Pixantrone

Indication
Monotherapy for relapsed / refractory Diffuse Large B-cell Lymphoma (DLBL) as 3rd or 4th line treatment for patients who have previously been treated with rituximab.

(NICE TA306)

ICD-10 codes
Codes with a prefix C83.3

Regimen details

Day	Drug	Dose	Route
Days 1,8 and 15	Pixantrone	50mg/m^2*/day	IV infusion

* (50mg/m^2 is equivalent to 85mg/m^2 pixantrone dimaleate)

Cycle frequency
28 days

Number of cycles
Up to 6 cycles

Administration
Pixantrone should be administered as an IV infusion in sodium chloride 0.9% (final volume 250mL) over a minimum of 60 minutes. (Final concentration < 0.58mg/mL).

Pre-medication
Pre-hydration may be required if bulky disease (e.g. 1000mL sodium chloride 0.9% over 4-6 hours).

Emetogenicity
This regimen has moderate emetic potential.

Additional supportive medication
Allopurinol 300mg OD (100mg OD if CrCl < 20mL/min) for 7 days (cycle 1 only)
Antiemetics as required
Antiviral and antifungal prophylaxis

Extravasation
Pixantrone is an exfoliant.

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+Es (including creatinine)	14 days
LFTs	14 days
LDH	14 days
Calcium	14 days
Magnesium	14 days
Glucose	14 days

ECG +/- echocardiogram
Pregnancy test for women of child bearing potential.

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	96 hours
U+Es (including creatinine)	7 days
LFTs	7 days

Standard limits for administration to go ahead on day 1

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

Investigation	Limit
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 75 x 10^9/L
Creatinine clearance	> 50mL/min
AST/ALT	See below
Bilirubin	See below

Dose modifications

- **Haematological toxicity**

On **day 1** if neutrophils <1.0 x 10^9/L or platelets < 75 x 10^9/L treatment should be delayed until recovery.

Doses on day 8 and 15 should be modified as below:

Day 8 and 15:

Neutrophils (x 10^9/L)		**Platelets** (x 10^9/L)	**Pixantrone dose**
> 1.0	And	> 50	100%
0.5-1.0	Or	25-50	Delay until neutrophils ≥1.0 x 10^9/L and platelets ≥ 50 x 10^9/L
< 0.5	Or	< 25	Delay until neutrophils ≥1.0 x 10^9/L and platelets ≥ 50 x 10^9/L Reduce dose to 80%

- **Renal impairment**

Pixantrone has not been studied in renal impairment, therefore use with caution.

- **Hepatic impairment**

Pixantrone has not been studied in patients with hepatic impairment. Use with caution in mild-moderate hepatic impairment and not recommended in severe hepatic impairment.

- **Other toxicities**

Cardiac toxicity:
If any grade 3-4 cardiac toxicity or persistent decline in LVEF: delay treatment until recovery to ≤ grade 1. Consider discontinuing treatment if ≥ 15% decline in LVEF from baseline.

Other toxicity:
Any grade 3-4 non cardiac toxicity: delay until recovery to ≤ grade 1 and recommence with 80% dose.

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

- **Serious side effects**

Myelosuppression
Cardiotoxicity
Tumour lysis syndrome

- **Frequently occurring side effects**

Myelosuppression
Photosensitivity reactions
Anorexia
Taste disturbance
Headache
Dyspnoea, cough
Nausea, vomiting
Altered LFTs

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

No drug interactions have been reported in human subjects and no drug-drug interaction studies in humans have been performed.

Additional comments

This medicinal product contains approximately 1000 mg (43 mmol) sodium per dose after dilution. To be taken into consideration by patients on a controlled sodium diet.
Patients should be advised regarding sun protection due to risk of photosensitivity reactions.

References

- Summary of Product Characteristics Pixantrone (CTI) accessed 10 May 2017 via www.medicines.org.uk
- Eyre TA, et al. Br J Haematol. 2016 Mar 9. doi: 10.1111/bjh.14021. Results of a multicentre UK-wide retrospective study evaluating the efficacy of pixantrone in relapsed, refractory diffuse large B cell lymphoma.
- Pettengell R, et al. Pixantrone dimaleate versus other chemotherapeutic agents as a single-agent salvage treatment in patients with relapsed or refractory aggressive non-Hodgkin lymphoma: a phase 3, multicentre, open-label, randomised trial. Lancet Oncol. 2012 Jul; 13(7):696-706

Written/reviewed by: Dr D Mannari (Consultant Haematologist, Yeovil District Hospital)

Checked by: Sarah Murdoch (Senior Oncology/Haematology Pharmacist, SW Clinical Network)

Authorised by: Dr J Braybrooke (Consultant Oncologist, UHBristol NHS Trust, SW Clinical Network)

Date: June 2017