Topotecan: Drug information

(For additional information see "Topotecan: Patient drug information" and see "Topotecan: Pediatric drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

ALERT: US Boxed Warning

Bone marrow suppression:

Topotecan may cause severe myelosuppression. Administer only to patients with baseline neutrophil counts of 1,500 cells/mm^3 or more and a platelet count of 100,000 cells/mm^3 or more. Monitor blood cell counts.

Brand Names: US

Hycamtin

Brand Names: Canada

Hycamtin; Topotecan For Injection; Topotecan Hydrochloride For Injection

Pharmacologic Category

Antineoplastic Agent, Camptothecin; Antineoplastic Agent, Topoisomerase I Inhibitor

Dosing: Adult

Note: Baseline neutrophil count should be ≥1500/mm^3 and platelets should be ≥100,000/mm^3 prior to treatment; for re-treatment, neutrophil count should be >1000/mm^3; platelets >100,000/mm^3 and hemoglobin ≥9 g/dL. Intravenous doses should generally not exceed 4 mg; verify dose prior to administration.

Cervical cancer, recurrent or resistant: IV: 0.75 mg/m^2/day for 3 days (in combination with cisplatin on day 1 only, [with hydration]) every 21 days

Ovarian cancer, metastatic: IV: 1.5 mg/m^2/day for 5 consecutive days every 21 days **or** (off-label dosing) 1.25 mg/m^2/day for 5 days every 21 days until disease progression or unacceptable toxicity or a maximum of 12 months (Sehouli 2011) **or** (weekly administration; off-label 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:

IV: 1.5 mg/m^2/day for 5 consecutive days every 21 days

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.

Ewing's sarcoma, relapsed/refractory or metastatic (off-label use): IV: 0.75 mg/m^2/day for 5

consecutive days every 21 days (in combination with cyclophosphamide) (Hunold 2006; Saylors 2001)

Primary CNS lymphoma, relapsed or refractory (off-label use): IV: 1.5 mg/m^2 for 5 days every 21 days for a maximum of 10 cycles or until disease progression or unacceptable toxicity (Voloschin 2008). Additional data may be necessary to further define the role of topotecan in this condition.

Rhabdomyosarcoma, metastatic (off-label use): Adults <21 years: IV: 0.75 mg/m^2/day for 5 consecutive days every 21 days for 2 cycles (window therapy; in combination with cyclophosphamide); if objective response occurred by week 6, follow with alternating cycles of vincristine, topotecan, and cyclophosphamide (VTC) with vincristine, dactinomycin, and cyclophosphamide (VAC) (Walterhouse 2004)

Dosing: Pediatric

(For additional information see "Topotecan: Pediatric drug information")

Note: Baseline neutrophil count should be ≥1500/mm^3 and platelets should be ≥100,000/mm^3 prior to treatment; for re-treatment, neutrophil count should be >1000/mm^3; platelets >100,000/mm^3 and hemoglobin ≥9 g/dL. Intravenous doses should generally not exceed 4 mg; verify dose prior to administration.

CNS malignancy, relapsed/refractory (off-label use; based on limited data): Oral: 0.8 mg/m^2/day for 21 consecutive days every 4 weeks for ≥12 cycles (Minturn 2011); additional data may be necessary to further define the role of topotecan in this condition

Ewing's sarcoma, relapsed/refractory or metastatic (off-label use): IV: 0.75 mg/m^2/day for 5 consecutive days every 21 days (in combination with cyclophosphamide) (Hunold 2006; Saylors 2001)

Neuroblastoma, relapsed/refractory (off-label use): IV: 0.75 mg/m^2/day for 5 days every 21 days (in combination with cyclophosphamide) (Ashraf 2013; London 2010) **or** 2 mg/m^2/day for 5 days every 21 days (monotherapy) (London 2010)

Rhabdomyosarcoma, metastatic (off-label use): IV: 0.75 mg/m^2/day for 5 consecutive days every 21 days for 2 cycles (window therapy; in combination with cyclophosphamide); if objective response occurred by week 6, follow with alternating cycles of vincristine, topotecan, and cyclophosphamide (VTC) with vincristine, dactinomycin, and cyclophosphamide (VAC) (Walterhouse 2004)

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

Manufacturer's labeling:

IV (single agent topotecan):

CrCl ≥40 mL/minute: No dosage adjustment necessary.

