DRUG NAME: Belinostat

SYNONYM(S): PXD101[1]

COMMON TRADE NAME(S): BELEODAQ®

CLASSIFICATION: miscellaneous

Special pediatric considerations are noted when applicable, otherwise adult provisions apply.

MECHANISM OF ACTION:

Belinostat is a histone deacetylase (HDAC) inhibitor which broadly inhibits all zinc-dependent HDAC enzymes. By inhibiting the enzymatic activity of HDAC, belinostat causes the accumulation of acetylated histones and other proteins, thus inducing cell cycle arrest and/or apoptosis of some transformed cells. Belinostat shows preferential cytotoxicity towards tumour cells and exhibits its activity at nanomolar concentrations.[2,3]

USES:

Primary uses:

Lymphoma, T-cell[2]

*Health Canada approved indication

Other uses:

SPECIAL PRECAUTIONS:

- ***tumour lysis syndrome*** has been reported in patients with advanced stage disease and/or high tumour burden; appropriate prophylaxis is recommended[2]
- in patients known to be ***homozygous*** for ***UGT1A1*28 allele***, reduce belinostat starting dose to 75% (i.e., 750 mg/m^2)[2]

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.

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
blood and lymphatic system/ febrile neutropenia	***anemia*** (32%, severe 11%)
	lymphopenia (43%)
	neutropenia (severe 6%)
	thrombocytopenia (16%, severe 7%)
gastrointestinal	*emetogenic potential:* low[4]
	abdominal pain (11%, severe 1%)

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
	constipation (23-26%, severe 1%)
	diarrhea (17-23%, severe 2%)
	dyspepsia (11%)
	nausea (38-63%, severe 1%)
	vomiting (24-29%, severe 1%)
general disorders and administration site conditions	*extravasation hazard:* irritant[5]
	chills (16%, severe 3%)
	edema, peripheral (13-20%)
	fatigue (26-37%, severe 5%)
	infusion site pain (14-17%)
	multi-organ failure (2%)
	phlebitis (10%, severe 1%)
	pyrexia (21-35%, severe 2%)
infections and infestations	***infection*** (3%, severe 3%)
	pneumonia (7%, severe 5%)
investigations	***AST/ALT increase*** (severe 10%)
	creatinine increase (2%)
	hypokalemia (12-13%, severe 4%)
	LDH increase (16%, severe 2%)
	QT prolongation (11%, severe 4%)
metabolism and nutrition	anorexia, appetite loss (15%, severe 2%)
nervous system	dizziness (10-21%)
	headache (13-15%)
respiratory, thoracic and mediastinal	cough (19%)
	dyspnea (11-22%, severe 6%)
skin and subcutaneous tissue	pruritus (16-17%, severe 3%)
	rash (13-20%, severe 1%)
vascular	hypotension (10%, severe 3%)

Adapted from standard reference[1-3] unless specified otherwise.

The ***most commonly observed*** adverse reactions include: nausea, fatigue, pyrexia, anemia, and vomiting. The most common ***serious*** adverse reactions include: pneumonia, pyrexia, infection, anemia, increased creatinine, thrombocytopenia, and multi-organ failure.[2]

Dosage modification is recommended for hematologic toxicity and any grade 3 or 4 non-hematologic adverse reaction. For thrombocytopenia and neutropenia, dose adjustments should be based on the nadir counts in the preceding cycle of therapy. Discontinue belinostat in patients who have recurrent ANC nadirs less than 0.5 x 10^9/L and/or recurrent platelet count nadirs less than 25 x 10^9/L after two dosage reductions. Non-hematologic toxicities

should have recovered to grade 2 or less prior to resuming treatment at a reduced dose (reduce by 25%). Discontinue belinostat for grade 3 or 4 non-hematologic toxicity which recurs after two dose reductions.[2]

SUPPLY AND STORAGE:

Injection: Spectrum Pharmaceuticals Inc. supplies belinostat as 500 mg vials of lyophilized powder. Store at room temperature in original packaging.[2]

For basic information on the current brand used at BC Cancer, see Chemotherapy Preparation and Stability Chart in Appendix.

SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at BC Cancer, see Chemotherapy Preparation and Stability Chart in Appendix.

Additional information:

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BC Cancer administration guideline noted in ***bold***, ***italics***

Subcutaneous	no information found
Intramuscular	no information found
Direct intravenous	no information found
Intermittent infusion	• ***over 30 minutes;*** infusion time may be extended to 45 minutes for injection site reactions (e.g., pain)[2] • administer with 0.22 micron inline filter[2]
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*:**

BC Cancer usual dose noted in ***bold, italics***

Intravenous:	Cycle Length: 3 weeks[1-3]:	1000 mg/m^2 IV once daily for 5 consecutive days starting on day 1 (total dose per cycle 5000 mg/m^2)

REFERENCES:

1. Foss F, Advani R, Duvic M, et al. A phase II trial of belinostat (PXD101) in patients with relapsed or refractory peripheral or cutaneous T-cell lymphoma. Br.J.Haematol. 2015;168(6):811-819.
2. Spectrum Pharmaceuticals Inc. BELEODAQ® full prescribing information. Irvine, CA, USA; April 2012.
3. O'Connor OA, Horwitz S, Masszi T, et al. Belinostat in patients with relapsed or refractory peripheral T-cell lymphoma: results of the pivotal phase II BELIEF (CLN-19) study. J Clin Oncol 2015;33(23):2492-2499.
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 Mar 2012.
5. 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; January 2016.