Chemotherapy Protocol

PROSTATE

MITOXANTRONE-PREDNISOLONE

Regimen

- Prostate-Mitoxantrone-Prednisolone

Indication

- Castrate resistant prostate cancer
- Performance status 0, 1, 2
- Palliative

Toxicity

Drug	Adverse Effect
Mitoxantrone	Cardiac toxicity, urinary discolouration
Prednisolone	Weight gain, GI disturbances, hyperglycaemia, CNS disturbances, cushingoid changes, osteoporosis

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBC, LFTs, PSA and U&Es prior to day one of treatment
- Consider an echocardiogram if there is a history of cardiac dysfunction

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Prior to Cycle 1 the following criteria should be met;

Criteria	Eligible Level
Neutrophils	$1x10^9$/L or greater
Platelets	$100x10^9$/L or greater

Dose modifications based on haematological parameters apply to mitoxantrone only.

Neutrophils ($x10^9$/L)	Dose Modifications (mitoxantrone)
1 or greater	100%
Less than 1 for less than 2 weeks	Delay until recovery to $1x10^9$/L or greater then continue at full dose
less than 1 for more than 2 weeks or nadir of less than 0.5	Delay until recovery to $1x10^9$/L or greater then give 8mg/m^2
Platelets ($x10^9$/L)	**Dose Modifications (mitoxantrone)**
100 or greater	100%
100 for less than 2 weeks	Delay until recovery to $100x10^9$/L or greater then continue at full dose
Less than 100 for more than 2 weeks or nadir of less than 50	Delay until recovery to $100x10^9$/L or greater then give 8mg/m^2

Hepatic Impairment

Drug	Bilirubin µmol/L		AST/ALT units/L	Dose (% of original dose)
Mitoxantrone	greater than 3xULN			For those with a WHO PS 0 or 1 then reduce the dose to 8mg/m^2. For those with a WHO PS of 2 or above stop treatment.

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Mitoxantrone	N/A	No dose adjustment needed

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose should then be reduced to 8mg/m^2 or discontinued as appropriate.

The recommendations apply to mitoxantrone only. Prednisolone should be continued if the mitoxantrone is delayed. It should be stopped if the mitoxantrone is stopped but may require a gradual reduction in dose.

Cardiac

Stop treatment if cardiotoxicity occurs

Regimen

21 day cycle for up to 10 cycles

Drug	Dose	Days	Administration
Mitoxantrone	12mg/m^2	1	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
Prednisolone	5mg twice a day	1-21 incl.	Oral

Dose Information

- Mitoxantrone dose will be rounded to the nearest 1mg (up if halfway).
- Mitoxantrone cardiac toxicity is more likely to occur at cumulative doses in excess of 160mg/m^2 or 100mg/m^2 after previous anthracycline therapy.
- Prednisolone is available as 5mg (uncoated) and 2.5mg and 5mg (enteric coated) tablets.

Administration Information

- Prednisolone should be taken with or after food.

Extravasation

- Mitoxantrone - vesicant

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy

  - ondansetron 8mg oral or intravenous

As take home medication

- metoclopramide 10mg oral three times a day for 3 days then 10mg three times a day as required

- Mouthwashes according to local or national policy on the treatment of mucositis
- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Additional Information

- Patients who stop mitoxantrone may require a gradual withdrawal of the prednisolone.

Coding (OPCS 4.6)

- Procurement – X70.2
- Delivery – X72.3

References
1.Berry W, Dakhil S, Modiano M et al. Phase III study of mitoxantrone plus low dose prednisolone versus low dose prednisone alone in patients with asymptomatic hormone refractory prostate cancer. J Urol 2002; 168 (6): 2451-2453.
2.Tannock IF, deWit R, Berry WR et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Engl J Med 2004; 351 (15): 1502-1512.
3.Tannock IF, Osoba D, Stockler MR et al. Chemotherapy with mitoxantrone plus prednisolone or prednisolone alone for symptomatic hormone resistant prostate cancer: a Canadian randomised trial with palliative end points. J Clin Oncol 1996; 14 (6): 1756-1764.

REGIMEN SUMMARY

Mitoxantrone-Prednisolone

Day 1

1. Ondansetron 8mg oral or intravenous

2. Mitoxantrone 12mg/m^2 intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

Take Home Medicines

3. Prednisolone 5mg twice a day for 21 days oral
   Administration Instructions
   Take with or after food. The dose of this medicine may need to be reduced gradually before stopping treatment.

4. Metoclopramide 10mg oral three times a day for 3 days then 10mg three times a day when required for nausea

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	February 2017	Mitoxantrone changed to vesicant as per EONS guidelines	Donna Kimber Pharmacy Technician	Dr Deborah Wright Pharmacist
1.1	May 2015	Header changed Metoclopramide dose changed to 10mg Bolus removed from intravenous bolus throughout text Mucositis recommendation changed Prednisolone admin instructions added. OPCS code updated Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	Jan 2012	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Joanna Gale Consultant Medical Oncologist Dr Mathew Wheater Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospitals NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.