Panitumumab

Indication

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

(NICE TA439)

ICD-10 codes

Codes prefixed with C18, C19, C20.

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

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

Dexamethasone 8mg IV should be administered 30 minutes prior to panitumumab infusion.

Ensure regular use of moisturiser. Additional medication may be required for skin toxicities, as per guidelines below.

Emetogenicity

This regimen has low emetogenic potential

Additional supportive medication

Loperamide if required.
See below for guidelines for management of skin toxicities.
Prophylactic antibiotics (such as doxycycline 100mg daily) as per local policy.

Extravasation

Panitumumab is neutral (Group 1)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
Magnesium	14 days
Calcium	14 days
CEA	14 days

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days
Magnesium	7 days
Calcium	7 days
CEA	Monthly

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**
Neutrophil count	≥1.0 x 10^9/L
Creatinine Clearance (CrCl)	≥ 30ml/min
Bilirubin	≤ 1.5 x ULN

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 table below
Electrolyte disturbance	Hypomagnesaemia, hypokalaemia, hypocalcaemia	Replace electrolytes 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	Withhold 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

Ensure regular use of moisturisers and sun protection (> SPF 15).
Skin reactions may be treated with mild topical corticosteroids and/or oral antibiotics.
Skin reactions ≥ grade 3 should be managed as below:

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

Nil

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.

References

- National Institute for Health and Clinical Excellence. TA439. Accessed 30 Aug 2017 via www.nice.org.uk
- Summary of Product Characteristics - Panitumumab (Amgen) accessed 30 Aug 2017 via www.emc.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.

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