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| <b>Indication</b>                          | For the treatment of metastatic castration resistant prostate cancer previously treated with a docetaxel-containing regimen.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Treatment Intent</b>                    | Palliative                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <b>Frequency and number of cycles</b>      | Repeat every 21 days<br><br>Continue until disease progression, unacceptable toxicity or to a maximum of 10 cycles whichever occurs first.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <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>• <b>Trusts must ensure that the patient has received 225mg/m<sup>2</sup> of docetaxel before starting cabazitaxel.</b></li> <li>• Monitor U&amp;Es and LFT's at each cycle.</li> <li>• Monitor FBC weekly during cycle 1 and then at each cycle thereafter.</li> <li>• If neuts <math>\geq 1.5</math> and PLT <math>\geq 100</math> continue with treatment. If neuts <math>&lt; 1.5</math> or Plts <math>&lt; 100</math> delay until neuts <math>\geq 1.5</math> and reduce dose, see dose modification section below.</li> <li>• Consider GCSF prophylaxis in at risk patients.</li> <li>• <b>Hepatic impairment:</b> In mild hepatic impairment (total bilirubin <math>&gt; 1</math> to <math>\leq 1.5 \times \text{ULN}</math> or AST <math>&gt; 1.5 \times \text{ULN}</math>), dose reduce cabazitaxel to 20 mg/m<sup>2</sup>. Treatment of patients with mild hepatic impairment should be undertaken with caution and close monitoring of safety.<br/>In moderate hepatic impairment (total bilirubin <math>&gt; 1.5</math> to <math>\leq 3.0 \times \text{ULN}</math>), the dose should not exceed 15 mg/m<sup>2</sup>.<br/>Cabazitaxel should not be given to patients with severe hepatic impairment (total bilirubin <math>&gt; 3 \times \text{ULN}</math>).</li> <li>• <b>Renal impairment:</b> No dosing information available for patients with CrCl <math>&lt; 50</math> ml/min – treat with caution and monitor carefully. No dose adjustment is necessary in patients with renal impairment, not requiring haemodialysis.</li> <li>• <b>Dose Modification:</b> Dose reduction should be considered for prolonged grade <math>\geq 3</math> neutropenia (longer than 1 week) despite appropriate treatment including G-CSF, or for febrile neutropenia. Delay until neutrophils <math>&gt; 1.5</math> and reduce dose to 20mg/m<sup>2</sup></li> <li>• Dose reduction should be considered if grade 3 or 4 diarrhoea or if grade <math>\geq 2</math> peripheral neuropathy. Delay until resolution or improvement of toxicity to <math>\leq</math> grade 1 and reduce dose to 20mg/m<sup>2</sup>.</li> <li>• If problems persist despite dosing at 20mg/m<sup>2</sup> further dose reduction to 15mg/m<sup>2</sup> or discontinuation of cabazitaxel should be considered. Data in patients treated below 20mg/m<sup>2</sup> is limited.</li> <li>• <b>Management of adverse reactions:</b></li> <li>• <b>Peripheral neuropathy:</b> Cases of peripheral neuropathy, peripheral sensory neuropathy (e.g., paraesthesias, dysaesthesias) and peripheral motor neuropathy have been observed in patients receiving cabazitaxel. Patients should be assessed for neuropathy before each dose, patients should be advised to report any symptoms of neuropathy such as pain, burning, tingling, numbness, or weakness. Dose interruption or reduction may be required if peripheral neuropathy occurs (see dose modification above).</li> <li>• <b>Pulmonary toxicity:</b> Interstitial lung disease (ILD), pneumonitis, and pneumonia syndrome have been reported in patients treated with cabazitaxel. Patients should report any new or worsening respiratory symptoms and evaluation performed. Consider withholding treatment during evaluation and resume if clinically appropriate on recovery.</li> </ul> |

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| Protocol No        | URO-019     | Kent and Medway SACT Protocol<br>Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere. |                         |
| Version            | V8          | Written by                                                                                                                                | M. Archer               |
| Supersedes version | V7 proforma | Checked by                                                                                                                                | C. Waters<br>M. Capomir |
| Date               | 03.11.2025  | Authorising consultant (usually NOG Chair)                                                                                                | C. Thomas               |

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|                   | <ul style="list-style-type: none"> <li>• <b>Common drug interactions (for comprehensive list refer to BNF/SPC):</b></li> <li>• Avoid concomitant administration with drugs that are either strong inducers (e.g. phenytoin, carbamazepine) or inhibitors (e.g. ketoconazole, itraconazole, clarithromycin) of CYP3A4, if patients require co-administration of a strong CYP3A inhibitor, a 25% cabazitaxel dose reduction should be considered.</li> <li>• If co-administration with OATP1B1 substrates (e.g. statins, valsartan, repaglinide) is required a time interval of 12 hours is recommended before the infusion or 3 hours after the end of the infusion before administering OATP1B1 substrates.</li> <li>• Patients should avoid St Johns Wort.</li> <li>• <b>Contraception measures:</b> Men should use contraceptive measures during treatment and for 4 months after cessation of treatment with cabazitaxel.</li> <li>• <b>Driving and Machinery:</b> Cabazitaxel may cause fatigue and dizziness, patients should be advised not to drive or use machines if they experience these adverse reactions.</li> <li>• <b>Ensure that famotidine pre-medication is prescribed and given to the patient at new patient chat.</b></li> </ul> |
| <b>References</b> | KMCC proforma URO-019 V7 SPC accessed online 14.07.2025 (genus pharmaceuticals) ARIA regimen URO-019                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |

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

**Repeat every 21 days**

| Day   | Drug                | Dose                      | Route | Infusion Duration                                                                                                                                        | Administration                                                                                                                                                               |
|-------|---------------------|---------------------------|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1     | Famotidine          | 40mg                      | PO    | stat                                                                                                                                                     | Ensure patient has taken TTO famotidine 4 hours before cabazitaxel.                                                                                                          |
|       | Chlorpheniramine    | 10mg                      | IV    | Slow bolus                                                                                                                                               | Please ensure that the pre-medication is given at least 30 minutes prior to administration of chemotherapy.                                                                  |
|       | Dexamethasone       | 8mg                       | IV    | bolus                                                                                                                                                    |                                                                                                                                                                              |
|       | Metoclopramide      | 20mg                      | IV    | bolus                                                                                                                                                    |                                                                                                                                                                              |
|       | <b>CABAZITAXEL</b>  | <b>25mg/m<sup>2</sup></b> | IV    | 1 hour                                                                                                                                                   | Usually in 250ml Sodium Chloride 0.9% (non-PVC bag and infusion set) via in-line 0.22-micron filter<br>Concentration of the infusion should be between 0.1mg/ml – 0.26mg/ml. |
| TTO   | Drug                | Dose                      | Route | Directions                                                                                                                                               |                                                                                                                                                                              |
| Day 1 | <b>PREDNISOLONE</b> | <b>5mg</b>                | PO    | BD continuously<br>Dispense 3 weeks supply.<br><br>When cabazitaxel is discontinued, the patient should commence a reducing dose of prednisolone.        |                                                                                                                                                                              |
|       | Metoclopramide      | 10mg                      | PO    | 10mg TDS for 3 days then 10mg up to TDS PRN<br><br>max. 30mg per day including 20mg pre-chemo dose<br><br>Do not take for more than 5 days continuously. |                                                                                                                                                                              |
|       | Famotidine          | 40mg                      | PO    | To be taken 4 hours prior to next cabazitaxel Treatment.                                                                                                 |                                                                                                                                                                              |

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