

<b>Indication</b>	First line treatment for RAS wild type colorectal cancer  NB: or as 2nd line treatment if treated with 1st line pembrolizumab (or 1st line nivolumab; previously available as an Interim COVID option) for MSI-H/dMMR disease.
<b>Treatment Intent</b>	Palliative / neo-adjuvant
<b>Frequency and number of cycles</b>	Repeat every 14 days  Treat to progression, patient choice or toxicity; or 3 to 6 month blocks of treatment, followed by a drug holiday or less intensive regimen (for patients who have responded, or have stable disease). Following a treatment break, please refer to NHSE Treatment Break Policy before restarting treatment. If being used neo-adjuvantly for potential resection of metastases, cetuximab is to be discontinued after surgery (adjuvant chemotherapy alone to be used post resection).  NB: Patients who have successful resection(s) after neoadjuvant cetuximab/panitumumab-containing combination chemotherapy for metastatic disease and who did not progress on such chemotherapy may receive cetuximab/panitumumab with subsequent first-line combination chemotherapy if they present later with progression of metastatic disease.  NB cetuximab is unlicensed for 2-weekly administration.
<b>Monitoring Parameters pre-treatment</b>	<ul style="list-style-type: none"> <li>• <b>Virology screening:</b> 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.</li> <li>• ECG prior to cycle 1.</li> <li>• Monitor FBC, LFTs and U&amp;Es prior to treatment and every 2 weeks thereafter, in particular Mg<sup>2+</sup>, K<sup>+</sup> and Ca<sup>2+</sup>.</li> <li>• Neuts &lt;1.5 and PLT&lt;100 delay one week.</li> <li>• <b>DPD testing</b> must be undertaken in all patients before starting treatment; the result must be checked before treatment is started.</li> <li>• <b>Renal Impairment:</b> <ul style="list-style-type: none"> <li>○ Oxaliplatin: Consider dose adjustment in severe impairment.</li> <li>○ Cetuximab: no data available in patients with impaired function.</li> <li>○ Fluorouracil, consider dose reduction in severe impairment.</li> </ul> </li> <li>• <b>Hepatic Impairment:</b> <ul style="list-style-type: none"> <li>○ Oxaliplatin- no dose adjustments required.</li> <li>○ Cetuximab: No dose reduction required.</li> <li>○ Fluorouracil - In moderate hepatic impairment consider reducing the dose by 30% and for severe impairment by 50%. If the bilirubin is &gt;85umol/L and / or AST &gt;180 fluorouracil is contra-indicated.</li> </ul> </li> <li>• <b>Cardiotoxicity:</b> caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris.</li> <li>• <b>Dose Modification:</b> <ul style="list-style-type: none"> <li>○ For guidance on the assessment and management of oxaliplatin induced neuropathy see KMCC website</li> </ul> </li> </ul>

Protocol No	COL-033	Kent and Medway SACT Protocol Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere.	
Version	V1	Written by	M.Archer
Supersedes version	New protocol	Checked by	C.Waters B.Willis
Date	09.03.2023	Authorising consultant (usually NOG Chair)	M.Durve

	<p><a href="http://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/sact-pathways-guidelines-for-the-management-of-sact-induced-adverse-reactions-and-nursing/">http://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/sact-pathways-guidelines-for-the-management-of-sact-induced-adverse-reactions-and-nursing/</a></p> <ul style="list-style-type: none"> <li>○ Dose reduction should be considered if any other grade 3 or 4 non-haematological toxicity or repeat appearance of grade 2 (except N&amp;V and alopecia). Delay until resolution of toxicity to &lt; grade 1.</li> <li>● <b>Adverse reactions:</b> <ul style="list-style-type: none"> <li>○ <b>Cetuximab infusion rate and infusion related reactions (IRRs):</b> Cetuximab can cause severe infusion related reactions, pre-meds must be given 30-60 minutes prior to the infusion and patients must be monitored every 30 minutes during the infusion and for a 1-hour period after. 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.</li> <li>○ <b>Interstitial lung disease (ILD):</b> Patients should report any new or worsening respiratory symptoms. Cetuximab should be permanently discontinued in patients with confirmed ILD.</li> <li>○ <b>Ocular toxicities:</b> Cetuximab should be used with caution in patients with a history of keratitis ulcerative keratitis or severe dry eye. If a diagnosis of ulcerative keratitis is confirmed, treatment with cetuximab should be interrupted or discontinued. If keratitis is diagnosed, the benefits and risks of continuing treatment should be carefully considered.</li> </ul> </li> <li>● <b>Common drug/food interactions (for comprehensive list refer to BNF/SPC):</b> <ul style="list-style-type: none"> <li>○ 5FU must not be given with concurrent sorivudine or derivatives (e.g. brivudine), see SPC.</li> <li>○ Monitor PT and INR regularly in patients taking coumarin-derivative anticoagulants.</li> <li>○ Monitor phenytoin levels with concomitant use.</li> <li>○ Caution with folic acid or folic acid – potential for increased toxicity.</li> </ul> </li> <li>● <b>Driving:</b> Oxaliplatin may cause dizziness, fatigue and nausea. Patients should be aware this may affect their ability to drive or operate machinery.</li> </ul>
<b>References</b>	North London cancer network Dosage Adjustment for Cytotoxics in Hepatic Impairment ARIA regimen COL-033 KMCC proforma COL-019 V6 and COL-027 V5

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

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**Repeat every 14 days**

Day	Drug	Dose	Route	Infusion Duration	Administration	
1	Chlorphenamine	10mg	IV	stat	To be administered 30-60 minutes prior to cetuximab	
	Dexamethasone	8mg	PO			
	<b>CETUXIMAB</b>	<b>500mg/m<sup>2</sup></b>	IV	1st dose 2hrs 2nd dose onwards – over 90mins (or 60mins if tolerated)	To be given undiluted or diluted in 0.9% sodium chloride to a total volume of 250ml  Flush line with sodium chloride 0.9% IV post cetuximab infusion.	
	<b>Give cytotoxic chemo at least 1 hour after MAb</b>					
	Ondansetron	<75yrs 16mg ≥75yrs 8mg	IV	15min	Sodium chloride 0.9% 50ml	
	<b>FLUSH WITH 5 % GLUCOSE BEFORE AND AFTER ADMINISTRATION OF OXALIPLATIN</b>					
	<b>OXALIPLATIN</b>	<b>85mg/m<sup>2</sup></b>	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 Folate.	
	<b>CALCIUM FOLINATE (flat dose) (calcium leucovorin)</b>	<b>350mg</b>	IV	2 hrs	Glucose 5% 250ml Can be run concurrently with oxaliplatin.	
<b>5-FLUOROURACIL</b>	<b>400mg/m<sup>2</sup></b>	IV	slow bolus	Through a fast running Sodium chloride 0.9% intravenous infusion		
<b>5-FLUOROURACIL</b>	<b>2400mg/m<sup>2</sup> over 46 hrs</b>	<b>IV</b>	46 hr pump	Continuous infusion		
<b>TTO</b>	<b>Drug</b>	<b>Dose</b>	<b>Route</b>	<b>Directions</b>		
	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.		
If required prescribe doxycycline 100mg OD at onset of rash.						

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