Indication	For first line use in RAS wild-type metastatic or locally advanced and inoperable colorectal cancer. Second line for RAS wild type metastatic colorectal cancer previously treated with 1st line pembrolizumab or 1st line nivolumab which was previously available as an Interim COVID option for MSI-H/dMMR disease. NB: The patient may have received neoadjuvant cytotoxic chemotherapy for potentially resectable metastatic colorectal cancer. NB: The patient will be ineligible for encorafenib plus cetuximab as a subsequent line of therapy if they receive a cetuximab/panitumumab-containing regimen as first-line therapy.
Treatment Intent	Palliative/ Neo-adjuvant treatment for potentially resectable metastatic disease.
Frequency and number of cycles	Repeat every 14 days. **Palliative:** Continue until disease progression, unacceptable toxicity or patient choice. Following a treatment break, please refer to NHSE Treatment Break Policy before restarting treatment. Assess after 12 weeks. **Neo-adjuvant:** If being used neo-adjuvantly for potential resection of metastases, panitumumab is to be discontinued after surgery (adjuvant chemotherapy alone to be used post resection). NB: Patients who have successful resection(s) after neoadjuvant panitumumab containing combination chemotherapy for metastatic disease and who did not progress on such chemotherapy may receive panitumumab with subsequent first-line combination chemotherapy if they present later with progression of metastatic disease.

Monitoring Parameters	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion.
	• **DPD testing** must be undertaken in all patients before starting treatment; the result must be checked before treatment is started.
	• **ECG** prior to cycle 1.
	• **Cardiotoxicity:** caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris.
	• If patient develops chest pain/ coronary artery syndrome: stop drug, emergency medical assessment. Please inform tumour site consultant after.
	• Patients should be assessed at each visit for symptoms of visual disturbance (see below).
	• **Blood parameters:** Monitor **FBC**, **LFTs** and **U&Es** prior to treatment and prior to each cycle thereafter, in particular $Mg2^+$, K^+ and $Ca2^+$ for up to 8 weeks after completion of treatment.
	• Neuts <1.5 and PLT<100 delay one week and inform treating consultant team.
	• **Hepatic Impairment:**
	  ○ **Oxaliplatin:** no dose adjustments recommended.
	  ○ **Panitumumab:** no available guidance clinical decision.
	  ○ **Fluorouracil:** In moderate hepatic impairment consider reducing the dose by 30% and for severe impairment by 50%. If the bilirubin is >85umol/L and / or AST >180 fluorouracil is contra-indicated.
	• **Renal Impairment:**
	  ○ **Panitumumab:** no available guidance clinical decision.

	○ **Oxaliplatin:** No dose reduction needed if CrCl >/=30ml/min. If CrCl <30ml/min d/w consultant. ○ **Fluorouracil:** consider dose reduction in severe renal impairment. • **Management of adverse reactions and dose adjustments:** • If the patient experiences excessive toxicity with oxaliplatin, panitumumab can be subsequently continued in combination with a fluoropyrimidine alone. • **PANITUMUMAB** ○ Panitumumab can cause severe infusion related reactions. If the patient experiences a mild or moderate infusion-related reaction, the infusion rate may be decreased. It is recommended to maintain this lower infusion rate in all subsequent infusions. For severe reactions discontinue treatment. infusion related reactions can occur more than 24 hours post infusion, patients should be made aware of this and report hypersensitivity reactions if they occur. ○ Interstitial lung disease (ILD): Patients should report any new or worsening respiratory symptoms. Panitumumab should be permanently discontinued in patients with confirmed ILD. ○ Patients presenting with signs and symptoms of keratitis should be referred to an ophthalmologist. If a diagnosis of ulcerative keratitis is confirmed, treatment with panitumumab should be interrupted or discontinued, the benefits and risks of continuing treatment should be carefully considered. ○ **Skin reactions:** Skin reactions are very common and treatment interruption or discontinuation may be required, see tables 1 and 2 for guidance. ○ All patients should use an emollient bd whilst on panitumumab preferably urea-containing (5-10%) ○ Advise all patients to take appropriate precautions against prolonged sun exposure. It is recommended that patients experiencing rash/dermatological toxicities wear sunscreen (> SPF 15), hat and limit sun exposure as sunlight can exacerbate any skin reactions that may occur. • **Oxaliplatin and 5-Fluorouracil** ○ Refer to KMCC website for oxaliplatin induced neuropathy guidance https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/guidelines-for-the-management-of-sact-induced-adverse-reactions/ ○ Dose reduction should be considered if any other grade 3 or 4 non-haematological toxicity or repeat appearance of grade 2 (except N&V and alopecia). Delay until resolution of toxicity to </= grade 1. • **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** ○ **Oxaliplatin:** ○ Caution is advised when oxaliplatin treatment is co-administered with other medicinal products known to cause QT interval prolongation. In case of combination with such medicinal products, the QT interval should be closely monitored. ○ Caution is advised when oxaliplatin treatment is administered concomitantly with other medicinal products known to be associated with rhabdomyolysis. ○ **5FU:** ○ 5FU must not be given with concurrent sorivudine or derivatives (e.g. brivudine), see SPC. ○ Monitor PT and INR regularly in patients taking coumarin-derivative anticoagulants. ○ Monitor phenytoin levels with concomitant use. ○ Caution with folinic acid or folic acid – potential for increased toxicity. • **Driving:** Panitumumab may affect vision and/or concentration and oxaliplatin may cause dizziness, fatigue and nausea. Patients should be advised to not drive or operate machinery if they are affected.
References	ARIA regimen COL-037 SPC accessed on line 26.04.2023 BNF accessed online 26.04.2023 V0.4.2 reviewed in NOG 10.02.2026 approved

