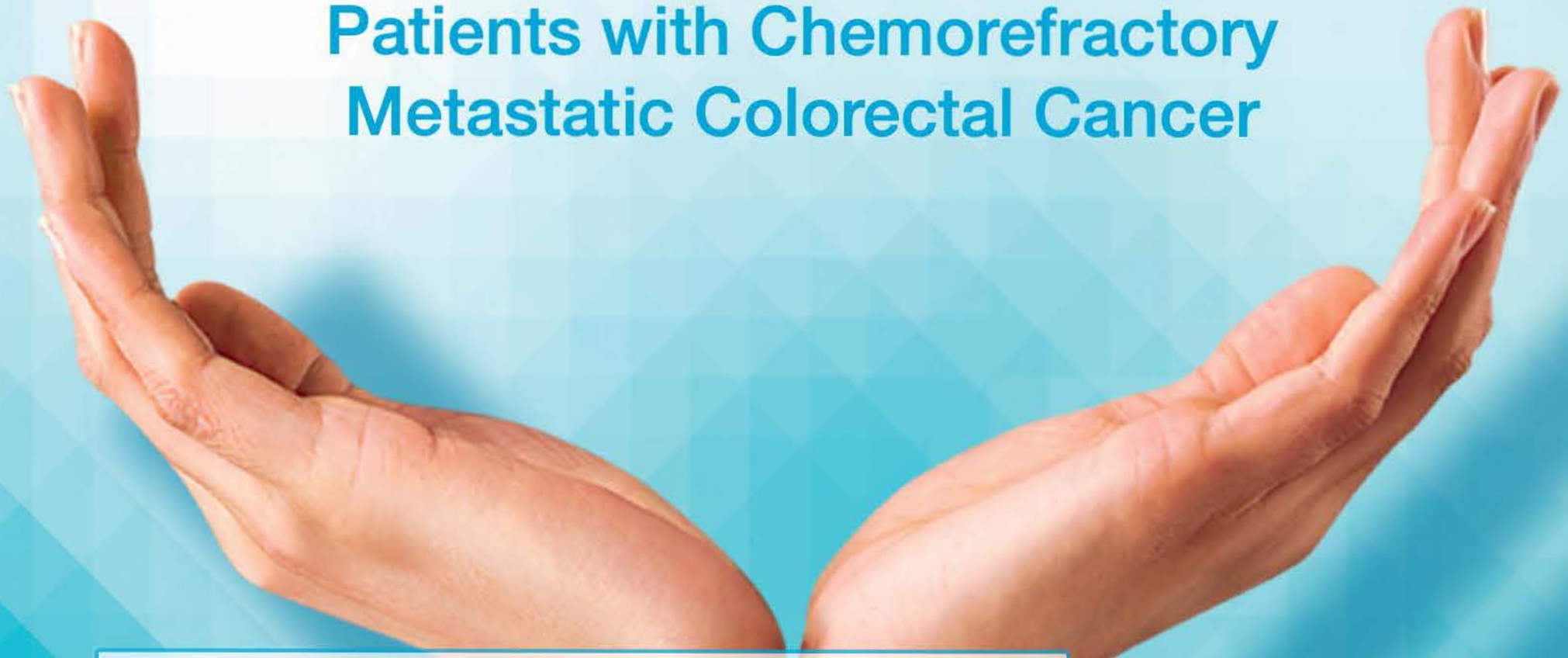
Weighing Vectibix®Treatment for Patients with Chemorefractory Metastatic Colorectal Cancer



Vectibix®, indicated as monotherapy for the treatment of patients with EGFR-expressing metastatic colorectal carcinoma with non-mutated (wild-type) *KRAS* after failure of fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens, has been issued marketing authorization with conditions, pending the results of studies to verify its clinical benefit. Patients should be advised of the nature of the authorization.

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 are available that demonstrate an increased survival with Vectibix®.

Vectibix®
(panitumumab)

Safety Profile

Clinical Use:

The safety and effectiveness of Vectibix® in pediatric patients have not yet been established.

Most Serious Warnings and Precautions:

Dermatologic and soft tissue toxicity:

Reported in 91% of patients, including 12% severe. Life-threatening and fatal infectious complications, including necrotizing fasciitis and/or sepsis, have been observed; withhold or discontinue Vectibix® for these reactions. Rare cases of Stevens-Johnson syndrome and toxic epidermal necrolysis observed in the post-marketing setting; discontinue Vectibix® in these rare cases.

