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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 / neo-adjuvant |
| **Frequency and number of cycles** | Repeat every 14 days<br><br>Treat to progression, patient choice or toxicity.<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><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>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 prior to 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>• **DPD testing** must be undertaken in all patients before starting treatment; the result must be checked before treatment is started.<br>• **Renal Impairment:**<br>  o Oxaliplatin: Consider dose adjustment in severe impairment.<br>  o Cetuximab: no data available in patients with impaired function.<br>  o Fluorouracil, consider dose reduction in severe impairment.<br>• **Hepatic Impairment:**<br>  o Oxaliplatin- no dose adjustments required.<br>  o Cetuximab: No dose reduction required.<br>  o 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.<br>• **Cardiotoxicity:** caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris.<br>• **Dose Modification:**<br>  o For guidance on the assessment and management of oxaliplatin induced neuropathy see KMCC website |

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| | http://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/sact-pathways-guidelines-for-the-management-of-sact-induced-adverse-reactions-and-nursing/<br>○ 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.<br>• **Adverse reactions:**<br>○ **Cetuximab infusion rate and infusion related reactions (IRRs):** 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:** Skin reactions are very common with cetuximab and treatment interruption or discontinuation may be required. 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>○ 5FU 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>• **Driving:** Oxaliplatin may cause dizziness, fatigue and nausea. Patients should be aware this may affect their ability to drive or operate machinery. |
| **References** | COL-033 V2 CDF list V1.322 |

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

**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 | | |
| | **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)<br>Can be run concurrently with Calcium Folinate. |
| | **CALCIUM FOLINATE (flat dose) (calcium leucovorin)** | **350mg** | IV | 2 hrs | Glucose 5% 250ml<br>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.<br>Do not take for more than 5 days continuously. | |
| | If required prescribe doxycycline 100mg OD at onset of rash. | | | | |