Chemotherapy Protocol

BREAST CANCER

CYCLOPHOSPHAMIDE (PO)-FLUOROURACIL-METHOTREXATE

(CMF-PO)

**Regimen**

- Breast Cancer – Cyclophosphamide (PO)-Fluorouracil-Methotrexate (CMF-PO)

**Indication**

- Adjuvant treatment of early breast cancer
- WHO Performance status 0, 1, 2

**Toxicity**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Dysuria, haemorrhagic cystitis, taste disturbances</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>Diarrhoea, stomatitis</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Stomatitis, conjunctivitis, renal toxicity</td>
</tr>
</tbody>
</table>

The presence of a third fluid compartment e.g. ascites or renal failure may delay methotrexate clearance hence increase toxicity.

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.

**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.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Eligible Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil</td>
<td>equal to or more than 1x10⁹/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>equal to or more than 100x10⁹/L</td>
</tr>
</tbody>
</table>

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 the neutrophils 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 cyclophosphamide, methotrexate and fluorouracil 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 stopping or changing treatment or growth factor support as per local guidelines.

Day eight treatment is seldom delayed for low blood counts.

**Kidney Impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Creatinine Clearance (ml/min)</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>More than 20</td>
<td>100%</td>
</tr>
<tr>
<td>(consider mesna)</td>
<td>10-20</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>Less than 10</td>
<td>50</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>Consider dose adjustments in severe renal impairment</td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>More than 80</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>65%</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>Less than 30</td>
<td>CI</td>
</tr>
</tbody>
</table>
Liver Impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin µmol/L</th>
<th>AST/ALT units</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Dose reduction may not be necessary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>Less than 85</td>
<td>Less than 180</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>More than 85</td>
<td>or More than 180</td>
<td>CI</td>
</tr>
<tr>
<td></td>
<td>In moderate hepatic impairment reduce the initial dose by one third. In severe hepatic impairment reduce initial dose by one half. These doses may be increased if no toxicity occurs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Less than 50</td>
<td>and Less than 180</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>51-85 and More than 180</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>More than 85</td>
<td>CI</td>
<td></td>
</tr>
</tbody>
</table>

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.

Regimen

28 day cycle for 6 cycles

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>100mg/m²</td>
<td>1-14 incl</td>
<td>Oral</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>600mg/m²</td>
<td>1,8</td>
<td>Intravenous bolus</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>40mg/m²</td>
<td>1,8</td>
<td>Intravenous bolus</td>
</tr>
</tbody>
</table>
Dose Information

- Cyclophosphamide will be dose rounded to the nearest 50mg (up if halfway)
- Fluorouracil will be dose banded as per the CSCCN agreed bands
- Methotrexate will be dose banded as per the CSCCN agreed bands

Extravasation

- Fluorouracil - inflammitant
- Methotrexate - inflammitant

Additional Therapy

- Antiemetics
  15-30 minutes prior to chemotherapy;
  - dexamethasone 8mg oral or equivalent intravenous dose
  - metoclopramide 10mg oral or intravenous

As take home medication:
  - dexamethasone 4mg once a day for 3 days oral
  - metoclopramide 10mg three times a day when required oral (may not be required on day eight)

- Folinic acid 15mg six hourly for 6 doses oral starting 24 hours after methotrexate administration.
- 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.

Additional Information

- The National Patient Safety Agency alert NPSA/2008/RRR001 must be followed when prescribing, dispensing or administering oral chemotherapy.
- It must be made clear to all staff, including those in the community, that this is a short course of oral chemotherapy that must not be continued.

Coding

- Procurement - X70.1
- Delivery - X 72.3, X72.4
References
REGIMEN SUMMARY

Cyclophosphamide (PO)-Fluorouracil-Methotrexate (CMF-PO)

Day One
1. Dexamethasone 8mg oral or equivalent intravenous dose
2. Metoclopramide 10mg oral or intravenous
3. Fluorouracil 600mg/m² intravenous bolus over 10 minutes
4. Methotrexate 40mg/m² intravenous bolus over 10 minutes

Take Home Medicines
5. Cyclophosphamide 100mg/m² once daily days 1-14 inclusive oral
6. Folinic acid 15mg six hourly for six doses oral starting 24 hours after methotrexate administration
7. Dexamethasone 4mg once a day for 3 days oral starting on the day after chemotherapy
8. Metoclopramide 10mg three times a day when required oral

Day Eight
1. Dexamethasone 8mg oral or equivalent intravenous dose
2. Metoclopramide 10mg oral or intravenous
3. Fluorouracil 600mg/m² intravenous bolus over 10 minutes
4. Methotrexate 40mg/m² intravenous bolus over 10 minutes

Take Home Medicines
5. Folinic acid 15mg six hourly for six doses oral starting 24 hours after methotrexate administration.
6. Dexamethasone 4mg once a day for 3 days oral starting on the day after chemotherapy
7. Metoclopramide 10mg three times a day when required oral*

*Only dispense if required
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.