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| <b>Indication</b>                     | <p>First line treatment for RAS wild type metastatic or locally advanced and inoperable colorectal cancer.</p> <p>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.</p>  |
| <b>Treatment Intent</b>               | Palliative / neo-adjuvant treatment for potentially resectable metastatic disease.  |
| <b>Frequency and number of cycles</b> | <p>Repeat every 14 days</p> <p>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).</p> <p>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.</p> <p>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.</p> <p>Review after 12 weeks.</p>   |
| <b>Monitoring Parameters</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>• <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>ECG</b> prior to cycle 1.</li> <li>• <b>Cardiotoxicity:</b> caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris.</li> <li>• Monitor FBC, LFTs and U&amp;Es prior to treatment.</li> <li>• At each cycle (every 2 weeks) monitor FBC, LFT's &amp; U&amp;Es, in particular Mg<sup>2+</sup>, K<sup>+</sup> and Ca<sup>2+</sup></li> <li>• Neuts <math>\geq 1.5</math> and PLT <math>\geq 100</math> continue with treatment.</li> <li>• Neuts <math>&lt; 1.5</math> and PLT <math>&lt; 100</math> delay one week.</li> <li>• Before starting treatment GFR (C+G) should be <math>\geq 50</math>ml/min</li> <li>• <b>Hepatic impairment:</b> <ul style="list-style-type: none"> <li>○ <b>Cetuximab:</b> no dose adjustment in patients with impaired hepatic function.</li> <li>○ <b>Capecitabine:</b> No dose adjustments in hepatic impairment (insufficient data of capecitabine to make a dose recommendation).</li> <li>○ <b>Irinotecan:</b> Consider dose reduction if bilirubin <math>\geq 26</math>μmol/L. Bilirubin <math>&gt; 51</math>μmol/L clinical decision.</li> </ul> </li> <li>• <b>Renal impairment:</b> <ul style="list-style-type: none"> <li>○ <b>Cetuximab:</b> no dose reduction required in patients with impaired renal function.</li> <li>○ <b>Capecitabine:</b> If CrCl <math>&lt; 30</math>-<math>50</math>ml/min dose reduce capecitabine (see SPC). Contraindicated if CrCl <math>&lt; 30</math>ml/min.</li> </ul> </li> <li>• <b>Management of adverse reactions and dose adjustments:</b></li> </ul> |

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| Version            | V1           | Written by  | M. Archer               |
| Supersedes version | New protocol | Checked by  | C. Waters<br>J. Sanders |
| Date               | 12.05.2026   | Authorising consultant (usually NOG Chair)  | M. Hill                 |

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|                   | <ul style="list-style-type: none"> <li>• Interrupt capecitabine in the event of <math>\geq</math> 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.</li> <li>• Dose reduction should be considered if 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 <math>\leq</math> grade 1</li> <li>• Patients with persistent diarrhoea for <math>\geq</math>24hrs should have a FBC and if neutropenic start a broad spectrum antibiotic in line with Trust antibiotic policy.</li> <li>• <b>Cetuximab:</b> <ul style="list-style-type: none"> <li>○ <b>Cetuximab infusion rate and infusion related reactions (IRRs):</b></li> <li>○ Cetuximab can cause severe infusion related reactions, pre-meds must be given 1 hour before 1st administration and then 30-60mins prior to subsequent administrations 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> <li>○ <b>Skin reactions:</b> Skin reactions are very common and treatment interruption or discontinuation may be required. For full guidance on cetuximab induced rashes see KMCC document "Guidelines for Cetuximab Induced Rashes" <a href="https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/guidelines-for-the-management-of-sact-induced-adverse-reactions/">https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/guidelines-for-the-management-of-sact-induced-adverse-reactions/</a></li> </ul> </li> <li>• <b>Capecitabine:</b> <ul style="list-style-type: none"> <li>○ <b>Skin reactions:</b> 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.</li> </ul> </li> <li>• <b>Common drug interactions (for comprehensive list refer to BNF/SPC):</b> <ul style="list-style-type: none"> <li>○ <b>Irinotecan:</b> St. John's Wort should not be administered with irinotecan.</li> <li>○ Concurrent administration with strong inhibitors (e.g. ketoconazole, itraconazole, clarithromycin) or inducers (e.g. phenytoin, rifampicin, carbamazepine, phenobarbital) of cytochrome P450 3A4 (CYP3A4) may alter the metabolism of irinotecan and should be avoided.</li> <li>○ <b>Capecitabine:</b> <ul style="list-style-type: none"> <li>○ 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> <li>○ Avoid concomitant allopurinol.</li> </ul> </li> </ul> </li> <li>• <b>Driving:</b> Capecitabine may cause dizziness, fatigue and nausea. Patients should be aware this may affect their ability to drive or operate machinery.</li> <li>• For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.</li> </ul> |
| <b>References</b> | SPC accessed online 17.09.2024 ARIA regimen COL-031 CDF List V1.322 accessed online 17.09.2024  |

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

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| Supersedes version | New protocol | Checked by  | C. Waters<br>J. Sanders |
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**Repeat every 14 days**

| Day   | Drug   | Dose   | Route | Infusion Duration   | Administration  |
|-------|--|--|-------|---|---|
| 1     | Dexamethasone  | 8mg  | PO    |   | To be administered 60 minutes prior to cetuximab on cycle 1.  |
|       | Chlorphenamine   | 10mg   | IV    | bolus   | From cycle 2 onwards administer 30-60 minutes prior to cetuximab.   |
|       | <b>CETUXIMAB</b>   | <b>500mg/m<sup>2</sup></b>                                       | IV    | <b>1st dose (week 1 only) 2hrs</b><br><b>2nd dose onwards – max rate of 10mg/min</b>  | To be given undiluted or diluted in 0.9% sodium chloride to a total volume of 250ml or 500ml.<br><br>If outsourcing, give in 500ml 0.9% sodium chloride non-PVC infusion.<br><br>Flush line with sodium chloride 0.9% IV post cetuximab infusion. |
|       | Cytotoxic chemotherapy to be administered 1 hour after the end of the cetuximab infusion |  |       |   |   |
|       | Ondansetron  | <75yrs 16mg<br>>=75yrs 8mg                                       | IV    | 15min   | In sodium chloride 0.9% 50ml  |
|       | Atropine   | 0.25mg   | SC    | bolus   | If required for acute cholinergic syndrome.   |
|       | <b>IRINOTECAN</b>  | <b>180mg/m<sup>2</sup></b>                                       | IV    | 30min   | In 250ml NaCl 0.9% or glucose 5% with a final volume of 180ml-240ml (pre-made bag)  |
| TTO   | Drug   | Dose   | Route | Directions  |   |
| Day 1 | <b>CAPECITABINE</b>  | <b>1600mg/m<sup>2</sup>/day</b><br><br><b>In 2 divided doses</b> | PO    | <b>For 9 days</b> (1st dose will be taken as the evening dose on day 1 and the last dose is taken the morning of day 10, followed by a 5 day rest period).<br>Take within 30 mins after food and approximately every 12 hours.<br><br>Available as 150mg and 500mg tablets. |   |
|       | 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.  |   |
|       | Loperamide   | 2mg  | PO    | Take TWO capsules (4mg) after first loose stool, then ONE capsule every 2 hrs for at least 12 hrs or until 12 hrs after last loose stool (for max. of 48hrs)  |   |
|       | Dioralyte  | 1 sachet   | PO    | Take the contents of ONE sachet dissolved in 200mls of water after each loose stool.  |   |
|       | If required prescribe <b>doxycycline 100mg OD</b> at onset of rash.                      |  |       |   |   |

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