Eribulin

Indication

Locally advanced or metastatic breast cancer in patients whose disease has progressed after 2 previous chemotherapy regimens for advanced disease. (This may include an anthracycline or a taxane and capecitabine).

(NICE TA423)

ICD-10 codes

Codes pre-fixed with C50.

Regimen details

Day	Drug	Dose	Route
1 and 8	Eribulin	1.23mg/m^2	IV infusion

Note: 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.

Cycle frequency

21 days

Number of cycles

Until disease progression or unacceptable toxicity.

Administration

Eribulin is administered as an IV infusion in 50-100mL sodium chloride 0.9% over 2-5 minutes.

Pre-medication

Nil

Emetogenicity

This regimen has moderate emetic potential.

Additional supportive medication

Antiemetics as per local policy.
H_2 antagonist or PPI, if required, as per local policy.
Mouthwashes as per local policy.

Extravasation

Eribulin is neutral (Group 1)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
Magnesium	14 days
Potassium	14 days

Baseline ECG

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours and within 24 hours of day 8
U+E (including creatinine)	7 days
LFTs	7 days
Magnesium	7 days
Potassium	7 days

ECG as clinically indicated.

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥ 1.5 x 10^9/L* see below for subsequent doses
Platelets	≥ 100 x 10^9/L
Creatinine clearance (CrCl)	≥ 50mL/min
Bilirubin	< 1 x ULN
AST/ALT	< 1.5 x ULN

Low magnesium and potassium should be corrected prior to commencing treatment.

Dose modifications

- **Haematological toxicity**

Prior to cycle 1 day 1, neutrophils must be ≥ 1.5 x 10^9/L and platelets > 100 x 10^9/L.

***For subsequent doses on day 1 or day 8:**
If neutrophils < 1.0 x 10^9/L **or** platelets < 75 x 10^9/L delay for 1 week. If recovered continue with 100% dose.

Reduce dose to **0.97mg/m²** if any of the following occur:
Neutrophils < 0.5 x 10^9/L for > 7 days
Neutrophils < 1.0 x 10^9/L with fever/infection
Platelets < 25 x 10^9/L
Platelets < 50 x 10^9/L with haemorrhage or needing transfusion

Reduce dose to **0.62mg/m²** if toxicity continues despite dose reduction.

Consider discontinuing treatment if toxicity persists despite this dose level.

- **Renal impairment**

Dose reduction is not recommended for patients with mild renal impairment. Close monitoring is required.
If CrCl < 50mL/min a dose reduction may be required (consultant decision).

- **Hepatic impairment**

For patients with impaired liver function due to liver metastases:

Degree of hepatic impairment	Eribulin dose
Mild (Child Pugh A)	0.97mg/m^2
Moderate (Child Pugh B)	0.62mg/m^2
Severe (Child Pugh C)	Consider discontinuing treatment (consultant decision)

Eribulin has not been studied in patients with impaired hepatic function due to cirrhosis. Doses as above may be used with close monitoring.

- **Other toxicities**

Patients should be closely monitored for signs of peripheral neuropathy.

For all grade 3-4 toxicities (except alopecia and nausea and vomiting) withhold until grade ≤ 1 and continue with 0.97mg/m^2 dose.
If further toxicity, consider further dose reduction to 0.62mg/m^2, discuss with consultant.

QT prolongation:
QT prolongation has been associated with eribulin. ECG monitoring is recommended for patients with congestive cardiac failure, bradycardias, electrolyte abnormalities and those who are taking medication known to prolong the QT interval.

Adverse effects - for full details consult product literature/ reference texts

- **Rare or serious side effects**

Myelosuppression
Infertility
Electrolyte disturbances
Hepatotoxicity
QT prolongation

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Diarrhoea, constipation
Peripheral neuropathy
Myalgia, arthralgia
Alopecia
Fatigue
Cough

- **Other side effects**

Reduced appetite
Headache
Insomnia
Depression

Significant drug interactions – for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

Inhibitors of hepatic transport proteins: (including cyclosporin, ritonavir, lopinavir) avoid - may increase eribulin levels leading to toxicity.

Enzyme inducers: (carbamazepine, phenytoin, St Johns Wort) avoid – may reduce plasma levels of eribulin.

Medications known to cause QT prolongation: avoid concomitant use.

Additional comments

References

- Summary of Product Characteristics Eribulin (Eisai) accessed 12 April 2017 via www.medicines.org.uk
- National Institute for Health and Clinical Excellence. TA423 accessed 12 April 2017 via www.nice.org.uk
- Cortes, J et al; Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer Lancet 2011; 377: 914 – 923

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