Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Dose Modifications | Adverse Effects | Interactions | Drug Administration and Special Precautions | Recommended Clinical Monitoring | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

BEND Regimen

Bendamustine

Disease Site	Hematologic - Lymphoma - Non-Hodgkin's Low Grade
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	Relapsed indolent B-cell non-Hodgkin Lymphoma (NHL) patients who did not respond to or progressed during or shortly following treatment with a rituximab regimen.

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B - Drug Regimen

bendamustine	120 mg /m²	IV	Days 1 and 2

(This drug is not currently publicly funded for this regimen and intent)

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

For up to 8 cycles unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

Other Supportive Care:

Also refer to CCO Antiemetic Summary

Hypertension should be controlled prior to starting treatment.

Pre-medication (only for patients with Grade 1 or 2 reactions with prior infusion):

- Analgesic/antipyretic (e.g. acetaminophen), corticosteroid and an antihistamine (e.g. diphenhydramine) should be considered in subsequent cycles.

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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 re-escalate after dose modification for toxicity.

Dosage with toxicity

Dose levels: 120 mg/m^2, 90 mg/m^2, 60 mg/m^2

Toxicity	Modification
Grade 4 Hematologic toxicities	Delay until ANC ≥ 1 x 10^9/L, platelets ≥ 75 x 10^9/L then reduce by 1 dose level
≥ Grade 3 Hypersensitivity reaction	Discontinue
≥ Grade 2 clinically significant Non-hematologic toxicities; ≥ Grade 3 Non-hematologic toxicities	Delay until recovered to ≤ grade 1, then reduce by one dose level

Hepatic Impairment

Bilirubin	AST or ALT or ALP	Bendamustine dose
≤ –1.5 x ULN	≤ 2.5 x ULN	Caution
> 1.5 x ULN	> 2.5 x ULN	Do not use

Renal Impairment

Creatinine Clearance (mL/min)	Bendamustine dose
>80	100%
40 - 80	Caution
< 40	Do not use

Dosage in the Elderly

No dose adjustment required. No clinically significant differences in efficacy and safety were observed in those aged 65 and older and younger patients.

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F - Adverse Effects

Refer to bendamustine 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
• Nausea, vomiting • Fatigue	• Diarrhea • Fever, chills • Constipation	• Anorexia, weight loss • Mucositis • Headache	• Arrhythmia, Prolonged QT • Arterial thromboembolism • Cardiotoxicity

		• Edema • Cough, dyspnea (may be severe) • Musculoskeletal pain • Rash (may be severe) • Abdominal pain • Immunosuppression, atypical infections • Abnormal electrolytes • Dizziness • Dysgeusia • Dyspepsia • Insomnia	• Hypertension • Hepatotoxicity • Infusion-related reaction • Renal failure • Secondary malignancy • Tumour lysis sydrome • Myelosuppression • ARDS

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G - Interactions

Refer to bendamustine drug monograph(s) for additional details

- CYP1A2 inhibitors my increase bendamustine concentration and toxicity; use with caution
- CYP1A2 inducers (including cigarette smoking) may reduce bendamustine concentration and/or efficacy

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H - Drug Administration and Special Precautions

Refer to bendamustine drug monograph(s) for additional details

Administration:

- NHL - infuse over 60 minutes
- Bendamustine infusions should be administered in a setting where full resuscitation facilities are immediately available, and under the close supervision of someone experienced and capable of dealing with severe infusion-related reactions.
- DO NOT administer as an IV push or bolus.
- Dilute to a final concentration of 0.2 - 0.6 mg/mL in 500 mL infusion bag of 0.9% sodium

chloride or 2.5% dextrose/0.45% sodium chloride.
- Reconstituted solution must be transferred to infusion bag within 30 minutes of reconstitution.
- Administer bendamustine through a dedicated line.
- Compatible with PVC or polyethylene bags.
- Do not admix with other drugs.

Contraindications:

- Patients who have a hypersensitivity to this drug or any of its components (including mannitol)
- Patients with CrCl < 40 mls/min or moderate/severe hepatic impairment
- Patients with serious infections

Other warnings/precautions:

- Avoid live vaccines, since they may result in serious or fatal infections in patients immunocompromised by bendamustine.
- Avoid in patients with relapsed indolent NHL who did not tolerate prior therapies (including other alkylating agents)
- Use with caution in patients with hypertension and patients with mild renal and hepatic impairment

Pregnancy and lactation:

- Bendamustine is not recommended for use in pregnancy. Adequate contraception should be used by both sexes 2 weeks before, during treatment, and for at least 4 weeks after the last dose.
- Breastfeeding is not recommended

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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 cycle
- Blood pressure; Baseline and before each dose
- Electrolytes, including sodium, potassium, magnesium and uric acid; Baseline and before each cycle
- Hepatitis B surface antigen; Baseline and as clinically indicated
- Liver function tests; Baseline and before each cycle
- Renal function tests; Baseline and before each cycle
- Clinical toxicity assessment for infection (including CMV and herpes zoster), renal, cardiac, hepatic and skin toxicity , infusion reactions and secondary malignancies; at each visit

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

Suggested Clinical Monitoring

- Blood glucose; Baseline and periodic
- ECG; As clinically indicated; periodic in the setting of cardiac disorders and electrolyte imbalances
- HIV status; Baseline
- CMV testing in febrile patients; as clinically indicated

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J - Administrative Information

Approximate Patient Visit	0.5 to 1 hour
Pharmacy Workload (average time per visit)	19.35 minutes
Nursing Workload (average time per visit)	36.667 minutes

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K - References

Bendamustine drug monograph, Cancer Care Ontario.

Garnock-Jones, K. Bendamustine: a review of its use in the management of indolent Non-Hodgkin's Lymphoma and Mantle Cell Lymphoma. Drugs 2010; 70(13):1703-1718.

Van der Jagt R, Lnaeuville P, MacDonald D, *et al*. A Canadian perspective on bendamustine for the tratment of chronic lymphocytic leukemia and non-Hodgkin lymphoma. *Curr Oncol* 2012; 19(3):160-167.

June 2017 added not publicly funded to drug regimen

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M - Disclaimer

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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