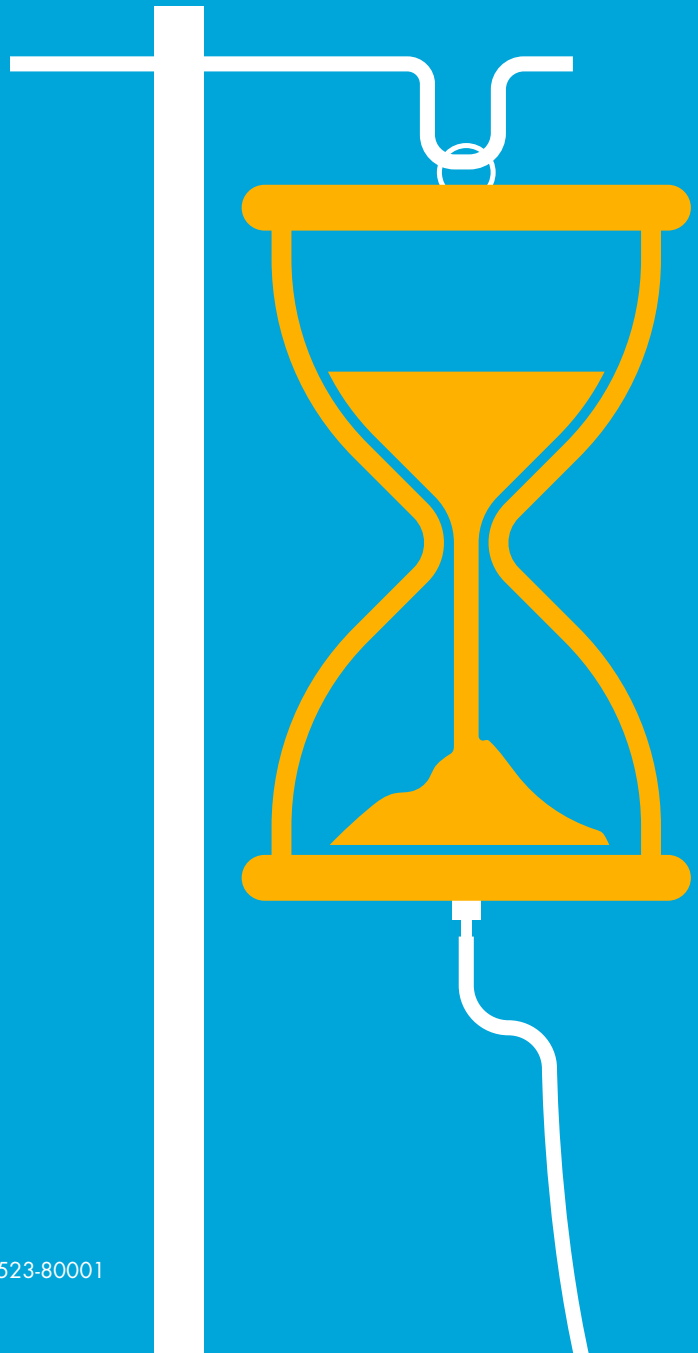
AMGEN

Vectibix®
panitumumab



SERVICE EVALUATIONS TO EVALUATE CAPACITY USE FOR METASTATIC COLORECTAL CANCER PATIENTS TREATED WITH EGFR INHIBITORS AND CHEMOTHERAPY

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

These service evaluations were conducted on behalf of the NHS trusts by 7i group Ltd. Funding was provided by Amgen Limited.