Infusion reactions:

Across all clinical studies, NCI-CTC grade 3-4 infusion reactions observed in ~~less than~~ 1% of patients. In the post-marketing setting, serious reactions observed in ~~less than~~ 1% of patients; fatal reactions reported in ~~less than~~ 0.01%. Stop infusion if a severe or life-threatening infusion reaction occurs.

Increased toxicity and decreased overall survival in combination with bevacizumab and chemotherapy:

Vectibix® is not indicated for use in combination with chemotherapy with or without bevacizumab.

Combination treatment with Irinotecan, bolus 5-Fluorouracil, and Leucovorin (IFL) regimen:

Vectibix® should not be combined with IFL due to increased NCI-CTC grade 3-5 diarrhea.

Other Relevant Warnings and Precautions:

- Hypersensitivity reactions.
- Fatal and non-fatal interstitial lung disease.
- Use with caution in patients with a history of keratitis, ulcerative keratitis or severe dry eye. Monitor patients who develop ocular toxicities.
- Contains sodium; advise patients on controlled sodium diets.
- If symptoms affect vision and/or ability to concentrate and react, driving or use of machines are not recommended.
- Electrolyte disturbances, including hypomagnesemia, hypocalcemia, and hypokalemia. Monitor prior to, during, and up to 8 weeks after treatment completion; replete as necessary.
- Acute renal failure associated with severe diarrhea and dehydration.
- May impair fertility.
- Not for use while nursing (during treatment and for 2 months post-dose) or in pregnant women. For women of childbearing potential appropriate contraceptive measures must be used during treatment with Vectibix® and for 6 months post-dose.

For More Information:

For important information relating to adverse reactions, drug interactions, and dosing (particularly, do not administer as an IV push or bolus; must use an IV infusion pump and a low protein binding 0.2 µm or 0.22 µm in-line filter), please consult the Product Monograph at www.amgen.ca/Vectibix_PM.pdf or by contacting Amgen Canada Medical Information at 1-866-502-6436.

Vectibix® (panitumumab)

Patient Profiles*

- 79 year old widower
- Diagnosed with stage IV mCRC 1.5 years ago
- Disease has progressed on 2 previous lines of therapy
- She is seeking further treatment options

- 64 year old lawyer
- Diagnosed with stage IV mCRC 8 months ago
- Disease has progressed on 2 previous lines of therapy
- He has asked about his remaining treatment options

- 73 year old living 2 hours from her local cancer centre
- Diagnosed with stage IV mCRC
- She received prior adjuvant chemotherapy & additional chemotherapy for metastatic disease

*Fictitious patients. Contents of these cases may not be reflective of individual patient diagnoses or outcomes.

Vectibix® (panitumumab)

408 Trial Primary Endpoint[1–2]: Progression-Free Survival in Patients with Wild-Type KRAS Status Tumours

55% Reduction in risk of disease progression or death shown in patients treated with Vectibix®+ Best Supportive Care (BSC)[1–2]

- Hazard Ratio = 0.45 (95% CI: 0.34-0.59); Stratified log-rank P < 0.0001[1-2]

- Significantly improved median progression-free survival (PFS):
  - Vectibix®+ BSC 12.3 weeks[1-2]
  - BSC alone 7.3 weeks[1-2]

Study Design[1–3]

Canadian KRAS Testing Recommendations[4]

Vectibix® (panitumumab)

