**Chemotherapy Protocol**

## BREAST CANCER

## CYCLOPHOSPHAMIDE-DOCETAXEL-DOXORUBICIN

## (TAC)

### Regimen

- Breast Cancer – Cyclophosphamide-Docetaxel-Doxorubicin (TAC)

### Indication

- Adjuvant therapy for node positive early breast cancer
- WHO Performance status 0, 1, 2

### Toxicity

| Drug | Adverse Effect |
|---|---|
| Cyclophosphamide | Dysuria, haemorrhagic cystitis, taste disturbances |
| Docetaxel | Hypersensitivity, fluid retention, neuropathy, joint pains, nail changes, fatigue |
| 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. 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 |
|---|---|
| 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/or platelets then delay treatment for seven days. Only re-start treatment when these levels are reached. If patients experience febrile neutropenia or treatment delay due to a neutrophil count of less than $0.5x10^9$/L or platelets less than $50x10^9$/L for more than seven days then reduce the doses of all agents to 80% of the original dose. If the neutropenia or thrombocytopenia recurs despite this decrease in dose intensity the doses should be either be further reduced to 50% of the original dose or treatment stopped.

### *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<br>If the bilirubin is between 51-85umol/L give 25% of the dose<br>If the bilirubin is greater than 85umol/L omit<br><br>If the AST is 2-3xULN give 75% of the dose<br>If the AST is greater than 3xULN give 50% of the dose | | | | | |
| Docetaxel | N/A | | 1.5xULN or greater | and | 2.5xULN or greater | Give 75% |
| | Greater than ULN | and/or | 3.5xULN or greater | and | 6xULN or greater | Not Recommended |

### *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 |
| Docetaxel | No dose reduction necessary | |
| Doxorubicin | No dose reduction generally required | |

## *Other*

*Docetaxel*

Peripheral neuropathy at NCI-CTC grade 3 or above should result in a dose reduction to 80% of the original dose in the first instance.

Excessive tearing / lacrimation are related to cumulative docetaxel doses and occur after a median of 400mg/m². Symptomatic treatment with hypromellose 0.3% eye drops four times a day may help. However, if the ocular irritation continues reduce the docetaxel dose to 80% of the original dose in the first instance.

Delay the docetaxel where a NCI-CTC grade 3 cutaneous toxicity is present on day one of the cycle until it resolves to NCI-CTC grade 1 or below. The subsequent doses of docetaxel should be reduced to 80% of the original dose. If there is no recovery after two weeks, docetaxel treatment should be stopped. Where a NCI-CTC grade 3 cutaneous toxicity occurs between cycles with recovery by day one then reduce the docetaxel dose to 80% of the original dose. Docetaxel should be stopped in response to a NCI-CTC grade 4 cutaneous toxicity.

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

Docetaxel is highly myelosuppressive and in those with poor bone marrow reserves (for example due to extensive prior treatment, bone metastasis or extensive skeletal radiation), consider a starting dose of 55mg/m² with a view to increase to 75mg/m² if well tolerated.

**21 day cycle for 6 cycles**

| Drug | Dose | Days | Administration |
|---|---|---|---|
| Cyclophosphamide | 500mg/m$^2$ | 1 | Intravenous bolus |
| Docetaxel | 75mg/m$^2$ | 1 | Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes |
| Doxorubicin | 50mg/m$^2$ | 1 | Intravenous bolus |

## Dose Information

- Cyclophosphamide will be dose banded as per the CSCCN agreed bands
- Docetaxel will be dose banded as per the CSCCN agreed bands
- Docetaxel induced fluid retention can lead to weight gain. This is not a reason to alter the doses
- Doxorubicin will be dose banded as per the CSCCN agreed bands
- The maximum lifetime cumulative dose of doxorubicin is 450mg/m$^2$

## Administration Information

- Hypersensitivity reactions tend to occur with the first or second infusion of Docetaxel. Docetaxel infusion should not be interrupted for minor symptoms such as flushing or localised rashes. Immediately discontinue the docetaxel infusion for severe reactions which include profound hypotension, bronchospasm and generalised erythema.
- Docetaxel doses greater than 190mg should be diluted in 500ml (maximum concentration 0.74mg/ml).

