Drug Monograph

Drug Name | Mechanism of Action and Pharmacokinetics | Indications and Status | Adverse Effects | Dosing | Administration Guidelines | Special Precautions | Interactions | Recommended Clinical Monitoring | Supplementary Public Funding | References | Disclaimer

A - Drug Name

brentuximab vedotin

COMMON TRADE NAME(S): Adcetris®

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B - Mechanism of Action and Pharmacokinetics

Brentuximab vedotin is an IgG1 antibody-drug conjugate (ADC) specific for CD30 on the surface of several types of tumor cells, including Hodgkin's disease and some lymphomas. The complex is internalized and transported to lysosomes where the antitumor agent monomethyl auristatin E (MMAE) is released by proteolytic cleavage. MMAE binds to tubulin and disrupts the microtubule network in the cell.

Absorption	Exposure is dose proportional, with no evidence of accumulation (q3w dosing). MMAE exposure falls with continued administration.	
	Time to reach steady state	21 days (q3w dosing)
	Peak plasma levels	Tmax = 1-3 days for MMAE
Distribution	PPB	68-82%, MMAE is unlikely displace or to be displaced by highly protein-bound drugs
Metabolism	Studies suggest that only a small fraction of MMAE released from brentuximab vedotin is metabolized.	
	Main enzymes involved	CYP3A4/5
	Active metabolites	Yes

	Inhibitor of	CYP3A4/5
Elimination	MMAE appears to follow metabolite kinetics, with elimination limited by its rate of release from ADC.	
	Half-life	4 to 6 days (3-4 for MMAE)
	Feces	72% (MMAE)
	Urine	28% (MMAE)

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C - Indications and Status

Health Canada Approvals:

- Hodgkin lymphoma (HL)
- Systemic anaplastic large cell lymphoma (sALCL)
- Peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS)
- Angioimmunoblastic T-Cell lymphoma (AITL)
- Primary cutaneous anaplastic large cell lymphoma (pcALCL)
- Mycosis fungoides (MF)

Refer to the product monograph for a full list and details of approved indications.

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D - Adverse Effects

Emetogenic Potential: Low

Extravasation Potential: None

The following adverse effects include those reported in the placebo-controlled phase III trial in high risk HL patients following ASCT where the incidence was 2% or more higher than reported for placebo. Severe adverse effects from other trials are included, where appropriate.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	Arrhythmia (<5%) (rare)	I E
	Arterial thromboembolism (rare)	E
	Hypotension (6%)	I
	Venous thromboembolism (rare)	E
Dermatological	Rash, pruritus (12%)	E
	Stevens-Johnson syndrome (rare)	E
	Toxic epidermal necrolysis (rare)	E
Gastrointestinal	Abdominal pain (14%)	E
	Anorexia, weight loss (19%)	E
	Constipation (13%)	E
	Diarrhea (20%)	E
	Dyspepsia (7%)	I E
	GI obstruction (rare)	E
	GI perforation (rare)	E
	Nausea, vomiting (22%)	I E
General	Fatigue (24%)	E
Hematological	Myelosuppression ± infection, bleeding (78%) (39% severe, including anemia, opportunistic infections)	E
Hepatobiliary	Hepatotoxicity (rare)	E D
	↑ LFTs (2%) (may be severe)	E
	Pancreatitis (rare)	D
Hypersensitivity	Infusion related reaction (15%) (may be severe)	I E
Metabolic / Endocrine	Hyperglycemia (2%)	E
	↓ K (6%)	E
	Tumour lysis syndrome (rare)	E

Musculoskeletal	Musculoskeletal pain (18%)	E
Nervous System	Headache (11%)	I E
	Insomnia (8%)	E
	Leukoencephalopathy (PML - rare)	E
	Peripheral neuropathy (56%) (sensory); motor (23%); (up to 10% severe)	E D
Renal	Renal failure (rare)	E D
Respiratory	Cough, dyspnea (21%)	E
	Pneumonitis (rare)	E

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.
"*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
D = *delayed* (weeks to months) L = *late* (months to years)

The most common side effects for brentuximab vedotin include myelosuppression ± infection, bleeding, peripheral neuropathy, fatigue, nausea/vomiting, cough, dyspnea, diarrhea, anorexia, weight loss, musculoskeletal pain, infusion related reaction and abdominal pain.

Infections with brentuximab vedotin may be serious (e.g. pneumonia, bacteremia, herpes zoster) and/or opportunistic (e.g. pneumocystis jiroveci pneumonia, oral candidiasis). JC virus related progressive multifocal leukoencephalopathy (PML) has been reported, may be fatal and may be associated with immunosuppressive therapies and underlying disease. Some cases have occurred within 3 months of initial drug exposure. Patients should be closely monitored and the drug held with any sign or symptom suggestive of PML, while undergoing further evaluation.

