

DRUG NAME: Irinotecan liposome

SYNONYM: irinotecan liposomal¹, liposomal irinotecan¹, nanoliposomal irinotecan², pegylated liposomal irinotecan hydrochloride¹

COMMON TRADE NAME(S): ONIVYDE®

CLASSIFICATION: Topoisomerase I inhibitor

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

MECHANISM OF ACTION:

The active substance of liposomal irinotecan is irinotecan encapsulated in a lipid bilayer vesicle or liposome.¹ Refer to conventional irinotecan monograph.

USES:**Primary uses:**

Pancreatic cancer

* Health Canada approved indication

Other uses:**SPECIAL PRECAUTIONS:****Caution:**

- **liposomal irinotecan** differs from conventional irinotecan in pharmacokinetic properties, dose concentration, and strength. It is **not interchangeable** with conventional irinotecan³
- **prior abdominal radiation** increases the risk of severe neutropenia and febrile neutropenia³
- **pulmonary toxicity**, including interstitial lung disease-like events, is more likely in patients with pre-existing lung disease or use of pneumotoxic drugs, colony stimulating factors, or prior radiation therapy³
- **hyperbilirubinemia** is associated with higher concentrations of total SN-38 (active metabolite) and therefore, increases the risk of neutropenia³
- patients with **Gilbert's syndrome** have increased risk of irinotecan toxicity, particularly myelosuppression, and may require greater dose reductions⁴

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.

| ORGAN SITE | SIDE EFFECT |
|---|--|
| Clinically important side effects are in bold, italics | |
| blood and lymphatic system/ febrile neutropenia | anemia (97%, severe 6%) |
| | lymphopenia (81%, severe 27%) |
| | neutropenia (52%, severe 20%) |
| | neutropenic fever (6%, severe 3%) |
| | thrombocytopenia (41%, severe 2%) |
| general disorders and administration site conditions | extravasation hazard: none ⁵ |

| ORGAN SITE | SIDE EFFECT |
|---|---|
| Clinically important side effects are in bold, italics | |
| gastrointestinal | <i>emetogenic potential</i> : low moderate ⁶ |
| | <i>diarrhea, early onset</i> (30%, severe 3%); see paragraph following Side Effects table |
| | <i>diarrhea, late onset</i> (43%, severe 9%); see paragraph following Side Effects table |
| | nausea (51%, severe 8%) |
| | stomatitis (32%, severe 0.7%) |
| | vomiting (51%, severe 11%) |
| immune system | infusion reaction (3%); see paragraph following Side Effects table |
| investigations | increased ALT (51%, severe 6%) |
| | increased creatinine (18%, severe 0%) |
| | hypoalbuminemia (43%, severe 2%) |
| | hypocalcemia (32%, severe 1%) |
| | hypokalemia (32%, severe 2%) |
| | hypomagnesemia (35%, severe 0%) |
| | hyponatremia (27%, severe 5%) |
| | hypophosphatemia (29%, severe 4%) |

Adapted from reference³ unless specified otherwise.

Early onset diarrhea occurs during or within 24 hours of administration of liposomal irinotecan and is usually transient. It may be accompanied by other **cholinergic symptoms** such as rhinitis, hypersalivation, miosis, bradycardia, diaphoresis, flushing, and abdominal cramping. Therapeutic or prophylactic atropine can be considered for early diarrhea of any severity.³

Late onset diarrhea occurs more than 24 hours after administration of liposomal irinotecan and can rarely lead to life-threatening dehydration and electrolyte imbalance. The diarrhea has a median onset of 8 days after liposomal irinotecan. Premedication with loperamide prior to irinotecan treatment is not required. However, patients should be instructed to have loperamide on hand and start treatment at the first poorly formed/loose stool or at the earliest onset of more frequent bowel movements than usual. Loperamide should be taken until diarrhea-free for 12 hours but should not be used for more than 48 hours. If diarrhea persists while patient is on loperamide for more than 24 hours, an oral antibiotic support (e.g., fluoroquinolone for 7 days) may be added. Patients with severe diarrhea should be carefully monitored for dehydration and given fluid and electrolyte replacement as needed. If diarrhea persists for more than 48 hours while on loperamide, stop loperamide, monitor and replace fluid electrolytes and continue antibiotic support until resolution of accompanying symptoms.³

Infusion reactions, primarily consisting of rash, urticaria, periorbital edema, or pruritus have been reported, mostly during the early therapy of liposomal irinotecan. **Hypersensitivity reactions**, including acute infusion reaction may occur.³

INTERACTIONS: Refer to conventional irinotecan monograph.

SUPPLY AND STORAGE:

Injection:

Servier Canada Inc. supplies irinotecan liposome as a liposomal dispersion (of the sucrose octasulfate salt) in single-use vials containing the equivalent of 43 mg irinotecan free base in a concentration of 4.3 mg/mL. Refrigerate. Protect from light.⁷

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 in **bold, italics**

| | |
|------------------------------|--|
| Subcutaneous | no information found |
| Intramuscular | no information found |
| Direct intravenous | do NOT use ¹ |
| Intermittent infusion | over 90 min¹ ; do NOT use in-line filters ³ |
| 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**

| | | |
|---------------------|---|--|
| <i>Intravenous:</i> | Cycle Length: 2 weeks⁴ | 70 mg/m² (irinotecan free base) (range 50-70 mg/m ²) IV for one dose on day 1 (total dose per cycle 70 mg/m ² [range 50-70 mg/m ²]) |
| | 2 weeks ^{1,3} : | 80 mg/m ² (irinotecan hydrochloride trihydrate) (range 40-80 mg/m ²) IV for one dose on day 1 (total dose per cycle 80 mg/m ² [range 40-80 mg/m ²]) |

Dosage in myelosuppression, renal failure, hepatic failure, and diarrhea^{1,4}:

| NCIC Grade | 1st event dose | 2nd event dose | 3rd event dose |
|------------|---|---|----------------|
| 1 and 2 | 100% | 100% | 100% |
| 3 and 4 | reduce to 60 mg/m ² (irinotecan hydrochloride trihydrate) or reduce to 50 mg/m ² (irinotecan free base) | reduce to 50 mg/m ² (irinotecan hydrochloride trihydrate) or reduce to 43 mg/m ² (irinotecan free base) | discontinue |

REFERENCES:

1. Baxalta. ONIVYDE® Summary of product characteristics. Vienna, Austria; undated.
2. Wang-Gillam A, Li C, Bodoky G, et al. Nanoliposomal irinotecan with fluorouracil and folinic acid in metastatic pancreatic cancer after previous gemcitabine-based therapy (NAPOLI-1): a global, randomised, open-label, phase 3 trial. *The Lancet* 2016;387(10018):545-557.
3. Merrimack Pharmaceuticals Inc. ONIVYDE® prescribing information. Cambridge, Massachusetts, USA; Oct 2015.
4. Baxalta Canada Corporation. ONIVYDE® product monograph. Toronto, Ontario; 11 August 2017.
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 Agency; January 2016.
6. 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.
7. Servier Canada Inc. ONIVYDE® product monograph. Laval, Quebec; 4 January 2019.