DRUG NAME: Polatuzumab vedotin

SYNONYM(S):

COMMON TRADE NAME(S): POLIVY® (USA)

CLASSIFICATION: miscellaneous

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

MECHANISM OF ACTION:

Polatuzumab vedotin is a CD79b-directed antibody-drug conjugate composed of polatuzumab, a humanized immunoglobulin G1 monoclonal antibody specific for human CD79b and the small molecule anti-mitotic agent monomethyl auristatin E (MMAE) covalently attached by a cleavable linker. Upon binding to CD79b on the B-cell surface, polatuzumab vedotin is internalized and the linker is cleaved by lysosomal proteases, thus enabling intracellular delivery of MMAE. The released MMAE inhibits cell division and induces apoptosis.[1,2] Polatuzumab vedotin is cell cycle phase-specific, inducing cell cycle arrest in the G2/M phase.[3]

USES:

Primary uses:

Lymphoma, non-Hodgkin's[1,2]

*Health Canada approved indication

Other uses:

SPECIAL PRECAUTIONS:

Contraindications:

- history of hypersensitivity reaction to polatuzumab vedotin or Chinese hamster ovary cell proteins[1]

Caution:

- ***premedicate*** with an ***antihistamine*** and ***antipyretic*** for all cycles to prevent infusion-related reactions[1]
- administer appropriate ***prophylaxis*** for ***Pneumocystis jiroveci pneumonia*** and ***herpesvirus*** throughout treatment with polatuzumab vedotin[1]
- ***myelosuppression*** can be severe; consider prophylactic ***granulocyte colony stimulating factor*** administration as needed[1]
- patients with rapidly proliferating tumour and high tumour burden are at risk of ***tumour lysis syndrome***[1]
- risk of ***hepatotoxicity*** from polatuzumab vedotin may be increased in patients with preexisting liver disease and/or concomitant hepatotoxic medications[1]
- MMAE may cause ***adverse developmental outcomes*** in the fetus if administered during pregnancy; effective contraception should be used during treatment and for up to 5 months after the last dose[1]

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. When placebo-controlled trials are available, adverse events will generally be included if the incidence is $\geq$5% higher in the treatment group.

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ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
blood and lymphatic system/ febrile neutropenia (see paragraph following **Side Effects** table)	***anemia*** (47%, severe 24%)
	febrile neutropenia (4-13%)
	neutropenia (49%, severe 42%)
	lymphopenia (severe 9-13%)
	pancytopenia (7%)
	thrombocytopenia (49%, severe 40%)
gastrointestinal	*emetogenic potential:* low[4]
	diarrhea (38%)
	vomiting (18%)
general disorders and administration site conditions	*extravasation hazard:* none[5]
	fever (9-33%)
hepatobiliary	hepatotoxicity (2%)
infections and infestations (see paragraph following **Side Effects** table)	pneumonia, including fungal (16-22%)
	sepsis (7%)
	upper respiratory tract infection (13%)
injury, poisoning, and procedural complications	***infusion related reaction*** (18%); see paragraph following **Side Effects** table
investigations	***ALT/AST increase*** (36-38%)
	serum amylase increase (24%)
	serum creatinine increase (87%)
	serum lipase increase (7-36%)
	weight loss (16%)
metabolism and nutrition	appetite loss (27%)
	hypoalbuminemia (13%)
	hypocalcemia (11-44%)
	hypokalemia (16%)
	hypophosphatemia (9%)
musculoskeletal and connective tissue	arthralgia (7%)
nervous system	dizziness (13%)
	peripheral neuropathy (40%; severe 2%); see paragraph following **Side Effects** table
	progressive multifocal encephalopathy (<1%)
respiratory, thoracic and mediastinal	pneumonitis (4%)

Adapted from standard reference[3] unless specified otherwise.

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Fatal and/or serious ***infections***, including opportunistic infections, have been reported in patients treated with polatuzumab vedotin. One-third of patients experience a grade 3 (or higher) infection. Closely monitor for signs of infection during treatment. Prophylaxis for *Pneumocystisi jiroveci* pneumonia and herpesvirus is recommended throughout treatment.[1]

Infusion related reactions include fever, chills, flushing, dyspnea, hypotension, and urticaria. The majority of reactions are grade 1 or 2, but more severe reactions have been reported. Reactions may be delayed, sometimes occurring 24 hours after polatuzumab vedotin administration. Premedication with an antihistamine and antipyretic is recommended prior to each infusion. Following a reaction, interrupt the infusion and administer supportive care as necessary. Upon resolution of symptoms, the infusion may be resumed at 50% of the prior rate. If tolerated, the rate may be increased in increments of 50 mg/h every 30 minutes. Permanently discontinue polatuzumab vedotin for grade 3 or recurrent grade 2 reactions.[1] For management of hypersensitivity reactions, see BC Cancer Protocol SCDRUGRX ***Management of Hypersensitivity Reactions to Chemotherapeutic Agents*.**

Polatuzumab vedotin can cause serious or severe ***myelosuppression***, including neutropenia, thrombocytopenia, and anemia. Management of cytopenia may include dose reduction, dose delay, or treatment discontinuation. Consider prophylactic administration of granulocyte colony stimulating factor as needed.[1]

Peripheral neuropathy is reported in up to 40% of patients receiving polatuzumab vedotin. It can occur as early as the first cycle of treatment and has a cumulative effect. Polatuzumab vedotin may also exacerbate pre-existing peripheral neuropathy. The neuropathy is predominantly sensory, however motor and sensorimotor neuropathy can occur. Management of new or worsening peripheral neuropathy may require dose reduction, dose delay, or treatment discontinuation depending on the severity. The majority of patients report improvement or resolution of symptoms after a median of one month.[1]

INTERACTIONS:

MMAE is a substrate of CYP 3A. Concomitant use with a strong CYP 3A inhibitor may increase the AUC of unconjugated MMAE; monitor for increased toxicity from polatuzumab vedotin. Concomitant use with a strong CYP 3A inducer may decrease the AUC of unconjugated MMAE; clinical significance is unknown.[1]

SUPPLY AND STORAGE:

Injection: Genentech, Inc. supplies polatuzumab vedotin as 140 mg vials of preservative-free, lyophilized powder. Refrigerate. Do not shake.[1]

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

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PARENTERAL ADMINISTRATION:

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

Subcutaneous	no information found
Intramuscular	no information found
Direct intravenous[1]	do not use
Intermittent infusion[1]	administer initial dose ***over 90 minutes*** using 0.2-0.22 micron inline filter; if well tolerated, subsequent infusions may be administered over 30 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:

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

	Cycle Length:	
Intravenous:	3 weeks[1,6]:	***1.8 mg/kg*** IV for one dose on day 1 (total dose per cycle 1.8 mg/kg)

REFERENCES:

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3. Lexi-Drugs® - Lexicomp Online (database on the Internet). Polatuzumab vedotin. Wolters Kluwer Clinical Drug Information Inc., 16 December 2019. Available at: http://online.lexi.com, 6 January 2020.
4. BC Cancer. (SCNAUSEA) Guidelines for Prevention and Treatment of Chemotherapy-induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer; 1 Dec 2018.
5. BC Cancer Provincial Systemic Therapy Program. Provincial Systemic Therapy Program Policy III-20: Prevention and Management of Extravasation of Chemotherapy. Vancouver, British Columbia: BC Cancer; January 2016.
6. Sehn LH, Herrera AF, Flowers CR, et al. Polatuzumab vedotin in relapsed or refractory diffuse large B-cell lymphoma. J Clin Oncol 2019;6 November 2019 Online Ahead of Print:1-22.

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