ESOPHAGEAL CARCINOMA

Etoposide is indicated in the management of the following neoplasms:

- Small Cell Lung Cancer
- Refractory Testicular Tumors
- Ewing's sarcoma and related small blue cell tumors
- Acute and chronic myelogenous leukemia
- Acute lymphocytic leukemia of childhood
- Hodgkin's disease
- Certain non-Hodgkin's lymphomas
- Metastatic colorectal cancer

INDICATIONS AND USAGE

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CONTRAINDICATIONS

Etoposide is contraindicated in patients who have demonstrated a previous hypersensitivity to etoposide or any component of the formulation.

WARNINGS

Physicians should be aware of the possible occurrence of an anaphylactic reaction manifested by: shivers, fever, tachycardia, bronchospasm, dyspnea, and hypotension. Higher ratios of anaphylactic-like reactions have been reported in children who received infusions at concentrations higher than those recommended. The need that concentration of infusion (or rate of infusion) plays in the development of anaphylactic-like reactions is uncertain. (See ADVERSE REACTIONS.) Treatment is symptomatic. The infusion should be terminated immediately, followed by the administration of pressor agents, anticonvulsants, antihistamines, or volume expanders at the discretion of the physician.

For parenteral administration, etoposide should be given only by slow intravenous infusion (usually over a 30- to 60-minute period) since hypotension has been reported as a possible side effect of rapid intravenous injection.

PRECAUTIONS

The risk of development of a pre-leukemic or leukemic syndrome is unclear. Carcinogenicity tests with etoposide have not been conducted in laboratory animals.

Etoposide is a potent carcinogen in humans. The occurrence of acute leukemia with or without a preleukemic phase has been reported in rare instances in patients treated with etoposide alone or in association with other anticancer agents. The risk of development of a pre-leukemic or leukemic syndrome is unclear. Carcinogenicity tests with etoposide have not been conducted in laboratory animals.

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. Reinstatement of etoposide therapy should be carried out with caution, and with adequate consideration of the further need for the drug and alternatives as to possible occurrence of toxicity. Patients with low serum albumin may be at an increased risk for etoposide associated toxicities. Physicians should be aware of the possible occurrence of an anaphylactic reaction manifested by: shivers, fever, tachycardia, bronchospasm, dyspnea, and hypotension. Higher ratios of anaphylactic-like reactions have been reported in children who received infusions at concentrations higher than those recommended. The need that concentration of infusion (or rate of infusion) plays in the development of anaphylactic-like reactions is uncertain. (See ADVERSE REACTIONS.) Treatment is symptomatic. The infusion should be terminated immediately, followed by the administration of pressor agents, anticonvulsants, antihistamines, or volume expanders at the discretion of the physician.

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

Administration Precautions: 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. The use of gloves is recommended. If etoposide contacts the skin or mucosa, immediately and thoroughly wash the skin with soap and water and flush the mucosa with water.

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 as concentrations above 0.4 mg/mL, etoposide injection should be refrigerated until reconstitution. Etoposide injection 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 factor.

Etoposide injection may also be used in patients with normal renal function. Parenteral drug products should be inspected visually for particulate matter and discoloration (see DESCRIPTION) prior to administration when solution and container are intact.

Stability: Unopened vials of Etoposide injection are stable for 24 months at room temperature (25°C). 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 illumination in glass and plastic containers.

Procedures for proper handling and disposal of antinecancer drugs should be considered. Several guidelines on this subject have been published. 8 There is no general agreement that all the procedures recommended in the guidelines are necessary or appropriate. 9

HOW SUPPLIED

Etoposide Injection USP, 20 mg/mL, is supplied as follows:

NDC 55390-291-01 100 mg/5 mL, Sterile Multiple Dose Vial, individually boxed.
NDC 55390-292-01 500 mg/25 mL, Sterile Multiple Dose Vial, individually boxed.
NDC 55390-293-01 1 g/50 mL, Sterile Multiple Dose Vial, individually boxed.
Stable from 20° to 25°C (68° to 77°F) (See Controlled Room Temperature).

REFERENCES

3. Mineau P, Jeffrey, Chairman, National Study Commission on Cytotoxic Exposure. Massachusetts College of Pharmacy and Allied Health Sciences, 179 Longwood Avenue, Boston, MA 02115.
7. Available from Louis P. Jeffrey, Chairman, National Study Commission on Cytotoxic Exposure. Massachusetts College of Pharmacy and Allied Health Sciences, 179 Longwood Avenue, Boston, MA.
8. Mineau P, Jeffrey, Chairman, National Study Commission on Cytotoxic Exposure. Massachusetts College of Pharmacy and Allied Health Sciences, 179 Longwood Avenue, Boston, MA.