### *Extravasation*

- Cyclophosphamide - neutral
- Docetaxel – exfoliant
- Doxorubicin – vesicant

## Additional Therapy

- Antiemetics

  15-30 minutes before chemotherapy

  - ondansetron 8mg oral or intravenous

  As take home medication

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

- To prevent fluid retention and hypersensitivity reactions prescribe dexamethasone 8mg twice a day oral for three days starting 24 hours before the docetaxel administration. On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg once only dose intravenous bolus.

- Growth factor as per local formulary choice. For example;

  - filgrastim or bioequivalent 300microgram once a day for seven days starting on day three of the cycle subcutaneous
  - lenograstim or bioequivalent 263microgram once a day for seven days starting on day three of the cycle subcutaneous
  - pegfilgrastim or bioequivalent 6mg once a day for one day on day two of the cycle

- 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 - X71.3

- Delivery – X72.2

References
1.Perez E A et al. TAC - A New Standard in Adjuvant Therapy for Breast Cancer? N Eng J Med; 352 (22): 2346-2348
2.Martin M, Lluch A, Segui MA et al. Toxicity and health-related quality of life in breast cancer patients receiving adjuvant docetaxel, doxorubicin, cyclophosphamide (TAC) or 5-fluorouracil, doxorubicin and Cyclophosphamide (FAC): impact of adding primary prophylactic granulocyte-colony stimulating factor to the TAC regimen. Ann Oncol 2006; 17: 1205-1212.
3.Martin M, Pienkowski T, Mackey J et al. Adjuvant Docetaxel for Node-Positive Breast Cancer. N Eng J Med 2005; 352:2302-13

## REGIMEN SUMMARY

## Cyclophosphamide-Docetaxel-Doxorubicin (TAC)

### Cycles 1, 2, 3, 4, 5

### Day Minus One

1. Dexamethasone 8mg twice a day oral*

### Day One

2. Dexamethasone 8mg twice a day oral (from TTO)*

3. Ondansetron 8mg oral or intravenous

4. Doxorubicin 50mg/m² intravenous bolus over 10 minutes

5. Docetaxel 75mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes

6. Cyclophosphamide 500mg/m² intravenous bolus over 10 minutes

### Take Home Medicines

7. Dexamethasone 8mg twice daily oral for 3 days starting the day before the docetaxel infusion

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

9. Ondansetron 8mg twice a day oral for 3 days starting on the evening of day one of treatment

10. Growth factor as per local formulary choice. For example;**

    - filgrastim or bioequivalent 300microgram once a day for seven days starting on day three of the cycle subcutaneous
    - lenograstim or bioequivalent 263microgram once a day for seven days starting on day three of the cycle subcutaneous
    - pegfilgrastim or bioequivalent 6mg once a day for one day on day two of the cycle

### Cycles 6

### Day Minus One

11. Dexamethasone 8mg twice a day oral*

### Day One

12. Dexamethasone 8mg twice a day oral (from TTO)*

13. Ondansetron 8mg oral or intravenous

14. Doxorubicin 50mg/m² intravenous bolus over 10 minutes

15. Docetaxel 75mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes

16. Cyclophosphamide 500mg/m² intravenous bolus over 10 minutes

**Take Home Medicines**

17. Dexamethasone 8mg twice a day oral for the day after chemotherapy*

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

19. Ondansetron 8mg twice a day oral for 3 days starting on the evening of day one of treatment

Growth factor as per local formulary choice. For example;**

- filgrastim or bioequivalent 300microgram once a day for seven days starting on day three of the cycle subcutaneous
- lenograstim or bioequivalent 263microgram once a day for seven days starting on day three of the cycle subcutaneous
- pegfilgrastim or bioequivalent 6mg once a day for one day on day two of the cycle

* In Aria Planner the dexamethasone 8mg twice daily will appear on days 1, 2, 3 of treatment. This is the supply for the next cycle. The administration instructions reflect this. On the last cycle no dexamethasone will appear for prescribing.

**Growth factors will appear as the drug in the regimen. The administration instructions reflect the guidance on agent, dose and duration.

## DOCUMENT CONTROL

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