Cabazitaxel and Prednisolone

Indication

Treatment of metastatic castration resistant prostate cancer (mCRPC) in patients who have had disease progression during or after docetaxel chemotherapy. Patients must have received 225mg/m2 or more of docetaxel prior to commencing cabazitaxel.

(NICE TA391)

ICD-10 codes

Codes with a prefix C61

Regimen details

Day	Drug	Dose	Route
1	Cabazitaxel	25mg/m^2*	IV infusion
1-21*	Prednisolone	10mg OD or 5mg BD	PO

*For some patients a reduced starting dose of 20mg/m^2 may be appropriate – consultant decision.
** Prednisolone is taken continuously during treatment

Cycle frequency

21 days

Number of cycles

Up to 10 cycles (maximum) or until disease progression or severe toxicity (whichever happens first).

Administration

Cabazitaxel is administered as an IV infusion in 250mL Sodium Chloride 0.9% over 60 minutes (PVC free).

Patients should be observed closely for hypersensitivity reactions, especially during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of cabazitaxel, thus facilities and equipment for the treatment of hypotension and bronchospasm should be available.

If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve re-started at a slower infusion rate. Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of cabazitaxel and appropriate therapy.

Pre-medication

30 minutes prior to each cabazitaxel infusion:

Ranitidine 50mg IV slow bolus
Chlorphenamine 10mg IV slow bolus
Dexamethasone 8mg IV slow bolus

Emetogenicity

This regimen has mild - moderate emetic potential.

Additional supportive medication

Antiemetics as per local policy
GCSF prophylaxis as per local policy
Antibiotics if required for secondary prophylaxis
Loperamide if required.

Extravasation

Cabazitaxel is an exfoliant (Group 4)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
PSA	14 days

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days
PSA	As required

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥ 1.5 x 10^9/L
Platelets	≥ 100 x 10^9/L
Creatinine Clearance (CrCl)	≥ 50mL/min
Bilirubin	< ULN
AST/ALT	< 1.5 x ULN

Dose modifications

- **Haematological toxicity**

If neutrophils <1.5 x 10^9/L and/or platelets <100 x 10^9/L delay 1 week or until recovery. Reduce dose to 20mg/m^2. Following symptomatic neutropenia or grade IV thrombocytopenia reduce dose to 20mg/m^2.

- **Renal impairment**

Cabazitaxel is minimally excreted through the kidney. No dose adjustment is necessary in patients with renal impairment not requiring haemodialysis. Treat with caution if CrCl <15mL/min.

Cabazitaxel should be discontinued if the patient experiences ≥ grade 3 renal toxicity.

- **Hepatic impairment**

Cabazitaxel is extensively metabolised by the liver. No formal studies have been carried out in patients with hepatic impairment. If bilirubin 1-1.5 x ULN and/or AST/ALT > 1.5 x ULN reduce dose to 20mg/m^2. If moderate hepatic impairment (bilirubin 1.5-3 x ULN) the maximum dose should not exceed 15mg/m^2 although efficacy data is limited at this dose.

Cabazitaxel is contraindicated in severe hepatic impairment (bilirubin > 3 x ULN).

- **Other toxicities**

Toxicity	Definition	Dose modification
Diarrhoea	≥ grade 3	Delay treatment until resolution and reduce dose to 20mg/m^2 If delayed for more than 2 weeks: discontinue
Peripheral neuropathy	≥ grade 2	Delay treatment until <grade 2 and reduce dose to 20mg/m^2 If delayed for more than 2 weeks: discontinue

Treatment should be discontinued if patient continues to experience any adverse effects at the reduced dose of 20mg/m^2.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Infusion related reactions
Anaphylaxis
Cardiac toxicity including arrhythmias
Secondary malignancy
Infertility
GI perforation

- **Frequently occurring side effects**

Diarrhoea
Constipation
Anorexia
Dysgeusia
Fatigue
Nausea and vomiting
Myelosuppression
Stomatitis and mucositis
Peripheral neuropathy
Arthralgia and myalgia

- **Other side effects**

Alopecia
Deranged liver function
Haematuria

Significant drug interactions – for full details consult product literature/ reference texts

CYP3A inhibitors: (e.g. ketoconazole, ritonavir, voriconazole, clarithromycin and erythromycin). Avoid: may increase plasma cabazitaxel levels.

CYP3A inducers: (e.g. rifampicin, phenytoin, carbamazepine and barbiturates). Avoid: may reduce cabazitaxel levels.

St Johns Wort: patients should not take St Johns Wort.

Vaccinations: live attenuated vaccinations are contraindicated during treatment.

OATP1B1 substrates: (e.g. statins, valsartan) cabazitaxel inhibits OATP1B1: substrates should not be taken 12 hours before or 3 hours after the cabazitaxel infusion.

Additional comments

Alcohol: The solvent contains 573.3mg ethanol 96% (15% v/v) equivalent to 14mL beer or 6mL wine: caution in alcoholism.

Contraception: Men should be advised to use effective barrier contraception throughout treatment and for 6 months after last dose.

References

- National Institute for Health and Clinical Excellence. NICE Technology Appraisal Guidance 391 accessed 21 December 2016 via www.nice.org.uk
- Summary of Product Characteristics Cabazitaxel (Jevtana) accessed 5 January 2017 via www.medicines.org.uk
- De Bono JS et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial *Lancet* 2010; 376: 1147-54.

Written/reviewed by: Dr A Bahl (Consultant Oncologist, UHBristol NHS Trust), Dr M Beresford (Consultant Oncologist, Royal United Hospital, Bath).

Checked by: Sarah Murdoch (Senior Oncology Pharmacist, SW Clinical Network)

Authorised by: Dr J Braybrooke (Consultant Oncologist, UHBristol NHS Trust, SW Clinical Network)

Date: January 2017