CrCl 20 to 39 mL/minute: Reduce dose to 0.75 mg/m^2/dose

CrCl <20 mL/minute: There are no dosage adjustments provided in manufacturer's U.S. labeling (insufficient data available for dosing recommendation); use is contraindicated in the Canadian labeling.

Oral:

CrCl ≥50 mL/minute: No dosage adjustment necessary.

CrCl 30 to 49 mL/minute: Reduce dose to 1.5 mg/m^2/day; may increase after the 1st cycle by 0.4 mg/m^2/day if no severe hematologic or gastrointestinal toxicities occur.

CrCl <30 mL/minute: Reduce dose to 0.6 mg/m^2/day; may increase after the 1st cycle by 0.4 mg/m^2/day if no severe hematologic or gastrointestinal toxicities occur.

Alternate recommendations:

Aronoff 2007: IV:

Adults:

CrCl >50 mL/minute: Administer 75% of dose

CrCl 10 to 50 mL/minute: Administer 50% of dose

CrCl <10 mL/minute: Administer 25% of dose

Hemodialysis: Avoid use

Continuous ambulatory peritoneal dialysis (CAPD): Avoid use

Continuous renal replacement therapy (CRRT): 0.75 mg/m^2

Children:

CrCl 30 to 50 mL/minute: Administer 75% of dose

CrCl 10 to 29 mL/minute: Administer 50% of dose

CrCl <10 mL/minute: Administer 25% of dose

Continuous renal replacement therapy (CRRT): Administer 50% of dose

Kintzel 1995: IV:

CrCl 46 to 60 mL/minute: Administer 80% of dose

CrCl 31 to 45 mL/minute: Administer 75% of dose

CrCl ≤30 mL/minute: Administer 70% of dose

Dosing: Hepatic Impairment **Manufacturer's labeling:**

IV:

US labeling: Bilirubin 1.7 to 15 mg/dL: There are no dosage adjustments provided in the manufacturer's labeling, although clearance is reduced up to 33%.

Canadian labeling: Bilirubin >1.5 to <10 mg/dL: No dosage adjustment is necessary (the half-life is increased slightly; usual doses are generally tolerated).

Oral: There is no dosage adjustment provided in the manufacturer's labeling; however, dosage

adjustment is likely not necessary as the pharmacokinetics of topotecan do not differ significantly based on serum bilirubin, ALT, or AST.

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

Cervical cancer (cisplatin may also require dosage adjustment): IV: 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).

If necessary, may further reduce dose to 0.45 mg/m^2/day for subsequent cycles.

Ovarian cancer: IV: 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.

Small cell lung cancer (SCLC):

IV: 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: Reduce dose by 0.4 mg/m^2/day for subsequent cycles.

Diarrhea (grade 3 or 4): Do not administer to patients with grade 3 or 4 diarrhea. Upon recovery to ≤grade 1 toxicity, reduce dose by 0.4 mg/m^2/day for subsequent cycles.

Dosage Forms

Excipient information presented when available (limited, particularly for generics); consult specific product labeling. [DSC] = Discontinued product

Capsule, Oral:

Hycamtin: 0.25 mg, 1 mg

Solution, Intravenous [preservative free]:

Generic: 4 mg/4 mL (4 mL)

Solution Reconstituted, Intravenous:

Generic: 4 mg (1 ea [DSC])

Solution Reconstituted, Intravenous [preservative free]:

Hycamtin: 4 mg (1 ea)

Generic: 4 mg (1 ea)

Generic Equivalent Available (US) May be product dependent

Administration

IV: Administer IVPB over 30 minutes. For combination chemotherapy with cisplatin, administer pretreatment hydration.

