## Breast Pathway Group – Eribulin in Advanced Breast Cancer

**Indication:** Treatment of advanced breast cancer in patients who have progressed after at least 2 prior chemotherapy regimens for advanced disease.

National Cancer Drug Fund application and approval is required prior to starting treatment.

**Regimen details:**
- **Eribulin** 1.23mg/m^2 IV Day 1 & 8

**Administration:**
- In 50-100ml Sodium Chloride 0.9% over 5 minutes

**Frequency:**
- Days 1 and 8, every 21 days, until progression

**Pre-medications:**
- Not routinely required

**Anti-emetics:**
- Low-moderate emetogenicity
- Follow Local Anti-emetic Policy

**Supportive medication:**
- Not routinely required

**Extravasation:**
- Non-vesicant

**Regular investigations:**
- Prior to cycle 1
  - FBC Day 1 (within 14 days)
  - LFTs Day 1 (within 14 days)
  - U&Es Day 1 (within 14 days)
  - ECG & electrolytes Baseline & periodically as appropriate (see comments: QT prolongation)

- Prior to Day 8 (all cycles):
  - FBC Day 8 (within 48 hours)

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**Disclaimer:** The Joint Delivery Chemotherapy Nurse/Oncology Pharmacist Group is a sub-group of the Medicines & Chemotherapy Steering Group (MCSG) working within the London Cancer Alliance Integrated Cancer System (LCA). The output of the LCA MCSG includes documentation that can be adopted by healthcare organisations at their discretion. It is the responsibility of each individual organisation to ensure that appropriate governance and safety clearance procedures within their own clinical service have been followed prior to implementation of any such pieces of work. LCA assume no responsibility for this process within individual organisations, and no responsibility for the clinical management of individual patients or patient groups. Any clinical queries regarding individual patients or documentation should be directed to the relevant clinical team within the most appropriate healthcare organisation.

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Breast Pathway Group – Eribulin in Advanced Breast Cancer

Prior to Day 1 (all cycles):
- FBC
- LFTs
- U&Es
- CT scan

Day 1 (within 72 hours)

Day 1 (within 72 hours)

Day 1 (within 72 hours)

Every 3 cycles

Toxicities: Neutropenia, leucopenia, anaemia, loss of appetite, peripheral neuropathy, headache, nausea, vomiting, pyrexia, GI symptoms, alopecia, arthralgia, myalgia, QT prolongation, lethargy

DOSE MODIFICATIONS

Haematological Toxicity

<table>
<thead>
<tr>
<th>Neutrophils (x $10^9$/L)</th>
<th>Platelets (x $10^9$/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.0</td>
<td>&amp;</td>
<td>100% dose</td>
</tr>
<tr>
<td>&lt; 1.0</td>
<td>or</td>
<td>Delay treatment until recovered to above these levels then reduce according to criteria below as appropriate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neutrophils (x $10^9$/L)</th>
<th>Platelets (x $10^9$/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 0.5 lasting for more than 7 days</td>
<td>≤ 25 thrombocytopenia</td>
<td>Delay until neutrophils ≥ 1.0 x $10^9$/L and platelets ≥ 75 x $10^9$/L then reduce to 0.97mg/m$^2$</td>
</tr>
<tr>
<td>≤ 1.0 complicated by fever or infection</td>
<td>≤ 50 thrombocytopenia complicated by haemorrhage or requiring blood or platelet transfusion</td>
<td>2\textsuperscript{nd} occurrence despite dose reduction</td>
</tr>
</tbody>
</table>

Do not escalate the dose after it has been reduced.

