TOPOSIDE

B.P Specs.
(ETOPOSIDE B.P)
100mg/5ml INJECTION

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Action And Clinical Pharmacology: Etoposide is a semisynthetic derivative of podophyllotoxin. Etoposide exhibits cytostatic activity in vitro by preventing cells from entering mitosis or by destroying them at a premitotic stage. Etoposide interferes with the synthesis of DNA and appears to arrest human lymphoblastic cells in the late S-G2 phases of the cell cycle.

The effects of etoposide on the human hematopoietic system are substantial. The effects evoked included leukopenia and thrombocytopenia. The toxic effects elicited by etoposide are described under Adverse Effects. Experiments using animals have revealed teratogenic and embryotoxic properties to etoposide.

Pharmacokinetics: In humans, administration of higher doses of etoposide resulted in higher levels of the drug in the plasma. Peak levels of etoposide in plasma were reached immediately following administration. Etoposide decayed from plasma in a biphasic manner. The values for t1/2â and t1/2ã ranged from 0.31 to 0.8 hours and 4.1 to 8.05 hours, respectively. The mean volume of distribution at steady state (VDss) was 25.2 L/m2, the mean plasma clearance rate was 28.0 mL/min/m2 and the mean renal clearance rate was 10.0 mL/min/m2.

Approximately 98% of etoposide was bound to proteins in plasma when incubated in vitro at 37°C. Protein binding was not affected by the concomitant administration of cisplatin. Analysis of biological fluids and tissues suggested that etoposide was present in nonsignificant amount in cerebrospinal fluid (CSF), pleural fluid, saliva and also in the tumors.

Of a dose of 220 to 290 mg/m2 of radioactive etoposide infused during 1 hour, 43.5% was recovered in the urine, of which 67% was unchanged etoposide. Recovery in the feces was inconsistent and ranged from <1.5 to 16.31% of the administered dose in 1 study. The levels of etoposide in bile were low and represented 1 to <3% of the original dose administered. The rest of the dose was not accounted for.

When etoposide was administered to children, the peak levels of the drug in plasma also coincided with the first time point after the beginning of the infusion. The decay of etoposide from plasma was biphasic. In a study of 8 children and adolescents receiving 200 mg/m2/day as 30- to 60-minute i.v infusions during 3 consecutive days, the mean values for t1/2â and t1/2ã were 0.82 hours and 6.5 hours, respectively. The mean systemic serum clearance rate was 20.9 mL/min/m2 and the mean VDss was 7.2 L/m2.

The metabolites of etoposide detected in urine included the blucuronate/sulfate conjugates, aglycone, cis-etoposide, trans isomer of the open ring lactone, cis/trans hydroxy acids and the picrolactones. Cis-etoposide was also detected in cerebrospinal fluid. The metabolites of etoposide observed in bile included the trans-hydroxy acid, glucuronide conjugate and cis-etoposide.

Indications And Clinical Uses: Small-cell Carcinoma of the Lung: As first-line therapy in combination with other antineoplastics. As second-line therapy or as a single agent in patients who have not relapsed or failed to respond after treatment with other chemotherapeutic protocols.

Nonsmall-cell Carcinoma of the Lung: In combination with cisplatin for patients who cannot be surgically treated. For patients requiring chemotherapy following surgery.

Malignant Lymphoma (histiocytic type): As first-line therapy in combination with other antineoplastics.

Testicular Malignancies (notably germ cell tumors including seminomas): In conjunction with other antineoplastics in patients who have received appropriate therapy.

Contra-Indications: Patients exhibiting previous hypersensitivity to etoposide; or severe leukopenia, thrombocytopenia, severe liver- and/or kidney-related impairment should not be treated with etoposide.

Caution: Etoposide is a potent antineoplastic agent. It should only be used by or under the direct supervision of qualified physicians who are experienced in using chemotherapeutic agents. Patients should be routinely tested for myelosuppression and for the toxic effects incurred to the renal and hepatic systems. If these tests indicate unacceptable levels of toxicity, therapy with etoposide should be discontinued.