Oral: Administer without regard to meals. Swallow whole; do not open, crush, chew, or divide capsule. If vomiting occurs after dose, do not take replacement dose. For patients unable to swallow capsules whole, reconstituted topotecan solution for injection (1 mg/mL concentration) may be mixed with up to 30 mL of acidic fruit juice (eg, apple, orange, grape) immediately prior to oral administration (Daw 2004).

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends double gloving, a protective gown, ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator), and closed system transfer devices (CSTDs) for IV preparation. Double gloving, a gown, and (if dosage form allows) CSTDs are required during IV administration. NIOSH recommends single gloving for administration of an intact tablet/capsule (NIOSH 2016). If manipulating tablets/capsules (eg, to prepare an oral suspension), NIOSH recommends double gloving, a protective gown, and preparation in a controlled device; if not prepared in a controlled device, respiratory and eye/face protection as well as ventilated engineering controls are recommended. NIOSH recommends double gloving, a protective gown, and (if there is a potential for vomit or spit up) eye/face protection for administration of an oral liquid/feeding tube administration.

Use

Cervical cancer, recurrent or resistant: Treatment of recurrent or resistant (stage IVB) cervical cancer (in combination with cisplatin) which is not amenable to curative treatment

Ovarian cancer, metastatic: Treatment of metastatic ovarian cancer (as a single agent) after disease progression on or after initial or subsequent chemotherapy

Small cell lung cancer, relapsed:

Injection: Treatment of small cell lung cancer (as a single agent) in patients with platinum-sensitive disease which has progressed at least 60 days after initiation of first-line chemotherapy

Oral: Treatment of relapsed small cell lung cancer in patients with a prior complete or partial response and who are at least 45 days from the end of first-line chemotherapy

Use: Off-Label

Acute myeloid leukemia (induction in older adults); CNS malignancy, relapsed/refractory; Ewing sarcoma; Neuroblastoma, relapsed/refractory; Ovarian cancer, metastatic (off-label [weekly] dosing); Primary CNS lymphoma, relapsed or refractory; Rhabdomyosarcoma

Medication Safety Issues

Sound-alike/look-alike issues:

Hycamtin may be confused with Mycamine

Topotecan may be confused with irinotecan

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Other safety concerns:

Topotecan overdoses have been reported; potential causes include omission of the leading zero and missing the decimal point when prescribing, preparing, and administering. Recommended intravenous doses should generally not exceed 4 mg; verify dose prior to administration.

Adverse Reactions

>10%:

Central nervous system: Fatigue (oral: 11% to 19%)

Dermatologic: Alopecia (oral: 10% to 20%)

Gastrointestinal: Nausea (oral: 27% to 33%), anorexia (intravenous: 32%; oral: 7% to 14%), diarrhea (oral: 14% to 22%, grade 3: 4%, grade 4: ≤1%; intravenous: grades 3/4: 6%), vomiting (oral: 19% to 21%)

Hematologic & oncologic: Anemia (oral: 94% to 98%; grades 3/4: 25%; grade 3: 15% to 18%; grade 4: 7% to 10%; intravenous: grades 3/4: 37% to 42%), neutropenia (oral: 83% to 91%; grade 3: 24% to 28%; grade 4: 32% to 33%; intravenous: grade 4: 70% to 80%; nadir 12 to 15 days; duration: 7 days), thrombocytopenia (oral: 81%; grade 3: 29% to 30%; grade 4: 6% to 7%; intravenous: grade 4: 27% to 29%; nadir: 15 days; duration: 3 to 5 days), febrile neutropenia (intravenous: grade 3/4: 23% to 28%; oral: grade 4: 4%), neutropenic infection (13% to 17%)

1% to 10%:

Gastrointestinal: Abdominal pain (intravenous: grades 3/4: 5% to 6%)

Hepatic: Increased liver enzymes (intravenous: 8%; transient)

