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| **Indication** | First line treatment for RAS wild-type metastatic or locally advanced and inoperable colorectal cancer.<br><br>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. |
| **Treatment Intent** | Palliative/ neoadjuvant |
| **Frequency and number of cycles** | Repeat every 14 days.<br><br>Continue until disease progression or unmanageable toxicity or patient choice.<br>Following a treatment break, please refer to NHSE Treatment Break Policy before restarting treatment.<br>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).<br>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.<br><br>Assess every 12 weeks.<br><br>NB cetuximab is unlicensed for 2-weekly administration, therefore Trust policy regarding the use of unlicensed treatments must be followed if using this dosing schedule. |
| **Monitoring Parameters pre-treatment** | • **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.<br>• ECG cycle 1<br>• Monitor FBC, LFTs and U&Es prior to treatment and every 2 weeks thereafter, in particular $Mg^{2+}$, $K^{+}$ and $Ca^{2+}$<br>• Neuts <1.5 and PLT<100 delay one week.<br>• Before starting treatment GFR (C+G) should be >/= 50ml/min<br>• **DPD testing** must be undertaken in all patients before starting treatment; the result must be checked before treatment is started.<br>• **Renal Impairment:**<br>  ○ Capecitabine is contraindicated if CrCl <30ml/min.<br>  ○ Oxaliplatin: Consider dose adjustment in severe renal impairment.<br>  ○ Cetuximab: no data available in patients with impaired function.<br>• **Hepatic Impairment:**<br>  ○ Capecitabine: No dose adjustments in hepatic impairment (insufficient data of capecitabine to make a dose recommendation).<br>  ○ Cetuximab: no dose reduction required.<br>  ○ Oxaliplatin: no dose reduction required.<br>• **Cardiotoxicity:** caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris.<br>• **Dose interruption and reduction**:<br>• Oxaliplatin: For guidance on oxaliplatin induced neuropathy see KMCC document "Guidance on the assessment and Management of Oxaliplatin induced Neuropathy" |

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| | see KMCC website https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/guidelines-for-the-management-of-sact-induced-adverse-reactions/ .<br>• Capecitabine:<br>  ○ Interrupt capecitabine in the event of >/= grade 2 non-haematological toxicity (with the exception of side effects such as alopecia, alteration in taste etc, considered to be not serious) until resolution of toxicity to grade 0-1.<br>  ○ Dose reduction should be considered if 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.<br>• **Adverse reactions:**<br>• **Cetuximab infusion rate and infusion related reactions (IRRs):**<br>• 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.<br>• **Skin reactions:** Capecitabine can induce severe skin reactions such as Stevens-Johnson syndrome and Toxic Epidermal Necrolysis. Patients should be informed of the possibility of such reactions and informed to seek urgent medical advice should any symptoms of a severe skin reaction occur. Treatment should be permanently discontinued in affected patients. For full guidance on cetuximab induced rashes see KMCC document "Guidelines for Cetuximab or Panitumumab Induced Rashes" https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/guidelines-for-the-management-of-sact-induced-adverse-reactions/<br>• **Interstitial lung disease (ILD):** Patients should report any new or worsening respiratory symptoms. Cetuximab should be permanently discontinued in patients with confirmed ILD.<br>• **Ocular toxicities:** 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.<br>• **Common drug/food interactions (for comprehensive list refer to BNF/SPC):**<br>  ○ Capecitabine must not be given with concurrent sorivudine or derivatives (e.g. brivudine), see SPC.<br>  ○ Monitor PT and INR regularly in patients taking coumarin-derivative anticoagulants.<br>  ○ Monitor phenytoin levels with concomitant use.<br>  ○ Caution with folinic acid or folic acid – potential for increased toxicity.<br>  ○ Avoid concomitant allopurinol.<br>• **Driving:** Capecitabine/Oxaliplatin may cause dizziness, fatigue and nausea. Patients should be aware this may affect their ability to drive or operate machinery.<br>• For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet. |
| **References** | COL-032 V3 CDF list V1.322 |

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

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| Protocol No | COL-032 | Kent and Medway SACT Protocol<br>Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere. | |
| Version | V4 | Written by | M.Archer |
| Supersedes version | V3 | Checked by | C.Waters V4<br>B.Willis V1<br>KMCC website link changes only to V2<br>Commissioning change V3 V4 minor change only |
| Date | 17.12.2024 | Authorising consultant (usually NOG Chair) | M.Hill V1 |

**Repeat every 14 days**

| Day | Drug | Dose | Route | Infusion Duration | Administration |
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| 1 | Chlorphenamine | 10mg | IV | stat | To be administered 30-60 minutes prior to cetuximab. |
| | Dexamethasone | 8mg | PO | | |
| | **CETUXIMAB** | **500mg/m²** | IV | 1st dose 2hrs<br>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 or 500ml.<br><br>Flush line with sodium chloride 0.9% IV post cetuximab infusion. |
| | **Give cytotoxic chemo at least 1 hour after MAb** | | | | |
| | Ondansetron | <75yrs 16mg<br>≥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). |

| TTO | Drug | Dose | Route | Directions |
|---|---|---|---|---|
| Day 1 | **CAPECITABINE** | **1600mg/m²/day**<br><br>In 2 divided doses | PO | BD<br>Take the first dose in the evening of **Day 1** and the last dose in the morning of **Day 10**, followed by a 5-day rest period.<br>Take within 30 minutes after food, and approximately every 12 hours.<br>Available as 500mg and 150mg tablets. |
| | Dexamethasone | 6mg | PO | OM for 3 days. |
| | Metoclopramide | 10mg | PO | 10mg three times a day for 3 days then 10mg up to 3 times a day as required.<br>Do not take for more than 5 days continuously. |
| | If required prescribe doxycycline 100mg OD at onset of rash. | | | |