Topotecan:

Class:
- Antineoplastic Agent, Camptothecin; Antineoplastic Agent, Topoisomerase I Inhibitor

Indications:
- **Cervical cancer**: Treatment of recurrent or resistant (stage IVB) cervical cancer (in combination with cisplatin)
- **Ovarian cancer**: Treatment of metastatic ovarian cancer
- **Small cell lung cancer (SCLC)**: Treatment of relapsed or refractory SCLC

Unlabeled use:
- Treatment of acute myeloid leukemia (induction in older adults),
- central nervous system lesions (metastatic from lung cancer),
- central nervous system lymphoma (primary),
- Ewing’s sarcoma,
- merkel cell cancer,
- osteosarcoma,
- rhabdomyosarcoma (pediatrics),
- neuroblastoma (pediatrics)

Available dosage form in the hospital:
- 4 mg / vial

Trade Names:
- Hycamtin , Oncotecam , Oncotecan , Topodria , Topokebir , Topotel

Dosage:  
**Note:** Baseline neutrophil count should be ≥1500/mm$^3$ and platelets should be ≥100,000/mm$^3$ prior to treatment; for retreatment, neutrophil count should be >1000/mm$^3$; platelets >100,000/mm$^3$ and hemoglobin ≥9 g/dL:

- **Cervical cancer, recurrent or resistant:** IVPB: 0.75 mg/m$^2$/day for 3 days (followed by cisplatin on day 1 only, [with hydration]) every 21 days

- **Ovarian cancer, metastatic:** IVPB: 1.5 mg/m$^2$/day for 5 consecutive days every 21 days, minimum of 4 cycles recommended in the absence of tumor progression or weekly administration; unlabeled dosing) 4 mg/m$^2$ on days 1, 8, and 15 every 28 days until disease progression or unacceptable toxicity or a maximum of 12 months (Sehouli, 2011)

- **Small cell lung cancer (SCLC), relapsed or refractory:**
  - IVPB: 1.5 mg/m$^2$/day for 5 consecutive days every 21 days, minimum of 4 cycles recommended in the absence of tumor progression
  - Oral: 2.3 mg/m$^2$/day for 5 consecutive days every 21 days (round dose to the nearest 0.25 mg); if patient vomits after dose is administered; do not give a replacement dose.

Geriatric
Refer to adult dosing.
**Renal Impairment:**

**Manufacturer’s recommendations:**

**I.V.:**
- \( \text{Cl}_\text{cr} \geq 40 \text{ mL/minute: No dosage adjustment necessary.} \)
- \( \text{Cl}_\text{cr} 20-39 \text{ mL/minute: Reduce dose to 0.75 mg/m}^2/\text{dose} \)
- \( \text{Cl}_\text{cr} < 20 \text{ mL/minute: No dosage adjustment provided in manufacturer’s U.S. labeling (insufficient data available for dosing recommendation); use is contraindicated in the Canadian labeling.} \)

**Note:** For topotecan in combination with cisplatin for cervical cancer, do not initiate treatment in patients with serum creatinine >1.5 mg/dL; consider discontinuing treatment in patients with serum creatinine >1.5 mg/dL in subsequent cycles.

**Oral:**
- \( \text{Cl}_\text{cr} \geq 50 \text{ mL/minute: No dosage adjustment necessary.} \)
- \( \text{Cl}_\text{cr} 30-49 \text{ mL/minute: Reduce dose to 1.8 mg/m}^2/\text{day} \)
- \( \text{Cl}_\text{cr} < 30 \text{ mL/minute: No dosage adjustment provided in manufacturer’s U.S. labeling (insufficient data available for dosing recommendation).} \)

**Alternate recommendations:**

*Arnonoff, 2007: I.V.:

**Adults:**
- \( \text{Cl}_\text{cr} > 50 \text{ mL/minute: Administer 75\% of dose} \)
- \( \text{Cl}_\text{cr} 10-50 \text{ mL/minute: Administer 50\% of dose} \)
- \( \text{Cl}_\text{cr} < 10 \text{ mL/minute: Administer 25\% of dose} \)

