ERIBULIN for locally advanced or metastatic breast cancer

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily dose</th>
<th>Route</th>
<th>Diluent</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 &amp; 8</td>
<td>Sodium chloride 0.9%</td>
<td>500ml</td>
<td>IV infusion</td>
<td></td>
<td>Fast running</td>
</tr>
<tr>
<td></td>
<td>Metoclopramide</td>
<td>10mg</td>
<td>Oral</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Eribulin</td>
<td>1.23 mg/m²</td>
<td>Fast IV infusion</td>
<td>100ml sodium chloride 0.9%</td>
<td>Over 2-5 mins</td>
</tr>
</tbody>
</table>

**DOSING INFORMATION (Caution confusing wording)**

Eribulin is supplied as vials labelled ‘each 2ml vial contains 0.88mg Eribulin (as Mesylate)’ which refers to the active substance (eribulin) and is equivalent to 1mg eribulin mesylate.

The product SPC recommends ‘In the EU the recommended dose refers to the base of the active substance (eribulin). Calculation of the individual dose to be administered to a patient must be based on the strength of the ready to use solution that contains 0.44 mg/ml eribulin and the dose recommendation of 1.23 mg/m²’

Note on dose rounding the reduced dose listed in SPC 0.97 mg/m² and 0.62 mg/m² have been rounded in this protocol for ease of prescribing to 1 mg/m² and 0.6 mg/m²

**CYCLE LENGTH AND NUMBER OF DAYS**

21 day cycle Day 1 & Day 8

**APPROVED INDICATION**

For use as monotherapy treatment of patients with locally advanced or metastatic breast cancer who have progressed after at least two chemotherapeutic regimens for advanced disease (which may include an anthracycline, or capecitabine).

**EXCLUSION CRITERIA**

First and second line treatment
Severe hepatic or renal impairment
Previous hypersensitivity to Eribulin
Pre-existing significant peripheral neuropathy.

**PREMEDICATION**

Metoclopramide oral as above

**RECOMMENDED TAKE HOME MEDICATION**

Metoclopramide 10 three times daily as required
*Suggested antiemetic regimen - may vary with local practice. See CINV policy for more details*

**INVESTIGATIONS / MONITORING REQUIRED/ CRITICAL TESTS**

FBC, U&E and LFT’s prior to each cycle
FBC Day 8: Limits ANC values ≥ 1.5 x 10⁹ and platelets ≥ 100 x 10⁹
ECG monitoring in selected patients (known congestive cardiac failure, bradyarrythmias, drugs known to prolong QT interval)

**ASSESSMENT OF RESPONSE**

Metastatic: Tumour size and patient symptomatic response
ERIBULIN for locally advanced or metastatic breast cancer

REVIEW BY CLINICIAN
To be reviewed by either a Nurse, Pharmacist or Clinician before every cycle.

NURSE / PHARMACIST LED REVIEW
On day 8 each cycle

ADMINISTRATION NOTES
There is no evidence that eribulin is a vesicant or irritant

TOXICITIES
- Nausea/vomiting
- Myelosuppression (Neutropenia common)
- Anorexia/weight loss
- Constipation/diarrhoea
- Peripheral Neuropathy
- Fatigue
- Alopecia
- QT interval prolongation (see monitoring)
- Arthralgia/myalgia
- Headache/backache
- Cough/dyspnoea
- Pyrexia

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

Day One and Day Eight:
- Day 1: Delay 1 week if neutrophil count < 1.5, plts < 100, unless directed by an oncology specialist.
- Day 8: patients whose bloods are not at the required level will miss that dose and proceed to the next cycle of treatment as planned
- If Hb < 10 & patient symptomatic will need blood transfusion, but may proceed with chemotherapy as planned if performance status (PS) stable.

Non-Haematological Toxicity:
- If pre-treatment U&E’s & LFT’s abnormal, delay treatment 1 week and discuss with Oncologist as may need dose reduction, On Day 8 patient will miss that dose and proceed to next dose of chemotherapy as planned.
- Patients with painful peripheral neuropathy or functional impairment - delay and discuss with Oncologist.
- If PS deteriorates to 3 or 4 and on assessment patient is more symptomatic withhold treatment and discuss with Oncologist

