Regimen Monograph

A - Regimen Name

BREN Regimen

Brentuximab vedotin

Disease Site

Hematologic
- Lymphoma - Non-Hodgkin's Intermediate Grade
- Lymphoma - T-cell
- Rare Diseases

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 CD30+ primary cutaneous anaplastic large-cell lymphoma (pcALCL) or mycosis fungoides (MF), in patients* who have good performance status

* Patients with MF must have received at least one prior systemic therapy and patients with pcALCL must have at least one prior systemic therapy or prior radiation therapy.

Supplementary Public Funding	**brentuximab vedotin** New Drug Funding Program (Brentuximab Vedotin - Previously Treated Primary Cutaneous Anaplastic Large Cell Lymphoma or Mycosis Fungoides) (NDFP Website)

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B - Drug Regimen

brentuximab vedotin	1.8* mg /kg	IV	Day 1

*Maximum dose 180mg for patients who are ≥ 100 kg

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until disease progression, unacceptable toxicity, or up to a maximum of 16 cycles, whichever comes first

Refer to NDFP form for details on brentuximab vedotin funding in retreatment.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Premedication (Prophylaxis for Infusion Reactions):

- Routine pre-medication is not recommended.
- May consider pre-medication with acetaminophen, H1-receptor antagonist and corticosteroid if an IR has occurred in the past.

Other supportive care:

- Patients at risk of tumour lysis syndrome should have appropriate prophylaxis and be monitored closely.
- Also refer to CCO Antiemetic Recommendations.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

Toxicity	Type / Grade	Brentuximab vedotin dose
Peripheral neuropathy	New or worsening Grade 2 or 3	Hold until improvement to Grade 1 or baseline, then restart at 1.2 mg/kg.^
	Grade 4	Discontinue.
Neutropenia	Grade 3 or 4	Hold until ≤ Grade 2. Consider growth factor support for subsequent cycles.
	Recurrent Grade 4 despite the use of growth factors	Consider discontinuing or reduce dose to 1.2 mg/kg when recovered to ≤ Grade 2.^
Thrombocytopenia	Grade 3 or 4	Monitor closely and consider platelet transfusions or dose delays.
SJS, TEN	Any	Discontinue and manage appropriately.
PML	Suspected, any grade	Hold and investigate; discontinue if confirmed.
Pancreatitis	Suspected, any grade	Hold and investigate; discontinue if confirmed.
Pulmonary symptoms	Any grade	Hold and investigate; consider discontinuing if pneumonitis confirmed.
Tumour lysis syndrome	Suspected, any grade	Hold and manage aggressively. May continue therapy after resolution with adequate preventative measures.
Hepatotoxicity	New, worsening or recurrent	Hold and consider reduced dose. Discontinue if severe.

^Maximum dose: 120 mg (for 1.2mg/kg dose) in patients ≥ 100 kg.

Management of Infusion-Related Reactions:

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Grade	Management	Re-challenge
1 or 2	• Stop or slow the infusion rate. • Manage the symptoms. **Restart:** • The infusion may be restarted at a slower rate once symptoms have resolved.	• Consider pre-medication with acetaminophen, H1-receptor antagonist and a corticosteroid for subsequent infusions.
3	• Stop treatment. • Aggressively manage symptoms. **Restart:** • The infusion may be restarted at a slower rate once symptoms have resolved.	
4	• Stop treatment. • Aggressively manage symptoms.	• Permanently discontinue (do not re-challenge).

Hepatic Impairment

The liver is a known route of clearance for brentuximab vedotin. MMAE exposure approximately doubled in patients with hepatic impairment; a reduced starting dose should be used.

Hepatic Impairment	Dose
Mild (Child-Pugh A)	Start at 1.2 mg/kg† and monitor closely.
Moderate (Child-Pugh B)	Avoid use.
Severe (Child-Pugh C)	Avoid use.

†Maximum dose: 120 mg (for 1.2 mg/kg dose) in patients ≥ 100 kg.

Renal Impairment

No dose adjustment for mild or moderate renal impairment. Avoid use in patients with severe renal impairment (CrCl <30mL/min). The kidneys are a known route of clearance for brentuximab vedotin. MMAE exposure approximately doubled and severe adverse effects were more frequent in patients with severe renal impairment.

