Chemotherapy Protocol

BREAST CANCER

CYCLOPHOSPHAMIDE-DOXORUBICIN-PACLITAXEL

(21 day)

Regimen

- Breast Cancer – Cyclophosphamide-Doxorubicin-Paclitaxel (21 day)

Indication

- Neoadjuvant / adjuvant therapy of early breast cancer
- WHO Performance status 0, 1

Toxicity

Drug	Adverse Effect
Cyclophosphamide	Dysuria, haemorrhagic cystitis, taste disturbances
Doxorubicin	Cardio toxicity, urinary discolourisation (red)
Paclitaxel	Hypersensitivity, hypotension, bradycardia, peripheral neuropathy, myalgia and back pain on administration

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
- Blood pressure and pulse to be monitored half hourly during the paclitaxel infusion

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
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 neutrophils and 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 cyclophosphamide, doxorubicin or paclitaxel to 80% of the original dose where a NCI-CTC grade 3 or above haematological event has occurred. If a second episode of neutropenia and / or thrombocytopenia occurs, despite dose reduction, or the time to reach the eligible level is longer than seven days consider changing or stopping therapy.

Hepatic Impairment

Drug	Bilirubin (µmol/L)	Dose
Cyclophosphamide	Dose reduction may not be necessary	
Doxorubicin	between 20-50 between 51-85 greater than 85	50% 25% omit
	If the AST is 2-3xULN give 75% of the dose If the AST is greater than 3xULN give 50% of the dose	
Paclitaxel	If bilirubin less than 1.25xULN and transaminase less than 10xULN, dose at 175 mg/m^2	
	less than 26 27-51 greater than 51	135mg/m² 75mg/m² 50mg/m²

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	
Paclitaxel	No dose reductions necessary	

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.

Paclitaxel

NCI-CTC grade 2 peripheral neuropathy withhold paclitaxel only until the neuropathy recovers to NCI-CTC grade 1 then dose reduce to 75% of the original dose. Where the peripheral neuropathy is NCI-CTC grade 3 again withhold the paclitaxel until it resolves to NCI-CTC grade 1 and then reduce the dose of paclitaxel to 50% of the original dose. Paclitaxel should be discontinued if the neuropathy does not resolve to NCI-CTC grade 1.

Regimen

21 day cycle for 4 cycles

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

Followed by

21 day cycle for 4 cycles

Drug	Dose	Days	Administration
Paclitaxel	175mg/m^2	1	Intravenous infusion in 500ml sodium chloride over 180 minutes

Dose Information

- Cyclophosphamide will be dose banded in accordance with the national dose bands (20mg/mL)
- Doxorubicin will be dose banded in accordance with the national dose bands (2mg/mL)

- 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.

- Paclitaxel will be dose banded in accordance with the national dose bands (6mg/ml)

Administration Information

- Hypersensitivity reactions tend to occur with the first or second infusion of paclitaxel. Paclitaxel infusions should be interrupted for minor symptoms such as flushing or localised rashes. If these resolve promptly (within 5 minutes) the infusion may be restarted at a lower rate with intensive monitoring. Immediately discontinue the infusion for severe reactions which include profound hypotension, bronchospasm and generalised erythema.

- Paclitaxel must be administered via a non-PVC administration set containing an in-line 0.22 micron filter.

Extravasation

- Cyclophosphamide - neutral

- Doxorubicin – vesicant

- Paclitaxel – vesicant

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy with **cyclophosphamide and doxorubicin**

  - 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

  15-30 minutes prior to chemotherapy with **paclitaxel**

  - metoclopramide 10mg oral or intravenous

  As take home medication

  - metoclopramide 10mg three times a day when required oral

- Premedication to reduce of risk of paclitaxel hypersensitivity reaction

30 minutes prior to chemotherapy with paclitaxel

- chlorphenamine 10mg intravenous
- dexamethasone 20mg intravenous
- H_2 antagonist according to local formulary choice and availability

- 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.

References
1. Henderson IC, Beryy D, Demetri G et al. Improved outcomes from adding sequential paclitaxel but not from escalating doxorubicin dose in an adjuvant chemotherapy regimen for patients with node positive primary breast cancer. J Clin Oncol 2003; 21 (6): 976-983
2. Tan-Chui E, Yothers G, Romond EH et al. Assessment of cardiac dysfunction in a randomised trial comparing doxorubicin and cyclophosphamide followed by paclitaxel with or without trastuzumab as adjuvant therapy in node positive HER2 over-expressing breast cancer. NSABP B-31. J Clin Oncol 2005; 23 (31): 7811-7819.

REGIMEN SUMMARY

Cyclophosphamide-Doxorubicin-Paclitaxel (21 day)

Cyclophosphamide-Doxorubicin

Cycles 1, 2, 3, 4 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 3 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 the cycle

Paclitaxel

Cycles 5, 6, 7, 8 Day One

1. Chlorphenamine 10mg intravenous

2. Dexamethasone 20mg intravenous

3. H_2 antagonist according to local formulary choice and availability

Administration Instructions:
Administer according to local formulary choice and availability one of the following 30 minutes prior to chemotherapy;

- ranitidine 50mg intravenous once only
- famotidine 20mg oral once only
- nizatidine 150mg oral once only
- ranitidine 150mg oral once only

If there is no stock of these products due to national shortages treatment may proceed without the H_2 antagonist provided there is no instruction in the ARIA journal indication the patient **must have** H_2 antagonist treatment.

All infusion related reactions must be recorded in the ARIA journal and reported to the appropriate consultantMany Trusts do not administer an H_2 antagonist from cycle three onwards. They have been left in the ARIA protocols so that decisions can be made on an individual Trust and patient basis.

4. Metoclopramide 10mg oral or intravenous

5. Paclitaxel 175mg/m² intravenous infusion in 500ml sodium chloride 0.9% over 180 minutes

Take Home Medicines

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

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	October 2020	Update of premedication due to shortage of IV ranitidine. IV ranitidine changed to H_2 antagonist according to local formulary choice and availability Dose banding updated Coding removed	Arum Shortland Pharmacist	Dr Deborah Wright Pharmacist
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	Dec 2011	None	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 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.