Etoposide

Brand names	Toposar, VePesid, VP-16, generic
Medication error potential	ISMP high-alert medication that has an increased risk of causing significant patient harm if it is used in error.[1] Etoposide may be confused with etoposide phosphate. Etoposide phosphate is a prodrug of etoposide. Each 100 mg of etoposide is equivalent to 114 mg of etoposide phosphate.
Contraindications and warnings	**U.S. boxed warning:** Etoposide should be administered under the supervision of a qualified physician. Severe myelosuppression with resulting infection or bleeding may occur.[2] **Contraindications:** Etoposide is contraindicated in patients who have a hypersensitivity to etoposide or any of the components of the formulation.[2] **Other warnings:** May cause myelosuppression, hypotension, severe emesis (see Significant Adverse Effects in the Comments section) and anaphylaxis.[2]
Infusion-related cautions	Hypotension has been reported with rapid administration of etoposide.[2] Stop or slow the rate of the infusion, and administer IV fluids if necessary. Infusing etoposide at a rate slower than 100 mg/m^2/hr (or 3.3 mg/kg/hr) has been shown to minimize hypotensive effects. Anaphylactic reactions have been seen with etoposide administration, manifesting as bronchospasm, tachycardia, dyspnea, and hypotension. Higher rates of anaphylaxis have been seen in children that receive higher than recommended concentrations of etoposide.[2] Extravasation has occurred but has rarely been associated with necrosis.[2] (See Appendix E for additional information regarding extravasation treatment.)
Dosage	Consult individual protocols for complete dosing information. Etoposide is used as a component of combination therapy or as single agent therapy in multiple pediatric and hematologic neoplasms. A general dosage regimen has included 60–150 mg/m^2/day IV for 2–5 days q 3–6 wk.[4,3] Specific regimens include the following: **Acute myeloid leukemia** **Remission induction:** Combination therapy[5] **BSA <0.6 m^2:** 3.3 mg/kg once daily on days 1–5 **BSA ≥0.6 m^2:** 100 mg/m^2 once daily on days 1–5 **Intensification**[5] **BSA <0.6 m^2:** 3.3 mg/kg once daily on days 1–5 **BSA ≥0.6 m^2:** 150 mg/m^2 once daily on days 1–5 **Consolidation:** 100 mg/m^2 once daily for 4–5 days (combination therapy)[6] **CNS tumor:** 150 mg/m^2 on days 1–3 or days 2–3 of treatment course[7] **Neuroblastoma:** 100 mg/m^2 over 1 hour on days 1–5 of cycle or 75 mg/m^2 over 1 hour on days 1–4 of weeks 4–9 in combination with other chemotherapeutic agents[8] **HSCT conditioning regimen:** 30 or 60 mg/kg as a single dose in combination chemotherapy 3 or 4 days prior to transplant[9,10] **Sarcoma (combination with ifosfamide and carboplatin):** 100 mg/m^2/dose once daily for 5 doses, days 0–4 q 3 wk[11] **Sarcoma (combination with vincristine, doxorubicin, cyclophosphamide, ifosfamide):** 150 mg/m^2/dose once daily for 3 doses, days 1–3[12] **Wilms tumor (combination therapy with ifosfamide and carboplatin):** 100 mg/m^2/dose once daily for 3–5 doses; repeat cycle q 21 days[13]

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Dosage adjustment in organ dysfunction	**GFR 10–50 mL/min/1.73 m²:** Administer 75% of normal dose.[14] **GFR <10 mL/min/1.73 m²:** Administer 50% of normal dose.[14] **Hemodialysis:** Administer 50% of normal dose after dialysis.[14] **Continuous renal replacement therapy (CRRT):** Administer 75% of normal dose.[14] Use caution in patients with hepatic dysfunction. One source recommends that if the serum bilirubin is 1.5–3 mg/dL or the aspartate aminotransferase (AST) is >3 times ULN, the dosage should be reduced by 50%.[15]
Maximum dosage	Not established
Additives	Each mL contains 30 mg benzyl alcohol.[2,16] (See Appendix C for more specific information about potential adverse effects and/or benzyl alcohol toxicity in neonates.) Contains polysorbate 80. In premature infants, life-threatening liver and renal failure, pulmonary compromise, thrombocytopenia and ascites have been associated with some products containing polysorbate 80.[2]
Suitable diluents	D5W or NS[2]
Maximum concentration	0.2–0.4 mg/mL.[2,16] Precipitation has developed with concentrations >0.4 mg/mL.[16] For high doses, may use 0.6 mg/mL (8-hour stability), but an in-line filter during infusion is recommended.[16]
Preparation and delivery	Must be diluted prior to use with D5W or NS to a final concentration of 0.2–0.4 mg/mL. Precipitation may occur at concentrations >0.4 mg/mL. The surfactant component may alter drop size. Administration with infusion devices that do not operate via drop size is recommended.[16] Administration devices made up of acrylic or acrylonitrile, butadiene, and styrene (ABS) should be avoided, as they have cracked and leaked when used with undiluted etoposide.[2]
IV push	Not recommended.[2,16] Rapid administration has been associated with the development of hypotension. (See the Infusion-Related Cautions section.)
Intermittent infusion	0.2–0.4 mg/mL may be infused over at least 30–60 minutes.[2,16] If volume is a concern, it may be infused over a longer time period, up to 210 minutes.[2] If infusion reaction occurs, may prolong infusion to 2–4 hours, but rate should not exceed 100 mg/m²/hr (3.3 mg/kg/hr).
Continuous infusion	Not recommended but prolonged infusions have been used. To minimize hypotensive reactions, rate should not exceed 100 mg/m²/hr (or 3.3 mg/kg/hr) at final concentration of 0.2–0.4 mg/mL. High-dose etoposide administered as a continuous infusion has been associated with more nonhematological toxicities compared to intermittent infusions.[17]
Other routes of administration	IT, IP, and intrapleural administration are not recommended.