Chemotherapy Protocol

BREAST CANCER

CYCLOPHOSPHAMIDE-EPIRUBICIN (100)- FLUOROURACIL

(\text{\textsc{FE}_{100}C})

Regimen

- Breast Cancer – Cyclophosphamide-Epirubicin (100)-Fluorouracil (\text{\textsc{FE}_{100}C})

Indication

- Neo-adjuvant /adjuvant therapy of 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>Epirubicin</td>
<td>Cardio-toxicity, urinary discolouration (red)</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>Diarrhoea, stomatitis</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Eligible Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>equal to or more than 1x10^9/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>equal to or more than 100x10^9/L</td>
</tr>
</tbody>
</table>

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

**In the adjuvant / neo-adjuvant setting, always check with the relevant consultant before delaying or reducing the dose in response to a toxicity.**

If counts on day one are below these criteria for neutrophil and/or platelets then delay treatment for seven days. Treatment should only be started when these levels are reached. On subsequent cycles, if the counts are below these levels on day one then delay treatment until these levels are reached and / or consider reducing the dose of epirubicin to 75% of the original dose. The dose intensity of fluorouracil and cyclophosphamide may be maintained. If a second episode of neutropenia / thrombocytopenia occurs or the time to reach the eligible level is longer than seven days consider changing treatment. If patients experience febrile neutropenia or treatment delay due to neutrophil less than 0.5x10^9/L or platelets less than 50x10^9/L for more than seven days then reduce the dose to 75% of the original dose. If neutropenia or thrombocytopenia recurs, the dosage should be either further reduce to 50% of the original dose or stop treatment.
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></td>
<td>10-20</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>Less than 10</td>
<td>50</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>Dose reduce in severe impairment only</td>
<td></td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>Consider dose reduction in severe renal impairment only</td>
<td></td>
</tr>
</tbody>
</table>

Liver Impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommendation</th>
<th>Bilirubin (umol/L)</th>
<th>Dose (% of original)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Dose reduction may not be necessary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epirubicin</td>
<td></td>
<td>24-51</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>51-85</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>85 or greater</td>
<td>Contra-indicated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If AST 2-4xULN give 50% of the dose, if the AST is greater than 4xULN then give 25% of the dose</td>
<td></td>
</tr>
</tbody>
</table>

<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>Fluorouracil</td>
<td>Less than 85</td>
<td>Less than 180</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>More than 85 or</td>
<td>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>
</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.

Epirubicin

Discontinue epirubicin if cardiac failure develops.
Regimen

21 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>500mg/m²</td>
<td>1</td>
<td>Intravenous bolus</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>100mg/m²</td>
<td>1</td>
<td>Intravenous bolus</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>500mg/m²</td>
<td>1</td>
<td>Intravenous bolus</td>
</tr>
</tbody>
</table>

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
- Fluorouracil will be dose banded as per the CSCCN agreed bands

Extravasation

- Cyclophosphamide – neutral
- Epirubicin – vesicant
- Fluorouracil - inflammitant

Additional Therapy

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

- Growth factor according to local formulary choice. For example;
  - filgrastim or bioequivalent 300microgram once a day subcutaneous for five
days starting on day five of the cycle
- lenograstim or bioequivalent 263microgram once a day subcutaneous for five days starting on day five of the cycle
- pegfilgrastim or bioequivalent 6mg once a day subcutaneous on day two

- 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**

- Procurement - X70.2

- Delivery - X72.3

**References**


REGIMEN SUMMARY

Cyclophosphamide-Epirubicin (100)-Fluorouracil (FE100C)

Day One

1. Dexamethasone 8mg oral or equivalent intravenous dose
2. Ondansetron 8mg oral or intravenous
3. Epirubicin 100mg/m² intravenous bolus over 10 minutes
4. Fluorouracil 500mg/m² intravenous bolus over 10 minutes
5. Cyclophosphamide 500mg/m² intravenous bolus over 10 minutes

Take Home Medicines

6. Dexamethasone 4mg twice a day for 3 days oral starting on day two of the cycle
7. Metoclopramide 10mg three times a day when required oral
8. Ondansetron 8mg twice a day for 3 days oral starting on the evening of day one of treatment
9. Growth factor according to local formulary choice. For example;
   - filgrastim or bioequivalent 300microgram once a day subcutaneous for five days starting on day five of the cycle
   - lenograstim or bioequivalent 263microgram once a day subcutaneous for five days starting on day five of the cycle
   - pegfilgrastim or bioequivalent 6mg once a day subcutaneous on day two
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.