Topotecan (toe-poe-tee-kan)

**Pharmacologic Class:** Antineoplastics

**Class:** Enzyme inhibitors

**Pregnancy Category:** D

## Indications

- **IV:** Metastatic ovarian cancer that has not responded to previous chemotherapy.
- **Small cell lung cancer** unresponsive to first-line therapy.
- **PO:** Relapsed small cell lung cancer in patients with a complete or partial prior response and who are at least 45 days from the end of first-line chemotherapy. Stage IV-B persistent or recurrent cervical cancer not amenable to treatment with surgery or radiation (with cisplatin).

## Action

Interferes with DNA synthesis by inhibiting the enzyme topoisomerase. Therapeutic Effects: Death of rapidly replicating cells, particularly malignant ones.

## Pharmacokinetics

- **Absorption:** IV administration results in complete bioavailability.
- **Distribution:** Unknown.
- **Metabolism and Excretion:** 30% excreted in urine; small amounts metabolized by the liver.
- **Half-life:** PO—3–6 hr; IV—2–3 hr.

### TIME/ACTION PROFILE (effects on WBCs)

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO</td>
<td>unknown</td>
<td>1–2 hr</td>
<td>24 hr</td>
</tr>
<tr>
<td>IV</td>
<td>within days</td>
<td>11 days</td>
<td>7 days</td>
</tr>
</tbody>
</table>

## Contraindications/Precautions

- **Contraindicated in:** Hypersensitivity; Pre-existing severe myelosuppression; OB, Lactation: Pregnancy or lactation.
- **Use Cautiously in:** Impaired renal function (adjust dose if CCr < 40 mL/min); Platelet count < 25,000 cells/mm³; History of interstitial lung disease, pulmonary fibrosis, lung cancer, thoracic radiation, or use of pneumotoxic drugs or colony-stimulating factors; OB: May require dose ↓ due to increased fetofetal transport.

## Adverse Reactions/Side Effects

- **CNS:** Headache, fatigue, weakness.
- **Resp:** Interstitial lung disease, dyspnea.
- **GI:** Abdominal pain, diarrhea, nausea, vomiting, anorexia, constipation, liver enzymes, stomatitis.
- **Derm:** Alopecia.
- **Hemat:** Anemia, leukopenia, thrombocytopenia.
- **MS:** Arthralgia.

## Interactions

**Drug-Drug:** Neutropenia is prolonged by concurrent use of filgrastim (do not use until day 6; 24 hr following completion of topotecan). Myelosuppression with other antineoplastics (especially platinum) or radiation therapy. May ↓ antibody response to and ↑ risk of adverse reactions from live virus vaccines.

## Route/Dosage

### PO (Adults):

- **Ovarian and Small Cell Lung Cancer:** 2.3 mg/m²/day for 5 days repeated every 21 days (round calculated oral dose to nearest 0.25 mg and prescribe the minimum number of 1 mg and 0.25 mg capsules with the same number of capsules prescribed for each of the 5 days).
- **Small Cell Lung Cancer—Cervical Cancer:** 1.5 mg/m²/day for 5 days starting on day 1 of a 21-day course; Cervical Cancer—75 mg/m² on Days 1, 2, and 3 followed by cisplatin on Day 1 and repeated every 21 days.

### IV (Adults):

- **Ovarian and Small Cell Lung Cancer—Cervical Cancer:** 0.75 mg/m²/day for 5 days starting on day 1 of a 21-day course.

## Renal Impairment

### PO (Adults):

- **Ovarian and Small Cell Lung Cancer—Cervical Cancer:** 1.8 mg/m²/day starting on day 1 of a 21-day course.
- **Small Cell Lung Cancer—Cervical Cancer—Administer at standard doses only if serum creatinine is < 1.5 mg/dL. Do not administer if serum creatinine > 1.5 mg/dL.

## Nursing Implications

### Assessment

- **Monitor vital signs frequently during administration.
- **Monitor for bone marrow depression.** Assess for bleeding (bleeding gums, bruising, petechiae, guaiac stools, urine, and emesis) and avoid IM injections and taking rectal temperatures if platelet count is low. Apply pressure to temperature sites for 10 min. Assess for signs of infection during neutropenia. Anemia may occur. Monitor for increased fatigue, dyspnea, and orthostatic hypotension.

## High Alert

- **Genetic Implication:** CAPI TALS indicate life-threatening, underlines indicate most frequent, strikethrough indicates discontinued.
Nausea and vomiting are common. Pretreatment with antiemetics should be considered.