Patient Case

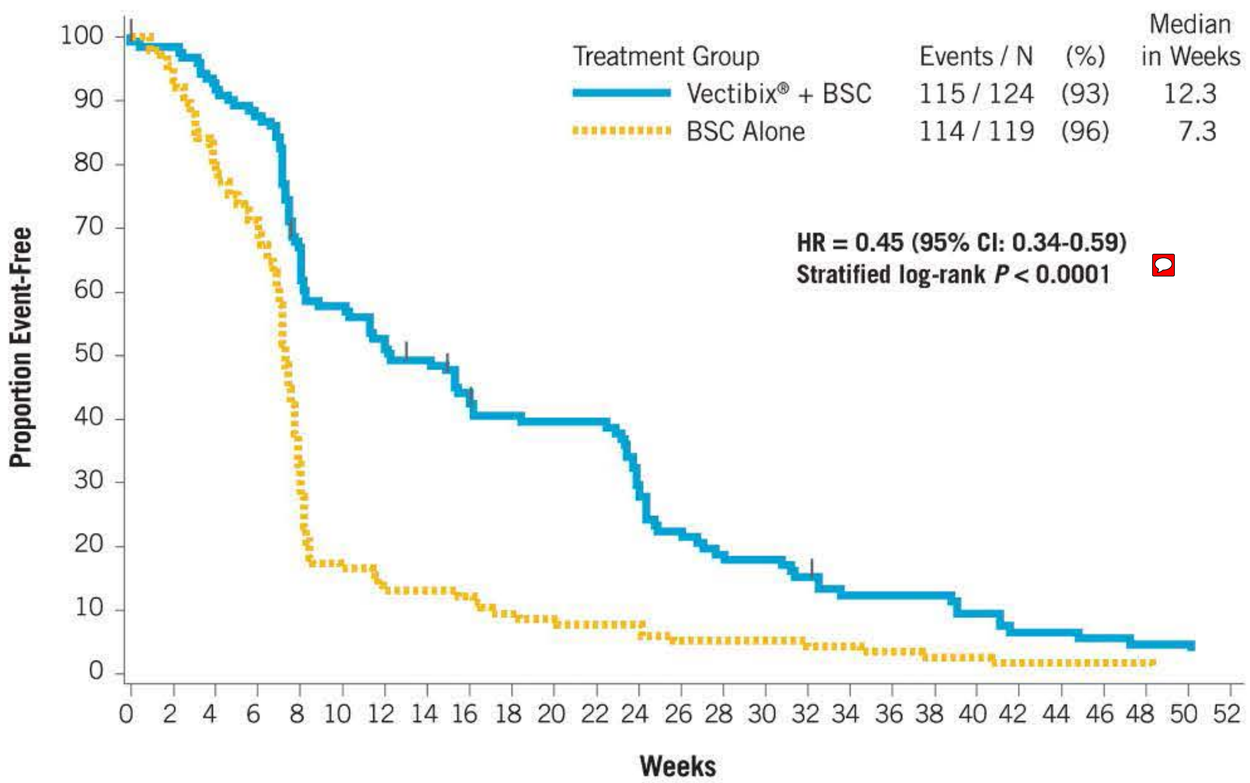
1 Vectibix® (panitumumab) Product Monograph. Amgen Canada Inc.

2 Amado RG, et al. J Clin Oncol. 2008;26:1626-34.

3 Van Cutsem E, et al. J Clin Oncol. 2007;25(13): 1658-64.

4 Aubin F, et al. Curr Oncol. 2011;18:e180-4.

Progression-Free Survival by Randomized Treatment in Wild-Type KRAS Stratum



Adapted from the Vectibix® Product Monograph[1] and Amado, et al[2].
BSC, best supportive care; HR, hazard ratio; CI, confidence interval.

Vectibix® (panitumumab)

Patient Case

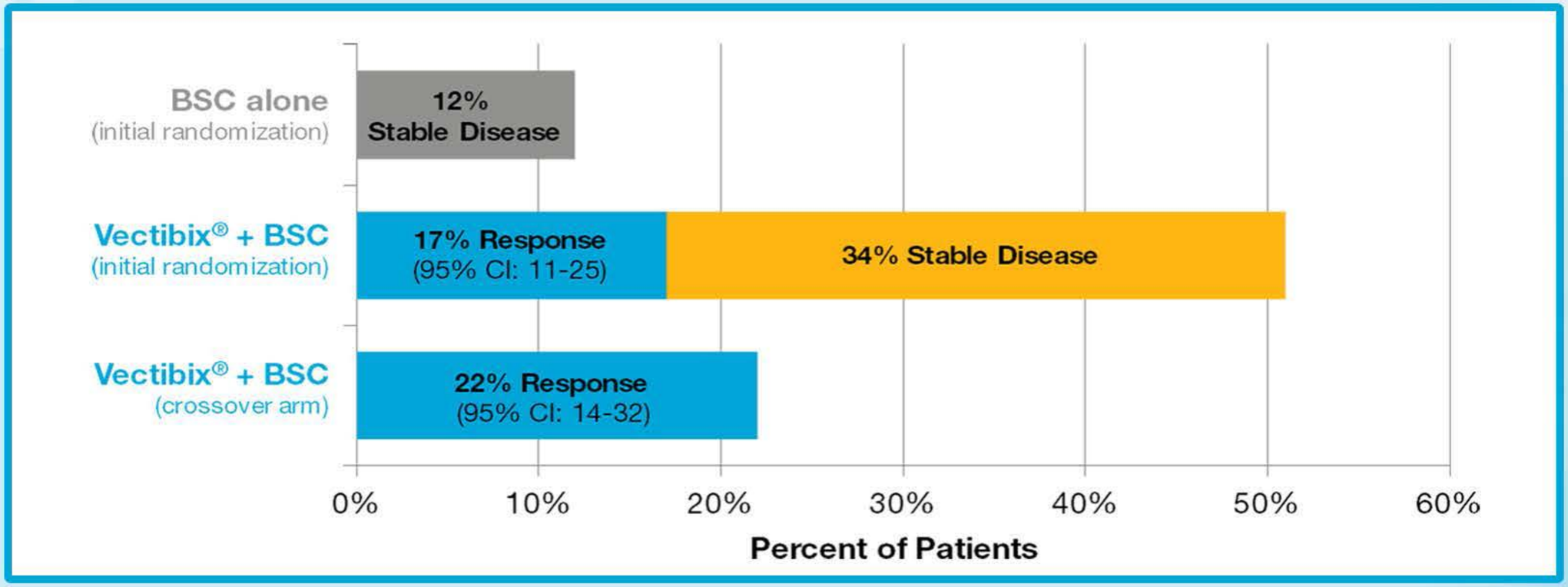
1 Vectibix® (panitumumab) Product Monograph. Amgen Canada Inc.