Severe **anemia, thrombocytopenia**, and **neutropenia** (with or without fever) have been observed.

Severe **rashes** including Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) have been described and may be fatal.

Transient or persistent **antibodies** to brentuximab vedotin have been observed in up to 27% of patients and are associated with a higher risk of infusion reactions.

Infusion reactions can be immediate or delayed, may be severe and can occur up to 2 days after the infusion.

Peripheral neuropathy (PN) is cumulative and may be sensory or motor. It is often reversible after treatment ends, but may be severe or not completely reversible in some patients.

Non-infectious pulmonary toxicity, including cough, dyspnea, and interstitial infiltration and/or inflammation on imaging has been reported with single-agent brentuximab vedotin and may be fatal. The risk appears to be higher with bleomycin (contraindicated).

Consider **pancreatitis** (fatal cases reported) as a diagnosis in patients who present with new or worsening abdominal pain.

GI complications, including those with fatal outcomes, have been reported. Lymphoma patients with pre-existing GI involvement may have an increased risk of perforation.

Serious cases of **hepatotoxicity** have occurred, including deaths, after the first dose or re-challenge. Risk may be increased with pre-existing liver disease or elevated baseline liver enzymes.

Hyperglycemia has been reported in patients with an elevated body mass index (BMI) with or without a history of diabetes mellitus.

Tumour lysis syndrome has been reported. Patients at risk (rapidly proliferating tumours or high tumour burden) should have appropriate prophylaxis and be monitored closely.

Responses had been reported when patients who had prior responses to brentuximab vedotin were retreated. There was an increased incidence of neuropathy and upper respiratory tract infections with treatment beyond 16 cycles.

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E - Dosing

Refer to protocol by which patient is being treated.

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:

- Primary G-CSF prophylaxis is recommended starting cycle 1 for patients on AVD+BREN or CHP+BREN.
- Antiviral and antibiotic prophylaxis post-ASCT should be followed per institutional guidelines.
- Patients at risk of tumour lysis syndrome should have appropriate prophylaxis and be monitored closely.

Adults:

Indication	Brentuximab Vedotin Dose*	Frequency
Previously untreated stage IV HL: • In combination with AVD	1.2 mg/kg	Q2 weeks
HL consolidation, Relapsed/refractory HL, Relapsed/refractory sALCL, pcALCL or CD-30-expressing MF: • Monotherapy Previously untreated sALCL, CD30-expressing PTCL-NOS, CD30-expressing AITL: • In combination with CHP	1.8 mg/kg	Q3 weeks^

*Maximum dose: 120 mg (for 1.2 mg/kg dose) or 180 mg (for 1.8 mg/kg dose) in patients ≥ 100 kg.
^For ASCT consolidation, start within 4-6 weeks post-ASCT or upon ASCT recovery.

Dosage with Toxicity:

Toxicity	Type / Grade	Brentuximab Vedotin Dose (AVD+BREN)	Brentuximab Vedotin Dose (CHP+BREN)	Brentuximab Vedotin Dose (Monotherapy)
Peripheral neuropathy	Grade 2	Reduce to 0.9 mg/kg q2w.^	Sensory neuropathy: No change. Motor neuropathy: Reduce to 1.2 mg/kg q3w.^	Hold until improvement to Grade 1 or baseline, then restart at 1.2 mg/kg q3w.^

	Grade 3	Hold until ≤ Grade 2 then restart at 0.9 mg/kg q2w.^ Consider discontinuing if already at 0.9 mg/kg q2w.^	Sensory neuropathy: Reduce to 1.2 mg/kg q3w.^ Motor neuropathy: Discontinue.	
	Grade 4	Discontinue.		
Neutropenia	Grade 3 or 4	Continue with growth factors.	Give growth factor prophylaxis for subsequent cycles in patients not on primary G-CSF prophylaxis.	Hold until ≤ Grade 2. Consider growth factor support for subsequent cycles.
	Recurrent Grade 4 despite the use of growth factors	Consider discontinuing, or reduce to 0.9 mg/kg q2w.^	Consider discontinuing, or reduce to 1.2 mg/kg q3w.^	Consider discontinuing, or reduce dose to 1.2 mg/kg q3w^ 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: 90 mg (for 0.9 mg/kg dose) or 120 mg (for 1.2 mg/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).

Dosage with 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 (In Combination with AVD)	Dose (Monotherapy or in Combination with CHP)
Mild (Child-Pugh A)	Start at 0.9 mg/kg† and monitor closely.	Start at 1.2 mg/kg† and monitor closely.
Moderate (Child-Pugh B)	Avoid use.	
Severe (Child-Pugh C)	Avoid use.	