Monitor IV site frequently for extravasation, which causes mild local erythema and bruising.

Lab Test Considerations: Monitor CBC with differential and platelet count prior to administration and frequently during therapy. Baseline neutrophil count of <1000 cells/mm³ and platelet count of <100,000 cells/mm³ are required before first dose. The nadir of neutropenia occurs in 11 days, with a duration of 7 days. The nadir of thrombocytopenia occurs in 15 days, with a duration of 5 days. The nadir of anemia occurs in 15 days. Subsequent doses should not be administered until neutrophils recover to >1000 cells/mm³, platelets recover to >75,000 cells/mm³, and hemoglobin levels recover to ≥9.0 mg/dL.

Monitor liver function. May cause transient increase in AST, ALT, and bilirubin concentrations.

Potential Nursing Diagnoses
Risk for infection (Adverse Reactions)

Implementation

High Alert: Fatalities have occurred with chemotherapeutic agents. Before administering, check all ambiguous orders, double check single dose, and course of therapy dose limits, have second practitioner independently double check original order, dose calculations and infusion pump settings.

PO: May be taken without regard to food. Capsules must be swallowed whole; do not open, crush, or chew. If patient vomits after taking dose, do not replace dose.

IV Administration

pH: 2.5–3.5

Solution should be prepared in a biologic cabinet. Wear gloves, gowns, and mask while handling IV medication. Discard IV equipment in specially designated containers.

Intermittent Infusion: Reconstitute each vial with 6 ml of sterile water for injection. Diluent: Dilute further in D10W or 0.9% NaCl. Infusion is stable for 24 hr at room temperature or up to 7 days if refrigerated. Solution is yellow to yellow-green. Concentration: 10–50 mcg/mL. Rate: Infuse over 30 min.

Y-Site Compatibility: alfuzosin, aztreonam, bezafibrate, bleomycin, carboplatin, cyclophosphamide, doxorubicin, dexamethasone, dextran, docetaxel, doxorubicin, emetine, fludarabine, gemcitabine, granisetron, heparin, levofloxacin, mitomycin, mitoxantrone, paclitaxel, carboplatin, oxaliplatin, paclitaxel, pazopanib, pamidronate, pentostatin, prednisone, tigecycline, thalidomide, vinorelbine, zoledronic acid.

Y-Site Incompatibility: amphotericin B lipid complex, docetaxel/cyclophosphamide, docetaxel/doxorubicin, docetaxel/5-fluorouracil, etoposide/cyclophosphamide, etoposide/paclitaxel, ifosfamide, methylprednisolone, metoclopramide, novantrone, octreotide, oxaliplatin, paclitaxel, prochlorperazine, doxorubicin, vinorelbine, voriconazole.

Patient/Family Teaching

Instruct patient to take as directed. If patient vomits after taking, do not replace dose; notify health care professional. Do not take missed doses; take next scheduled dose at usual time. If any capsules are broken or leaking, do not touch with bare hands; dispose of capsules and wash hands with soap and water. Patient should be instructed to read the Patient Information guide prior to first dose and with each refill; new information may be available.

May cause drowsiness or sleepiness during and for several days after therapy. Caution patient to avoid driving and other activities requiring alertness until response to medication is known.

Instruct patient to notify health care professional of fever, chills, sore throat, or signs of infection. Bloody or black stools may be an early sign of bleeding. Thrombosis, pulmonary embolism, blood in stool, nosebleeds, or other signs and symptoms of interstitial lung disease occur. Caution patient to avoid crowds and persons with known infections. Instruct patient to use nonsteroidal anti-inflammatory drugs (NSAIDs) with caution. Instruct patient to use sunscreen and protective clothing to avoid sunburn. Caution patient to avoid progestin and estrogen-containing products.

May cause diarrhea. Advise patient to notify health care professional if diarrhea occurs with fever or abdominal cramps or cramping diarrhea that occurs more than 3 times/day.

Advise patient to notify health care professional of all Rx or OTC medications, vitamins, or herbal products being taken and to consult with health care professional before taking other medications.

© 2015 F.A. Davis Company

CONTINUED
topotecan

- Discuss with patient the possibility of hair loss. Explore methods of coping.
- Instruct patient not to receive any vaccinations without advice of health care professional.
- Advise patient that this medication may have teratogenic effects. Contraception should be used during therapy and breastfeeding avoided.
- Emphasize the need for periodic lab tests to monitor for side effects.

**Evaluation/Desired Outcomes**

- Decrease in size and spread of malignancy.

Why was this drug prescribed for your patient?