2 Amado RG, et al. J Clin Oncol. 2008;26:1626-34.

Clinical Efficacy PFS 2 of 2

408 Trial[1–2] Secondary Endpoints: Response Rates in Patients with Wild-Type KRAS Status Tumours

Response rates* of 17% and 22% in patients with non-mutated (wild-type) KRAS mCRC receiving Vectibix®



BSC, best supportive care; CI, confidence interval.
*Response rate = complete response (CR) + partial response (PR).

Vectibix® (panitumumab)

Patient Case

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2 Amado RG, et al. J Clin Oncol. 2008;26:1626-34.

Tolerability Profile

Infusion Reactions

Low incidence of infusion reactions (occurring within 24 hours of any dose):

- 3% of Vectibix®-treated patients
- <1% were severe (grade 3-4)

Most symptoms of potential infusion reactions were:

- Mild in intensity
- Resolved without treatment
- Isolated occurrences
- Did not require alteration or interruption of Vectibix® administration

Across all clinical studies, NCI-CTC grade 3-4 infusion reactions observed in less than 1% of patients. In the post-marketing setting, serious reactions observed in less than 1% of patients; fatal reactions reported in less than 0.01%. Stop infusion if a severe or life-threatening infusion reaction occurs

1 Vectibix® (panitumumab) Product Monograph. Amgen Canada Inc.

Tolerability Profile

Study Discontinuation Rates

In 789 patients with mCRC treated with Vectibix® monotherapy:

- 3% of Vectibix®-treated patients
- Predominantly due to skin-related events

In a clinical study comparing Vectibix® + BSC to BSC alone, of the of 123 patients with wild-type KRAS mCRC who were treated with Vectibix® + BSC:

- Efficacy results and qualitative safety were similar between 52 patients ≥ 65 years old and 71 patients < 65 years old
- Incidence of adverse events leading to permanent discontinuation was higher in patients ≥ 65 years old (10%) compared to patients < 65 years old (6%).

1 Vectibix® (panitumumab) Product Monograph. Amgen Canada Inc.

Toxicity Management of Selected Adverse Events

Additional information about the management of the following selected toxicities are available:

Dermatologic & Soft Tissue Toxicity
- General Guidance[1]
- Dry Skin[1-2]
- Fissures[1-2]
- Paronychia[2]
- Pruritus[1-2]
- Rash[1-3]
- Trichomegaly[2]

Electrolytes
- Hypomagnesemia[1]

To help you manage your patients' treatment, Vectibix® Patient Management Kits and skin care sample kits are also available.

Dermatologic and soft tissue toxicity: Reported in 91% of patients, including 12% severe. Life-threatening and fatal infectious complications, including necrotizing fasciitis and/or sepsis, have been observed; withhold or discontinue Vectibix® for these reactions. Rare cases of Stevens-Johnson syndrome and toxic epidermal necrolysis observed in the post-marketing setting; discontinue Vectibix® in these rare cases.

