DRUG NAME: Pentostatin

SYNONYM(S): 2'-deoxycoformycin (DCF)[1]

COMMON TRADE NAME(S): NIPENT®

CLASSIFICATION: antimetabolite

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

MECHANISM OF ACTION:

Pentostatin is a purine antimetabolite isolated from fermentation cultures of *Streptomyces antibioticus.* It is a potent inhibitor of the adenosine deaminase (ADA) enzyme. The cytotoxicity of pentostatin is believed to be due to the intracellular elevation of dATP which occurs following the inhibition of ADA and causes DNA synthesis to be blocked through the inhibition of ribonucleotide reductase. Pentostatin can also cause increased DNA damage and may inhibit RNA synthesis.[1,2]

USES:

Primary uses:
Leukemia, hairy cell[1]

Other uses:
Leukemia, chronic lymphocytic[2]
Leukemia, lymphocytic[2]
Lymphoma, cutaneous T-cell[2]

*Health Canada approved indication

SPECIAL PRECAUTIONS:

Caution:
- ***myelosuppression*** may occur, primarily during early treatment courses; preexisting infections may worsen with pentostatin treatment[1]
- terminal half-life is prolonged with ***renal dysfunction***; dose adjustment may be required[1]
- severe or fatal ***pulmonary toxicity*** has been reported in patients treated with pentostatin in combination therapy (e.g., with fludarabine, carmustine, etoposide, and cyclophosphamide)[1]
- ***hydration*** is recommended with each pentostatin administration (e.g., 500 – 1000 mL D5W or NS prior and 500 mL after)[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. **The association of some adverse events with pentostatin are uncertain as they may be associated with the disease course itself (e.g., infection, myelsuppression)**.[1]

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Revised:

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
blood and lymphatic system/ febrile neutropenia	***anemia*** (8-35%)
	febrile neutropenia
	hemolytic uremic syndrome
	leukopenia (22-60%)
	neutropenia
	thrombocytopenia (6-32%)
	thrombotic thrombocytopenic purpura
cardiac	cardiac arrhythmias (<3%); includes AV block, bradycardia, tachycardia
	chest pain (3-10%)
eye	conjunctivitis (4%)
gastrointestinal	*emetogenic potential:* low[2] to moderate[3]
	abdominal pain (4-16%)
	diarrhea (15-17%)
	nausea (22-63%)
	stomatitis (5-12%)
	vomiting (10-53%)
general disorders and administration site conditions	*extravasation hazard:* none[1,4]
	chills (11-19%)
	fatigue (29-42%)
	fever (42-46%)
	pain (8-20%)
immune system	autoimmune thrombocytopenia
	hypersensitivity reaction (2-11%)
infections and infestations	***infection***, various (7-38%)
	pharyngitis (8-10%)
	pneumonia (5%)
	upper respiratory infection (13-16%)
	viral infection (8%)
investigations	***creatinine elevation*** (3-10%)
	serum transaminase elevation (2-19%)
metabolism and nutrition	anorexia (13-16%)
musculoskeletal and connective tissue	arthralgia (3-6%)
	asthenia (10-12%)
	myalgia (11-19%)

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ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
nervous system	headache (13-17%)
	neurologic disorder/CNS toxicity (1-11%)
	paresthesia (3-10%)
psychiatric	anxiety, nervousness (3-10%)
	confusion (3-10%)
	depression (3-10%)
	hallucination (<3%)
	hostility (<3%)
	insomnia (3-10%)
renal and urinary	genitourinary disorder (15%)
	renal insufficiency, renal failure (<3%)
respiratory, thoracic and mediastinal	acute respiratory failure
	cough (17-20%)
	dyspnea (8-11%)
	lung disorder (12%)
	rhinitis (10-11%)
skin and subcutaneous tissue	exfoliative dermatitis
	diaphoresis (8-10%)
	pruritus (10-21%)
	rash (26-43%)
	skin disorder, changes (4-17%)
vascular	hypertension (<3%)
	hypotension (3-10%)

Adapted from standard reference[1,2] unless specified otherwise.

Most adverse events were mild to moderate in severity and diminished in frequency with continued therapy.[1]

Dosage reductions are not recommended at the start of therapy in patients with anemia, neutropenia, or thrombocytopenia. In addition, dosage reductions are not recommended during treatment in patients with anemia or thrombocytopenia if the patients can otherwise be supported hematologically. Hold pentostatin in patients who develop neutropenia during treatment and resume when neutrophil count returns to predose levels.[1]

SUPPLY AND STORAGE:

Injection: Hospira Inc. supplies pentostatin as a lyophilized powder in 10 mg single-dose (preservative free) vials. Refrigerate.[1]

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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	has been given[1]
Intermittent infusion	***over 20-30 min[1]***
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:	***2 weeks[1,2]***:	***4 mg/m^2 IV for one dose on day 1*** (total dose per cycle 4 mg/m^2)
	1-4 weeks[2]:	4 mg/m^2 (range 2-5 mg/m^2) IV for one dose on day 1 (total dose per cycle 4 mg/m^2 [range 2-5 mg/m^2])
Dosage in renal failure:	dosage reduction is recommended; however, data is insufficient to recommend a starting or subsequent dose for CrCl < 60 mL/min	

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REFERENCES:

1. Hospira Inc. NIPENT® full prescribing information. Lake Forest, Illinois USA; Oct 2019.
2. Lexi-Drugs® - Lexicomp Online (database on the Internet). Pentostatin. Wolters Kluwer Clinical Drug Information Inc., 3 Sep 2020. Available at: http://online.lexi.com. Accessed 1 Oct 2020.
3. BC Cancer. (SCNAUSEA) Guidelines for Prevention and Treatment of Chemotherapy-induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer; 1 Dec 2018.
4. 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.

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