Neuromuscular & skeletal: Weakness (3% to 7%)

Respiratory: Dyspnea (intravenous: 6% to 9%)

Miscellaneous: Fever (oral: 5% to 7%), sepsis (intravenous: grades 3/4: 5%; oral: 2%)

<1%, postmarketing, and/or case reports: Anaphylactoid reactions, angioedema, arthralgia, chest pain, cough, dermatitis (severe), extravasation, headache, hemorrhage (severe, associated with thrombocytopenia), hypersensitivity reaction, interstitial pulmonary disease, leukopenia, myalgia, neutropenic enterocolitis, pancytopenia, paresthesia, pruritus (severe), skin rash, stomatitis, typhlitis

Contraindications

Hypersensitivity to topotecan or any component of the formulation

Canadian labeling: Additional contraindications (not in U.S. labeling): Severe renal impairment (CrCl <20 mL/minute); pregnancy; breast-feeding; severe bone marrow depression

Warnings/Precautions

Concerns related to adverse effects:

• Bone marrow suppression: **[US Boxed Warning]: May cause severe myelosuppression. Monitor blood counts frequently. Do NOT administer to patients with baseline neutrophils <1500/mm^3 and platelets <100,000/mm^3.** The dose-limiting toxicity is bone marrow suppression (primarily neutropenia); may also cause thrombocytopenia and anemia. Grade 3 and 4 events were common. Severe myelotoxicity has also been reported when used in combination with cisplatin. Neutropenia is not cumulative over time. The median duration of neutropenia and thrombocytopenia was 7 days and 5 days, respectively. Nadir neutrophil and platelet counts occurred at a median of 15 days (when administered orally). In a clinical study comparing IV to oral topotecan, G-CSF support was administered in a higher percentage of patients receiving oral topotecan (Eckardt 2007). Bone marrow suppression may require dosage reduction and/or growth factor support.

• Extravasation: Extravasation injuries have been reported (some severe); if extravasation occurs, discontinue infusion immediately and manage appropriately. Ensure proper needle or catheter placement prior to and during infusion. Avoid extravasation.

• Gastrointestinal toxicity: Diarrhea has been reported with oral topotecan; may be severe (requiring hospitalization); educate patients on early recognition and proper management, including diet changes, increase in fluid intake, antidiarrheals, and antibiotics. The median time to onset of diarrhea (grade 2 or worse) was 9 days. The incidence of diarrhea may be higher in the elderly. Do not administer in patients with grade 3 or 4 diarrhea; reduce dose upon recovery to ≤grade 1 toxicity.

• Interstitial lung disease (ILD): ILD (with fatalities) has been reported; monitor for pulmonary signs/symptoms (eg, dyspnea, fever, cough, hypoxia) and discontinue use in patients with confirmed ILD diagnosis. Risk factors for ILD include a history of ILD, pulmonary fibrosis, lung cancer, thoracic radiation, and the use of colony-stimulating factors or medication with pulmonary toxicity.

• Neutropenic enterocolitis: Topotecan-induced neutropenia may lead to typhlitis (neutropenic enterocolitis), including fatalities; should be considered in patients presenting with neutropenia, fever, and abdominal pain.

Disease-related concerns:

• Renal impairment: Use with caution in patients with renal impairment; may require dose adjustment. Use in severe renal impairment is contraindicated in the Canadian labeling.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information. Topotecan exposure is increased when oral topotecan is used concurrently with P-glycoprotein inhibitors; avoid concurrent use.

Other warnings/precautions:

• Safety issue: Topotecan overdoses have been reported; potential causes include omission of the leading zero and missing the decimal point when prescribing, preparing, and administering. Recommended intravenous doses should generally not exceed 4 mg in adults; verify dose prior to administration.

