Chemotherapy Protocol

BREAST CANCER

CYCLOPHOSPHAMIDE-DOXORUBICIN

Regimen

- Breast Cancer – Cyclophosphamide-Doxorubicin

Indication

- Primary systemic (neoadjuvant) therapy of breast cancer
- Adjuvant therapy of high risk (greater than 5%) node negative breast cancer
- WHO Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Cyclophosphamide	Dysuria, haemorrhagic cystitis, taste disturbances
Doxorubicin	Cardio toxicity, urinary discolourisation (red)

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

Monitoring

Regimen

- FBC, U&E's and LFT's prior to each cycle.
- Ensure adequate cardiac function before starting treatment with doxorubicin. Baseline LVEF should be measured, particularly in patients with a history of cardiac problems or in the elderly.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function 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. The following is a general guide only.

Haematological

Prior to prescribing the following treatment criteria must be met on day 1 of treatment.

Criteria	Eligible Level
Neutrophil	equal to or more than $1x10^9$/L
Platelets	equal to or more than $100x10^9$/L

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

If counts on day one are below these criteria for neutrophil and/or platelets then delay treatment for seven days. Treatment should only be re-started when these levels are reached. Treatment may be resumed at the original dose or reduce the original dose of doxorubicin and cyclophosphamide to 80% of the original dose depending on clinical circumstances. If a second episode of neutropenia and / or thrombocytopenia occurs or the time to reach the eligible level is longer than seven days consider changing or stopping therapy.

Hepatic Impairment

Drug	Bilirubin (µmol/L)		AST/ALT (units)		Alk Phos (units)	Dose (% of original dose)
Cyclophosphamide	Dose reduction may not be necessary					
Doxorubicin	If the bilirubin is between 20-51umol/L give 50% of the dose If the bilirubin is between 51-85umol/L give 25% of the dose If the bilirubin is greater than 85umol/L omit If the AST is 2-3xULN give 75% of the dose If the AST is greater than 3xULN give 50% of the dose					

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cyclophosphamide (consider mesna)	More than 20	100
	10-20	75
	Less than 10	50
Doxorubicin	No dose reduction generally required	

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.

Doxorubicin

Discontinue doxorubicin if cardiac failure develops.

Regimen

21 day cycle for 6 cycles

Where the intention is to follow this regimen with another such as paclitaxel only **FOUR** cycles may be necessary. Always check on prescribing cycle one what is required.

Drug	Dose	Days	Administration
Cyclophosphamide	600mg/m^2	1	Intravenous bolus
Doxorubicin	60mg/m^2	1	Intravenous bolus

Dose Information

- Cyclophosphamide will be dose banded as per the CSCCN agreed bands
- Doxorubicin will be dose banded as per the CSCCN agreed bands
- The maximum lifetime cumulative dose of doxorubicin is 450mg/m^2. However prior radiotherapy to mediastinal/pericardial area should not receive a lifetime cumulative doxorubicin dose of more than 400mg/m^2.

Administration Information

Extravasation

- Cyclophosphamide - neutral
- Doxorubicin – vesicant

Additional Therapy

- Antiemetics;

  15-30 minutes prior to chemotherapy;

  - dexamethasone 8mg oral or intravenous
  - ondansetron 8mg oral or intravenous

  As take home medication;

  - dexamethasone 4mg twice a day oral for 3 days

- metoclopramide 10mg three times a day when required oral
- ondansetron 8mg twice a day oral for 3 days

- 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.

Coding

- Procurement - X70.2

- Delivery - X72.3

References
1. Coskan U, Gunel N, Onuk E et al. Effect of different neoadjuvant chemotherapy regimens on locally advanced breast cancer. Neoplasma 2003; 50 (3): 210-216
2. Wolmark N, Wang J, Mamounas E et al. Preoperative chemotherapy in patients with operable breast cancer: nine-year results from the National Surgical Adjuvant Breast and Bowel Project B-18. J Natl Cancer Inst Monogr 2001; 30: 96-102

REGIMEN SUMMARY

Cyclophosphamide-Doxorubicin

Day One

1. Dexamethasone 8mg oral or intravenous

2. Ondansetron 8mg oral or intravenous

3. Doxorubicin 60mg/m² intravenous bolus over 10 minutes.

4. Cyclophosphamide 600mg/m² intravenous bolus over 10 minutes.

Take Home Medicines

5. Dexamethasone 4mg twice a day oral for three days starting on day two of the cycle

6. Metoclopramide 10mg three times a day when required oral

7. Ondansetron 8mg twice a day oral for three days starting on the evening of day one of treatment

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	August 2014	Header changed Toxicities removed Adverse effects tabulated ≥ removed and written in full Dose modification tabulated Hepatic impairment updated Regimen tabulated Metoclopramide dose changed to 10mg Bolus removed from intravenous bolus throughout text Mucositis recommendation changed OPCS code updated Dexamethasone TTO clarified Ondansetron TTO clarified Disclaimer added	Donna Kimber Pharmacy Technician	Dr Debbie Wright Pharmacist
1	June 2011	None	Anna Bunch Pharmacist Dr Debbie Wright Pharmacist	Dr Ellen Copson Consultant Medical Oncologist Dr Caroline Archer 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 Hospital 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.