SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

# EC (Epirubicin Cyclophosphamide) Adjuvant / Neo-adjuvant regimen

PROTOCOL REF: MPHAECANBR
(Version No. 1.1)

## Approved for use in:

**ER positive, HER2 negative:**

For Adjuvant or Neo-adjuvant intent.

For fit but lower risk – node negative, intermediate risk oncotype or 1-3 node positive patients in whom the consultant wishes to avoid taxane;

EC x 6

**Or**

EC x 4 for lowest risk patients.

**Triple negative breast cancer, adjuvant use:**

Use EC x 6 (or EC x 4 if lower risk) if wish to avoid a taxane.

## Dosage:

| Drug | Dose | Route | Frequency |
|---|---|---|---|
| **Epirubicin** | **90mg/m²** | **IV** | Every 21 days<br>For 4 to 6 cycles |
| **Cyclophosphamide** | **600mg/m²** | **IV** | |

## Administration:

**Consider IV access, PICC line insertion is recommended for this regimen**

- Nasal stuffiness can occur immediately with administration of cyclophosphamide, if uncomfortable for the patient the drug can be slowed down and administered over 45 minutes.
- Encourage an oral fluid intake of 2 litres per day to promote urinary output & prevent chemical cystitis with cyclophosphamide.
- Remind patient that red colouration of urine can occur 1-2 days after epirubicin administration

## Emetogenic risk:

Moderately emetogenic.

## Supportive treatments:

Dexamethasone 4mg orally twice a day for three days

Ondansetron 8mg orally twice a day for three days

Metoclopramide 10mg tablets three times a day when required

Filgrastim subcutaneous injection daily for 7 days from day 3

- 300 micrograms for patients below 70kg
- 480 micrograms for those 70kg and above

## Extravasation risk:

Refer to the CCC policy for the Prevention and Management of Extravasation Injuries

**Epirubicin:** vesicant. Erythematous streaking along the vein proximal to the site of injection has been reported, and must be differentiated from an extravasation event. This reaction usually subsides within 30 minutes.

**Cyclophosphamide** – neutral

## Dosing in renal and hepatic impairment:

<table>
<tr><td rowspan="5">Renal</td><td>Epirubicin</td><td colspan="2">No dose adjustment required, however for patients requiring Haemodialysis(HDx) - consider weekly dosing.</td></tr>
<tr><td rowspan="4">Cyclophosphamide</td><td>Creatinine Clearance</td><td>Dose (%)</td></tr>
<tr><td>≥ 30 ml/min</td><td>100</td></tr>
<tr><td>10-29 ml/min</td><td>75</td></tr>
<tr><td><10ml/min or HDx</td><td>Not recommended. If unavoidable consider 50% of the original dose</td></tr>
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<table>
<tr><td>Hepatic</td><td>Epirubicin</td><td>
<table>
<tr><th>Bilirubin (µmol/L)</th><th></th><th>AST</th><th>Epirubicin dose</th></tr>
<tr><td>21 to 51</td><td>OR</td><td>2-4 x ULN</td><td>50%</td></tr>
<tr><td>52 to 86</td><td>OR</td><td>>4x ULN</td><td>25%</td></tr>
<tr><td>Above 86</td><td>OR</td><td>Child-Pugh C</td><td>omit</td></tr>
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| | | |
|---|---|---|
| | | **Child-Pugh Class**<br>A (5-6 points)<br>B (7-9 points)<br>C (10 or more points)<br><br>**Child-Pugh Scoring**<br>**Parameters** / **1 point** / **2 points** / **3 points**<br>Total bilirubin (µmol/L) / < 34 / 34–50 / > 50<br>Serum albumin (g/L) / > 35 / 28–35 / < 28<br>Prothrombin time, prolongation (s) *Or* INR / < 4<br>< 1.7 / 4–6<br>1.7-2.3 / > 6<br>>2.3<br>Ascites / None / Mild to Moderate (diuretic responsive) / Severe (diuretic refractory)<br>Hepatic encephalopathy / None / Grade I–II (or suppressed with medication) / Grade III–IV (or refractory to medication)<br>INR: International Normalised Ratio.<br>**Please note**: assessment of Child-Pugh Class is to help guide clinical teams when prescribing and pharmacists when screening. |
| | **Cyclophosphamide** | No dose adjustments needed for mild to moderate impairment. Not recommended in severe impairment |

