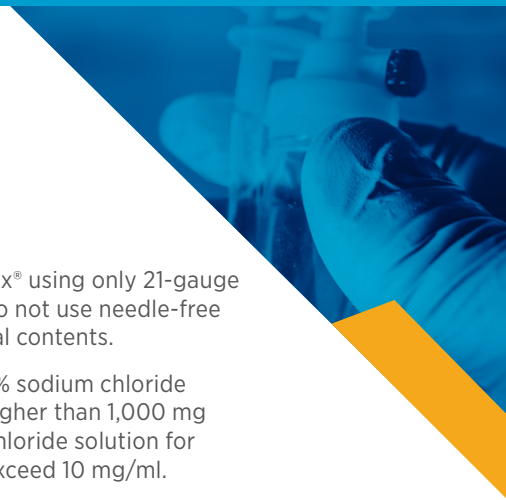
Administered as:
- 1 whole 20 ml vial (400 mg)
- 1 whole 5 ml vial (100 mg)
- 0.5 ml from a second 5 ml vial (10 mg)

Administered dose (ml)				
Weight (kg)	**Dose (mg)**	**5 ml vial**	**5 ml vial**	**5 ml vial**
40	240	5.0	5.0	2.0
41	246	5.0	5.0	2.3
42	252	5.0	5.0	2.6
43	258	5.0	5.0	2.9
44	264	5.0	5.0	3.2
45	270	5.0	5.0	3.5
46	276	5.0	5.0	3.8
47	282	5.0	5.0	4.1
48	288	5.0	5.0	4.4
49	294	5.0	5.0	4.7
50	300	5.0	5.0	5.0

Weight (kg)	Dose (mg)	20 ml vial	5 ml vial	5 ml vial
51	306	15.3	-	-
52	312	15.6	-	-
53	318	15.9	-	-
54	324	16.2	-	-
55	330	16.5	-	-
56	336	16.8	-	-
57	342	17.1	-	-
58	348	17.4	-	-
59	354	17.7	-	-
60	360	18.0	-	-
61	366	18.3	-	-
62	372	18.6	-	-
63	378	18.9	-	-
64	384	19.2	-	-
65	390	19.5	-	-
66	396	19.8	-	-
67	402	20	0.1	-
68	408	20	0.4	-
69	414	20	0.7	-

Administered dose (ml)				
Weight (kg)	**Dose (mg)**	**5 ml vial**	**5 ml vial**	**5 ml vial**
70	420	20	1.0	-
71	426	20	1.3	-
72	432	20	1.6	-
73	438	20	2.2	-
74	444	20	2.5	-
75	450	20	2.8	-
76	456	20	3.1	-
77	462	20	3.4	-
78	468	20	3.7	-
79	474	20	4.0	-
80	480	20	4.3	-
81	486	20	4.6	-
82	492	20	4.9	-
83	498	20	5.0	-
84	504	20	5.0	0.2
85	510	20	5.0	0.5
86	516	20	5.0	0.8
87	522	20	5.0	1.1
88	528	20	5.0	1.4
89	534	20	5.0	1.7
90	540	20	5.0	2.0
91	546	20	5.0	2.3
92	552	20	5.0	2.6
93	558	20	5.0	2.9
94	564	20	5.0	3.2
95	570	20	5.0	3.5
96	576	20	5.0	3.8
97	582	20	5.0	4.1
98	588	20	5.0	4.4
99	594	20	5.0	4.7
100	600	20	5.0	5.0

Preparation and Administration



Recommended dose is 6 mg/kg once every two weeks, administered as an IV infusion via an infusion pump with a low protein binding filter.[1]

- Vectibix® treatment should be supervised by a physician experienced in the use of anti-cancer therapy.
- Vectibix® must not be administered as an intravenous push or bolus.
- Vectibix® should be inspected visually prior to administration. The solution should be colourless and may contain visible translucent-to-white, amorphous, proteinaceous particulates (which will be removed by in-line filtration).
- Do not administer Vectibix® if its appearance is not as described.
- Modification of the dose may be necessary in cases of severe (grade ≥ 3) dermatological reactions.
- A reduction in the rate of infusion of Vectibix® may be necessary in cases of infusion-related reactions.