Vectibix® (panitumumab)

Patient Case

1 Vectibix® (panitumumab) Product Monograph. Amgen Canada Inc.

2 Lacouture ME, et al. Support Care Cancer. 2011;19(8): 1079-95.

3 Melosky B, et al. Curr Oncol. 2009;16(1):14-24.

Dermatologic & Soft Tissue Toxicity: General Guidance*

- When prescribed by a physician, the following skin treatments may be useful in the management of skin toxicities:
  - Moisturizers
  - Sunscreens (SPF > 15 UVA and UVB)
  - Topical steroid creams (not stronger than 1% hydrocortisone)
  - Oral antibiotics (eg, doxycycline)

- Withhold or discontinue Vectibix® for dermatologic or soft tissue toxicity associated with severe or life-threatening inflammatory or infectious complications.

- For dose modifications related to dermatological toxicity, refer to the Vectibix® Product Monograph.

*Any treatment decisions are the sole responsibility of the healthcare professional. Please consult the Product Monograph of any treatment option before use.

Dry Skin: Management Guidelines*

Proactive Treatment Options

- Avoid extreme temperatures and direct sunlight[1]
- Bathing in tepid water with bath oils or mild cleansers[1]
- Moisturizing creams[1]

Reactive Treatment Options

- Petroleum-based creams; emollients containing urea, colloidal oatmeal[1]
- Zinc oxide (13-40%); urea creams (10-40%)[1]
- Topical corticosteroids[1-2] (not stronger than 1% hydrocortisone[2])

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Vectibix® (panitumumab)

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2 Vectibix® (panitumumab) Product Monograph. Amgen Canada Inc.

Fissures: Management Guidelines*

Proactive Treatment Options

- Protective footwear and gloves
- Avoid friction with fingertips, toes, ~~heals~~

Reactive Treatment Options

- Thick moisturizers; zinc oxide (13-40%) creams
- Wound sealing: Cyanoacrylate preparations
- Hydrocolloid dressings; topical antibiotics
- Bleach soaks to prevent infection (¼ cup of bleach to 3 gal of water)

*Any treatment decisions are the sole responsibility of the healthcare professional. Please consult the Product Monograph of any treatment option before use.

1 Lacouture ME, et al. Support Care Cancer. 2011;19(8): 1079-95.

Paronychia: Management Guidelines*

Proactive Treatment Options

- Diluted bleach soaks (recommended final concentration of approximately 0.005% [¼ - ⅛ cup of 6% bleach to 3 - 5 gal of water])[1]
- Avoid irritants[1]

Reactive Treatment Options

- Topical corticosteroids[1-2] (not stronger than 1% hydrocortisone[2])
- Systemic tetracycline antibiotics[1]

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Vectibix® (panitumumab)

Patient Case

1 Lacouture ME, et al. Support Care Cancer. 2011;19(8): 1079-95.

2 Vectibix® (panitumumab) Product Monograph. Amgen Canada Inc.

Pruritus: Management Guidelines*

Proactive Treatment Options

- Gentle skin care[1]

Reactive Treatment Options

- Treatment of underlying rash[1]
- Topical menthol 0.5%[1]; topical pramoxine 1%[1]
- Topical corticosteroids[1-2] (not stronger than 1% hydrocortisone[2])
- Systemic antihistamines[1]

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Vectibix® (panitumumab)

Patient Case

1 Lacouture ME, et al. Support Care Cancer. 2011;19(8): 1079-95.

2 Vectibix® (panitumumab) Product Monograph. Amgen Canada Inc.

Rash: Management Guidelines*

Proactive Treatment Options

A proactive skin regimen should be discussed before treatment, and may include[1-3]:

- Avoiding harmful products and/or activities
- Minimizing sun exposure
- Protecting high-risk areas of the body
- Monitoring changes proactively

Proactive recommendations

Reactive Treatment Options

Treatment options are based on severity[1]:

- Mild / Grade 1
- Moderate / Grade 2
- Severe / Grade 3

Reactive recommendations

*Any treatment decisions are the sole responsibility of the healthcare professional. Please consult the Product Monograph of any treatment option before use.

1 Melosky B, et al. Curr Oncol. 2009;16(1):14-24.

2 Vectibix® (panitumumab) Product Monograph. Amgen Canada Inc.

3 Lacouture ME, et al. Support Care Cancer. 2011;19(8):1079-95.

Trichomegaly: Management Guidelines*

Proactive Treatment Options

- Lash clipping every 2-4 weeks

Reactive Treatment Options

- Refer to ophthalmologist for irritation or persistent discomfort

*Any treatment decisions are the sole responsibility of the healthcare professional.

