Indication: Locally advanced or metastatic breast cancer
- Progression after at least two chemotherapy regimens for advanced disease
- Prior therapy should have included an anthracycline and a taxane unless these were unsuitable treatment options

LCNDG criteria to be met:
- Progression within 6 months of last chemotherapy
- ECOG PS ≤ 2

Ensure funding is confirmed before treatment initiation.

Regimen details: Eribulin 1.23mg/m² (1.4 mg/m² Eribulin mesylate) IV D1 and D8

Administration: Eribulin is supplied as ready to use solution, administer IV over 2-5 minutes
May be diluted in 100ml Sodium Chloride 0.9% solution for injection

Frequency: Days 1 and 8, every 21 days

Extravasation: Non vesicant

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

Regular investigation: FBC D1 and D8
LFTs D1
U&Es D1
ECG & electrolytes Pre-treatment & periodically when appropriate (see QT prolongation section)

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

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.

DOSE MODIFICATIONS

Haematological Toxicity, Day 1 and Day 8

WBC < 3.0 x 10⁹/L or Neutrophils < 1.0 x 10⁹/L or Platelets < 75 x 10⁹/ L Delay for 1 week.
See dose reduction table below for haem & non-haem toxicities for next cycle when appropriate.
Do not administer next dose until FBC has recovered to these values.
Omit Day 8. dose if not recovered within 2 weeks.
Haematological & Non-haematological dose reductions for subsequent cycles:

<table>
<thead>
<tr>
<th>Adverse reaction after previous administration</th>
<th>Recommended dose (once any toxicity recovered to normal values following delay)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haematological:</strong></td>
<td></td>
</tr>
<tr>
<td>Neutrophils &lt; 0.5 x 10⁹/L</td>
<td>0.97mg/m²</td>
</tr>
<tr>
<td>Neutrophils &lt; 1.0 x 10⁹/L, Neutropenia complicated by fever or infection</td>
<td>0.97mg/m²</td>
</tr>
<tr>
<td>Platelets &lt; 25 x 10⁹/L thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td>Platelets &lt; 50 x 10⁹/L thrombocytopenia complicated by haemorrhage or requiring blood or platelet transfusion</td>
<td>0.97mg/m²</td>
</tr>
<tr>
<td><strong>Non- Haematological:</strong></td>
<td></td>
</tr>
<tr>
<td>Any Grade 3 or 4 in the previous cycle</td>
<td>0.97mg/m²</td>
</tr>
<tr>
<td>Re-occurrence of any haematological or non-haematological adverse reactions as specified above</td>
<td>0.97mg/m²</td>
</tr>
<tr>
<td>Despite reduction to 0.97mg/m²</td>
<td>0.62mg/m²</td>
</tr>
<tr>
<td>Despite reduction to 0.62mg/m²</td>
<td>Consider discontinuation</td>
</tr>
</tbody>
</table>

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

**Renal Impairment**

No specific dose adjustments are recommended for patients with mild to moderate renal impairment.
Discuss with the consultant, or consider discontinuation if Creatinine Clearance < 40ml/min.

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>Eribulin dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40ml/min</td>
<td>Discuss with the consultant, consider discontinuation</td>
</tr>
</tbody>
</table>

**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Hepatic impairment</th>
<th>Eribulin dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild impairment (Child Pugh A)</td>
<td>0.97mg/m²</td>
</tr>
<tr>
<td>Moderate impairment (Child Pugh B)</td>
<td>0.62mg/m²</td>
</tr>
<tr>
<td>Severe impairment (Child Pugh C)</td>
<td>Discuss with the consultant, consider discontinuation</td>
</tr>
</tbody>
</table>

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

ALT or AST > 3 x ULN (and possibly Bilirubin > 1.5 x ULN, limited data) increases the incidence of Grade 4 neutropenia and febrile neutropenia.

**Dose modifications for other toxicities as appropriate**

**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 Eribulin treatment.
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) cyclosporine, 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:  
www.medicines.org.uk,  
www.micromedex.com  
CDF SELCN documentation, Sept-2011  
Vahdat L. T et al. J Clin Oncol (2009); 27 (18) 2954-2961