

## Regimen Monograph

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## A - Regimen Name

**BREN Regimen**

Brentuximab vedotin (sALCL)

**Disease Site**

Hematologic

Lymphoma - Non-Hodgkin's Intermediate Grade

Lymphoma - T-cell

**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+ systemic anaplastic large cell lymphoma (sALCL) after failure of at least one multi-agent chemotherapy regimen, in patients who have an ECOG performance status of 0 or 1. Treatment beyond 16 cycles may be funded (documentation showing continued evidence of benefit is required).

Not funded for use in the first-line setting or as a bridge to allogeneic stem cell transplant. Not funded for retreatment after disease progression or relapse.

**Supplementary Public Funding****[brentuximab vedotin](#)**

New Drug Funding Program (Brentuximab Vedotin - Systemic Anaplastic Large Cell Lymphoma) ([NDFP Website](#) )

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## B - Drug Regimen

<a href="#">brentuximab vedotin</a>	1.8* mg /kg	IV	Day 1
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\*Maximum dose 180mg for patients who are  $\geq 100$  kg

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## C - Cycle Frequency

### REPEAT EVERY 21 DAYS

For up to 16 cycles unless disease progression or unacceptable toxicity occurs

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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**

<b>Toxicity</b>	<b>Type / Grade</b>	<b>Brentuximab vedotin dose</b>
<b>Peripheral neuropathy</b>	New or worsening Grade 2 or 3	Hold until improvement to Grade 1 or baseline, then restart at 1.2 mg/kg. <sup>^</sup>
	Grade 4	Discontinue.
<b>Neutropenia</b>	Grade 3 or 4	Hold until $\leq$ 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 $\leq$ Grade 2. <sup>^</sup>
<b>Thrombocytopenia</b>	Grade 3 or 4	Monitor closely and consider platelet transfusions or dose delays.
<b>SJS, TEN</b>	Any	Discontinue and manage appropriately.
<b>PML</b>	Suspected, any grade	Hold and investigate; discontinue if confirmed.
<b>Pancreatitis</b>	Suspected, any grade	Hold and investigate; discontinue if confirmed.
<b>Pulmonary symptoms</b>	Any grade	Hold and investigate; consider discontinuing if pneumonitis confirmed.
<b>Tumour lysis syndrome</b>	Suspected, any grade	Hold and manage aggressively. May continue therapy after resolution with adequate preventative measures.
<b>Hepatotoxicity</b>	New, worsening or recurrent	Hold and consider reduced dose. Discontinue if severe.

<sup>^</sup>Maximum dose: 120 mg (for 1.2mg/kg dose) in patients  $\geq$  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	<ul style="list-style-type: none"> <li>Stop or slow the infusion rate.</li> <li>Manage the symptoms.</li> </ul> <p><b>Restart:</b></p> <ul style="list-style-type: none"> <li>The infusion may be restarted at a slower rate once symptoms have resolved.</li> </ul>	<ul style="list-style-type: none"> <li>Consider pre-medication with acetaminophen, H1-receptor antagonist and a corticosteroid for subsequent infusions.</li> </ul>
3	<ul style="list-style-type: none"> <li>Stop treatment.</li> <li>Aggressively manage symptoms.</li> </ul> <p><b>Restart:</b></p> <ul style="list-style-type: none"> <li>The infusion may be restarted at a slower rate once symptoms have resolved.</li> </ul>	
4	<ul style="list-style-type: none"> <li>Stop treatment.</li> <li>Aggressively manage symptoms.</li> </ul>	<ul style="list-style-type: none"> <li>Permanently discontinue (do not re-challenge).</li> </ul>

### 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  $\geq 100$  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. Efficacy and safety of monotherapy have not been established in geriatric patients with relapsed/refractory sALCL. Older age was a risk factor for febrile neutropenia for brentuximab in combination with chemotherapy.

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## F - Adverse Effects

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

Very common ( $\geq 50\%$ )	Less common (10-24%)	Uncommon ( $< 10\%$ ), but may be severe or life-threatening
<ul style="list-style-type: none"> <li>• Myelosuppression +/- infection and bleeding (may be severe, includes anemia, opportunistic infections)</li> <li>• Peripheral neuropathy (may be severe)</li> </ul>	<ul style="list-style-type: none"> <li>• Fatigue</li> <li>• Nausea, vomiting</li> <li>• Cough, dyspnea</li> <li>• Diarrhea</li> <li>• Anorexia, weight loss</li> <li>• Musculoskeletal pain</li> <li>• Infusion-related reaction (may be severe)</li> <li>• Abdominal pain</li> <li>• Constipation</li> <li>• Rash, pruritus</li> <li>• Headache</li> </ul>	<ul style="list-style-type: none"> <li>• Arterial / venous thromboembolism</li> <li>• Arrhythmia</li> <li>• GI perforation</li> <li>• GI obstruction</li> <li>• Pancreatitis</li> <li>• Hepatotoxicity</li> <li>• Tumour lysis syndrome</li> <li>• Leukoencephalopathy (PML)</li> <li>• Pneumonitis</li> <li>• Renal failure</li> <li>• Stevens-Johnson syndrome</li> <li>• Toxic epidermal necrolysis</li> </ul>

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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).

Deng C, Pan B, O'Connor OA. Brentuximab vedotin. Clin Cancer Res 2012;19(1):22-27.

Minich SS. Brentuximab vedotin: a new age in the treatment of Hodgkin lymphoma and anaplastic large cell lymphoma. Ann Pharmacother 2012;46:377-83.

Pro B, Advani R, Brice P et al. Brentuximab vedotin (SGN-35) in patients with relapsed or refractory systemic anaplastic large-cell lymphoma: results of a phase II study. J Clin Oncol 2012;30(18):2190-6.

Younes A, Yasotheam U, Kirkpatrick P. Brentuximab vedotin. Nat Rev Drug Discov 2012;11:19-20.

**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.

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*provided in the Formulary.*

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*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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