Prescribing information

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TREATING PATIENTS WITH RAS WILD-TYPE METASTATIC COLORECTAL CANCER (mCRC)

Vectibix® (panitumumab) and cetuximab are both recommended by The National Institute for Health and Care Excellence (NICE) for previously untreated RAS wild-type mCRC in combination with FOLFOX or FOLFIRI.[1-3] These two targeted therapies target the EGFR receptor and both are administered by intravenous infusion.[1,2] A number of NHS Trusts across the UK have investigated how the choice of anti-EGFR treatment affects the amount of time a patient occupies a treatment chair ("chair-time"), which in turn affects how many patients can be treated in a given clinic ("capacity").[4-6]

IT ALL ADDS UP

PRE-MEDICATIONS:
Pre-medications are not routinely required for Vectibix.[1] Prior to the first infusion, patients must receive pre-medication with an antihistamine and a corticosteroid at least 1 hour prior to administration of cetuximab.[2] This is also recommended for all subsequent infusions.[2]

INFUSION TIME:
Infusion chair time for Vectibix ranges from 0.5-1.5 hours, compared with 1-2 hours for cetuximab.*[1,2]

POST INFUSION, CHEMOTHERAPY CAN BE STARTED IMMEDIATELY:
After Vectibix infusion, chemotherapy can be started immediately without monitoring. For cetuximab, close monitoring is required during the infusion and for at least 1 hour after the end of the infusion.†[1,2]

DOSING SCHEDULE:
The recommend dose of Vectibix is once every 2 weeks, whereas the recommended dose of cetuximab is once a week.[1,2]

Vectibix is a recombinant, fully human anti-epidermal growth factor receptor inhibitor (EGFRI) monoclonal antibody.[1] Cetuximab is a chimeric monoclonal IgG1 antibody produced in a mammalian cell line (Sp2/0) by recombinant DNA technology.[2]

*Doses higher than 1,000mg should be infused over approximately 90 minutes. †Patients should be periodically monitored for hypomagnesaemia and accompanying hypocalcaemia both prior to initiating Vectibix treatment and periodically afterwards for up to eight weeks following completion of treatment.

Prescribing information

References

NHS TRUSTS UNDERTOOK SERVICE EVALUATIONS TO ASSESS CAPACITY

22

PATIENTS RECEIVED CETUXIMAB*

37

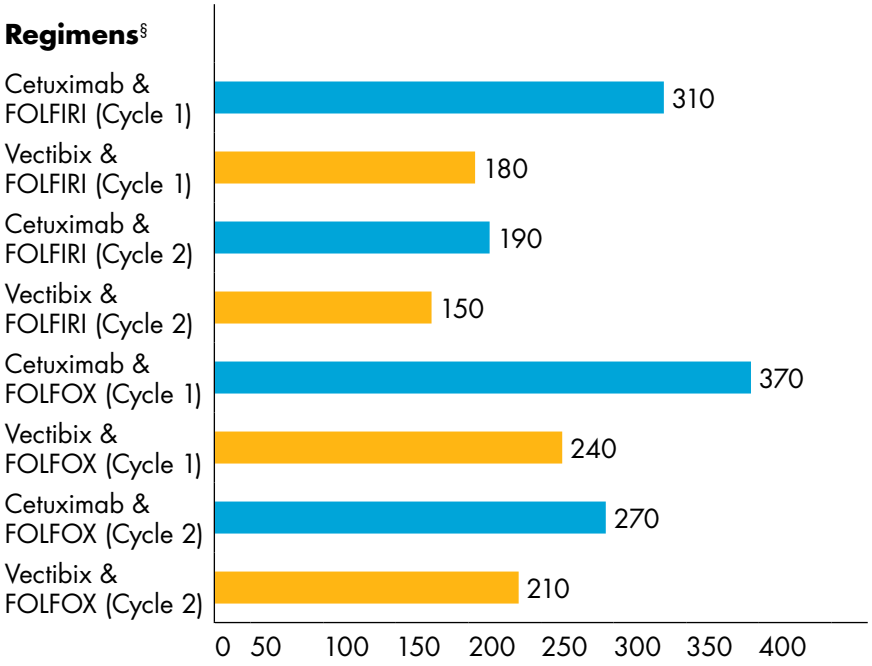
PATIENTS RECEIVED VECTIBIX*

DATA COLLECTION

• 59 patient records were retrospectively collected between December 2015 and March 2020†

PATIENT RECORD CRITERIA

• Attended the Royal Marsden NHS Foundation Trust[4] • Aged 18 and over • Diagnosed with RAS wild-type stage 3/4 mCRC
• Treated with at least 3 cycles of EGFR therapy in combination with chemotherapy



Data in graph adapted from Cortez et al., 2021.

