Topotecan HCl

Brand names	Hycamtin
Medication error potential	ISMP high-alert medication that has an increased risk of causing significant patient harm if it is used in error.[1] Look-alike, sound-alike drug names USP reports that topotecan has been confused with irinotecan; no patient harm resulted.[2]
Contraindications and warnings	**U.S. boxed warning:** Must be administered under the supervision of an experienced physician. Topotecan may cause severe bone marrow suppression, primarily neutropenia, and should not be administered to patients with baseline neutrophil counts <1500 cells/mm^3 and platelets <100,000/mm^3. Monitor blood counts before and during therapy.[3] (See Monitoring in the Comments section.) **Contraindications:** Should not be used in patients with a history or known hypersensitivity to topotecan or any of the components. Should not be used in pregnant or breastfeeding patients.[3] **Other warnings:** May also cause thrombocytopenia and anemia.[3] (See Monitoring in the Comments section.)
Infusion-related cautions	Extravasation, causing mild reactions such as erythema and bruising, has been reported.[3,4] See Appendix E for additional information regarding extravasation treatment.
Dosage	Consult institutional protocols for complete dosing information. Topotecan is a component of combination therapy or as single agent therapy to treat multiple pediatric solid tumors, including osteosarcoma, neuroblastoma, rhabdomyosarcoma, Ewing sarcoma, retinoblastoma, ependymoma, as well as pediatric leukemia. **Acute lymphoblastic leukemia, refractory, recurrent:** 2.4 mg/m^2/day once daily for 7–9 days.[5,6] Combination therapy of topotecan 1 mg/m^2/day continuous infusion for 5 days with vinorelbine, clofarabine,and thiotepa has been investigated.[7] **Acute myeloid leukemia; refractory, recurrent:** 4 mg/m^2/dose once on day 1, with dosing on days 2–5 determined by pharmacokinetic analysis (median dose reported at 4 mg/m^2/day.[8] **Neuroblastoma induction** **≤12 kg:** 0.04 mg/kg/dose once daily for 5 days in combination with cyclophosphamide. Repeat every 21 days for 6 cycles.[9] **>12 kg:** 1.2 mg/m^2/dose once daily for 5 days in combination with cyclophosphamide. Repeat every 21 days for 6 cycles.[9] **Neuroblastoma, recurrent refractory or untreated metastatic:** 0.75 mg/m^2/dose once daily for 5 days in combination with cyclophosphamide. Repeat every 21 days.[10-14] **Hematopoietic stem cell transplant conditioning:** 2 mg/m^2/dose on days −8 through −4 prior to stem cell transplant in combination with carboplatin and thiotepa[15] **Pediatric solid tumors:** 1 mg/m^2/day (range: 0.6–1.9 mg/m^2/day) for 3 days as a continuous infusion; repeat q 21 days[16,17] or over 30 minutes 5 days a week for 2 consecutive weeks; repeat q 24–28 days.[18] **Combination therapy:** 0.75 mg/m^2/day for 5 days; repeat q 21 days.[19] **Single-agent therapy for refractory solid tumors:** 1.4–2.4 mg/m^2/day for 5 days; repeat q 21 days.[20-22]

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Dosage adjustment in organ dysfunction	No dosage adjustment necessary in patients with hepatic dysfunction or mild renal impairment (CrCl 40–60 mL/min).[3] One reference recommends that patients with moderate renal failure (CrCl 20–39 mL/min) receive 50% of the standard dose and those with CrCl <20 mL/min have doses held until recovery.[23] Another reference recommends a 25% dose reduction for patients with CrCl <50 mL/min, a 50% reduction for CrCl of 10–50 mL/min, and a 75% reduction with CrCl <10 mL/min.[24] There is evidence that obese patients have increased clearance of topotecan due to upregulation of tubular secretion. No dose adjustments have been recommended.[25] **Continuous renal replacement thearpy (CRRT):** Administer 50% of dose or decrease dose by 0.75 mg/m^2/dose.[24]
Maximum dosage	Not established. One *adult* patient received a single dose of 35 mg/m^2 and developed reversible severe neutropenia.[3]
Additives	None
Suitable diluents	Reconstitution with SW; further dilution with D5W or NS.[3,4]
Maximum concentration	0.5 mg/mL[23]
Preparation and delivery	Do not dilute in alkaline solutions.[4]
IV push	Not recommended
Intermittent infusion	Dilute reconstituted drug (1 mg/mL) in 50–250 mL D5W or NS and infuse over 30 minutes.[3,4]
Continuous infusion	Has been administered via continuous infusion for up to 120 hours at 1 mg/m^2/day.[7]
Other routes of administration	Periocular, intra-arterial topotecan has been used for treatment of retinoblastoma.[26,27] IT doses have been used in pediatric patients with refractory leptomeningeal leukemia.[28]
Comments	**Significant adverse effects:** Topotecan is associated with a low (10% to 30%) risk of emesis.[29] Patients should receive antiemetic therapy to prevent acute and delayed nausea and vomiting. The recommended therapy is a corticosteroid on every day chemotherapy is administered; alternatives are a phenothiazine (e.g., prochlorperazine) or a butyrophenone (e.g., droperidol).[29-31] Therapy for delayed nausea and vomiting is generally not needed. Breakthrough medications should also be offered. Selection should be based on what the patient is currently receiving for acute emesis prophylaxis. **Monitoring:** Monitor CBC with platelets, renal function, and bilirubin.[3,23] Patients should have a baseline absolute neutrophil count >1500 cells/mm^3 and a platelet count >100,000 cells/mm^3 before drug administration.[3] The manufacturer recommends dose adjustments with severe neutropenia or thrombocytopenia.[3] (See the Contraindications and Warnings section.) **Drug interactions:** BCRP/ABCG2 inhibitors (e.g., filgrastim, denosumab, platinum derivatives) may increase serum concentrations of topotecan.[23] Consult appropriate resources for dosing recommendations before combining any drug with topotecan.