†Maximum dose: 90 mg (for 0.9 mg/kg dose) or 120 mg (for 1.2 mg/kg dose)in patients ≥ 100 kg.

Dosage with 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.

Efficacy and safety of monotherapy have not been established in geriatric patients with HL at high risk of relapse, relapsed/refractory HL or relapsed/refractory sALCL.

Older age was a risk factor for febrile neutropenia in AVD+BREN and CHP+BREN clinical trials. Patients ≥ 65 years of age had higher incidences of ≥ Grade 3 and serious adverse effects compared with younger patients on CHP+BREN.

Dosage based on gender:

Females have been found to have a lower antibody-drug conjugate volume of distribution than males. Dosage adjustment is not needed.

Children:

Efficacy and safety in children aged less than 18 years have not been established.

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F - Administration Guidelines

- 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.

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G - Special Precautions

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)

Other Warnings/Precautions:

- Patients with significant pre-existing cardiovascular disease should be monitored closely as the potential cardiotoxicity of brentuximab vedotin is unknown.
- Patients with baseline neuropathy, including asymptomatic Grade 1 neuropathy, were excluded from the AVD+BREN clinical trial. Benefit-risk must be carefully considered before starting AVD+BREN for previously untreated patients with stage IV HL who have pre-existing neuropathy.
- Use live vaccines with caution.

Other Drug Properties:

- Carcinogenicity: Unknown

Pregnancy and Lactation:

- Genotoxicity: Yes
- Crosses placental barrier: Documented in animals
- Fetotoxicity: Documented in animals
- Teratogenicity: Documented in animals
- Pregnancy:
  Brentuximab is not recommended for use in pregnancy. Adequate contraception (including a barrier method) should be used by patients and their partners during treatment, and for at least **6 months** after the last dose.
- Excretion into breast milk: Unknown
  Breastfeeding is not recommended.
- Fertility effects: Probable
  Documented in animal studies. Partially reversible in male animals.

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H - Interactions

MMAE is a P-gp and CYP3A4/5 substrate. Although MMAE is an in vitro inhibitor of CYP3A4/5, it is not expected to change the exposure to drugs that are metabolized by CYP3A4.

AGENT	EFFECT	MECHANISM	MANAGEMENT
CYP3A4 inducers (i.e. phenytoin, rifampin, dexamethasone, carbamazepine, phenobarbital, St. John's Wort, etc)	↓ exposure to MMAE (up to 46%)	↑ metabolism of MMAE	Caution; monitor for efficacy.
CYP3A4 inhibitors (i.e. ketoconazole, clarithromycin, ritonavir, fruit or juice from grapefruit, Seville oranges or starfruit)	↑ exposure to MMAE (up to 34%)	↓ metabolism of MMAE	Caution with strong inhibitors; monitor for adverse reactions closely.
P-glycoprotein inhibitors (i.e. quinidine, verapamil, cyclosporine)	↑ exposure to MMAE	MMAE is a P-gp substrate	Caution; monitor for adverse reactions closely.
Bleomycin	↑ risk of pulmonary toxicity	Unknown mechanism	CONTRAINDICATED.

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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

Monitor Type	Monitor Frequency
CBC	Baseline and prior to each dose; more frequent monitoring should be considered for patients with Grade 3 or 4 neutropenia or thrombocytopenia
Liver function 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

Monitor Type	Monitor Frequency
Blood glucose	Baseline and as clinically indicated, especially for patients with a history of diabetes mellitus

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J - Supplementary Public Funding

New Drug Funding Program (NDFP Website)

- Brentuximab Vedotin - In Combination with Chemotherapy for Previously Untreated Peripheral T-cell Lymphoma (PTCL)
- Brentuximab Vedotin - Consolidation Post-Autologous Stem Cell Transplant (ASCT) for Hodgkin Lymphoma
- Brentuximab Vedotin - Relapsed or Refractory Hodgkin Lymphoma
- Brentuximab Vedotin - Systemic Anaplastic Large Cell Lymphoma
- Brentuximab Vedotin - Previously Treated Primary Cutaneous Anaplastic Large Cell Lymphoma or Mycosis Fungoides
- Brentuximab Vedotin - In Combination with Chemotherapy for Pediatric High-Risk Hodgkin Lymphoma
- Brentuximab Vedotin - In Combination with Chemotherapy for Previously Untreated Advanced Stage Hodgkin Lymphoma

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K - References

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

Product Monograph: Adcetris® (brentuximab vedotin). Seattle Genetics, Inc., June 2021.

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

June 2025 Added NDFP forms

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L - 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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