Systemic Anti Cancer Treatment Protocol

Docetaxel Weekly
Prostate Cancer

PROCTOCOL REF: MPHADOCWE
(Version No: 1.1)

Approved for use in:

For the treatment of patients with, hormone resistant metastatic prostate cancer that have a WHO performance status 0-2.

*Option for patients unable to tolerate 3 weekly regimen

Dosage:

Drug	Dose	Route	Frequency
Dexamethasone 30 minutes before chemotherapy	8mg	IV	Bolus injection
Docetaxel	**30mg/m^2**	IV	Weekly for 5 weeks followed by a week break
Prednisolone	10mg once daily	Oral	Once daily in the morning (continuous throughout treatment)

Repeat at 7 day intervals for 5 weeks followed by a week break up to 5 cycles (one cycle = six weeks)

Supportive Treatments:

Domperidone 10mg three times a day

Steroid Aftercare

Abrupt withdrawal after a prolonged period can lead to acute adrenal insufficiency, hypotension or death. Withdrawal can also be associated with fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and weight loss.

The magnitude and speed of dose reduction in corticosteroid withdrawal should be determined on a case-by–case basis, taking into consideration the underlying condition that is being treated, and individual patient factors such as the likelihood of relapse and the duration of corticosteroid treatment. *Gradual* withdrawal of systemic corticosteroids should be considered in those whose disease is unlikely to relapse.

Once the patient has completed their chemotherapy regime the steroid dose should be tapered as follows:

1. Stop pre-docetaxel dexamethasone tablets.
2. Taper prednisolone to 10mg daily for seven days then reduce to 5mg daily for seven days then stop.*

*This can be customised to suit each patient on an individual basis.

Extravasation risk:

Docetaxel: Non-vesicant

Administration:

Day	Drug	Dose	Route	Diluent and rate
1, 8, 15, 22 and 29	**Dexamethasone** 30 minutes before chemotherapy	**8mg**	**IV**	Bolus injection
	Docetaxel	**30mg/m^2**	**IV**	Sodium Chloride 0.9% 250mL over 1 hour
	Prednisolone	**10mg once daily in the morning**	**PO**	Continuous throughout treatment

Interactions with other medicinal products

Concomitant use of medicines which induce, inhibit or are metabolised by cytochrome P450-3A such as ciclosporin, ketoconazole, erythromycin, may affect levels of docetaxel refer to summary of product of characteristics for more detailed information.

In case of a combination with CYP3A4 inhibitors, the occurrence of docetaxel adverse reactions may increase, as a result of reduced metabolism. Therefore, close clinical surveillance is warranted and a dose-adjustment of docetaxel may be suitable during the treatment with the strong CYP3A4 inhibitor

Main Toxicities:

Docetaxel	
Haematological	Myelosuppression - Neutropenia is the most frequent adverse reaction of docetaxel. Neutrophil nadirs usually occur at a median of 7 days but this interval may be shorter in heavily pre-treated patients.

Gastrointestinal	Stomatitis, abdominal pain, diarrhoea - may be early manifestations of serious gastrointestinal toxicity and should be evaluated and treated promptly.
Cardiovascular	Congestive heart failure (CHF) Fluid retention - Patients with severe fluid retention such as pleural effusion, pericardial effusion and ascites should be monitored closely
Neuropathies	Peripheral neurotoxicity
Hypersensitivity	Patients should be observed closely for hypersensitivity reactions especially during the first and second infusions. Hypersensitivity reactions may occur within a few minutes. Minor symptoms such as flushing or localised cutaneous reactions do not require interruption of therapy. Severe reactions, such as severe 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.
Ocular	Cystoid macular oedema (CMO). patients with impaired vision should undergo a prompt and complete ophthalmologic examination.
Respiratory disorders	Epistaxis, dyspnoea, cough Acute respiratory distress syndrome, interstitial pneumonia/pneumonitis, interstitial lung disease, pulmonary fibrosis and respiratory failure have been reported and may be associated with fatal outcome. If new or worsening pulmonary symptoms develop, patients should be closely monitored, promptly

	investigated, and appropriately treated.
Additional side effects	Cutaneous reactions - Localised skin erythema of the extremities (palms of the hands and soles of the feet) with oedema followed by desquamation has been observed. Nail changes, fluid retention, alopecia, steroid side effects Infertility - contraceptive measures must be taken by both men and women during treatment and for men at least 6 months after cessation of therapy

Investigations:

	Pre	C1	C1	C1 D	C1	C1 D	C1 D	C2D1	Ongoing
Week		1	2	3	4	5	6	7	→
Medical Assessment	X	X					TREATMENT BREAK	X	Every 6 weeks
Nursing Assessment		X	X	X	X	X		X	Every treatment
SACT assessment		X	X	X	X	X		X	Every treatment
FBC	X	X	X	X	X	X		X	Every treatment
U&E & LFTs	X			X				X	Every 3 weeks
PSA	X	X						X	Every 6 weeks
CT scan	X								Every 12 weeks
Informed Consent	X								
PS recorded	X	X	X	X	X	X		X	Every treatment
Toxicities documented	X	X	X	X	X	X		X	Every treatment
Weight recorded	X	X	X	X	X	X		X	Every treatment

Dose Modifications and Toxicity Management:

A dose reduction to 70-80% of the full dose is required for patients with a WHO performance status of 2.

Consider dose reduction to 25mg/m^2 for any grade 2 reaction that has required a treatment delay

Docetaxel	**Recommended dose reduction for toxicity management**
First dose reduction of 80%	**25mg/m^2**

Haematological Toxicity:

Proceed on each treatment day if-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 100 x 10^9/L

Omit treatment for 1 week and refer to advice below-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 99 x 10^9/L

- In the event of febrile neutropenia or neutrophils < 0.5 x 10^9/L for more than 1 week, give docetaxel 25mg/m^2 for all further cycles.
- If platelets < 50 x 10^9/L, consider dose reduction to 25mg/m^2 after recovery - discuss with Consultant first.
- If the patient continues to experience these side effects at the lower dose, review treatment plan

Hepatic impairment:

Docetaxel
For those patients with serum bilirubin > ULN and/or ALT and AST > 3.5 times the ULN associated with alkaline phosphatase > 6 times the ULN, no dose-reduction can be recommended and docetaxel should not be used unless strictly indicated.

Renal impairment:

Docetaxel
Excretion is predominately via hepatic metabolism. Renal impairment is unlikely to affect elimination. No dose reduction required.

References:

Docetaxel Accord 160 mg/8 ml concentrate for solution for infusion, summary of Product Characteristics, Accord Healthcare limited, Middlesex. 22/05/2012. Available from www.medicines.org.uk/emc/medicine. Last updated 10/10/2014.

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