

Chemotherapy Protocol

BREAST CANCER

CYCLOPHOSPHAMIDE-EPIRUBICIN

Regimen

- Breast Cancer – Cyclophosphamide-Epirubicin

Indication

- Primary systemic (neoadjuvant) therapy of breast cancer
- Adjuvant therapy of breast cancer
- WHO Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Cyclophosphamide	Dysuria, haemorrhagic cystitis, taste disturbances
Epirubicin	Cardio-toxicity, urinary discolouration (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. 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 one of treatment.

Criteria	Eligible Level
Neutrophils	equal to or more than $1 \times 10^9/L$
Platelets	equal to or more than $100 \times 10^9/L$

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 epirubicin and cyclophosphamide to 80% of the original dose depending on clinical circumstances. If a second episode of neutropenia / thrombocytopenia occurs or the time to reach the eligible level is longer than seven days consider changing treatment or growth factors as per local policy.

Kidney Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cyclophosphamide	more than 20	100
	10-20	75
	10 or less	50
Epirubicin	Dose reduce in severe impairment only	

Liver Impairment

Drug	Recommendation	
Cyclophosphamide	Dose reduction may not be necessary	
Epirubicin	Bilirubin (umol/L)	Dose (% of original)
	24-51	50
	51-85	25
	85 or greater	Contra-indicated
If AST 2-4 x ULN or bili 21-51µmol/L give 50% dose , if AST greater than 4 x ULN or bili greater than 51 µmol/L then give 25% dose		

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.

Epirubicin

Discontinue epirubicin 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
Epirubicin	90mg/m ²	1	Intravenous bolus

Dose Information

- Cyclophosphamide will be dose banded as per the CSCCN agreed bands
- Epirubicin will be dose banded as per the CSCCN agreed bands
- The maximum lifetime cumulative dose of epirubicin is 900mg/m²

Extravasation

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

- Mouthwashes according to local or national policy on the treatment of mucositis
- Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Coding (OPCS 4.6)

- 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

REGIMEN SUMMARY

Cyclophosphamide-Epirubicin

Day One

1. Dexamethasone 8mg oral or intravenous
2. Ondansetron 8mg oral or intravenous
3. Epirubicin 90mg/m² intravenous bolus over 10 minutes
4. Cyclophosphamide 600mg/m² intravenous bolus over 10 minutes

Take Home Medicines

4. Dexamethasone 4mg twice a day for 3 days oral starting on day two of the cycle
5. Metoclopramide 10mg three times a day when required oral
6. Ondansetron 8mg twice a day for 3 days oral starting on the evening of day one of the cycle

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	August 2014	Hepatic and renal dose modifications updated Bolus removed from intravenous bolus throughout text Metoclopramide dose changed to 10mg Mucositis recommendation changed Dexamethasone and Ondansetron TTO clarified	Donna Kimber Pharmacy Technician	Dr Deborah Wright Pharmacist
1.1	June 2013	Header changed to NHS badge. Name changed to Cyclophosphamide-Epirubicin (90). Adverse effects, liver and renal dose modifications, and dose recommendations tabulated. Renal dose changed to 21 or greater. Liver modified for epirubicin. Named Trusts added.	Dr Deborah Wright Pharmacist	Alison Burgin Pharmacist
1	Aug 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.