Chair time booked for each regime[4]

Regimens	Number of patients	Total number of cycles	Total chair time (hours)	Total chair time (days)
Cetuximab & FOLFIRI	**18**	**300**	**985.0**	**123.1**
Vectibix & FOLFIRI	**12**	**153**	**388.5**	**48.6**
Cetuximab & FOLFOX	**4**	**67**	**308.2**	**38.5**
Vectibix & FOLFOX	**25**	**300**	**132.8**	**16.5**

Chair available 8 hours per day (09:00 – 17:00)
Chair time data was collected based on allocated infusion times‡

*In combination with either FOLFOX or FOLFIRI. †All patients had: stage 3/4 mCRC, RAS wild-type status, previous treatment with three cycles of EGFR therapy + chemotherapy. ‡The data for chair time came from the Royal Marsden's infusion time for each treatment regimen. §The allocated time for each treatment regimen per patient for first and second cycles are as follows: Vectibix and FOLFIRI: 180, 150; Vectibix and FOLFOX: 240, 210; cetuximab and FOLFIRI: 310, 190; cetuximab and FOLFOX: 370, 270.

This service evaluation was conducted on behalf of The Royal Marsden NHS Foundation Trust by 7i Group Ltd. Funding was provided by Amgen Limited.

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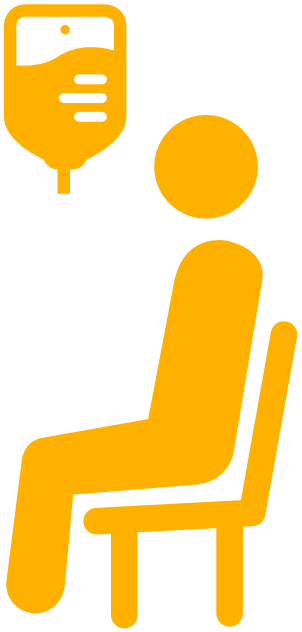
References

CHAIR TIME OCCUPIED*

Cetuximab
1,293.2 hours or
161.6 chair days



Vectibix
521.3 hours or
65.1 chair days

It was estimated that if all patients received Vectibix, the potential savings could have been made over the study period:[4]

297.6
hours of chair time saved

37.1
chair days saved

50%
less treatment time

86
more cycles of treatment could be delivered

16
more patients could have potentially been treated with 5 cycles of Vectibix and FOLFOX

*Chair available 8 hours per day (09:00 – 17:00)

