LONDON CANCER ALLIANCE
West and South

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-medication:	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)

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

Prior to Day 1 (all cycles):

FBC	Day 1 (within 72 hours)
LFTs	Day 1 (within 72 hours)
U&Es	Day 1 (within 72 hours)
CT scan	Every 3 cycles

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

DOSE MODIFICATIONS

Haematological Toxicity

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Dose
≥ 1.0	&	≥ 75	100% dose
< 1.0	or	< 75	Delay treatment until recovered to above these levels then reduce according to criteria below as appropriate

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Dose
≤ 0.5 lasting for more than 7 days	or	≤ 25 thrombocytopenia	Delay until neutrophils ≥ 1.0 x 10^9/L and platelets ≥ 75 x 10^9/L then reduce to 0.97mg/m^2
≤ 1.0 complicated by fever or infection		≤ 50 thrombocytopenia complicated by haemorrhage or requiring blood or platelet transfusion	
2nd occurrence despite dose reduction			Delay until neutrophils ≥ 1.0 x 10^9/L and platelets ≥ 75 x 10^9/L then reduce to 0.62mg/m^2
3rd occurrence despite dose reduction			Consider discontinuation

Do not escalate the dose after it has been reduced.

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Non-haematological Toxicities

Renal Impairment

Creatinine Clearance	Dose
> 40ml/min	1.23mg/m^2
< 40ml/min	Discuss with the Consultant, consider dose reduction

Hepatic Impairment

Impaired liver function due to metastases

Degree of Impairment	Dose
Mild impairment (Child-Pugh A)	Reduce to 0.97mg/m^2
Moderate impairment (Child-Pugh B)	Reduce to 0.62mg/m^2
Severe impairment (Child-Pugh C)	Discuss with the consultant, consider discontinuation

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:

Score	1	2	3
Bilirubin (µmol/L)	< 34	34 - 50	> 50
Albumin	> 35	28 - 35	< 28
PT (seconds prolonged)	< 4	4 - 6	> 6
Encephalopathy	none	mild	marked
Ascites	none	mild	marked

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

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Dose modifications for other toxicities

Non-haematological toxicities including peripheral neuropathy	**Dose**
Any Grade 3 or 4 toxicities in the previous cycle – first occurrence	Delay until recovered to <Grade 2 then reduce to 0.97mg/m^2
2nd occurrence despite dose reduction	Reduce to 0.62mg/m^2
3rd occurrence despite dose reduction	Consider discontinuation

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 abnomalities. 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:

Eisai Ltd. 2013. Summary of product characteristics: Halaven (eribulin). Available at www.medicines.org.uk [accessed 07/11/2013]

Cortes J. et al. Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomised study. *Lancet* 2011; 377: 914–23

LCA Breast Cancer Clinical Guidelines October 2013