**Systemic Anti-Cancer Treatment Protocol**

# CABAZITAXEL
## Prostate Cancer

**PROCTOCOL REF: MPHACABAZ**
**(Version No: 1.0)**

## Approved for use in:

Cabazitaxel in combination with prednisolone is a treatment option for treating metastatic hormone-relapsed prostate cancer where disease has progressed during or after docetaxel chemotherapy, if:

- PS 0 or 1
- At least 225mg/m$^2$ docetaxel has been administered

## Dosage:

| Drug | Dosage | Route | Frequency |
|---|---|---|---|
| Cabazitaxel | 25mg/m$^2$ | IV infusion | 21 days |
| Prednisolone | 10mg | Oral | Once daily throughout treatment |

Treatment is repeated every 21 days for 10 cycles maximum.

**Supportive treatments:**

Domperidone 10mg three times daily as required

## Extravasation risk:

**Cabazitaxel:** Not known, but has potential to be a vesicant. In the absence of data, manage as for paclitaxel and docetaxel.

## Patient counselling points

There is a small amount of ethanol in the solvent used to prepare the infusion. Prednisolone tablets should be taken every morning, after breakfast, and not stopped abruptly. It is important that the patient tells other healthcare professionals they are taking steroids. The patient should be advised to report any significant change in daily urinary volume immediately.

## Administration:

| Day | Drug | Dose | Route | Diluent and rate |
|---|---|---|---|---|
| 1 | **Chlorphenamine Maleate** 30imns before chemotherapy | 10mg | IV | Bolus |
| | **Dexamethasone** 30imns before chemotherapy | 8mg | oral | Oral |
| | **Ranitidine hydrochloride** 30imns before chemotherapy | 50mg | IV | Bolus over 2 minutes |
| | **Cabazitaxel** | **25mg/m$^2$** | IV | Sodium chloride 0.9% 250mL over 60 minutes, using a 0.2 micron in line filter |
| | **Prednisolone** | 10mg | Oral | Once daily (continuous throughout treatment) |

## Drug Interactions

| Interactions with other medicinal products |
|---|
| Cabazitaxel is predominately metabolised through CYP3A (80% to 90%)<br><br>CYP3A inhibitors: Concomitant administration of strong CYP3A inhibitors (e.g. ketoconazole, itraconazole, clarithromycin, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, voriconazole) should be avoided as an increase of plasma concentrations of cabazitaxel may occur |
| CYP3A inducers: Concomitant administration of strong CYP3A inducers (e.g. phenytoin, carbamazepine, rifampin, rifabutin, rifapentin, phenobarbital) should be avoided as a decrease of plasma concentrations of cabazitaxel may occur. In addition, patients should also avoid taking St. John's Wort. |
| OATP1B1: The risk of interaction with OATP1B1 substrates (e.g. statins, valsartan, repaglinide) is possible, notably during the infusion duration (1 hour) and up to 20 minutes after the end of the infusion. A time interval of 12 hours is recommended before the infusion and at least 3 hours after the end of infusion before administering the OATP1B1 substrates. |

## Main Toxicities:

| | |
|---|---|
| **Heamatological** | Neutropenia, anaemia, leukopenia, thrombocytopenia |
| **Hypersensitivity** | All patients should be pre-medicated prior to the initiation of the infusion of cabazitaxel. Patients should be observed closely for hypersensitivity reactions especially during the first and second infusions. |
| **Hepatotoxicity** | Increased AST, ALT, and bilirubin |
| **Renal toxicity** | Acute renal failure associated with dehydration, dysuria, haematuria, hydronephrosis, urinary retention, urinary incontinence.<br><br>Cabazitaxel treatment should be discontinued in case of renal failure ≥CTCAE 4.0 Grade 3. |
| **Nervous system** | Neuropathy (pain, burning, tingling, numbness, or weakness). |
| **Gastrointestinal disorders** | Diarrhoea and dehydration, nausea, vomiting, D dyspepsia, mucosal inflammation, hyperglycaemia.<br><br><u>Serious gastrointestinal (GI) reactions</u><br>GI hemorrhage and perforation, ileus, colitis, including fatal outcome, have been reported.<br>Caution is advised with treatment of patients most at risk of developing gastrointestinal complications: those with neutropenia, the elderly, concomitant use of NSAIDs, anti-platelet therapy or anti-coagulants, and patients with a prior history of pelvic radiotherapy or gastrointestinal disease, such as ulceration and GI bleeding. |
| **Cardiovascular** | Cardiac arrhythmias, most commonly tachycardia and atrial fibrillation |
| **General disorders and administration site conditions** | Fatigue, arthralgia, muscle spasms, myalgia |
| | **Dermatological**<br>Alopecia, dry skin, erythema |
| | **Ear and labyrinth disorders**<br>Conjunctivitis, Tinnitus, Vertigo |