Dose reduction recommendations

<table>
<thead>
<tr>
<th>Adverse reaction after previous Eribulin</th>
<th>Recommended dose reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematological:</td>
<td></td>
</tr>
<tr>
<td>ANC &lt; 0.5 x 10^9/l lasting more than 7 days</td>
<td></td>
</tr>
<tr>
<td>ANC &lt; 1 x 10^9/l neutropenia complicated by fever or Infection</td>
<td>1 mg/m² (75%)</td>
</tr>
<tr>
<td>Platelets &lt; 25 x 10^9/l thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td>Platelets &lt; 50 x 10^9/l thrombocytopenia complicated by haemorrhage or requiring blood or platelet transfusion</td>
<td></td>
</tr>
<tr>
<td>Non-haematological:</td>
<td></td>
</tr>
<tr>
<td>Any Grade 3 or 4 in the previous cycle</td>
<td></td>
</tr>
</tbody>
</table>
ERIBULIN for locally advanced or metastatic breast cancer

Reoccurrence of any haematological or non haematological adverse reactions as specified above

<table>
<thead>
<tr>
<th></th>
<th>Recommended dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Despite reduction to 1 mg/m²</td>
<td>0.6 mg/m² (50%)</td>
</tr>
<tr>
<td>Despite reduction to 0.6 mg/m²</td>
<td>Consider discontinuation</td>
</tr>
</tbody>
</table>

Do not re-escalate the eribulin dose after it has been reduced.

**Impaired liver function due to metastases:**
- The recommended dose of eribulin in patients with mild hepatic impairment (Child-Pugh A - see appendix 1) is **1 mg/m²** administered intravenously over 2 to 5 minutes on Days 1 and 8 of a 21-day cycle.
- The recommended dose of eribulin in patients with moderate hepatic impairment (Child-Pugh B) is **0.6 mg/m²** administered intravenously over 2 to 5 minutes on Days 1 and 8 of a 21-day cycle.
- Severe hepatic impairment (Child-Pugh C) routine usage **not recommended** as it has not been studied.

**Patients with renal impairment**
Some patients with moderately or severely impaired renal function (creatinine clearance <50 ml/min) may have increased eribulin exposure. Caution and close safety monitoring is advised and consideration should be made to reducing the dose.

**TREATMENT LOCATION**
Can be given at Cancer Centre or Cancer Unit

**REFERENCES:**

**APPENDIX 1**
Assigning a Child-Pugh score (for an adult patient)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Score</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Mild</td>
<td>Moderate or Severe</td>
<td></td>
</tr>
<tr>
<td>Encephalopathy (grade)</td>
<td>None</td>
<td>1-2</td>
<td>3-4</td>
<td></td>
</tr>
<tr>
<td>Bilirubin (micromole/L)</td>
<td>&lt;35</td>
<td>35-50</td>
<td>&gt;50</td>
<td></td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>&gt;35</td>
<td>28-35</td>
<td>&lt;28</td>
<td></td>
</tr>
<tr>
<td>INR</td>
<td>&lt;1.7</td>
<td>1.8-2.3</td>
<td>&gt;2.3</td>
<td></td>
</tr>
</tbody>
</table>

**Child-Pugh Score**
- 5-6: Indicates a well functioning liver = Grade A
- 7-9: Indicates significant functional compromise = Grade B
- 10-15: Indicates decomposition of the liver = Grade C
# ERIBULIN for locally advanced or metastatic breast cancer

## Document Control

<table>
<thead>
<tr>
<th>Document Title:</th>
<th>Eribulin protocol CRP11 B0026</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Document No:</strong></td>
<td>CRP11 B0026</td>
</tr>
<tr>
<td><strong>Current Version:</strong></td>
<td>4.3</td>
</tr>
<tr>
<td><strong>Reviewer:</strong></td>
<td>Chris Beck Chemotherapy Pharmacist Northern Cancer Alliance</td>
</tr>
<tr>
<td><strong>Date Approved:</strong></td>
<td>28.02.18</td>
</tr>
<tr>
<td><strong>Approved by:</strong></td>
<td>Steve Williamson Consultant Pharmacist Northern Cancer Alliance</td>
</tr>
<tr>
<td><strong>Due for Review:</strong></td>
<td>01.03.21</td>
</tr>
</tbody>
</table>

## Summary of Changes

- **2.0**: Updated dosing to mesylate and added caution regarding dosing
- **3.0**: Confirmed dosing recommendations
- **4.0**: Final version (10.2.12)
- **4.1**: Addition of ‘bolus’ option as well as bag.
- **4.2**: Protocol reviewed and reissued, Antiemetic advice updated
- **4.3**: Antiemetics & parameters updated from chemocare
  Updated approval criteria and Alliance references