**Hemodialysis:** Avoid use

**Continuous ambulatory peritoneal dialysis (CAPD):** Avoid use

**Continuous renal replacement therapy (CRRT):** 0.75 mg/m²

*Kintzel, 1995: I.V.:*

- \( \text{Cl}_\text{cr} 46-60 \text{ mL/minute: Administer 80\% of dose} \)
- \( \text{Cl}_\text{cr} 31-45 \text{ mL/minute: Administer 75\% of dose} \)
- \( \text{Cl}_\text{cr} \leq 30 \text{ mL/minute: Administer 70\% of dose} \)

**Hepatic Impairment:**

**Manufacturer’s labeling:**

**I.V.:** Bilirubin 1.7-15 mg/dL (U.S. labeling) or >1.5 - <10 mg/dL (Canadian labeling): No dosage adjustment necessary (the half-life is increased slightly; usual doses are generally tolerated).

**Oral:** Bilirubin >1.5 mg/dL: No dosage adjustment necessary.

**Dosing: Obesity**

*ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer:* Utilize patient’s actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider resumption of
full weight-based dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs, 2012).

**Dosing: Adjustment for Toxicity**

1. **Cervical cancer (cisplatin may also require dosage adjustment):** I.V.: Severe febrile neutropenia (<1000/mm$^3$ with temperature of 38°C) or platelet count <25,000/mm$^3$: Reduce topotecan to 0.6 mg/m$^2$/day for subsequent cycles (may consider G-CSF support [beginning on day 4] prior to instituting dose reduction for neutropenic fever.  

   *For neutropenic fever despite G-CSF use, reduce dose to 0.45 mg/m$^2$/day for subsequent cycles.*

2. **Ovarian cancer:** I.V.: Dosage adjustment for hematological effects: Severe neutropenia (<500/mm$^3$) or platelet count <25,000/mm$^3$: Reduce dose to 1.25 mg/m$^2$/day for subsequent cycles (may consider G-CSF support [beginning on day 6] prior to instituting dose reduction for severe neutropenia). **Note:** The Canadian labeling states that the dose may be further reduced to 1 mg/m$^2$/day if necessary.

3. **Small cell lung cancer (SCLC):**
   - **I.V.:** Dosage adjustment for hematological effects: Severe neutropenia (<500/mm$^3$) or platelet count <25,000/mm$^3$: Reduce dose to 1.25 mg/m$^2$/day for subsequent cycles (may consider G-CSF support [beginning on day 6] prior to instituting dose reduction for severe neutropenia). **Note:** The Canadian labeling states that the dose may be further reduced to 1 mg/m$^2$/day if necessary.
   - **Oral:** Severe neutropenia (neutrophils <500/mm$^3$ associated with fever or infection or lasting ≥7 days) or prolonged neutropenia (neutrophils ≥500/mm$^3$ to ≤1000/mm$^3$ lasting beyond day 21) or platelets <25,000/mm$^3$ or grades 3/4 diarrhea: Reduce dose by 0.4 mg/m$^2$/day for subsequent cycles (may consider same dosage reduction for grade 2 diarrhea if clinically indicated).

**Common side effect:**

- Central nervous system: Fatigue (6% to 29%), fever (5% to 28%), pain (5% to 23%), headache (18%)
- Dermatologic: Alopecia (10% to 49%), rash (16%)
- Gastrointestinal: Nausea (8% to 64%), vomiting (10% to 45%), diarrhea (6% to 32%); Oral: grade 3: 4%; grade 4: ≤1%; onset: 9 days), constipation (5% to 29%), abdominal pain (5% to 22%), anorexia (7% to 19%), stomatitis (18%)
- Hematologic: Anemia (89% to 98%; grade 4: 7% to 37%; nadir: 15 days), neutropenia (83% to 97%; grade 4: 32% to 80%; nadir 12-15 days; duration: 7 days), leukopenia (86% to 97%; grade 4: 15% to 32%), thrombocytopenia (69% to 81%; grade 4: 6% to 27%; nadir: 15 days; duration: 3-5 days), neutropenic fever/sepsis (2% to 43%)
- Neuromuscular & skeletal: Weakness (3% to 25%)
- Respiratory: Dyspnea (6% to 22%), cough (15%)
- Miscellaneous: Infection (≤17%)

**Pregnancy Risk Factor:** D