16

PATIENTS RECEIVED CETUXIMAB*

4

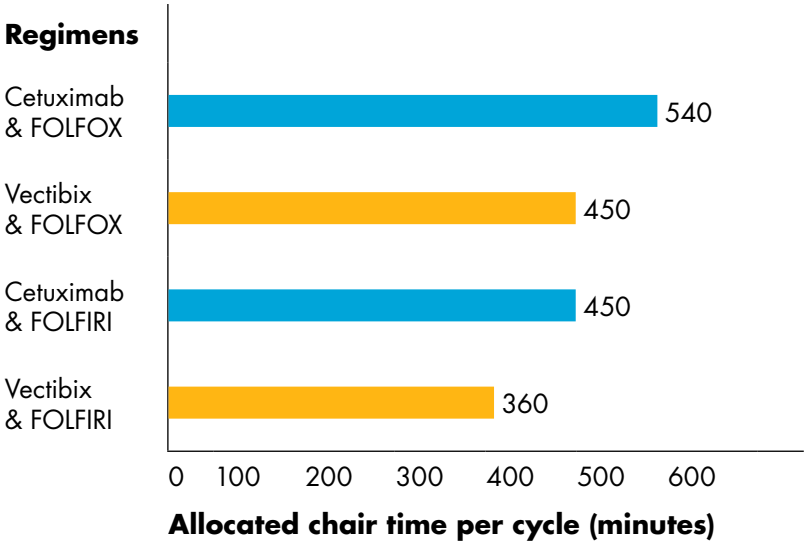
PATIENTS RECEIVED VECTIBIX*

DATA COLLECTION

- 20 patient records were retrospectively collected between January 2019 and December 2019†

PATIENT RECORD CRITERIA

- Attended the Singleton Hospital[5] • Aged 18 and over • Diagnosed with RAS wild-type stage 3/4 mCRC
- Treated with at least 2 cycles of EGFR therapy in combination with chemotherapy



Chair time booked for each regime[5]

Regimens	Number of patients	Total number of cycles	Total chair time (hours)	Total chair time (days)
Cetuximab & FOLFOX	**5**	**24**	**216**	**27.0**
Vectibix & FOLFOX	**4**	**14**	**105**	**13.1**
Cetuximab & FOLFIRI	**11**	**66**	**495**	**61.9**
Vectibix & FOLFIRI	**0**	**0**	**0**	**0**

Chair available 8 hours per day (09:00 – 17:00)
Chair time data was collected based on allocated infusion times‡

*In combination with either FOLFOX or FOLFIRI. †All patients diagnosed with RAS wild-type metastatic CRC, aged 18 and over. ‡The data for chair time came from Singleton Hospital's infusion time for each treatment regimen.

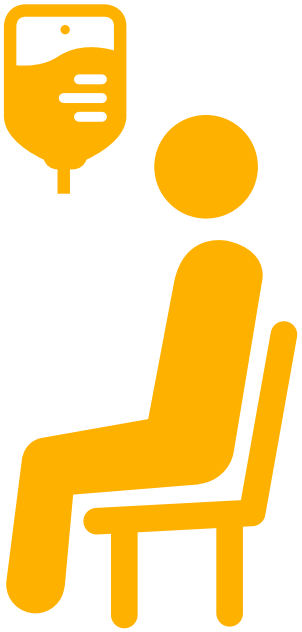
This service evaluation was conducted on behalf of Singleton Hospital (Swansea Bay University Health Board) by 7i Group Ltd. Funding was provided by Amgen Limited.

Prescribing information

References

CHAIR TIME OCCUPIED*

Cetuximab
711 hours or
88.9 chair days



Vectibix
105 hours or
13.1 chair days

It was estimated that if all patients received Vectibix, the potential savings could have been made over the study period:[5]

135
hours of chair time saved

16.9
chair days saved

Total recorded chair time was found to be
19%
less than the total allocated chair time

14
more cycles of treatment could be delivered

3.6
more patients could have potentially been treated with 5 cycles of Vectibix and FOLFOX

*Chair available 8 hours per day (09:00 – 17:00)