Pregnancy and the Use of Birth Control: Etoposide displayed teratogenicity and embryotoxicity when administered to pregnant rats. Etoposide also caused reduced spermatogenesis in monkeys and a reduction in the weights of testes in rats and monkeys. Thus, administration of etoposide during pregnancy is not recommended. Patients receiving etoposide who are able to conceive or bear children are advised to use appropriate methods of birth control. Ovarian dysfunction was experienced after treatment with etoposide, therefore etoposide should be administered with caution to postpubertal women.

Precautions: Etoposide should only be administered by those experienced in the use of chemotherapeutic antineoplastics. Blood counts and renal and hepatic function should be evaluated frequently. The count of white blood cells, platelets, and granulocytes, will alter the recommended dose.

Administration of etoposide should be terminated if the absolute granulocytic count falls below 1 000; or the number of platelets fall below 50 000 cells/µL. The number of neutrophils and platelets reach their lowest levels at 7 to 14 days and 9 to 16 days respectively, after initial treatment with etoposide. Approximately 20 days are required for recovery of the bone marrow.

As hypotension has been reported after bolus administration, etoposide should be mixed with normal saline or 5% dextrose and administered over a period of at least 30 minutes. Vital signs should be monitored during this period.

Interaction of vincristine and etoposide have resulted in severe neuropathies in 0.7% of the patients.

Children: Inadequate use of etoposide in children, currently, does not permit the recommendation of dosages to be used for children.

Lactation: As etoposide may be secreted in human milk, mothers should be advised not to breast-feed while undergoing chemotherapy with etoposide.

Adverse Reactions: The following section summarizes the toxic side effects of etoposide.

The major dose-limiting toxic side effect was myelosuppression, manifested mainly as leukopenia, thrombocytopenia and anemia. The nadirs of granulocytes and platelets occurred at 7 to 14 days and 9 to 16 days after treatment, respectively. Recovery of the bone marrow generally occurred by 20 days after treatment. The occasional deaths observed after treatment with combinations containing etoposide were usually associated with myelosuppression.

Nausea and emesis were the main gastrointestinal toxic effects. These effects were usually prevented by antinausea/antiemetic regimens. When etoposide was administered at high doses, stomatitis was often the dose-limiting toxicity.

Anaphylactic reactions were reported after infusion of etoposide. A fatality due to respiratory distress syndrome was also reported. The reactions were controlled by terminating the infusion and administering vasopressors, corticosteroids, anti-histamines and plasma volume expanders are required. In one case, a longer period of infusion resolved the reactions.

Symptoms And Treatment Of Overdose: Symptoms and Treatment: There are currently no known antidotes for the adverse effects experienced after administration of etoposide. In the event of overdosage, treatment should be directed at alleviating the symptoms presented and ensuring the survival of the patient through the period of toxicity. The symptoms of overdosage are expected to be associated with hematopoietic toxicity. The functions of the renal and hepatic systems should be monitored for at least 3 to 4 weeks, in case of delayed or persistent toxicity of etoposide.

Dosage And Administration: A dose of 50 to 100 mg/m2/day may be administered by i.v. infusion (over at least 30 minutes) for 5 days. The dose should be adjusted depending on the toxic effects experienced by each patient; whether etoposide is used as a single agent or in combination with other antineoplastics; and the specific protocol used to treat the patient.

Due to reports of leukopenia and thrombocytopenia after treatment with etoposide, blood counts should be performed to determine the platelets and white blood cells prior to each new administration of etoposide.

Functions of the liver and kidneys should be monitored regularly. In patients with renal failure and hepatic failure, modifications are suggested.

Administration: Etoposide should not be administered by i.v. push. It should be mixed with normal saline or 5% dextrose injection and should be administered immediately by the i.v. route over a period of not less than 30 minutes.

Etoposide should be diluted as follows: Diluted solutions of etoposide should not exceed a concentration of 0.4 mg/mL. The diluted solution should be inspected visually for discoloration and particulate matter prior to administration. Diluted etoposide should be administered immediately after dilution. Discard unused portion.

COMPOSITION:
TOPOSIDE INJECTION;
Each ml contains: Etoposide BP.....20mg
(Product complies BP specs.)

AVAILABILITY:
Etoposide BP 100mg/5mL in a clear glass vial.

DOSAGE: As directed by the physician.

INSTRUCTIONS: Store below 25°C , Protect from heat and light. Keep all medicines out of the reach of children.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات: 25 ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی اور روشنی سے بچائیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

Manufactured by :
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