## Interactions:

For detailed list of interactions please refer to the relevant SmPC

## Treatment schedule:

| Day | Drug | Dose | Route | Diluent and rate |
|---|---|---|---|---|
| 1 | Ondansetron | 24mg | PO | 30 mins before chemotherapy |
| | Dexamethasone | 12mg | PO | 30 mins before chemotherapy |
| | **Epirubicin** | **90mg/m$^2$** | **IV** | IV bolus over 10–15 minutes |
| | **Cyclophosphamide** | **600mg/m$^2$** | **IV** | IV bolus over 30 minutes |

## Main toxicities:

| | |
|---|---|
| **Haematological** | Neutropenia, thrombocytopenia and anaemia. |
| **Gastrointestinal** | Nausea, vomiting, stomatitis, diarrhoea, mucositis |
| **Cardiotoxicity** | Epirubicin - sinus tachycardia and/or electrocardiogram (ECG) abnormalities such as non-specific ST-T wave changes. Congestive heart failure. Other cardiac events have been reported, included delayed toxicity. |
| **Dermatological** | Alopecia, normally reversible |
| **Ocular** | Watery eyes, gritty and irritated |
| **Urological** | Red colouration of urine for 1 to 2 days after administration following epribucin<br>Urotoxicity can occur with short-term and long-term use of cyclophosphamide. Hemorrhagic cystitis, pyelitis, ureteritis, and haematuria. Mesna can be given if required. |
| **Infertility** | Amenorrhea, risk of premature menopause<br>However ensure appropriate contraceptive advice is given.<br>Pregnancy status should be confirmed prior to administration. |

## Investigations and treatment plan:

| | Pre | Cycle 1 | Cycle 2 | Cycle 3 | Ongoing |
|---|---|---|---|---|---|
| Informed Consent | X | | | | |
| Clinical Assessment | X | | | X | As clinically indicated or at the end of treatment |
| SACT Assessment (to include PS and toxicities) | X | X | X | X | Every cycle |
| FBC | X | X | X | X | Every cycle |
| U&E & LFTs & Magnesium | X | X | X | X | Every Cycle |
| CrCl (Cockcroft and Gault) | X | | | | If clinically indicated |
| CT scan | | | | | If clinically indicated based on the stage of cancer and clinical history |
| ECG/ECHO | X* | | | | *At baseline if pre-existing cardiac risk factors and if clinically indicated |
| Observation measurements | X | | | | Repeat if clinically indicated |
| Weight recorded | X | X | X | X | Every cycle |
| Height recorded | X | | | | |

## Dose Modifications and Toxicity Management:

## Haematological toxicity:

Proceed on day 1 if-

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|---|---|
| ANC ≥ 1.0 x $10^9$/L | Platelets ≥ 100 x $10^9$/L |

Delay 1 week on day 1 if-

| | |
|---|---|
| ANC ≤ 0.9 x $10^9$/L | Platelets ≤ 99 x $10^9$/L |

**Second episode or severe neutropenic sepsis: Defer** by 7 days or until blood counts recovered if neutrophils $\leq$ 1.0 **or** platelets $\leq$ 100 x $10^9$/L **and reduce** to 80% dose

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

## References:

1. https://www.medicines.org.uk/emc
2. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e201–08.
3. BNF available via: https://bnf.nice.org.uk/
4. Smith JW et al Epirubicin with cyclophosphamide followed by docetaxel with trastuzumab and bevacizumab as neoadjuvant therapy for HER2 positive locally advanced breast cancer NSABP FB-5 Clin Breast Cancer 2016 17(1)48-54
5. Jones, RL et al A randomised pilot phase II study of AC or EC given 2 weekly with pegfilgrastim vs 3 weekly for women with early breast cancer British Journal of Cancer 2009 100: 305-310

## Circulation/Dissemination

| | |
|---|---|
| Date added into Q-Pulse | 28th April 2023 |
| Date document posted on the Intranet | N/A |

## Version History

| Date | Version | Author name and designation | Summary of main changes |
|---|---|---|---|
| March 2023 | 1.1 | **Gabriella Langton** | Updated to new template, changed supportive medication domperidone to metoclopramide |
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