## Investigations and Treatment Plan:

| | Pre | C1 | C2 | C3 | C4 | C5 | Ongoing |
|---|---|---|---|---|---|---|---|
| Medical Assessment | X | X | X | X | | | Every 12 weeks |
| Nursing Assessment | | X | X | X | X | X | Every cycle |
| FBC | X | | X | X | X | X | Every cycle |
| U&E & LFTs | X | | X | X | X | X | Every Cycle |
| PSA | X | X | X | X | X | X | Every 4 weeks |
| CT scan | X | | | | X | | Every 12 weeks |
| Informed Consent | X | | | | | | |
| Blood pressure measurement | X | X | X | X | X | X | Every cycle |
| PS recorded | X | X | X | X | X | X | Every cycle |
| Toxicities documented | X | X | X | X | X | X | Every cycle |
| Weight recorded | X | X | X | X | X | X | Every cycle |

## Dose Modifications and Toxicity Management:

### Haematological Toxicity:

Proceed on day 1 if-

| | |
|---|---|
| ANC ≥ 1.0 x $10^9$/L | Plt ≥ 100 x $10^9$/L |

Delay 1 week if -

| | |
|---|---|
| ANC ≤ 0.9 x $10^9$/L | Plt ≤ 99 x $10^9$/L |

| Cabazitaxel Toxicity | Recommended dose modification |
|---|---|
| Prolonged grade ≥3 neutropenia (longer than 1 week) despite appropriate treatment | Delay treatment until neutrophil count is >1.5 x $10^9$/L, and reduce dose to 20 mg/$m^2$ |
| Febrile neutropenia or neutropenic infection | Delay treatment until improvement or resolution, and until neutrophil count is >1.5 x $10^9$/L, and reduce dose to 20 mg/$m^2$ |
| Grade ≥3 diarrhoea or persisting diarrhoea despite appropriate treatment, including fluid and electrolytes replacement | Delay treatment until improvement or resolution, and reduce dose to 20 mg/$m^2$. |
| Grade ≥2 peripheral neuropathy | Delay treatment until improvement, and reduce dose to 20 mg/$m^2$ |
| The treatment should be discontinued if a patient continues to experience any of these reactions at 20 mg/$m^2$ | |

## Hepatic impairment

Cabazitaxel is extensively metabolised by the liver prior to excretion via the faeces as numerous metabolites (76% of the dose);

No formal studies have been carried out in patients with hepatic impairment. As a precautionary measure, cabazitaxel should not be given to patients with hepatic impairment (bilirubin ≥1 x Upper Limit of Normal (ULN), or AST and/or ALT ≥1.5 x ULN)

## Renal impairment

Minimally excreted via the kidney (2.3% of the dose). No formal pharmacokinetic studies were conducted with cabazitaxel in patients with renal impairment. However, mild to moderate renal impairment does not have significant effects on the pharmacokinetics of cabazitaxel. For patients with calculated renal function below 30ml/min treatment decisions should be reviewed by a consultant oncologist

## References:

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Carbazitaxel, Jevtana 40mg/ml. Summary of Product Characteristics, Sanofi. Surrey 17/03/2011 Available from www.medicines.org.uk/emc/medicine. Last Updated 10/07/2015

Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH (Version 3 - updated January 2009)

Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009 UCLH (Version 3 - updated January 2009)