22

PATIENTS RECEIVED CETUXIMAB*

22

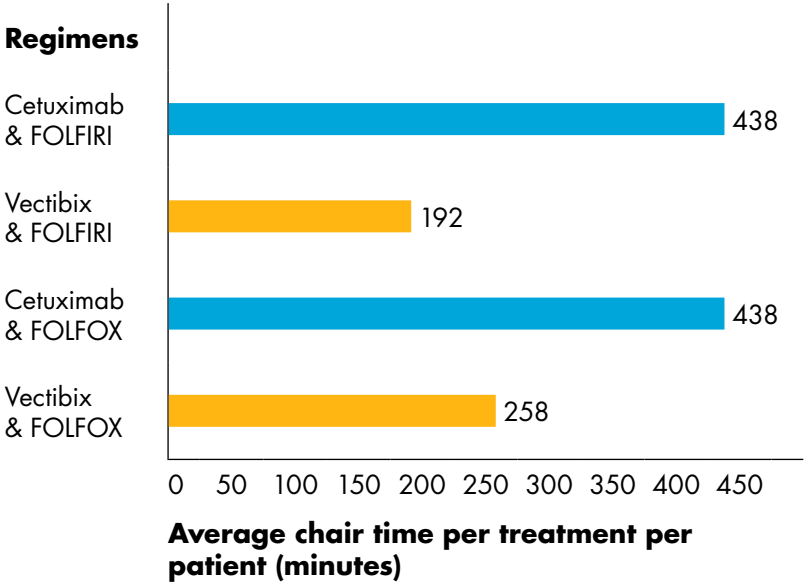
PATIENTS RECEIVED VECTIBIX*

DATA COLLECTION

• Retrospective data was collected from 44 patients who attended Canisc and Chemocare between February 2018 and January 2019†

PATIENT RECORD CRITERIA

• Attended the Velindre Cancer Centre[6] • Aged 18 and over • Diagnosed with RAS wild-type stage 3/4 mCRC
• Treated with at least 5 cycles of EGFR therapy in combination with chemotherapy



Chair time booked for each regime[6]

Regimens	Number of patients	Total number of cycles	Total chair time (hours)	Total chair time (days)
Cetuximab & FOLFIRI	**10**	**52**	**377**	**41.8**
Vectibix & FOLFIRI	**5**	**28**	**89**	**9.8**
Cetuximab & FOLFOX	**12**	**70**	**507.5**	**56.3**
Vectibix & FOLFOX	**16**	**80**	**344**	**38.2**

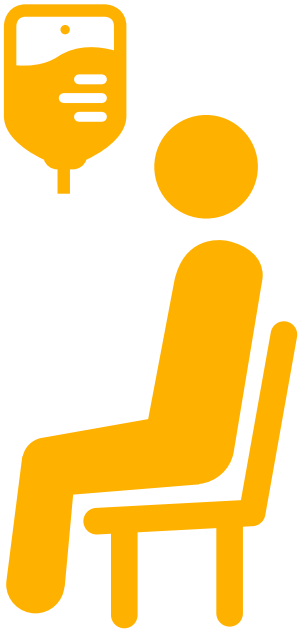
Chair available 9 hours per day (08:30 – 17:30)
Chair time data was collected based on allocated infusion times‡

*In combination with either FOLFOX or FOLFIRI. †All patients diagnosed with RAS wild-type metastatic CRC, aged 18 and over. ‡The data for chair time came from the Velindre Cancer Centre's infusion time for each treatment regimen.

Prescribing information
References

CHAIR TIME OCCUPIED*

Cetuximab
906.25 hours or
100.7 chair days



Vectibix
440 hours or
48.9 chair days

It was estimated that if all patients received Vectibix, the potential savings could have been made over the study period:[6]

466.25
hours of chair time saved

51.8
chair days saved

Less than half
the chair time

14
more cycles of treatment could be delivered

2.8
more patients could have potentially been treated with 5 cycles of Vectibix and FOLFOX

*Chair available 9 hours per day (08:30 – 17:30)

Prescribing information

References

SUMMARY

All of the hospitals that took part in the service evaluations found that chair time could be saved, and capacity improved by treating RAS wild-type mCRC patients with Vectibix in combination with chemotherapy instead of cetuximab in combination with chemotherapy.

IT ALL ADDS UP. VECTIBIX PATIENTS:

Don't routinely need pre-medications.

Have shorter infusion times compared with cetuximab.

Can start their chemotherapy immediately after their infusion.

Attend hospital every 2 weeks, instead of weekly, cutting the number of hospital visits in half.

PRESCRIBING INFORMATION

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. **Contra-indications:** 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)

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References

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2. Cetuximab Summary of Product Characteristics.
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