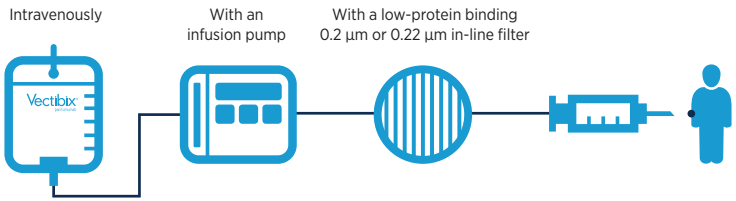
For full information, always refer to the Vectibix® (panitumumab) Summary of Product Characteristics.[1]

Stability and storage[1]

- Store vials in the original carton under refrigeration at 2°C to 8°C until time of use. Protect from light. **DO NOT FREEZE**.
- Since Vectibix® does not contain preservatives, any unused portion remaining in the vial should be discarded.
- Vectibix® should be used immediately after dilution. If not used immediately, it should be used within 24 hours at 2°C to 8°C.
- Look for discolouration prior to administration. Vectibix® is a colourless solution that may contain translucent-to-white, visible amorphous, proteinaceous panitumumab particles.

Six steps to prepare and administer Vectibix®[1]

1. Withdraw the necessary amount of Vectibix® using only 21-gauge or smaller diameter hypodermic needle. Do not use needle-free devices (e.g. vial adapters) to withdraw vial contents.
2. Dilute in a total volume of 100 ml with 0.9% sodium chloride injection using aseptic technique. Doses higher than 1,000 mg should be diluted in 150 ml 0.9% sodium chloride solution for injection. Final concentration should not exceed 10 mg/ml.
3. Mix diluted solution by gentle inversion. **DO NOT SHAKE** or vigorously agitate.
4. Administer using an IV infusion pump with a low-protein binding 0.2 µm or 0.22 µm in-line filter.
5. Infuse over approximately 60 minutes through a peripheral line or indwelling catheter. If the first infusion is tolerated, then subsequent infusions may be administered over 30 to 60 minutes. Doses higher than 1,000 mg should be infused over approximately 90 minutes.
6. Flush infusion line before and after Vectibix® administration with 0.9% sodium chloride solution to avoid mixing with other drug products or IV solutions.



Monitoring Requirements[1]

- In patients experiencing a mild or moderate (CTCAE v 4.0 grades 1 and 2) infusion-related reaction the infusion rate should be reduced for the duration of the infusion. It is recommended to maintain this lower infusion rate in all subsequent infusions.
- In the post-marketing setting, serious infusion-related reactions have been reported, including rare post-marketing reports with a fatal outcome. If a severe or life-threatening reaction occurs during an infusion or at any time post-infusion (e.g. presence of bronchospasm, angioedema, hypertension, need for parenteral treatment, or anaphylaxis), Vectibix® should be permanently discontinued.
- Hypersensitivity reactions occurring more than 24 hours after infusion have been reported including a fatal case of angioedema that occurred more than 24 hours after the infusion. Patients should be informed of the possibility of a late-onset reaction and instructed to contact their physician if symptoms of hypersensitivity reaction occur.
- Progressively decreasing serum magnesium levels leading to severe (grade 4) hypomagnesaemia have been observed in some patients. Patients should be periodically monitored for hypomagnesaemia and accompanying hypocalcaemia prior to initiating Vectibix® treatment, and periodically thereafter for up to 8 weeks after the completion of treatment. Magnesium repletion is recommended, as appropriate.
- Other electrolyte disturbances, including hypokalaemia, have also been observed. Monitoring as above and repletion as appropriate of these electrolytes is also recommended.

For any other monitoring requirements, please refer to the Vectibix® Summary of Product Characteristics for further details.[1]

References

1. Vectibix® (panitumumab) Summary of Product Characteristics. Amgen Ltd. Available at: https://www.medicines.org.uk/emc/product/6178/smpc#about-medicine [updated June 2023]. Accessed September 2023.

2. Köhne CH, *et al.* First-line panitumumab plus irinotecan/5-fluorouracil/leucovorin treatment in patients with metastatic colorectal cancer. J Cancer Res Clin Oncol. 2012;138(1):65-72.