Metabolism/Transport Effects **Substrate** of BCRP

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

BCG (Intravesical): Immunosuppressants may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

BCG (Intravesical): Myelosuppressive Agents may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

BCRP/ABCG2 Inhibitors: May increase the serum concentration of Topotecan. *Risk D: Consider therapy modification*

CloZAPine: Myelosuppressive Agents may enhance the adverse/toxic effect of CloZAPine. Specifically, the risk for neutropenia may be increased. *Risk C: Monitor therapy*

Coccidioides immitis Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioides immitis Skin Test. *Risk C: Monitor therapy*

Deferiprone: Myelosuppressive Agents may enhance the neutropenic effect of Deferiprone. *Risk X: Avoid combination*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Dipyrone: May enhance the adverse/toxic effect of Myelosuppressive Agents. Specifically, the risk for agranulocytosis and pancytopenia may be increased *Risk X: Avoid combination*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Fingolimod: Immunosuppressants may enhance the immunosuppressive effect of Fingolimod. Management: Avoid the concomitant use of fingolimod and other immunosuppressants when possible. If combined, monitor patients closely for additive immunosuppressant effects (eg, infections). *Risk D: Consider therapy modification*

Fosphenytoin-Phenytoin: May decrease the serum concentration of Topotecan. Management: Monitor topotecan response closely, and consider alternatives to phenytoin when possible. No specific guidelines for topotecan dose adjustment are available. *Risk D: Consider therapy modification*

Granulocyte Colony-Stimulating Factors: May enhance the myelosuppressive effect of Topotecan. *Risk D: Consider therapy modification*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Lenograstim: Antineoplastic Agents may diminish the therapeutic effect of Lenograstim. *Risk D: Consider therapy modification*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Nivolumab: Immunosuppressants may diminish the therapeutic effect of Nivolumab. *Risk D: Consider therapy modification*

Ocrelizumab: May enhance the immunosuppressive effect of Immunosuppressants. *Risk C: Monitor therapy*

Palifermin: May enhance the adverse/toxic effect of Antineoplastic Agents. Specifically, the duration and severity of oral mucositis may be increased. Management: Do not administer palifermin within 24 hours before, during infusion of, or within 24 hours after administration of myelotoxic chemotherapy. *Risk D: Consider therapy modification*

P-glycoprotein/ABCB1 Inhibitors: May increase the serum concentration of Topotecan. *Risk X: Avoid combination*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Platinum Derivatives: May enhance the adverse/toxic effect of Topotecan. *Risk D: Consider therapy modification*

Promazine: May enhance the myelosuppressive effect of Myelosuppressive Agents. *Risk C: Monitor therapy*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Tertomotide: Immunosuppressants may diminish the therapeutic effect of Tertomotide. *Risk C: Monitor therapy*

Tofacitinib: Immunosuppressants may enhance the immunosuppressive effect of Tofacitinib. Management: Concurrent use with antirheumatic doses of methotrexate or nonbiologic disease modifying antirheumatic drugs (DMARDs) is permitted, and this warning seems particularly focused on more potent immunosuppressants. *Risk X: Avoid combination*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). Management: Vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

Velpatasvir: May increase the serum concentration of Topotecan. *Risk X: Avoid combination*

Pregnancy Risk Factor

D (show table)

Pregnancy Implications

Adverse effects were observed in animal reproduction studies. May cause fetal harm in pregnant women. Women of childbearing potential should use highly effective contraception to prevent pregnancy during treatment and for at least 1 month after therapy discontinuation. Males with female partners of childbearing potential should use highly effective contraception during treatment and for 3 months after therapy discontinuation. Topotecan may have both acute and long-term effects on fertility in women; fertility in males may be impaired due to effects on spermatogenesis.

Breast-Feeding Considerations

It is not known if topotecan is excreted in breast milk. Due to the potential for serious adverse reactions in the nursing infant, the manufacturer recommends to discontinue breast-feeding in women who are receiving topotecan.

