DRUG NAME: Lurbinectedin

SYNONYM(S): PM01183,[1] PM1183[1]

COMMON TRADE NAME(S):

CLASSIFICATION: miscellaneous

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

MECHANISM OF ACTION:

Lurbinectedin is a selective inhibitor of oncogenic transcription. It binds preferentially to guanines located in DNA gene promoters. Transcription factors are prevented from binding to their recognition sequences, which inhibits oncogenic transcription, and leads to tumour cell apoptosis. Secondary to this, lurbinectedin may also degrade transcribing RNA Pol II and inhibit DNA damage repair to cause DNA double strand breaks and apoptosis.[1,2]

USES:

Primary uses:

Lung cancer, small cell[1,2]

*Health Canada approved indication

Other uses:

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

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*** (93%, severe 17%)
	febrile neutropenia (6.5%)
	leukopenia (73%, severe 30%)
	lymphopenia (79%, severe 33%)
	neutropenia (64%, severe 41%)
	pancytopenia (<1%)
	thrombocytopenia (49%, severe 10%)
cardiac	arrhythmia, supraventricular (<1%)
	myocardial infarction (<1%)

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ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
gastrointestinal	*emetogenic potential:* low[1,3]
	abdominal pain (9%)
	constipation (17%)
	diarrhea (13%, severe 1%)
	nausea (51%, severe 3%)
	stomatitis (3%)
	vomiting (25%, severe 3%)
general disorders and administration site conditions	*extravasation hazard:* irritant[1,4]
	extravasation (1%)
	fatigue (53%, severe 7%)
	infusion site thrombosis (<1%)
	injection site reaction, phlebitis (2%, severe 1%)
infections and infestations	***infections***, including bacterial, viral, fungal (6%)
	sepsis, septic shock (<1%)
investigations	***alkaline phosphatase increase*** (46%, severe 5%)
	ALT increase (66%, severe 6%)
	AST increase (50%, severe 3%)
	bilirubin increase (12%, severe 2%)
	creatine phosphokinase increase (9%, severe <1%)
	creatinine increase (83%, severe 2%)
	gamma-glutamyl transferase increase (71%, severe 20%)
metabolism and nutrition	appetite decrease (17%)
musculoskeletal and connective tissue	arthralgia (3%)
	muscle weakness, spasms (2%)
	musculoskeletal pain (5%)
	osteonecrosis (<1%)
neoplasms	myelodysplastic syndrome (<1%)
nervous system	dizziness, balance disorder (3%)
	dysgeusia (4%)
	headache (4%)
	peripheral neuropathy (7%)
	toxic encephalopathy (<1%)
psychiatric	insomnia (2%)
	dyspnea (3%)

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ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
respiratory, thoracic and mediastinal	epistaxis (1%)
skin and subcutaneous tissue	alopecia (1%)
	pigmentation changes (1%)
	pruritus (1%)
	rash (3%)
vascular	embolism, venous embolism (1%)
	hypotension (1%)
	phlebitis, thrombophlebitis (1%)
	thrombosis, deep vein thrombosis (1%)

Adapted from standard reference[1] unless specified otherwise.

Reversible ***myelosuppression*** is the most frequent and serious adverse effect related to single-agent lurbinectedin. Dose reduction and secondary prophylaxis with GCSF may be required. Concurrent use of aprepitant or other NK-1 antagonists with lurbinectedin may cause more severe and prolonged myelosuppression and should be avoided.[1]

INTERACTIONS:

AGENT	EFFECT	MECHANISM	MANAGEMENT
aprepitant[1]	aprepitant reduced lurbinectedin clearance and Vd by 42% and 40% respectively	inhibition of CYP 3A4 by aprepitant	avoid concurrent use of aprepitant and other NK-1 antagonists with lurbinectedin

Lurbinectedin is a substrate of CYP 3A4. CYP 3A4 is the major isoform involved in the metabolism of lurbinectedin. If possible, avoid concomitant therapy with drugs which induce or inhibit CYP 3A4; monitor for reduced effect or increased toxicity as applicable.[1]

SUPPLY AND STORAGE:

Injection:

Jazz Pharmaceuticals Canada Incorporated supplies lurbinectedin as 4 mg vials of preservative free lyophilized powder. Refrigerate.[5]

Pharma Mar SA supplies lurbinectedin (via Health Canada Special Access Program) as 4 mg vials of lyophilized powder. Refrigerate.[1,6]

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

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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:

- for administration through a ***peripheral*** line, dilute lurbinectedin in at least 250 mL of suitable diluent (e.g., NS or D5W); if administered via a ***central line***, lurbinectedin may be diluted in a minimum volume of 100 mL[5]
- filters are not required for administration of lurbinectedin; however, if a filter is to be used, infusion sets containing ***nylon*** membrane filters should NOT be used when lurbinectedin is diluted with NS[5] (NOTE: BD Alaris pump infusion/syringe sets have polyethersulfone membrane in-line filters)[7]

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 1 hour***[1,2,8]
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[1,2,8]:	***3.2 mg/m²*** (range 2-3.2 mg/m²) ***IV for one dose on day 1*** (total dose per cycle 3.2 mg/m² [range 2-3.2 mg/m²])

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6. Pharma Mar. Lurbinectedin Compassionate Use: Preparation Guide for Infusion - edition 1. Madrid, Spain; April 2019
7. Linda Ewing.BD US Market Manager. WW Infusion Disposables. Personal communication. Feb2018
8. Paz-Ares L, Trigo Perez JM, Besse B, et al. Efficacy and safety profile of lurbinectedin in second-line SCLC patients: Results from a phase II single-agent trial. J Clin Oncol 2019;37(15 suppl):abstract 8506

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