Vectibix® (panitumumab) Brief Prescribing Information

Please refer to the Summary of Product Characteristics before prescribing Vectibix. **Pharmaceutical Form:** Vectibix 20 mg/ml concentrate for solution for infusion. Each vial contains either 100 mg of panitumumab in 5 ml or 400 mg of panitumumab in 20 ml. Excipients: sodium chloride, sodium acetate trihydrate, acetic acid (glacial [for pH adjustment]), water for injection. **Indication:** Vectibix is indicated for the treatment of adult patients with wild-type *RAS* metastatic colorectal cancer (mCRC): in first-line in combination with FOLFOX or FOLFIRI; in second-line in combination with FOLFIRI for patients who have received first-line fluoropyrimidine–based chemotherapy (excluding irinotecan); as monotherapy after failure of fluoropyrimidine–, oxaliplatin–, and irinotecan-containing chemotherapy regimens. **Dosage and Administration:** The recommended dose of Vectibix is 6 mg/kg of bodyweight given once every two weeks. The recommended infusion time is approximately 60 minutes. Doses higher than 1000 mg should be infused over approximately 90 minutes. Evidence of wild-type RAS (*KRAS* and *NRAS*) status is required before initiating treatment with Vectibix. Mutational status should be determined by an experienced laboratory using validated test methods for detection of KRAS (exons 2, 3, and 4) and NRAS (exons 2, 3, and 4) mutations. If Vectibix is to be used in combination with FOLFOX or FOLFIRI then it is recommended that mutational status be determined by a laboratory that participates in a *RAS* European Quality Assurance programme or wild-type status be confirmed in a duplicate test. **Contraindications:** History of severe or life-threatening hypersensitivity to the active substance or to any of the excipients, interstitial pneumonitis or pulmonary fibrosis and combination of Vectibix with oxaliplatin-containing chemotherapy for patients with mutant *RAS* mCRC or for whom *RAS* mCRC status is unknown. **Special Warnings and Precautions:** ***Traceability*:** Clearly record name and batch number of administered product to improve traceability of biological products. ***Dermatologic reactions and soft tissue toxicity***: Dermatologic reactions are experienced with nearly all patients (approximately 94%) treated with Vectibix; with 23% severe (grade 3 NCI-CTC) and < 1% life threatening (grade 4 NCI-CTC). If a patient develops dermatologic reactions that are grade 3 (CTCAE v4.0) or higher or considered intolerable, dose modification, interruption, or discontinuation as per the Summary of Product Characteristics should be followed. Rare cases of Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in patients treated with Vectibix in the post-marketing setting. Proactive skin treatment may be useful in the management of dermatological reactions please refer to the Summary of Product Characteristics for more details. ***Pulmonary complications*:** If interstitial lung disease (ILD) is diagnosed, Vectibix should be permanently discontinued and the patient should be treated appropriately. In patients with a history of interstitial pneumonitis or pulmonary fibrosis, a risk benefit assessment should be conducted. ***Electrolyte disturbances*:** Patients should be periodically monitored for hypomagnesaemia and accompanying hypocalcaemia prior to initiating Vectibix treatment, and periodically for up to 8 weeks after the completion of treatment. Repletion of magnesium and other electrolytes is also recommended, as appropriate. ***Acute Renal Failure:*** Acute renal failure has been observed in patients who develop severe diarrhoea and dehydration. ***Infusion Related Reactions*:** Across monotherapy and combination mCRC clinical studies, infusion-related reactions (occurring within 24 hours of an infusion) were reported in Vectibix-treated patients, including severe infusion-related reactions (NCI-CTC grade 3 and 4). In the post-marketing setting, serious infusion-related reactions have been reported, including rare reports with a fatal outcome. If a severe or life-threatening reaction occurs during an infusion or at any time post-infusion, Vectibix should be permanently discontinued. In patients experiencing a mild or moderate infusion-related reaction, the infusion rate should be reduced, then maintain this lower infusion rate in all subsequent infusions. Hypersensitivity reactions occurring more than 24 hours after infusion have been reported including a fatal case of angioedema. Patients should be informed of the possibility of a late onset reaction and instructed to contact their physician if symptoms of a hypersensitivity reaction occur. ***Ocular toxicities:*** Serious cases of keratitis and ulcerative keratitis, which may lead to corneal perforation, have been reported. Patients presenting with signs and symptoms suggestive of keratitis should be referred promptly to an ophthalmology specialist. If a diagnosis of ulcerative keratitis is confirmed, treatment with Vectibix should be interrupted or discontinued. If keratitis is diagnosed, the benefits and risks of continuing treatment should be carefully considered. Vectibix should be used with caution in patients with a history of keratitis, ulcerative keratitis or severe dry eye. ***ECOG 2 performance status*:** For patients with ECOG 2 performance status, assessment of benefit-risk is recommended prior to initiation of Vectibix in combination with chemotherapy for treatment of mCRC. A positive benefit-risk balance has not been documented in patients with ECOG 2 performance status. ***Elderly