

DRUG NAME: Bendamustine**SYNONYM(S):****COMMON TRADE NAME(S):** TREANDA®**CLASSIFICATION:** Alkylating agent, cytotoxic¹*Special pediatric considerations are noted when applicable, otherwise adult provisions apply.***MECHANISM OF ACTION:**

Bendamustine is a bifunctional mechlorethamine derivative containing a purine-like benzimidazole ring. Its exact mechanism of action is unknown, but it may cause apoptotic and non-apoptotic death of malignant cells by damaging both single- and double-strand DNA, increasing the expression of pro-apoptotic genes, and inhibiting mitotic control. Bendamustine is active against both quiescent and dividing cells.²

USES:**Primary uses:****Other uses:²**

- Lymphoma, non-Hodgkin's
- Leukemia, chronic lymphocytic

*Health Canada approved indication

SPECIAL PRECAUTIONS²:**Contraindications:** history of hypersensitivity reaction to bendamustine or mechlorethamine.**Caution:**

- **infusion reactions**, including fever, chills, pruritus and rash commonly occur. Severe **anaphylactic** and anaphylactoid reactions have occurred rarely, particularly in the second and subsequent cycles of therapy. Consider pre-treatment with antihistamines, antipyretics and corticosteroids for patients experiencing Grade 1 or 2 infusion reactions; consider discontinuing treatment for patients experiencing Grade 3 or 4 infusion reactions.
- **tumour lysis syndrome** has been associated with bendamustine, possibly leading to acute renal failure and death. Usual onset occurs during the first cycle. Maintain adequate volume status and monitor blood chemistry, including potassium and uric acid levels. Allopurinol has been used, but the concomitant use of bendamustine and allopurinol can cause increased risk of severe skin toxicity.
- **CYP1A2 inhibitors** can potentially decrease plasma concentration of bendamustine; **CYP1A2 inducers** can potentially increase plasma concentration of bendamustine.

Pregnancy: FDA Pregnancy Category D.² There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important.

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in bold, italics	
allergy/immunology	hypersensitivity (5%, severe 1%)
	infusion reactions, anaphylaxis
blood/bone marrow/ febrile neutropenia	decreased hemoglobin (88-89%, severe 11-13%)
	febrile neutropenia (6%, severe 6%)
	leucopenia (61-94%, severe 28-56%)
	lymphopenia (68-99%, severe 47-94%)
	neutropenia (75-86%, severe 43-60%)
	thrombocytopenia (77-86%, severe 7-25%)
cardiovascular (arrhythmia)	tachycardia (7%)
cardiovascular (general)	hypotension (6%, severe 1%)
constitutional symptoms	chills (14%)
	dehydration (5%)
	fatigue (9-57%, severe 1-5%)
	hyperhidrosis (5%)
	night sweats (5%)
	pyrexia (24-34%, severe 4%)
	weight loss (7-18%, severe 2%)
dermatology/skin	<i>extravasation hazard: non-vesicant</i> ³
	dry skin (5%)
	pruritus (5-6%)
	rash (8-28%, severe 3%); may be progressive and increase in severity, may require treatment cessation
	toxic epidermal necrolysis
gastrointestinal	<i>emetogenic potential: low-moderate</i> ⁴
	anorexia (23%, severe 2%)
	constipation (15%, severe <1%)
	dehydration (14%, severe 5%)
	diarrhea (9-37%, severe 1%)
	dry mouth (9%)
	dyspepsia (11-16%, severe 2%)
	nausea (20-75%, severe <1%)
	stomatitis (15%, severe <1%)
vomiting (16-40%, severe <1%)	
infection	herpes simplex (3%)
	herpes zoster (10%, severe 3%)
	infection (6%, severe 2%)

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in bold, italics	
	nasopharyngitis (6-7%)
	oral candidiasis (6%, severe 1%)
	pneumonia (8%, severe 5%)
	sinusitis (9%)
	upper respiratory tract infection (10%)
	urinary tract infection (10%, severe 2%)
lymphatics	edema peripheral (13%, severe <1%)
metabolic/laboratory	hyperuricemia (7%, severe 2%)
	hypokalemia (9%, severe 5%)
musculoskeletal	arthralgia (6%)
	asthenia (11%, severe 2%)
neurology	anxiety 8%
	depression 6%
	dizziness 14%
	insomnia 13%
pain	abdominal pain (13%, severe 1%)
	back pain (14%, severe 3%)
	bone pain (5%)
	catheter site pain (5%)
	chest pain (6%)
	headache (21%)
	infusion site pain (6%)
	pain (6%)
	pain in extremity (5%, severe 1%)
	pharyngolaryngeal pain (8%, severe <1%)
pulmonary	cough (4-22%, severe <1%)
	nasal congestion (5%)
	wheezing (5%)
secondary malignancy	pre-malignant and malignant diseases
syndromes	tumour lysis syndrome
	Stevens-Johnson syndrome

Adapted from standard reference² unless specified otherwise.

SUPPLY AND STORAGE:

Injection: Cephalon supplies single-use vials containing either 25 mg or 100 mg of bendamustine HCL as lyophilized powder. Store at room temperature.²

For basic information on the current brand used at the BC Cancer Agency, see [Chemotherapy Preparation and Stability Chart](#) in Appendix.

SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at the BC Cancer Agency, see [Chemotherapy Preparation and Stability Chart](#) in Appendix.

Additional information:

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BCCA administration guideline noted in ***bold, italics***

Subcutaneous	no information found
Intramuscular	no information found
Direct intravenous	no information found
<i>Intermittent infusion²</i>	For CLL: over 30 minutes For NHL: over 60 minutes
Continuous infusion	no information found
Intraperitoneal	no information found
Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical	no information found

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response and concomitant therapy. Guidelines for dosing also include consideration of absolute neutrophil count (ANC). Dosage may be reduced, delayed or discontinued in patients with bone marrow depression due to cytotoxic/radiation therapy or with other toxicities.

Adults:

BCCA usual dose noted in ***bold, italics***

Cycle Length:

Intravenous²: 4 weeks: 100 mg/m² IV for one dose on days 1 and 2

BCCA usual dose noted in ***bold, italics***

Cycle Length:

3 weeks: 120 mg/m² IV for one dose on days 1 and 2

REFERENCES:

1. National Institute for Occupational Safety and Health (NIOSH). Preventing occupational exposures to antineoplastic and other hazardous drugs in healthcare settings. Cincinnati, Ohio: NIOSH - Publications Dissemination; September 2004. p. 31-40.
2. Cephalon. TREANDA® prescribing information. Frazer, PA; October 2009.
3. BC Cancer Agency Provincial Systemic Therapy Program. Provincial Systemic Therapy Program Policy III-20: Prevention and Management of Extravasation of Chemotherapy. Vancouver, British Columbia: BC Cancer Agency; 1 December 2007.
4. BC Cancer Agency. (SCNAUSEA) Guidelines for Prevention and Treatment of Chemotherapy-induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer Agency; 1 March 2008.