Panitumumab 6mg/kg Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of adult patients with wild-type RAS metastatic colorectal cancer (mCRC) as monotherapy after failure of fluoropyrimidine, oxaliplatin, and irinotecan containing chemotherapy regimens.	C18	00225c	Hospital

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Panitumumab is administered every once every 14 days until disease progression or unacceptable toxicity occurs.

Availability of resuscitation equipment **MUST** be ensured while administering treatment.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Panitumumab	6mg/kg	IV infusion	[a]100ml 0.9% sodium chloride over 60min[b]using a 0.22 micron in-line filter	Repeat every 14 days
[a]In 150ml over 90min if dose > 1000mg Final concentration should not exceed 10mg/ml [b]If the first infusion is tolerated, then subsequent infusions may be administered over 30 to 60 minutes					
Panitumumab is incompatible with glucose solutions, Ensure IV administration sets are flushed with sodium chloride 0.9% pre and post administration.					

ELIGIBILITY:

- Indications as above
- Wild type RAS tumours verified by a validated test method.
- ECOG 0-2.
- Adequate marrow reserve.
- Adequate renal and liver function.

EXCLUSIONS:

- Patients with mutant RAS mCRC or unknown RAS mCRC status.
- Patients with interstitial pneumonitis or pulmonary fibrosis.
- Renal impairment.
- Hepatic impairment.
- Hypersensitivity to panitumumab or to any of the excipients.

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, liver and renal profile

Regular tests:

- FBC, liver and renal profile prior to each treatment.
- Post treatment: monthly electrolytes, magnesium, calcium for 2 months after last panitumumab treatment.

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.

Renal and Hepatic Impairment;

Table 1: Dose modification of panitumumab in renal and hepatic impairment

Renal Impairment	Hepatic Impairment
Safety and efficacy of panitumumab has not been studied in patients with renal impairment	Safety and efficacy of panitumumab has not been studied in patients with hepatic impairment

Management of adverse events:

Table 2: Dose modification schedule based on skin reactions.

Local skin care policy for the prevention and treatment of EGFR-inhibitor adverse skin reactions should be instigated as appropriate.

Occurrence of skin symptom(s): ≥ grade 3	Administration of panitumumab	Outcome	Dose regulation
Initial occurrence	Hold 1 or 2 doses	Improved (< grade 3)	Continue infusion at 100% original dose
		Not recovered	Discontinue
2nd occurrence	Hold 1 or 2 doses	Improved (< grade 3)	Continue infusion at 80% of original dose
		Not recovered	Discontinue
3rd occurrence	Hold 1 or 2 doses	Improved (< grade 3)	Continue infusion at 60% of original dose
		Not recovered	Discontinue
4th occurrence	Discontinue		

Table 3: Dose Modification of Panitumumab for Adverse Events

Adverse reactions	Recommended dose modification
Infusion reaction	Decrease infusion rate and maintain lower rate for subsequent infusions
Severe infusion reaction	Discontinue
Interstitial lung disease	Discontinue
Ulcerative keratitis	Discontinue

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Low (**Refer to local policy).**

PREMEDICATIONS:

Not usually required

OTHER SUPPORTIVE CARE:

See local skin care policy for the prevention and treatment of EGFR-inhibitor adverse skin reactions

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Infusion-related reactions**:
  - In cases of mild or moderate infusion-related reaction, the infusion rate may be decreased and maintained at the lower rate in all subsequent infusions.
  - Occurrence of a severe infusion-related reaction requires immediate and permanent discontinuation of panitumumab therapy and may necessitate emergency treatment.
  - Hypersensitivity reactions occurring more than 24 hours after infusion have been reported.Patients should be warned of the possibility of such a late onset and instructed to contact their physician if symptoms occur.
- **Respiratory disorders:** Interstitial lung disease (ILD) has been observed with EGRF inhibitors. Treatment should be withheld in the event of onset or worsening respiratory symptoms. If ILD is confirmed, treatment should be discontinued.
- **Acute renal failure:** This has been observed in patients who develop severe diarrhoea and dehydration.
- **Skin reactions:** This is the main adverse reaction of panitumumab. Refer to local policy for skin care regime and to Table 1 under Dose Modifications for management of treatment if patient experiences skin reactions.
- **Electrolyte disturbances:** Hypomagnesaemia, hypokalaemia or hypocalcaemia may occur. Electrolyte repletion is recommended, as appropriate.
- **Ocular toxicities:** Patients presenting with signs and symptoms suggestive of keratitis such as acute or worsening: eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain and/or red eye should be referred promptly to an ophthalmology specialist. If a diagnosis of ulcerative keratitis is confirmed, treatment should be interrupted or discontinued. If keratitis is diagnosed, the benefits and risks of continuing treatment should be carefully considered.

DRUG INTERACTIONS:

- No formal drug-drug interaction studies have been conducted with panitumumab.
- Panitumumab should not be administered in combination with IFL chemotherapy or with bevacizumab-containing chemotherapy.

- The combination of panitumumab with oxaliplatin-containing chemotherapy is contraindicated for patients with mutant *RAS* mCRC or for whom *RAS* mCRC status is unknown.
- Current drug interaction databases should be consulted for more information.

ATC CODE:

Panitumumab - L01XC08

COMPANY SUPPORT RESOURCES/Useful Links:

Please note that this is for information only and does not constitute endorsement by the NCCP
Physician Brochure: https://www.hpra.ie/img/uploaded/swedocuments/edumat_auto_c5038c9d-3ed9-4692-9ecd-dda83b67eeeb.pdf

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2. Amado RG,Wolf M, Peeters M, et al:Wild-type KRAS is required for panitumumab efficacy in patients with metastatic colorectal cancer. J Clin Oncol. 2008;26:1626-34.
3. Douillard, J. Y., S. Siena, J. Cassidy, 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(31):4697-4705
4. Douillard, JY, Oliner KS, Siena S, et al. Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer. N Engl J Med 2013;369(11):1023-1034.
5. Kohne CH, Hofheinz R 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
6. VECTIBIX® Summary of Product Characteristics. Accessed Oct 2020 Available at https://www.ema.europa.eu/en/documents/product-information/vectibix-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	05/04/2014		Prof Maccon Keane
2	30/05/2015	Change of title to Panitumumab 6mg/kg Therapy Addition of new indications, drug interactions and references	Prof Maccon Keane
3	11/11/2016	Amendment of indications to allow combination with FOLFIRI in first line as per SmPC	Prof Maccon Keane
4	26/11/2018	Updated to new NCCP template Removal of combination therapy indications- separate NCCP regimens available for these	Prof Maccon Keane
5	10/11/2020	Reviewed	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.