Temsirolimus

Brand names	Torisel
Medication error potential	None
Contraindications and warnings	**Contraindications:** Patients with bilirubin >1.5 × ULN (upper limit of the normal range) should not receive temsirolimus.[1] **Other warnings:** Hypersensitivity, including anaphylaxis, can occur early in the first infusion of temsirolimus. Patients should be closely monitored throughout the duration of the infusion. Appropriate medical care should be available in the event of anaphylaxis. Discontinuation of the infusion and administration of antihistamine should be used to treat hypersensitivity reactions. Once resolved the infusion may be restarted at a slower rate.[1] Administer an H_1 antagonist and/or an IV H_2 antagonist 30 minutes prior to resuming infusion.[1] Use with caution in patients with mild hepatic impairment. Dose reduction may be necessary.[1] Use with caution in the perioperative period, as abnormal wound healing may occur.[1]
Infusion-related cautions	See the Contraindications and Warnings section.
Dosage	**Premedication with IV diphenhydramine, 30 minutes prior to each dose is recommended. Dosage should be held for absolute neutrophil counts <1000/mm³, platelet count <75,000/mm³, or CTCAE (common terminology criteria for adverse events) grade 3 or greater adverse reactions.**[1] **Recurrent/refractory solid tumors:** 75 mg/m² IV once weekly.[2] In a phase II trial in children 1–21 years of age with neuroblastoma, rhabdomyosarcoma or high-grade glioma, one complete response was seen in a neuroblastoma patient. Stable disease was noted in 7 of 17 patients with high-grade glioma and 6 of 19 patients with neuroblastoma. A partial response at week 18 was seen in 1 of 16 patients with rhabdomyosarcoma.[2] **Combination therapy, cixutumumab:** 8 mg/m² once weekly temsirolimus with cixutumumab was found to be the optimal dose in children with recurrent solid or central nervous system tumors (median age 11. 8 years).[3] However, in a Phase II trial at this dose, this drug combination did not result in objective responses.[4] **Advanced or metastatic Ewing sarcoma:** 25–37.5 mg IV once weekly with cixutumumab 6 mg/kg IV weekly.[5] Twenty patients with Ewing sarcoma or desmoplastic, small round cell tumor, ages 14–41 were administered combination therapy on 4-week cycles. Complete response was seen in 1 of 17 Ewing sarcoma patients with tumor regression in 5 of 17.[5] **Advanced renal cell carcinoma (*adults*):** 25 mg IV once weekly[1]
Dosage adjustment in organ dysfunction	In *adults*, mild hepatic impairment, defined as bilirubin >1–1.5 × ULN or AST (aspartate aminotransferase) >ULN with bilirubin ≤ULN: 15 mg once weekly.[1] **Moderate-to-severe hepatic impairment, defined as bilirubin >1.5 × ULN:** Contraindicated[1]
Maximum dosage	220 mg/m²[1]
Additives	Polysorbate 80, propylene glycol, dehydrated alcohol, alpha-tocopherol 0.75 mg[1]
Suitable diluents	NS. Do not mix with other solutions or medications.[1]

Temsirolimus

Maximum concentration	10 mg/mL[1]
Preparation and delivery	Protect from excessive room light and sunlight during preparation. Use two-step process for preparation: (1) dilute vial of temsirolimus with 1.8 mL of supplied diluent to produce 30 mg/3 mL (mix well and allow air bubbles to subside); (2) withdraw the required amount of concentrate-diluent mixture as prepared in step 1 and further dilute into a 250-mL bag of NS (mix by inversion and avoid excessive shaking; protect from excessive room light and sunlight; administer within 6 hours).[1] Administration materials should be glass, polyolefin, or polyethylene to avoid excessive loss of product and diethylhexyl phthalate (DEHP) extraction.[1] When PVC administration has to be used, it should not contain DEHP.[1] Use with an in-line polyethersulfone filter with pore size <5 microns.[1]
IV push	Not recommended
Intermittent infusion	Infuse over 30–60 minutes weekly via infusion pump.[1]
Continuous infusion	Not recommended
Other routes of administration	Not recommended
Comments	**Significant adverse effects:** Hyperglycemia, immunosuppression, interstitial lung disease, hyperlipidemia, bowel perforation, renal failure, wound healing complications, intracerebral hemorrhage have been reported.[1] Patients should be closely monitored. The most common adverse reactions (≥30%) are rash, asthenia, mucositis, nausea, edema, and anorexia.[1] There is a low risk for emesis. The most common laboratory abnormalities (≥30%) are anemia, hyperglycemia, hyperlipidemia, hypertriglyceridemia, lymphopenia, elevated alkaline phosphatase, elevated SCr, hypophosphatemia, thrombocytopenia, elevated AST, and leukopenia.[1] **Significant drug interactions:** Strong inducers of CYP3A4/5, such as dexamethasone, carbamazepine, phenytoin, phenobarbital, rifampin, and rifampicin, may decrease exposure of the active metabolite (sirolimus). A dose adjustment should be considered.[1,6] Concomitant use of St. John's Wort should be avoided due to unpredictable temsirolimus concentrations.[1] Strong inhibitors of CYP3A4 such as atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, and telithromycin may increase concentrations of the active metabolite sirolimus. A dose adjustment should be considered.[1,7] Concomitant use of temsirolimus and sunitinib has resulted in dose-limiting toxicity requiring hospitalization.[1] Concomitant use of temsirolimus and valproic acid has been shown to significantly decrease the MTD of temsirolimus, with mucositis as the major dose-limiting toxicity.[8] **Other:** Live virus vaccines (measles, mumps, rubella; varicella; rotavirus) should be avoided during treatment.[1]