Version: 1.0  Supersedes: all other versions
Approved by LCA Breast Pathway Chemotherapy Lead: Mark Harries November 2014

Reason for Update: LCA Protocol Development
Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl

Prepared by: Lisa Yuen
Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson

Second check by: Laura Cameron
Date prepared: November 2014  Review Date: November 2016

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Non-haematological Toxicities

Renal Impairment

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 40ml/min</td>
<td>1.23mg/m²</td>
</tr>
<tr>
<td>&lt; 40ml/min</td>
<td>Discuss with the Consultant, consider dose reduction</td>
</tr>
</tbody>
</table>

Hepatic Impairment

Impaired liver function due to metastases

<table>
<thead>
<tr>
<th>Degree of Impairment</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild impairment (Child-Pugh A)</td>
<td>Reduce to 0.97mg/m²</td>
</tr>
<tr>
<td>Moderate impairment (Child-Pugh B)</td>
<td>Reduce to 0.62mg/m²</td>
</tr>
<tr>
<td>Severe impairment (Child-Pugh C)</td>
<td>Discuss with the consultant, consider discontinuation</td>
</tr>
</tbody>
</table>

ALT/AST > 3 x ULN (and possibly bilirubin > 1.5 x ULN, limited data) increases the incidence of grade 4 neutropenia and febrile neutropenia.

Monitor carefully if liver impairment is due to cirrhosis, doses may require further re-adjustment.

Child-Pugh Classification:

<table>
<thead>
<tr>
<th>Score</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin (μmol/L)</td>
<td>&lt; 34</td>
<td>34 - 50</td>
<td>&gt; 50</td>
</tr>
<tr>
<td>Albumin</td>
<td>&gt; 35</td>
<td>28 - 35</td>
<td>&lt; 28</td>
</tr>
<tr>
<td>PT (seconds prolonged)</td>
<td>&lt; 4</td>
<td>4 - 6</td>
<td>&gt; 6</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>none</td>
<td>mild</td>
<td>marked</td>
</tr>
<tr>
<td>Ascites</td>
<td>none</td>
<td>mild</td>
<td>marked</td>
</tr>
</tbody>
</table>

If there is primary biliary cirrhosis or sclerosing cholangitis then bilirubin is classified as < 68 = 1; 68 – 170 = 2; > 170 = 3.

The individual scores are summed and then grouped as:

- < 7 = A
- 7 – 9 = B
- > 9 = C
**Dose modifications for other toxicities**

<table>
<thead>
<tr>
<th>Non-haematological toxicities including peripheral neuropathy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Grade 3 or 4 toxicities in the previous cycle – first occurrence</td>
<td>Delay until recovered to &lt;Grade 2 then reduce to 0.97mg/m²</td>
</tr>
<tr>
<td>2(^{nd}) occurrence despite dose reduction</td>
<td>Reduce to 0.62mg/m²</td>
</tr>
<tr>
<td>3(^{rd}) occurrence despite dose reduction</td>
<td>Consider discontinuation</td>
</tr>
</tbody>
</table>

**Location of regimen delivery:**
Outpatient setting

**Comments:**
Contains small amount of ethanol (less than 100mg/ dose)
Eribulin may cause dizziness and may affect the ability to drive or use machines on the day of treatment.

**QT Prolongation**
ECG monitoring is recommended in patients with congestive cardiac failure, bradyarrhythmias, other medication known to prolong QT interval (including class Ia and III antiarrhythmics) and electrolyte abnormalities. Hypokalaemia and hypomagnesemia should be corrected prior to initiating treatment and monitored periodically. Avoid eribulin in patients with congenital long QT syndrome.

**Drug interactions:**
Concomitant administration of substances which inhibit hepatic transport proteins such as organic anion-transporting proteins, p-glycoprotein or multidrug resistant proteins. Transport inhibitors include (but are not limited to) cyclosporin, ritonavir, saquinavir, lopinavir; and protease inhibitors efavirenz, emtricitabine, verapamil, clarithromycin, quinine, quinidine, disopyramide etc. Concomitant administration with enzyme inducers such as rifampicin, carbamazepine, phenytoin, St John’s Wort is not recommended.
Eribulin may inhibit CYP3A4 enzyme.

**References:**


**LCA Breast Cancer Clinical Guidelines October 2013**