Monitoring Parameters

CBC with differential and platelet count, renal function tests, bilirubin; monitor for symptoms of interstitial lung disease; diarrhea symptoms/hydration status

Mechanism of Action

Binds to topoisomerase I and stabilizes the cleavable complex so that religation of the cleaved DNA strand cannot occur. This results in the accumulation of cleavable complexes and single-strand DNA breaks. Topotecan acts in S phase of the cell cycle.

Pharmacodynamics/Kinetics

Note: Pharmacokinetic data in pediatric patients and young adults (0.4-22 years) demonstrated a high level of interpatient variability (43% to 57% dependent upon parameter evaluated) as well as intrapatient variability (20% to 22% dependent upon parameter evaluated) (Schaiquevich 2007)

Absorption: Oral: Rapid

Distribution: V_d:

Pediatric patients and young adults (0.4-22 years): Mean range: 32.2-32.7 L/m^2 (Schaiquevich, 2007)

Adults: 25 to 75 L/m^2 (Hartmann 2006)

Protein binding: ~35%

Metabolism: Undergoes a rapid, pH-dependent hydrolysis of the lactone ring to yield a relatively inactive hydroxy acid in plasma; metabolized in the liver to N-demethylated metabolite

Bioavailability: Oral: Capsule: Adults: ~40%; data from pediatric patients (1-18 years) showed that, while highly variable, the reported median oral bioavailability with oral administration of the reconstituted parenteral solution is similar to adults (Daw 2004; Zamboni 1999)

Half-life elimination:

Pediatric patients (0-18 years): Lactone moiety: 2.58 hours ± 0.15 (range: 0.2-7.1 hours) (Santana 2005)

Adults: IV: 2 to 3 hours; renal impairment: ~5 hours; Oral: 3 to 6 hours

Time to peak, plasma:

Pediatric patients (1-18 years): Parenteral formulation (reconstituted lyophilized formulation): 0.75-2 hours (Zamboni 1999)

Adults: Oral: 1 to 2 hours; delayed with high-fat meal (3 to 4 hours)

Excretion:

IV: Urine (51%; ~3% as N-desmethyl topotecan); feces (18%; ~2% as N-desmethyl topotecan)

Oral: Urine (20%; 2% as N-desmethyl topotecan); feces (33%; <2% as N-desmethyl topotecan)

Clearance:

Pediatric patients (0.4-18 years): GFR most significant determinant of clearance; a linear model with GFR has been observed; BSA is also a significant determinant of clearance and AUC more so than patient weight; infants <6 months have decreased clearance (Schaiquevich 2007). However, pharmacokinetic data from six pediatric patients with severe renal impairment (n=5: Unilateral nephrectomy; n=1: Anephric on hemodialysis) suggests that other mechanisms than GFR may assist with renal clearance; in these patients, overall systemic clearance was shown to be similar to matched controls (age, BSA, and Scr) despite decreased GFR (Iacono 2003; Iacono 2004)

Adults: Topotecan plasma clearance is 24% higher in males than in female patients

Pricing: US

Capsules (Hycamtin Oral)

0.25 mg (10): $1205.92

1 mg (10): $4823.58

Solution (Topotecan HCl Intravenous)

4 mg/4 mL (4 mL): $134.66

Solution (reconstituted) (Hycamtin Intravenous)

4 mg (1): $1389.00

Solution (reconstituted) (Topotecan HCl Intravenous)

4 mg (1): $282.00

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

Camtoop (CR, DO, GT, HN, NI, PA, SV); Firotex (VN); Hikamtyn (UA); Hycamtin (AE, AR, AT, AU, BE, BG, BH, BR, CH, CL, CN, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IL, IS, IT, JO, KR, KW, LB, LT, LU, MT, MY, NL, NO, NZ, PH, PK, PL, PT, QA, RO, RU, SA, SE, SG, SI, SK, TH, TR, TW, UY, VE, VN, ZW); Oncotecan (CO, EC, PE); Potactasol (LV, MT); Potekam (PY); Topodria (CO); Topokebir (AR); Topotel (IN, PH, ZW); Toranex (CR, DO, GT, HN, NI, PA, SV)

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