Panitumumab

Indication
First line treatment of RAS wild type, metastatic colorectal cancer in combination with FOLFOX or FOLFIRI chemotherapy.

ICD-10 codes
Codes prefixed with C18-20.

Regimen details

Day	Drug	Dose	Route
1	Panitumumab	6mg/kg	IV infusion

RAS status must be confirmed prior to commencing treatment

Cycle frequency
14 days

Number of cycles
Continued until disease progression or unacceptable toxicity

Administration
Panitumumab is administered in sodium chloride 0.9% over 60 minutes via a 0.2 micron in line filter. The final concentration must not exceed 10 mg/mL.

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

Patients should be observed for fever and chills and other symptoms of infusion-related reaction during the infusion. Interruption and slowing down the infusion rate may help control such symptoms.

If a mild or moderate infusion-related reaction occurs, the infusion should be interrupted, and necessary supportive medication administered. The infusion may be resumed once the symptoms abate. It is recommended to maintain the lower infusion rate for all subsequent infusions.

Severe infusion-related reactions have been documented and require immediate and permanent discontinuation of panitumumab therapy and may necessitate emergency treatment. Resuscitation equipment must be available during administration.

Hypersensitivity reactions occurring more than 24 hours after infusion have been reported. Patients should be informed of the possibility of a late onset reaction and instructed to seek medical advice if symptoms of a hypersensitivity reaction occur.

Panitumumab should be administered prior to chemotherapy

Pre-medication
None

Emetogenicity

This regimen has low emetogenic potential

Additional supportive medication

Patients should be prescribed skin reaction prophylaxis from cycle 1 as per the skin management pathway:

Emollient: Light emollient cream (e.g. Cetraben) and soap substitute (e.g. Dermol 500 lotion)

Topical Steroid: Hydrocortisone cream 1% (prn/QDS)

Sunscreen: SPF50 (can be requested from GP as not on trust formulary)

Oral antibiotics: Doxycycline 100mg OD

Extravasation

Panitumumab is neutral (Group 1)

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
Bone profile	14 days
Calcium	14 days
Magnesium	14 days
CEA	14 days
Hepatitis B serology (HBsAG, HBcAb)	none
HbA1c	3 months
Random glucose	14 days

RAS status must be confirmed prior to commencing treatment

Investigations - pre subsequent cycles

FBC, U&E (including creatinine), LFT, magnesium, calcium, random glucose, CEA (4 weekly)

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Note: Refer to parameters in relevant chemotherapy protocol in addition to below.

Investigation	Limit
Neutrophils	≥ 1.0 x 10^9/L
Bilirubin	< 1.5 x ULN
Creatinine Clearance (CrCl)	≥ 30 mL/min

Electrolyte disturbances should be corrected prior to treatment

Dose modifications

- ### Haematological toxicity

Refer to relevant chemotherapy protocol for advice. If chemotherapy is delayed panitumumab should also be delayed.

- ### Renal impairment

The safety and efficacy of panitumumab has not been studied in patients with renal impairment. Discuss with consultant if CrCl <30ml/min

- **Hepatic impairment**

The safety and efficacy of panitumumab has not been studied in patients with impaired hepatic function.

- **Other toxicities**

Refer to appropriate chemotherapy protocol for advice regarding chemotherapy toxicity.

Toxicity	Definition	Dose adjustment
Severe skin reaction	≥ grade 3	See guidance below
Electrolyte disturbance	Hypomagnesaemia, hypokalaemia, hypocalcaemia	Replace electrolyte as appropriate
Dyspnoea	May occur as result of infusion related reaction but may occur several weeks into treatment	Discontinue panitumumab treatment if interstitial lung disease is diagnosed.
Any other toxicity	≥ grade 3	Withold until resolved to < grade 2

Interstitial lung disease ILD, which may be acute in onset, has been observed and some cases have been fatal. If patients experience worsening of respiratory symptoms such as dyspnoea, cough and fever, panitumumab should be interrupted and the patient should be promptly investigated. If ILD is confirmed, panitumumab should be discontinued and the patient treated appropriately.
Panitumumab is contra-indicated in patients with interstitial pneumonitis or pulmonary fibrosis.

Skin reactions

Management of patients with mild, moderate and severe skin reactions should be as per the below guidance:

https://northwest-nhs.iqemo.com/authenticated/documents/159b8f96-aa48-4b4d-b566-75c3f6ac8a7b.pdf

Occurrence of ≥ grade 3 skin reaction	Management
1st occurrence	Withhold 1-2 doses If improved to < grade 3 continue 100% If no recovery: discontinue
2nd occurrence	Withhold 1-2 doses If improved to < grade 3 continue 80% If no recovery: discontinue
3rd occurrence	Withhold 1-2 doses If improved to < grade 3 continue 60% If no recovery: discontinue
4th occurrence	Discontinue

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Infusion related toxicity
Interstitial lung disease
Acute renal failure
Severe skin reactions and risk of secondary bacterial infection, including necrotising fasciitis

- **Frequently occurring side effects**

Skin reactions
Nausea and vomiting
Abdominal pain
Diarrhoea, constipation
Headache
Mucositis
Dyspnoea, cough
Electrolyte imbalances particularly hypomagnesaemia, hypokalaemia, hypocalcaemia.
Ocular disorders, keratitis

- **Other side effects**

Cardiovascular disorders
Eye disorders- ulcerative keratitis

Significant drug interactions – for full details consult product literature/ reference texts

Panitumumab should not be administered in combination with bevacizumab containing chemotherapy.

Additional comments

It is recommended to warn patients of the possibility of late onset infusion reactions and instruct them to contact their doctor/nurse team if symptoms of an infusion-related reaction occur. If severe, a reaction requires immediate and permanent discontinuation of panitumumab therapy and may necessitate emergency treatment.

Panitumumab causes sun-sensitivity that may exacerbate skin reactions. Protect from sun.

Fertility/Contraception

Patients should use an acceptable method of birth control to avoid pregnancy for the duration of treatment and for 6 months afterwards. Breastfeeding should be discontinued during treatment. Women using hormonal contraceptive must also use a barrier contraceptive method.

References

- Colorectal NICE guideline NG151 (updated 15 Dec 2021) accessed 19 May 2022
- National Institute for Health and Clinical Excellence. TA439. (Updated 25 September) 2017 Accessed 19 May 2022 via www.nice.org.uk
- Summary of Product Characteristics - Panitumumab (Amgen) accessed 19 May 2022 via www.medicines.org.uk/
- Douillard JY, Oliner KS, Siena S, et al. Panitumumab–FOLFOX4 treatment and RAS mutations in colorectal cancer. N Engl J Med 2013;369:1023-34.
- 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;28:4697-705.

THIS PROTOCOL HAS BEEN DIRECTED BY DR WILLIAMSON DESIGNATED LEAD CLINICIAN FOR COLORECTAL CANCER
RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

Date:	June 2022
Review:	June 2024
Version	4