patients:*** No overall differences in safety or efficacy were observed in elderly patients (≥ 65 years of age) treated with Vectibix monotherapy. However, an increased number of serious adverse events were reported in elderly patients treated with Vectibix in combination with FOLFIRI or FOLFOX chemotherapy compared to chemotherapy alone. The most increased serious adverse events were diarrhoea in patients treated with Vectibix in combination with either FOLFOX or FOLFIRI, and dehydration and pulmonary embolism when patients were treated with Vectibix in combination with FOLFIRI. ***Sodium content*:** Vectibix contains 3.45 mg sodium per ml, equivalent to 0.17% of the WHO recommended daily intake for an adult. **Interactions:** Vectibix should not be administered in combination with IFL chemotherapy or with bevacizumab-containing chemotherapy. A high incidence of severe diarrhoea was observed when Vectibix was administered in combination with IFL and increased toxicity and deaths were seen when Vectibix was combined with bevacizumab and chemotherapy. **Fertility, pregnancy and lactation:** There are no adequate data from the use of Vectibix in pregnant women. In women of childbearing potential, appropriate contraceptive measures must be used during treatment and for 2 months following the last dose. It is recommended that women do not breast-feed during treatment with Vectibix and for 2 months after the last dose. **Undesirable Effects:** Very common (≥ 1/10): Anaemia, conjunctivitis, paronychia, diarrhoea, nausea, vomiting, abdominal pain, stomatitis, constipation, fatigue, pyrexia, asthenia, mucosal inflammation, oedema peripheral, weight decreased, hypokalaemia, hypomagnesaemia, decreased appetite, back pain, insomnia, dyspnoea, cough, dermatitis acneiform, rash, erythema, pruritus, dry skin, skin fissures, acne and alopecia. Common (≥ 1/100 to < 1/10): Leucopenia, tachycardia, blepharitis, growth of eyelashes, lacrimation increased, ocular hyperaemia, dry eye, eye pruritus, eye irritation, rectal haemorrhage, dry mouth, dyspepsia, aphthous ulcer, cheilitis, gastrooesophageal reflux disease, chest pain, pain, chills, hypersensitivity, rash pustular, cellulitis, urinary tract infection, folliculitis, localised infection, decreased blood magnesium, hypocalcaemia, dehydration, hyperglycaemia, hypophosphataemia, pain in extremity, headache, dizziness, anxiety, pulmonary embolism, epistaxis, palmar-plantar erythrodysaesthesia syndrome, skin ulcer, skin exfoliation, exfoliative rash, dermatitis, rash papular, rash pruritic, rash erythematous, rash generalised, rash macular, rash maculo-papular, skin lesion, skin toxicity, scab, hypertrichosis, onychoclasis, nail disorder, hyperhidrosis, deep vein thrombosis, hypotension, hypertension and flushing. Uncommon (≥ 1/1000 to < 1/100): Anaphylactic reaction, cyanosis, ulcerative keratitis, keratitis, infusion-related reaction, interstitial lung disease, bronchospasm, toxic epidermal necrolysis, skin necrosis, Stevens-Johnson syndrome, and angioedema. The safety profile of Vectibix in combination with chemotherapy consisted of the reported adverse reactions of Vectibix (as a monotherapy) and the toxicities of the background chemotherapy regimen. No new toxicities or worsening of previously recognised toxicities beyond the expected additive effects were observed. Skin reactions were the most frequently occurring adverse reactions in patients receiving Vectibix in combination with chemotherapy. Other toxicities that were observed with a greater frequency relative to monotherapy included hypomagnesaemia, diarrhoea, and stomatitis. As with all therapeutic proteins, there is potential for immunogenicity. Please consult the Summary of Product Characteristics for a full list and more detailed description of side effects. **Overdose:** Doses up to 9 mg/kg have been tested in clinical trials. Overdose at doses up to approximately twice the recommended therapeutic dose have been reported. Adverse events observed included skin toxicity, diarrhoea, dehydration and fatigue. **Pharmaceutical Precautions:** Store in a refrigerator (2°C – 8°C). Do not freeze. Store in the original carton in order to protect from light. The product should be used immediately after dilution. Vectibix should be diluted in 0.9% sodium chloride injection using aseptic technique. Do not shake or vigorously agitate the vial. Do not administer Vectibix if discolouration is observed. **Legal Category:** POM. **Presentation, Basic NHS Costs and Marketing Authorisation Numbers Great Britain (GB):** Vectibix 100mg: Pack of 1: £379.29, 400mg: Pack of 1: £1517.16, PLGB 13832/0045. **Marketing Authorisation Holder GB:** Amgen Limited, 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK. **Presentation, Basic NHS Costs and Marketing Authorisation Numbers Northern Ireland (XI):** Vectibix 100mg: Pack of 1: £379.29, EU/1/07/423/001, 400mg: Pack of 1: £1517.16, EU/1/07/423/003. **Marketing Authorisation Holder XI:** Amgen Europe B.V., Minervum 7061, 4817 ZK Breda, The Netherlands. Further information is available from Amgen Limited, 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK. Vectibix is a registered trademark of Amgen Inc. **Date of PI preparation:** December 2021 (Ref: GB-VBX-1121-00001)

Adverse events should be reported. Reporting forms and information can be found at **https://yellowcard.mhra.gov.uk** or search for MHRA Yellow Card in the Google Play or Apple App store. Adverse events should also be reported to Amgen Limited on **+44 (0)1223 436441**

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