epiRUBicin 90 + cycloPHOSphamide (EC90) Therapy-21 day

INDICATIONS FOR USE:

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Regimen Code</th>
<th>Reimbursement status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjuvant treatment for operable breast carcinoma</td>
<td>C50</td>
<td>00262a</td>
<td>Hospital</td>
</tr>
</tbody>
</table>

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.

epiRUBicin and cycloPHOSphamide are administered once every 21 days for 4 cycles until disease progression or unacceptable toxicity occurs.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

<table>
<thead>
<tr>
<th>Order of Admin</th>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
<th>Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>epiRUBicin</td>
<td>90mg/m²</td>
<td>IV Bolus</td>
<td>Via the tubing of a free-running intravenous saline infusion over a period of up to 30min.</td>
<td>Every 21 days</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>cycloPHOSphamide</td>
<td>600mg/m²</td>
<td>IV infusion³</td>
<td>250ml 0.9% NaCl over 30min</td>
<td>Every 21 days</td>
</tr>
</tbody>
</table>

³ cycloPHOSphamide may also be administered as an IV bolus over 5-10mins

Lifetime cumulative dose for epiRUBicin is 900mg/m²

In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors outlined below and to the age of the patient.

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ELIGIBILITY:

- indications as above.
- ECOG status 0-2.
- Adequate haematological, renal and liver status.

EXCLUSIONS:

- Hypersensitivity to epiRUBicin, cycloPHOSphamide or any of the excipients.
- Uncontrolled high blood pressure, unstable angina, symptomatic congestive heart failure, myocardial infarction within the preceding 6 months, serious uncontrolled cardiac dysrhythmia.
- Patients previously treated with maximum cumulative doses of epiRUBicin or any other anthracycline.
- Pregnancy and lactation.

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- ECG
- MUGA scan or echocardiogram if clinically indicated

Regular tests:

- FBC, renal and liver profile prior to each cycle
- If clinically indicated creatinine, MUGA scan or echocardiogram
Disease monitoring:

Disease monitoring should be in line with the patient’s treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant

Haematological:

Table 1: Dose modifications for haematological toxicity

<table>
<thead>
<tr>
<th>ANC (x 10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose (Day 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1 and &gt; 100</td>
<td>&gt; 100</td>
<td>100%</td>
</tr>
<tr>
<td>&lt; 1.0 or &lt; 100</td>
<td>&lt; 100</td>
<td>Delay for 1 week</td>
</tr>
</tbody>
</table>

Consider decreasing to 75% if an episode of febrile neutropenia* occurs with the prior cycle of treatment.

*May consider the use of G-CSF in adjuvant therapy after an episode of febrile neutropenia or neutropenic sepsis.

Renal and Hepatic Impairment:

Table 2: Dose modification of epiRUBicin and cycloPHOSphamide in renal and hepatic impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>epiRUBicin</td>
<td>Dose reduction may need to be considered where CrCl &lt;10ml/min. Clinical decision.</td>
<td>Bilirubin (micromol/L)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24-51</td>
</tr>
<tr>
<td></td>
<td></td>
<td>51-85</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;85</td>
</tr>
<tr>
<td>cycloPHOSphamide</td>
<td>CrCl (mL/min)</td>
<td>Dose</td>
</tr>
<tr>
<td>≥ 20</td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>10-20</td>
<td></td>
<td>75%</td>
</tr>
</tbody>
</table>

NCCP Regimen: EC (90-600) Therapy-21 day
Published: 29/04/2015
Review: 12/05/2026
Version number: 7
Tumour Group: Breast
NCCP Protocol Code: 00262
ISMO Contributor: Prof Maccon Keane
Page 3 of 6
SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Potency</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>epiRUBicin</td>
<td>High</td>
<td>(Refer to local policy)</td>
</tr>
<tr>
<td>cycloPHOSphamide</td>
<td>High</td>
<td>(Refer to local policy)</td>
</tr>
</tbody>
</table>

PREMEDICATIONS: None usually required

OTHER SUPPORTIVE CARE:

Patients should have an increased fluid intake of 2-3 litres on day 1 to prevent haemorrhagic cystitis associated with cycloPHOSphamide.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated appropriately.
- **Extravasation**: epiRUBicin causes pain and tissue necrosis if extravasated (Refer to local extravasation guidelines).
- **Cardiac Toxicity**: Clinical cardiac assessment is required prior to epiRUBicin if cardiac function is equivocal and recommended at any time if clinically indicated with a formal evaluation of LVEF.

DRUG INTERACTIONS:

- CYP3A inhibitors decrease the conversion of cycloPHOSphamide to both its active and inactive metabolites. Patients should also be counselled with regard to consumption of grapefruit juice.
- CYP3A inducers may also increase the conversion of cycloPHOSphamide to both its active and inactive metabolites.
- Current drug interaction databases should be consulted for more information.
REFERENCES:


<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Approved By</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29/04/2015</td>
<td></td>
<td>Dr Maccon Keane</td>
</tr>
<tr>
<td>2</td>
<td>14/06/2017</td>
<td>Updated title, clarified administration order and dosing in renal and hepatic impairment, applied new NCCP regimen template</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>3</td>
<td>19/06/2019</td>
<td>Treatment table standardised. Tallman lettering</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>4</td>
<td>16/08/2019</td>
<td>Amended dosing in renal impairment.</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>5</td>
<td>27/12/2019</td>
<td>Updated recommendations in hepatic impairment</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>6</td>
<td>12/05/2021</td>
<td>Reviewed. Amended emetogenic potential.</td>
<td>Prof Maccon Keane</td>
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<tr>
<td>7</td>
<td>15/09/2023</td>
<td>Amended emetogenic potential.</td>
<td>Prof Maccon Keane</td>
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1 Cardiotoxicity is a risk associated with anthracycline therapy that may be manifested by early (acute) or late (delayed) effects.

Risk factors for developing anthracycline-induced cardiotoxicity include:

• high cumulative dose, previous therapy with other anthracyclines or anthracenediones
• prior or concomitant radiotherapy to the mediastinal/pericardial area
• pre-existing heart disease
• concomitant use of other potentially cardiotoxic drugs

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