Dosage in the Elderly

No specific dose adjustment is recommended by the manufacturer.

No meaningful safety or efficacy difference was observed between patients ≥ 65 years compared to younger patients with pcALCL or CD30-expressing MF.

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F - Adverse Effects

Refer to brentuximab vedotin drug monograph(s) for additional details of adverse effects.

Very common (≥ 50%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Myelosuppression +/- infection and bleeding (may be severe, includes anemia, opportunistic infections) • Peripheral neuropathy (may be severe)	• Fatigue • Nausea, vomiting • Cough, dyspnea • Diarrhea • Anorexia, weight loss • Musculoskeletal pain • Infusion-related reaction (may be severe) • Abdominal pain • Constipation • Rash, pruritus • Headache	• Arterial / venous thromboembolism • Arrhythmia • GI perforation • GI obstruction • Pancreatitis • Hepatotoxicity • Tumour lysis syndrome • Leukoencephalopathy (PML) • Pneumonitis • Renal failure • Stevens-Johnson syndrome • Toxic epidermal necrolysis

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G - Interactions

Refer to brentuximab vedotin drug monograph(s) for additional details.

- Concomitant use of bleomycin is **contraindicated** given increased risk of pulmonary toxicity.

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H - Drug Administration and Special Precautions

Refer to brentuximab vedotin drug monograph(s) for additional details.

Administration

- DO NOT administer as an IV push or bolus.
- Reconstitute based on product monograph instructions to yield a single-use 5 mg/mL solution.
- After reconstitution, immediately add to an infusion bag containing at least 100 mL volume to achieve a final concentration of 0.4-1.8 mg/mL.
- Can be diluted into normal saline, 5% dextrose or lactated Ringer's injection.
- Infuse IV over 30 minutes.
- Do not mix with, or administer as an infusion with, other medicinal products.
- Store unopened vials at 2-8°C in the original carton to protect from light.

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Contraindications

- Patients who are hypersensitive to this drug or any of its components
- Concomitant use with bleomycin due to increased risk of pulmonary toxicity
- Patients who have, or have had progressive multifocal leukoencephalopathy (PML)

Warnings/Precautions

- Patients with significant pre-existing cardiovascular disease should be monitored closely as the potential cardiotoxicity of brentuximab vedotin is unknown.
- Use live vaccines with caution.

Pregnancy/Lactation

- This regimen is not recommended for use in pregnancy. Adequate contraception (including a barrier method) should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Effects in fertility: Probable

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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.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- CBC; Baseline and prior to each dose; more frequent monitoring should be considered for patients with Grade 3 or 4 neutropenia or thrombocytopenia
- Liver functions tests; Baseline and before each cycle, also as clinically indicated in patients with liver impairment
- Renal function tests; Baseline and before each cycle, also as clinically indicated in patients with renal impairment
- Clinical toxicity assessment for TLS, PML, infusion-related reactions, infections, bleeding, neuropathy, pneumonitis, pancreatitis, thromboembolism, GI or skin effects, fatigue, pain; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Blood glucose; Baseline and as clinically indicated, especially for patients with a history of diabetes mellitus

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J - Administrative Information

Approximate Patient Visit	0.5 hour
Pharmacy Workload (average time per visit)	19.589 minutes
Nursing Workload (average time per visit)	47.5 minutes

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K - References

Brentuximab drug monograph, Ontario Health (Cancer Care Ontario).

pCODR expert review committee final recommendation (brentuximab vedotin treatment of adult patients with primary cutaneous anaplastic large cell lymphoma or CD30-expressing mycosis fungoides). December 3, 2020.

Prince HM, Kim YH, Horwitz SM, et al. Brentuximab vedotin or physician's choice in CD30-positive cutaneous T-cell lymphoma (ALCANZA): an international, open-label, randomised, phase 3, multicentre trial. Lancet 2017;390(10094):555-66. doi: 10.1016/S0140-6736(17)31266-7.

September 2024 Updated Pregnancy and Lactation section

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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 information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

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.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management

information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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