EriBULin Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement status
Treatment of locally advanced or metastatic breast cancer which has progressed after at least one chemotherapeutic regimens for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless patients were not suitable for these treatments.	C50	00228a	ODMS 1/1/2014

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 patients individual clinical circumstances.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1 and 8	[a, b]eriBULin	1.23mg/m^2	IV infusion	[c]100ml 0.9% sodium chloride over 5 minutes	Repeat every 21 days

[a]Note: eriBULIn may be used in combination with trastuzumab therapy (Ref NCCP Regimen 00200 Trastuzumab (IV) Monotherapy -21 days)

[b]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/m^2.

The dose reduction recommendations shown below (Table 1, 2 and 3) are also shown as the dose of eriBULin to be administered based on the strength of the ready to use solution.

In the pivotal EMBRACE trial, the corresponding publication and in some other regions e.g. the US and Switzerland, the recommended dose is based on the salt form (eriBULin mesylate). The equivalent dose of eriBULin mesylate is 1.4mg/m^2

[c]EriBULin should not be diluted in 5% glucose.

ELIGIBILITY:

- Indications as above
- ECOG 0-2
- Platelets > 100 x 10^9/L and ANC ≥ 1.5x10^9/L

EXCLUSIONS:

- Hypersensitivity to eriBULin or to any of the excipients
- Breast feeding
- Congenital long QT syndrome

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile
- ECG monitoring if therapy initiated in patients with congestive heart failure, bradyarrhythmias, medicinal products known to prolong the QT interval, including Class Ia and III antiarrhythmics, and electrolyte abnormalities.

Regular tests:

- FBC, renal and liver profile at the start of each cycle.
- ECG monitoring if clinically indicated as above.

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.
- The administration of eriBULin should be delayed on day 1 or day 8 for any of the following:
  - ANC < 1 x 10^9/L
  - Platelets < 75 x 10^9/L
  - Grade 3 or 4 non-haematological toxicities

Thereafter the dose modifications in table 1 apply

Haematological:

Table 1: Dose modification of eriBULin in haematological toxicity

ANC (x10^9/L)	**Dose**
<0.5 lasting > 7 days	0.97mg/m^2
<1. complicated by fever or infection	
Platelets(x10^9/L)	
< 25	
< 50 complicated by haemorrhage or requiring blood or platelet transfusion	
Reoccurrence of any haematological adverse reactions as specified above	
Despite reduction to 0.97mg/m^2	0.62mg/m^2
Despite reduction to 0.62mg/m^2	Consider discontinuation
Do not re-escalate the eriBULin dose after it has been reduced.	

Renal and Hepatic Impairment:

Table 2: Dose modification of eriBULin in renal and hepatic impairment

Renal Impairment		Hepatic Impairment	
Cr Cl (ml/min)	**Dose**		**Dose**
<50ml/min	Patients may have increased eriBULin exposure and may need a reduction of the dosage. For all patients with renal impairment, caution and close safety monitoring is advised	Mild (Child-Pugh A)	0.97mg/m^2
		Moderate (Child-Pugh B)	0.62mg/m^2
		Severe	Has not been studied Expect more marked reduction required if eriBULin is used in these patients

Management of adverse events:

Table 3: Dose Modification of eriBULin for Adverse Events

Adverse reactions	Recommended dose modification
Grade 3 or 4 non haematological toxicity in previous cycle.	Reduce dose from 1.23mg/m^2 to 0.97mg/m^2. If there is any reoccurrence despite the dose reduction, reduce dose further to 0.62mg/m^2. If there is any reoccurrence despite dose reduction to 0.62mg/m^2, consider discontinuation.. Do not re-escalate the eriBULin dose after it has been reduced.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Low **(Refer to local policy).**

PREMEDICATIONS: Not usually required

OTHER SUPPORTIVE CARE:

- Severe neutropenia may be managed by the use of G-CSF.
- EriBULin may cause adverse reactions such as tiredness and dizziness which may lead to a minor or moderate influence on the ability to drive or use machines. Patients should be advised not to drive or use machines if they feel tired or dizzy.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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

- **Haematology:** Myelosuppression is dose dependent and manifests primarily as neutropenia. Patients experiencing febrile neutropenia, severe neutropenia or thrombocytopenia should be treated according to the recommendations in table 1 above. Patients with ALT or AST >3 x ULN experienced a higher incidence of Grade 4 neutropenia and febrile neutropenia. Although data are limited, patients with bilirubin >1.5 x ULN also have a higher incidence of Grade 4 neutropenia and febrile neutropenia.
- **Peripheral neuropathy:** Patients should be closely monitored for signs of peripheral motor and sensory neuropathy. The development of severe peripheral neurotoxicity requires a delay or reduction of dose.
- **QT prolongation:** In an uncontrolled open-label ECG study in 26 patients, QT prolongation was observed on Day 8, independent of eriBULin concentration, with no QT prolongation observed on Day 1. ECG monitoring is recommended if therapy is initiated in patients with congestive heart failure, bradyarrhythmias, medicinal products known to prolong the QT interval, including Class Ia and III anti-arrhythmics, and electrolyte abnormalities. Hypokalemia, hypocalcaemia or hypomagnesaemia should be corrected prior to initiating eriBULin and these electrolytes should be monitored periodically during therapy.

DRUG INTERACTIONS:

- Possible risk of drug interactions causing decreased concentrations of eriBULin with CYP3A inducers.
- Increased risk of QT prolongation with drugs that disrupt electrolyte levels and Class Ia and III anti-arrhythmics.
- Current drug interaction databases should be consulted for more information.

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Version	Date	Amendment	Approved By
1	20/12/13		Dr Cathy Kelly
2	15/9/15	Update of dose modification in renal impairment as per change to SmPC	Dr Maccon Keane
3	4/11/15	Update of indication based on change to SmPC to allow treatment after one previous chemotherapeutic regimen	Dr Maccon Keane
4	15/11/17	Applied new NCCP regimen template, Updated Title and included equivalent dose of eriBULin mesylate	Prof Maccon Keane
5	22/5/19	Standardisation of treatment table. Update on use of eriBULin with trastuzumab. Updated adverse effects/ regimen specific complications as per update in SmPC for QT prolongation.	Prof Maccon Keane
6	28/04/21	Reviewed. Amended Management of adverse effects (Table 3), updated drug interactions.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.