Bendamustine 120 (Relapsed/refractory NHL)

Indication

Monotherapy for relapsed/refractory non-Hodgkin's lymphoma in patients who have progressed during or within 6 months following treatment with rituximab or a rituximab-containing regimen.

Note: funding should be secured prior to commencing treatment.

There are a number of bendamustine protocols – please ensure this is the correct one for your patient. This protocol should NOT be used in combination with rituximab. Refer to alternative protocol.

ICD-10 codes

Codes with a prefix C88, C82, C83

Regimen details

Day	Drug	Dose	Route
1 and 2	Bendamustine	120mg/m^2	IV infusion

Cycle frequency

21 days

Number of cycles

Up to 6 cycles

Administration

Bendamustine is administered in 500mL sodium chloride 0.9% over 30-60 minutes.

Pre-medication

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

Emetogenicity

This regimen has moderate emetic potential

Additional supportive medication

Allopurinol 300mg OD (100mg OD if CrCl < 20mL/min) for the first 2 weeks. Some patients may require for subsequent cycles. (**Omit allopurinol on days of bendamustine administration** – see interactions section).
Antiviral and PCP prophylaxis as per local policy.

Extravasation

Bendamustine is an irritant (Group 3)

Investigations – pre first cycle

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

Hepatitis B and C serology: HBV serology (aAg and cAb) must be checked before first dose rituximab. Avoid rituximab in active hepatitis B. Consider anti-viral (eg entecavir 500micrograms OD) where there is evidence of past infection.
HIV status.
TP53 mutational status (R-bendamustine has limited efficacy if TP53 mutated)

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC*	72 hours
U+E (including creatinine)	72 hours
LFTs	72 hours

*Serum potassium must be monitored in all patients with cardiac disorders. If serum potassium <3.5mml/L start potassium supplementation and perform an ECG.

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	≥ 1.0 x 10^9/L
Platelets	≥ 100 x 10^9/L
Creatinine clearance (CrCl)	≥ 10ml/min
Bilirubin	≤ ULN

Dose modifications

- **Haematological toxicity**

If neutrophils < 1.0x 10^9/L and/or platelets < 100 x 10^9/L delay treatment until recovery. Consider bendamustine dose reduction – discuss with consultant.

- **Renal impairment**

There is no information regarding use of bendamustine if CrCl ≤ 10mL/min. Discuss with consultant.

- **Hepatic impairment**

Bilirubin (x ULN)	**Bendamustine dose**
≤ ULN	100%
1-3	70%
> 3	Discuss with consultant (no information)

- **Other toxicities**

For any grade 3-4 toxicity (except alopecia) delay treatment until toxicity ≤ grade 1 and consider reducing subsequent bendamustine doses to 50% - discuss with consultant.

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

- **Serious side effects**

Myelosuppression
Cardiotoxicity including arrhythmia
Infertility
Stevens-Johnson syndrome and toxic epidermal necrolysis (bendamustine with allopurinol)
Possible risk of secondary malignancies

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Mucositis, stomatitis
Diarrhoea, constipation
Hypokalaemia
Renal impairment

- **Other side effects**

Raised transaminases
Alopecia
Fatigue
Insomnia
Rash, urticaria

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.

Allopurinol: reports of Stevens-Johnson syndrome and toxic epidermal necrolysis – avoid concurrent administration.

CYP 1A2 inhibitors: metabolism of bendamustine by cytochrome P450 (CYP) 1A2 isoenzyme is a significant route of hepatic clearance so interaction with CYP1A2 inhibitors such as fluvoxamine, ciprofloxacin, aciclovir and cimetidine is possible. May increase toxicity – avoid concomitant use.

Additional comments

Patients must receive irradiated blood products for all future transfusions.

References

- Summary of Product Characteristics Bendamustine (Napp) accessed 9 March 2017 via www.medicines.org.uk
- Weidmann E, et al. Bendamustine is effective in relapsed or refractory aggressive non-Hodgkin's lymphoma. Ann Oncol. 2002 Aug;13(8):1285-9
- Friedberg JW, et al. Bendamustine in patients with rituximab-refractory indolent and transformed non-Hodgkin's lymphoma: results from a phase II multicenter, single-agent study. J Clin Oncol. 2008 Jan 10;26(2):204-10

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