

PANITUMUMAB (Vectibix) OXALIPLATIN Modified de Gramont

INDICATION (ICD10) C18, C20

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (PAN2)

1. Panitumumab in combination with oxaliplatin based chemotherapy for chemotherapy-naive RAS wild-type metastatic colorectal cancer either 1st line treatment for metastatic colorectal cancer or as 2nd line treatment if treated with 1st line pembrolizumab for MSI-H/dMMR disease. (TA439)

REGIMEN

Day 1	PANITUMUMAB	6mg/kg	IV infusion	#ml sodium chloride 0.9%
	CALCIUM FOLINATE	350mg	IV infusion	250ml glucose 5% over 2 hours
	OXALIPLATIN	85mg/m ²	IV infusion	#ml glucose 5% IV infusion over 2 hours
	FLUOROURACIL	400mg/m ²	IV bolus	
	FLUOROURACIL	2400mg/m ²	IV infusion	continuous over 46 hours

diluent and diluent volume for dose prescribed as per national standardised product specification or licensed dose

NB Calcium folinate (calcium leucovorin) is not the same as calcium levofolinate. (Calcium levofolinate is a single isomer of folinic acid and the dose is generally half that of calcium folinate).

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 14 days until disease progression

ANTI-EMETICS

Moderately emetogenic day 1

Low emetogenic risk day 2

CONCURRENT MEDICATION REQUIRED

Fluorouracil	Mouth and bowel support eg Loperamide, benzydamine mouthwash
Oxaliplatin	Flush with glucose 5% before and after infusion

ADMINISTRATION

Calcium folinate	concurrently with oxaliplatin via a Y site placed immediately before the injection site.
Panitumumab	The initial dose should be administered over 60 minutes, if tolerated well the subsequent infusions may be administered over 30 to 60 minutes. Doses higher than 1000mg should be infused over 90 minutes.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Fluorouracil – inflammitant

Oxaliplatin – exfoliant

Panitumumab - neutral

Administer panitumumab via low protein binding 0.2 or 0.22micron filter

Central line (single lumen)

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E including Mg ⁺⁺ and LFTs Neutrophils $\geq 1.5 \times 10^9/L$ (1.0-1.5x10 ⁹ /L retest and if on an upward trend then can go ahead, if no access to retest then contact Dr) Platelets $\geq 75 \times 10^9/L$	baseline and every cycle
EDTA GFR or calculated CrCl at consultant's discretion.	baseline and every cycle
Serum creatinine	baseline and every cycle
DPYD (dihydropyrimidine dehydrogenase) test	baseline
Weight	baseline and every cycle

MAIN TOXICITIES AND ADVERSE REACTIONS

Fluorouracil	Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds Diarrhoea – treat with loperamide or codeine Cardiotoxicity – monitor cardiac function (consider ECG at baseline). Special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil. Stomatitis
Oxaliplatin	Peripheral sensory neuropathy and laryngeal spasm – avoid cold drinks and touching cold items
Panitumumab	Dermatologic related reactions, a pharmacologic effect observed with epidermal growth factor receptor (EGFR) inhibitors, are experienced with nearly all patients. Electrolyte disturbances - hypomagnesaemia, hypokalaemia and hypocalcaemia. Repletion required. Hypersensitivity – reactions may occur more than 24 hours after infusion. Mild or moderate infusion-related reaction the infusion rate should be reduced for the duration of that infusion. Maintain this lower infusion rate in all subsequent infusions. If a severe or life-threatening reaction occurs during an infusion or at any time post-infusion eg bronchospasm, angioedema, hypotension, need for parenteral medication, or anaphylaxis, discontinue permanently. Pulmonary interstitial disease

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Fluorouracil	Cimetidine slightly increases exposure to fluorouracil Metronidazole increased toxicity Phenytoin concentration increased Warfarin
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DOSE MODIFICATIONS

Haematological

Neutrophils $< 1.5 \times 10^9/L$ and/or platelet count $< 100 \times 10^9/L$	delay one week, only treat when neutrophils and platelets are above these limits.
Grade 4 neutropenia	consider giving 50% oxaliplatin and fluorouracil in palliative disease.
If > 1 delay or 1 delay ≥ 2 weeks give 80% oxaliplatin and fluorouracil for future cycles. A further dose reduction may be made at the clinician's discretion	

Non-haematological

Oxaliplatin

If patients develop acute laryngopharyngeal dysaesthesia infuse the next cycle over 4 hours.

If symptoms persist give 80% dose.

If persistent sensory symptoms occur, withdraw treatment

Panitumumab

Ocular

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.

Skin

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

Hepatic impairment

Fluorouracil

Significantly impaired hepatic function eg bilirubin >50micromol/L may be a sign of disease progression and require cessation of, or change in, treatment.

Always discuss deteriorating liver function with consultant.

If hepatic function is impaired, the recommended dose can be reduced to give 50% to 70% dose, but no need for dose adjustment is expected in mild and moderate (without renal impairment).

Bilirubin >85micromol/L	not recommended
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Oxaliplatin

No dose adjustment is needed.

Panitumumab

No dose adjustment is needed.

Renal impairment

Fluorouracil

If renal function is impaired, the recommended dose can be reduced to give 50% to 70% dose, but no need for dose adjustment is expected.

Oxaliplatin

CrCl >30ml/min	give 100% dose
CrCl <30ml/min	Dose reduce (consider 50% of original dose)

Panitumumab

No dose adjustment is expected.

REFERENCES

CDF list

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing	Last cycle
Clinical assessment	X		Pre cycle		Pre cycle	Alternate cycles or team discretion	
SACT assessment (PS and toxicities)	X	X	X	X	X	Every cycle	Check has OPD
FBC	X	X	X	X	X	Every cycle	X
U&E, calcium, magnesium & LFT	X	X	X	X	X	Every cycle	X
CrCl	X	X	X	X	X	Every cycle	X
CEA	X	X	X	X	X	Every cycle	X
Dihydropyrimidine dehydrogenase (DPYD) deficiency test	X					This test is required for every patient newly started on capecitabine or fluorouracil for the first time. The result MUST be available before administration of chemotherapy unless clear documentation from the consultant is available to the contrary.	
CT scan	X					Inform consultant team if not booked	Check has date for CT
Informed consent	X					Verbal each cycle	
Height	X						
Weight recorded	X	X	X	X	X	Every cycle	X