

DRUG NAME: Lurbinectedin

SYNONYM(S): PM01183,¹ PM1183¹

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 $\geq 5\%$ higher in the treatment group.

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in <i>bold, italics</i>	
blood and lymphatic system/ febrile neutropenia (see paragraph following Side Effects table)	<i>anemia</i> (93%, severe 17%)
	<i>febrile neutropenia</i> (6.5%)
	leukopenia (73%, severe 30%)
	lymphopenia (79%, severe 33%)
	<i>neutropenia</i> (64%, severe 41%)
	pancytopenia (<1%)
	<i>thrombocytopenia</i> (49%, severe 10%)
cardiac	arrhythmia, supraventricular (<1%)
	myocardial infarction (<1%)
gastrointestinal	<i>emetogenic potential: low</i> ^{1,3}
	abdominal pain (9%)

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in <i>bold, italics</i>	
	constipation (17%)
	diarrhea (13%, severe 1%)
	<i>nausea</i> (51%, severe 3%)
	stomatitis (3%)
	<i>vomiting</i> (25%, severe 3%)
general disorders and administration site conditions	<i>extravasation hazard: irritant</i> ^{1,4}
	extravasation (1%)
	<i>fatigue</i> (53%, severe 7%)
	infusion site thrombosis (<1%)
	<i>injection site reaction, phlebitis</i> (2%, severe 1%)
infections and infestations	<i>infections</i> , including bacterial, viral, fungal (6%)
	sepsis, septic shock (<1%)
investigations	<i>alkaline phosphatase increase</i> (46%, severe 5%)
	<i>ALT increase</i> (66%, severe 6%)
	<i>AST increase</i> (50%, severe 3%)
	<i>bilirubin increase</i> (12%, severe 2%)
	creatinine phosphokinase increase (9%, severe <1%)
	<i>creatinine increase</i> (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%)
respiratory, thoracic and mediastinal	dyspnea (3%)
	epistaxis (1%)
skin and subcutaneous	alopecia (1%)

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in <i>bold, italics</i>	
tissue	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 reference¹ 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: Pharma Mar SA supplies lurbinectedin as 4 mg vials of lyophilized powder. Refrigerate.^{1,5}

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.

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	<i>over 1 hour</i> ^{1,2,6}
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^{1,2,6}: ***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])

REFERENCES:

1. Pharma Mar. Lurbinectedin Investigator's Brochure - version 12. Madrid, Spain; 9 March 2020.
2. Trigo J, Subbiah V, Besse B, Moreno V, et al. Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial. *Lancet Oncol* 2020; Available online 27 March 2020:1-9.
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.
5. Pharma Mar. Lurbinectedin Compassionate Use: Preparation Guide for Infusion - edition 1. Madrid, Spain; April 2019.
6. 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.