NB for funding information, refer to CDF and NICE Drugs Funding List

Table 1: Panitumumab induced acneiform rash: Treatment Principles	
At development of **GRADE 1 CTCAE V5: Rash acneiform:** Papules and/or pustules covering <10% BSA, which may or may not be associated with symptoms of pruritus or tenderness; psychosocial impact limiting instrumental ADLs	**Continue panitumumab at current dose** **Commence** Doxycycline 100mg bd OR Minocycline 50mg bd OR Oxytetracycline 500mg bd Ensure emollient use Reinforce precautions against sun exposure Consider antihistamine Consider analgesia **Reassess** After 2 weeks
If reaction worsens or does not improve. Up to **GRADE 2 CTCAE V5: Rash acneiform:** Papules and/or pustules covering 10-30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; papules and/or pustules covering > 30% BSA with or without mild symptoms	**Continue panitumumab at current dose** **Continue** Doxycycline 100mg bd OR Minocycline 50mg bd OR Oxytetracycline 500mg bd **Add** Topical low/ moderate steroid – hydrocortisone 1 to 2.5% Ensure emollient use Reinforce precautions against sun exposure Consider antihistamine Consider analgesia **Reassess** After 2 weeks
If deterioration to GRADE **3 CTCAE V5** (or intolerable GRADE 2): Rash acneiform: Papules and/or pustules covering >30%. BSA with moderate or severe symptom; limiting self-care ADL; associated with local superinfection	**Interrupt** panitumumab until resolution to grade 0-2 Consultant referral required SEE TABLE 2 for dose reductions on reintroduction of panitumumab. **Continue oral antibiotic for 6 weeks:** Doxycycline 100mg bd OR Minocycline 50mg bd OR Oxytetracycline 500mg bd **Consider** Topical low to topical moderate steroid **Add** Systemic corticosteroids (prednisolone 0.5-1mg/kg for 7 days) **Reassess** After 2 weeks If reaction worsens or does not improve for dose interruption or discontinuation Consider dermatology input for consideration of isotretinoin at low doses (20-30mg/day)
	• **GENERAL REMARKS** • All patients should use an emollient bd whilst on panitumumab preferably urea-containing (5-10%) • All patients should avoid excessive sun exposure and use sun protection products UVA/UVB>15 • Oral tetracyclines: treat for a prolonged period to benefit from their anti-inflammatory properties. Advise patients to take appropriate precautions against prolonged sun exposure

Table 2 Panitumumab dose modification following treatment interruption due to Grade 3 acneiform skin rash

Occurrence of skin symptom(s): ≥ grade 3	**Management**
1st occurrence	Withhold 1 or 2 doses Improved (< grade 3): continue at 100% of original dose Not recovered: Discontinue
2nd occurrence	Withhold 1 or 2 doses Improved (< grade 3): continue at 80% of original dose Not recovered: Discontinue
3rd occurrence	Withhold 1 or 2 doses Improved (< grade 3): continue at 60% of original dose Not recovered: Discontinue
4th occurrence	Discontinue

Repeat every 14 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**PANITUMUMAB**	**6mg/kg**	IV	1st dose 60mins 2nd dose onwards Over 30-60mins (if previously tolerated) Doses higher than 1,000 mg should be infused over approximately 90 minutes.	To be given diluted in 0.9% sodium chloride to 100ml via an in-line 0.22-micron filter. The final concentration should not exceed 10mg/ml.
	Flush line with sodium chloride 0.9% IV before and after panitumumab infusion.				
	Dexamethasone	8mg	PO		
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15min	Sodium chloride 0.9% 50ml
	FLUSH WITH 5 % GLUCOSE BEFORE AND AFTER ADMINISTRATION OF OXALIPLATIN				
	OXALIPLATIN	**85mg/m²**	IV	2- 6 hrs	250-500ml 5% glucose (to give a concentration between 0.2 mg/ml and 0.70 mg/ml) Can be run concurrently with Calcium Folinate.
	CALCIUM FOLINATE (flat dose) (calcium leucovorin)	**350mg**	IV	2 hrs	Glucose 5% 250ml Can be run concurrently with oxaliplatin.
	5-FLUOROURACIL	**400mg/m²**	IV	slow bolus	Through a fast running Sodium chloride 0.9% intravenous infusion
	5-FLUOROURACIL	**2400mg/m² over 46 hrs**	IV	**46 hr pump**	Continuous infusion

TTO	Drug	Dose	Route	Directions
Day 1	Dexamethasone	6mg	PO	OM for 3 days
	Metoclopramide	10mg	PO	10mg TDS for 3 days then 10mg up to 3 times a day as required. Do not take for more than 5 days continuously.
	NB If required prescribe doxycycline 100mg OD at onset of rash.			