Regimen Monograph

A - Regimen Name

ERIB Regimen

eriBULin

Disease Site	Breast
Intent	Palliative
Regimen Category	**Evidence-Informed :** Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.
Rationale and Uses	Treatment of metastatic or incurable locally advanced breast cancer patients meeting the following criteria: • have had previous treatment with a taxane and an anthracycline, and • whose disease has progressed following at least two chemotherapy regimens for metastatic or locally recurrent disease, and • whose disease has progressed after the last therapy, and • have good performance status (ECOG ≤2)
Supplementary Public Funding	**eriBULin** New Drug Funding Program (Eribulin - Metastatic or Incurable Locally Advanced - Breast Cancer) (NDFP Website)

back to top

B - Drug Regimen

eriBULin[1]	1.4 mg /m²	IV	Days 1 and 8

[1] as eriBULin mesylate

back to top

C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until disease progression, no evidence of further response, or unacceptable toxicity.

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Low

back to top

E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations have been adapted from clinical trials or product monographs and could be considered. Do not start the first dose until platelets are > 100 x 10^9/L and ANC ≥ 1.5 x 10^9/L. Correct electrolyte abnormalities prior to treatment, especially potassium, calcium and magnesium. Do not re-escalate a dose reduced for toxicity.

Starting Dose *	Dose level -1 *	Dose level -2 *	Dose level -3 *
1.4 mg/m^2	1.1 mg/m^2	0.7 mg/m^2	Discontinue

*as eriBULin mesylate

Dosage with toxicity

Dose adjustments on Day 1 or Day 8:

Worst toxicity in previous period / on day of dosing	**Day 1***	**Day 8 */#**
Platelets < 75-100 x 10^9/L or ANC <1-1.5 x 10^9/L on day of dosing	Do not treat *	Delay for one week; if no recovery, omit for that cycle
Grade 4 ANC > 7 days, Grade 4 thrombocytopenia, Febrile neutropenia, Platelets < 50 requiring transfusion or Thrombocytopenic bleeding	Hold until recovered*, then ↓ 1 dose level	Delay for one week; if no recovery, omit for that cycle
≥ grade 3 non-hematologic	Hold until recovered*, then ↓ 1 dose level	Delay for one week until ≤ grade 2; if no recovery, omit for that cycle
Delay or dose modification for day 8 in previous cycle	↓ one dose level for all subsequent doses	
* Do not treat until ANC ≥ 1 x 10^9/L and platelets ≥ 75 x 10^9/L and other toxicity ≤ grade 2. # If delay day 8, the cycle length is also increased (next cycle must be ≥2 weeks after the delayed "day 8").		

Hepatic Impairment

eriBULin exposure is increased in mild and moderate hepatic impairment. Starting doses should be reduced and patients monitored closely for toxicity.

Hepatic function	**Recommended Dose on Days 1 and 8 (mg/m^2)**
Normal (bilirubin < 1.5 x ULN, transaminases ≤ 3 x ULN)	1.4
Mild impairment (Child Pugh A)	1.1
Moderate impairment (Child Pugh B)	0.7
Severe impairment (Child Pugh C)	OMIT

Renal Impairment

Mild or moderate renal impairment may decrease eriBULin clearance. Exposure may increase up to 1.5-fold in moderate or severe renal impairment. Monitor for adverse effects, especially myelosuppression.

Renal impairment	Starting dose
Mild (50-80 mL/min)	No change in starting dose
Moderate or severe (15-50 mL/min)	Caution; ↓ starting dose to 1.1 mg/m^2
End-stage (<15 mL/min)	No data; OMIT

Dosage in the Elderly

No dose adjustments required.

back to top

F - Adverse Effects

Refer to eribulin drug monograph(s) for additional details of adverse effects

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Increased LFTs (may be severe) • Myelosuppression +/- infection, bleeding (may be severe) • Fatigue	• Alopecia • Abnormal electrolytes • Nausea, vomiting • Neuropathy (may be severe) • Constipation	• Musculoskeletal pain • Anorexia, weight loss • Headache • Diarrhea • Cough, dyspnea • Increased creatinine (may be severe)	• Atrial fibrillation • QT prolongation • Venous thromboembolism • Disseminated intravascular coagulation • Rash (SJS, TENS) • Hypersensitivity • Hand-foot

			syndrome • Pancreatitis • Pneumonitis

back to top

G - Interactions

Refer to eribulin drug monograph(s) for additional details

- Avoid drugs that prolong QT interval, where possible. Monitor with ECG if used together.
- Caution and monitor ECG with drugs that disrupt electrolyte levels.
- Caution and monitor for toxicity with inhibitors of P-gp (i.e. quinidine, verapamil, cyclosporine).

back to top

H - Drug Administration and Special Precautions

Refer to eribulin drug monograph(s) for additional details

Administration

- Give IV over 2 to 5 minutes
- Dose may be administered in a syringe without dilution or may dilute in up to 100mL NS.
- Does not require premedications with steroids and/or antihistamines for hypersensitivity.

- Do not admix eriBULin with other medicinal products.
- Do not dilute or administer with dextrose-containing solutions.

- Store unopened vials at room temperature in their original cartons.
- Diluted solutions may be stored for up to 48 hours refrigerated, or for up to 24 hours at room temperature.

Contraindications

- Patients who have a hypersensitivity to this drug, halichondrin B or any of its components
- Severe hepatic impairment
- End-stage renal disease

Precautions

- Avoid use in patients with congenital long QT syndrome.
- Avoid concomitant use of QT-prolonging drugs, where possible (see Drug Interactions).
- Correct any hypocalcemia, hypokalemia and hypomagnesemia prior to starting eriBULin.
- Exercise extreme caution with significant cardiovascular impairment (congestive heart failure > grade 2, unstable angina or myocardial infarction within the last 6 months) as the safety of eriBULin in this population has not been established.
- Use with caution in patients with pre-existing neuropathy as eriBULin may aggravate the condition.

Pregnancy & lactation

- eriBULin is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least 3 months after the last dose. Breastfeeding is not recommended.
- Fertility effects may be irreversible. Male patients should seek advice on conservation of sperm prior to treatment.

back to top

I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Recommended Clinical Monitoring

- CBC; Baseline and before each dose; more frequent in patients who develop severe myelosuppression.
- ECG in patients with risk factors for torsade de pointes (i.e. patients with cardiac disease or concomitant QT-prolonging medications); Baseline and as clinically indicated

- Liver and renal function tests, including electrolytes; Baseline and before each dose
- Clinical toxicity assessment for neuropathy, cardiotoxicity, hepatic, musculoskeletal, fatigue, GI symptoms and thromboembolism; At each visit

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

back to top

J - Administrative Information

Approximate Patient Visit	30 minutes
Pharmacy Workload (average time per visit)	15.15 minutes
Nursing Workload (average time per visit)	36.667 minutes

back to top

K - References

Cortes J, O'Shaughnessy J, Loesch D, 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.

Eribulin drug monograph, Cancer Care Ontario.

January 2018 updated adverse effects; added interactions, admin & precautions

back to top

M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the

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Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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back to top