Etopor™ 100

Etoposide Injection BP

DESCRIPTION

Etopor™ is a preparation of Etoposide. Etoposide has been shown to cause metaphase arrest in chick fibroblasts. Its main effect, however, appears to be at the G_2 portion of the cell cycle in mammalian cells. Two different dose-dependent responses are seen. At high concentrations (10 µg/mL or more), lysis of cells entering mitosis is observed. At low concentrations (0.3 to 10 µg/mL), cells are inhibited from entering prophase. It does not interfere with microtubular assembly. The predominant macromolecular effect of Etoposide appears to be the induction of DNA strand breaks by an interaction with DNA topoisomerase II or the formation of free radicals.

INDICATIONS

• **Refractory Testicular Tumors:** Etoposide injection in combination therapy with other approved chemotherapeutic agents in patients with refractory testicular tumors who have already received appropriate surgical, chemotherapeutic, and radiotherapeutic therapy.

• **Small Cell Lung Cancer:** Etoposide injection in combination with other approved chemotherapeutic agents as first line treatment in patients with small cell lung cancer.

DOSAGE AND ADMINISTRATION

The usual dose of Etoposide injection in testicular cancer in combination with other approved chemotherapeutic agents ranges from 50 to 100 mg/m^2/day on days 1 through 5 to 100 mg/m^2 /day on days 1, 3, and 5.

In small cell lung cancer, the Etoposide injection dose in combination with other approved chemotherapeutic drugs ranges from 35 mg/m^2/day for 4 days to 50 mg/m^2/day for 5 days.

Renal Impairment

In patients with impaired renal function, the following initial dose modification should be considered based on measured creatinine clearance:

Measured Creatinine Clearance	>50 mL/min	15-50 mL/min
Etoposide	100% of dose	75% of dose

Subsequent Etoposide dosing should be based on patient tolerance and clinical effect. Chemotherapy courses are repeated at 3- to 4-week intervals after adequate recovery from any toxicity.

The dosage should be modified to take into account the myelosuppressive effects of other drugs in the combination or the effects of prior x-ray therapy or chemotherapy which may have compromised bone marrow reserve.

CONTRAINDICATIONS

• Hypersensitivity

ADVERSE EFFECTS

• **Hematologic toxicity:** Leukopenia, thrombocytopenia, anemia
• **Gastrointestinal toxicity:** Nausea and vomiting, abdominal pain, anorexia, diarrhea, stomatitis, hepatic.
• **Others:** Alopecia, peripheral neurotoxicity, hypotension, allergic reaction

WARNING AND PRECAUTION

Patients being treated with Etoposide must be frequently observed for myelosuppression both during and after therapy. Myelosuppression resulting in death has been reported. Dose-limiting bone marrow suppression is the most significant toxicity associated with Etoposide therapy. Therefore, the following studies should be obtained at the start of therapy and prior to each subsequent cycle of Etoposide: platelet count, hemoglobin, white blood cell count, and differential. The occurrence of a platelet counts below 50,000/mm^3 or an absolute neutrophil count below 500/mm^3 is an indication to withhold further therapy until the blood counts have sufficiently recovered. Physicians should be aware of the possible occurrence of an anaphylactic reaction manifested by chills, fever, tachycardia, bronchospasm, dyspnea, and hypotension. Higher rates of anaphylactic-like reactions have been reported in children who received infusions at concentrations higher than those recommended.

In all instances where the use of Etoposide is considered for chemotherapy, the physician must evaluate the need and usefulness of the drug against the risk of adverse reactions. Most such adverse reactions are reversible if detected early. If severe reactions occur, the drug should be reduced in dosage or discontinued and appropriate corrective measures should be taken according to the clinical judgment of the physician. Reinstitution of Etoposide therapy should be carried out with caution, and with adequate consideration of the further need for the drug and alertness as to possible recurrence of toxicity. Patients with low serum albumin may be at an increased risk for Etoposide associated toxicities.

USE IN PREGNANCY AND LACTATION

Pregnancy category D. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Etoposide, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

DRUG INTERACTIONS

High-dose Cyclosporin A resulting in concentrations above 2000 ng/mL administered with oral etoposide has led to an 80% increase in etoposide exposure with a 38% decrease in total body clearance of etoposide compared to etoposide alone.

PRECAUTION FOR HANDLING AND DISPOSAL

As with other potentially toxic compounds, caution should be exercised in handling and preparing the solution of Etoposide. Skin reactions associated with accidental exposure to Etoposide may occur. During preparation a strictly aseptic working technique should be used, protective measures should include the use of gloves, mask, safety goggles and protective clothing. Use of a vertical laminar airflow (LAF) hood is recommended. If Etoposide solution contacts the skin or mucosa, immediately and thoroughly wash the skin with soap and water and flush the mucosa with water. Any unused product or waste material should be disposed of in accordance with local requirements.

PREPARATION FOR INTRAVENOUS ADMINISTRATION

Etoposide injection must be diluted prior to use with either 5% Dextrose Injection, or 0.9% Sodium Chloride Injection to give a final concentration of 0.2 to 0.4 mg/mL. If solutions are prepared at concentrations above 0.4 mg/mL, precipitation may occur. Hypotension following rapid intravenous administration has been reported, hence, it is recommended that the Etoposide solution be administered over a 30 to 60-minute period. A longer duration of administration may be used if the volume of fluid to be infused is a concern. Etoposide should not be given by rapid intravenous injection. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

PHARMACEUTICAL PRECAUTION

Store at or below 25° C temperature. Keep away from light and wet place. Keep out of reach of children.

STABILITY

Vials diluted as recommended to a concentration of 0.2 to 0.4 mg/mL are stable for 96 and 24 hours, respectively, at room temperature (25° C) under normal room fluorescent light in both glass and plastic containers.

PACKAGING

Etopor™ 100 IV Injection: Each box contains one multiple dose vial of Etoposide BP 100 mg/5 mL injection.

SK+F ONCOLOGY

Manufactured by
ESKAYEF PHARMACEUTICALS LIMITED
RUPGANJ, NARAYANGANJ, BANGLADESH
TM TRADEMARK
R/PM0937 V01