Docetaxel and Prednisolone (prostate)

Indication

First line chemotherapy for hormone refractory metastatic prostate cancer.

(NICE TA101)

Hormone naïve metastatic prostate cancer in men who are commencing (or who have started within 12 weeks), long term androgen deprivation therapy (ADT) for the first time and who have sufficient performance status to receive 6 cycles of docetaxel chemotherapy. Note: this is an unlicensed indication.

(Funding via NHS England commissioning)

ICD-10 codes

Codes with a prefix C61

Regimen details

Day	Drug	Dose	Route
1	Docetaxel	75mg/m^2	IV infusion
1-21	Prednisolone	5mg BD	PO

Cycle frequency

21 days

Number of cycles

Hormone refractory metastatic prostate cancer: up to 10 cycles or until disease progression or severe toxicity.
Hormone naïve metastatic prostate cancer: maximum of 6 cycles.

Administration

Docetaxel is administered as an IV infusion in 250mL or 500mL (concentration dependent) PVC free Sodium Chloride 0.9% over 60 minutes.

Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions.

Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of docetaxel and therefore facilities for the treatment of hypotension and bronchospasm must 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 docetaxel and appropriate therapy.

Patients who have developed severe hypersensitivity reactions should not be re-challenged with docetaxel.

Pre-medication

Dexamethasone 8 mg BD (morning and lunchtime) for 3 days starting 24h prior to chemotherapy. Or dexamethasone 8mg 12 hours, 3 hours and 1 hour before docetaxel infusion. (Note: Patients must receive 3 doses of dexamethasone prior to treatment).

In the case where 3 doses have not been taken, dexamethasone 16-20mg IV should be administered 30-60 minutes prior to chemotherapy and the remaining 3 oral doses should be taken as normal.

Emetogenicity

This regimen has mild - moderate emetic potential

Additional supportive medication

Mouthwashes as per local policy

H_2 antagonist or proton-pump inhibitor if required

Loperamide if required.

Extravasation

Docetaxel 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
Calcium	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	Every 2 cycles or as clinically indicated

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
Bilirubin	≤ ULN
AST/ALT	≤ 1.5 x ULN
Alkaline Phosphatase*	< 2.5 x ULN

* unless due to bone metastases only

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.

If delayed on 2 occasions reduce dose to 60mg/m^2. It may be appropriate, for hormone refractory prostate cancer patients, to consider further dose reductions to 45mg/m^2, however in hormone naïve patients if toxicity occurs at a 60mg/m^2 dose, docetaxel should be discontinued.

If delayed for more than 2 weeks discuss with consultant and consider stopping treatment.

Following symptomatic neutropenia or grade IV thrombocytopenia reduce dose to 60mg/m^2.

- **Renal impairment**

There is no data available on the use of docetaxel in severe renal impairment. No modifications required.

- **Hepatic impairment**

AST/ALT (x ULN)		**Alkaline phosphatase*** (x ULN)	**Docetaxel dose**
≤ 1.5	and	< 2.5	100%
> 1.5	or	≥ 2.5- 6	75%
> 3.5	or	≥ -6	Discuss with consultant

*unless due to bone metastases only.
If bilirubin > 1.0 x ULN withhold dose (or consultant decision to treat)

- **Other toxicities**

Grade 3 cutaneous reactions – once recovered reduce dose to 60mg/m^2. If symptoms return, discontinue treatment.

Grade 2 neuropathy - once recovered reduce dose to 60mg/m^2. If symptoms return, discontinue treatment.

Grade 3 or 4 neuropathy – discontinue treatment permanently.

Any other grade 3 or 4 toxicity- discuss with consultant.

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

- **Serious side effects**

Secondary malignancy
Myelosuppression
Infusion related reactions
Anaphylaxis
Interstitial pneumonitis
Teratogenicity
Infertility
Cardiotoxicity

- **Frequently occurring side effects**

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

- **Other side effects**

Alopecia
Fluid retention
Deranged liver function
Phlebitis
Skin toxicity
Nail changes

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

CYP3A4 Enzyme inducers/inhibitors: in vitro studies suggest that CYP3A inhibitors (such as ketoconazole, ritonavir, clarithromycin and erythromycin) may raise docetaxel levels, whereas CYP3A inducers (such as rifampicin and barbiturates) may reduce docetaxel levels.

Additional comments

Nil

References

- National Institute for Health and Clinical Excellence. NICE Technology Appraisal Guidance 101 accessed 2 Apr 2014 via www.nice.org.uk
- Tannock et al. Docetaxel plus prednisolone or mitoxantrone plus prednisolone for advanced prostate cancer. NEJM2004:351(15):1502-1512
- Aus G, et al. EAU Guidelines on Prostate Cancer. European Urology. 2005; 546-551
- Summary of Product Characteristics Docetaxel (Sanofi Aventis) accessed 2 Apr 2014 via www.medicines.org.ukNHS England commissioning policy statement Jan 2016 accessed 27 Jan 2016 via https://www.england.nhs.uk/wp-content/uploads/2016/01/b15psa-docetaxel-policy-statement.pdf

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