Urinary system
Urotoxicity consisted of hemorrhagic cystitis, dysuria, urinary frequency and other symptoms of bladder irritation. The incidence and severity of hematuria can be significantly reduced by using vigorous hydration, a fractionated dose schedule and a protector such as mesna.
Renal toxicity occurred in 6% of the patients treated with ifosfamide as a single agent. Clinical signs, such as elevation in BUN or serum creatinine or decrease in creatinine clearance, were usually transient.
Close monitoring of serum and urine chemistries including phosphorus, potassium, alkaline phosphatase and other appropriate laboratory studies is recommended.

Central Nervous System
Those most commonly seen were somnolence, confusion, depressive psychosis and hallucinations.
Other less frequent symptoms include dizziness, disorientation, and cranial nerve dysfunction.

Others
Alopecia occurred in approximately 83% of the patients treated with Ifosfamide for Injection USP as a single agent.
Increases in liver enzymes and/or bilirubin were noted in 3% of the patients.
Other less frequent side effects included phlebitis, pulmonary symptoms, fever of unknown origin, allergic reactions, stomatitis, cardiotoxicity and polyneuropathy.

Overdosage
No specific antidote for Ifosfamide for Injection USP is known. Management of overdosage would include general supportive measures to sustain the patient through any period of toxicity that might occur.

Storage
Ifosfamide for Injection USP should not be stored above 25° C.

Presentation

IFOS 1g	1 gm vial
IFOS 2g	2 gm vial

Cipla

041W A

For the use only of a Cancer Specialist.

IFOSFAMIDE FOR INJECTION USP

IFOS 1g
IFOS 2g

Composition
IFOS 1g
Each vial of Ifosfamide for Injection USP contains 1 gm of sterile ifosfamide USP.

IFOS 2g
Each vial of Ifosfamide for Injection USP contains 2 gm of sterile ifosfamide USP.

Description
Ifosfamide is a chemotherapeutic agent chemically related to the nitrogen mustards and a synthetic analogue of cyclophosphamide.

Indication and Usage
Ifosfamide for Injection USP used in combination with certain other approved antineoplastic agents, is indicated for third line chemotherapy of germ cell testicular cancer. It should ordinarily be used in combination with a prophylactic agent for hemorrhagic cystitis, such as mesna.

Dosage and Administration
Ifosfamide for Injection USP should be administered intravenously at a dose of 1.2 g/m² per day for 5 consecutive days. Treatment is repeated every 3 weeks or after recovery from hematologic toxicity (Platelets ≥ 100,000/µL, WBC ≥ 4,000 µL).
In order to prevent bladder toxicity, Ifosfamide for Injection USP should be given with extensive hydration consisting of at least 2 liters of oral or intravenous fluid per day.
A protector, such as mesna, should also be used to prevent hemorrhagic cystitis. Ifosfamide for Injection USP should be administered as a slow intravenous infusion lasting a minimum of 30 minutes.
Although, Ifosfamide for Injection USP has been administered to a small number of patients with compromised hepatic and/or renal function, studies to establish optimal dose schedules of Ifosfamide for Injection USP in such patients have not been conducted.

Preparation for Intravenous Administration/Stability
Injections are prepared for parenteral use by adding

Sterile Water for Injection, USP, or Sterile Bacteriostatic Water for Injection, USP (benzyl alcohol or parabens; preserved), to the vial and shaking to dissolve. Use the quantity of diluent shown below to constitute the product:

Dosage Strength	Quantity of Diluent	Final Concentration
1 gram	25 mL	50 mg/mL

Solutions of ifosfamide may be diluted further to achieve concentrations of 0.6 to 20 mg/mL in the following fluids:

5% Dextrose Injection, USP
0.9% Sodium Chloride Injection, USP
Lactated Ringer's Injection, USP
Sterile Water for Injection, USP

Because essentially identical stability results were obtained for Sterile Water admixtures as for the other admixtures (5% Dextrose Injection, 0.9% Sodium Chloride Injection, and Lactated Ringer's Injection), the use of large volume parenteral glass bottles, Viaflex bags or PAB bags that contain intermediate concentrations or mixtures of excipients (e.g. 2.5% Dextrose Injection, 0.45% Sodium Chloride Injection, or 5% Dextrose and 0.9% Sodium Chloride Injection) is also acceptable.
Constituted or constituted and further diluted solutions of **Ifosfamide for Injection USP** should be refrigerated and used within 24 hours.
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

Contraindication

Continued use of **Ifosfamide for Injection USP** is contraindicated in patients with severely depressed bone marrow function.
Ifosfamide for Injection USP is also contraindicated in patients who have demonstrated a previous hypersensitivity to it.

Warnings & Precautions

General

Ifosfamide for Injection USP should be given cautiously to patients with impaired renal function as well as to those with compromised bone marrow reserve, as indicated by: leukopenia, granulocytopenia, extensive bone marrow metastases, prior radiation therapy, or prior therapy with other cytotoxic agents.

Laboratory Tests

During treatment, the patient's hematologic profile (particularly neutrophils and platelets) should be monitored regularly to determine the degree of hematopoietic suppression. Urine should also be examined regularly for red cells which may precede hemorrhagic cystitis.

Drug Interactions

The physician should be alert for possible combined drug actions, desirable or undesirable, involving ifosfamide even though ifosfamide has been used successfully concurrently with other drugs, including other cytotoxic drugs.

Wound Healing

Ifosfamide may interfere with normal wound healing.

Pregnancy

Ifosfamide can cause fetal damage when administered to a pregnant woman. If **Ifosfamide for Injection USP** is used during pregnancy, or if the patient becomes pregnant while taking this drug; the patient should be apprised of the potential hazard to the fetus.

Nursing Mothers

Ifosfamide is excreted in breast milk. Because of the potential for serious adverse events and the tumorigenicity shown for ifosfamide in animal studies, 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.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Ifosfamide has been shown to be carcinogenic in rats, with female rats showing a significant incidence of leiomyosarcomas and mammary fibroadenomas.
The mutagenic potential of ifosfamide has been documented in bacterial systems *in vitro* and mammalian cells *in vivo*.

Adverse Reactions

Hematologic Toxicity

Myelosuppression was dose related and dose limiting. It consisted mainly of leukopenia and, to a lesser extent, thrombocytopenia. A WBC count < 3000/μL is expected in 50% of the patients treated with **Ifosfamide for Injection USP** single agent at doses of 1.2 g/m² per day for 5 consecutive days.
At this dose level, thrombocytopenia (platelets < 100,000/μL) occurred in about 20% of the patients.
Myelosuppression was usually reversible and treatment can be given every 3 to 4 weeks. When **Ifosfamide for Injection USP** is used in combination with other myelosuppressive agents, adjustments in dosing may be necessary. Patients who experience severe myelosuppression are potentially at increased risk for infection.