Vectibix® (panitumumab)

Patient Case

1 Lacouture ME, et al. Support Care Cancer. 2011;19(8): 1079-95.

Hypomagnesemia: Management Guidelines*

Monitoring[1]

- Monitor electrolytes periodically:
  - Prior to initiating Vectibix® treatment
  - During treatment
  - For 8 weeks after completion of Vectibix® treatment

Grading[2]

Grade 1	Grade 2	Grade 3	Grade 4
< LLN - 1.2 mg/dL < LLN - 0.5 mmol/L	< 1.2 - 0.9 mg/dL < 0.5 - 0.4 mmol/L	< 0.9 - 0.7 mg/dL < 0.4 - 0.3 mmol/L	< 0.7 mg/dL < 0.3 mmol/L

Treatment[1]

- Institute appropriate treatment, eg, oral or intravenous electrolyte repletion, as needed

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Vectibix® (panitumumab)

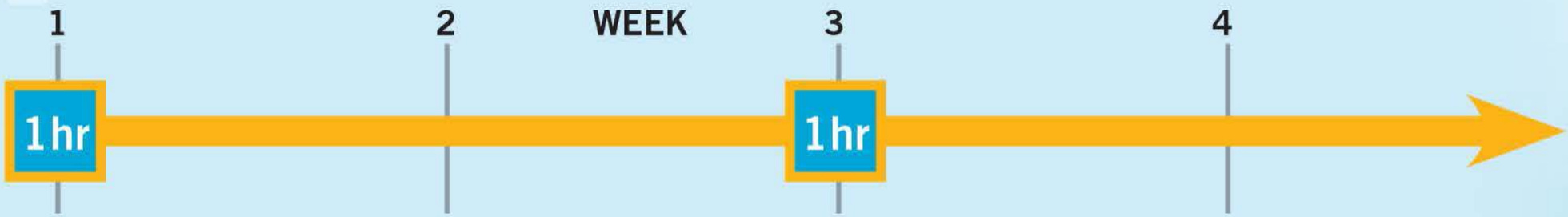
Patient Case

1 Vectibix® (panitumumab) Product Monograph. Amgen Canada Inc.

2 National Cancer Institute Cancer therapy evaluation program. Common terminology criteria for adverse events, v4.03 (CTCAE).

Dosing Schedule

Vectibix®: The ONLY fully human IgG2 anti-EGFR monoclonal antibody for mCRC with Q2W dosing*



- Recommended dose: 6 mg/kg
- Dosing frequency: Every 2 weeks
- Infusion time:
  - 60 minutes for infusion volumes of 100 mL
  - 90 minutes for infusion volumes greater than 150 mL

*Comparative clinical significance unknown.

Vectibix® (panitumumab)

Patient Case

1 Vectibix® (panitumumab) Product Monograph. Amgen Canada Inc.

Vectibix® Preparation

- Prepare using appropriate aseptic technique
- Withdraw the necessary amount of Vectibix® for a dose of 6 mg/kg as appropriate
- Dilute in a total volume of 100 mL in 0.9% sodium chloride injection USP*; final concentration should not exceed 10 mg/mL
- Mix diluted solution by gentle inversion; do not shake

If a patient's actual body weight requires a volume greater than 150 mL infusion, Vectibix® may be administered over approximately 90 minutes

Vectibix® (panitumumab)

Patient Case

1 Vectibix® (panitumumab) Product Monograph. Amgen Canada Inc.

Vectibix® Administration

- Infuse over approximately 60 minutes through a peripheral line or indwelling catheter*
  - **Vectibix® must be administered using an IV infusion pump**
  - **Do not administer Vectibix® as an IV push or bolus**
  - **Administer using a low protein binding 0.2 µm or 0.22 µm in-line filter**

- Flush line before and after Vectibix® administration with 0.9% sodium chloride injection USP to avoid mixing with other drug products or IV solutions

- Vectibix® should not be mixed with, or administered as, an infusion with other medicinal products and should not be administered if discolouration is observed.

*If a patient's actual body weight requires a volume greater than 150 mL infusion, Vectibix® may be administered over approximately 90 minutes

Vectibix® (panitumumab)

Patient Case

1 Vectibix® (panitumumab) Product Monograph. Amgen Canada Inc.

Vectibix® Storage

Vials

- Store vials under refrigeration at 2° to 8°C (36° to 46°F)
- Do not freeze
- Protect from light
- Do not shake
- Since Vectibix® does not contain preservatives, any unused portion remaining in the vial must be discarded

Diluted Infusion Solution

- Use immediately after dilution
- If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user & should be no longer than 24 hours at 2° to 8°C (36° to 46°F)
- Do not freeze or shake

Vectibix® (panitumumab)

Patient Case

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