MES-D

Mesna BP 400 mg Injection

Composition: Mes-D : Each Vial contains mesna BP 400 mg/4ml Injection.

Description: Mesna is a drug used to reduce the undesired side effects of certain chemotherapy drugs. It is referred to as a "chemoprotectant."

Clinical Pharmacology:

Mechanism of Action

Mesna was developed as a prophylactic agent to reduce the risk of hemorrhagic cystitis induced by ifosfamide. Analogous to the physiological cysteine-cystine system, Mesna is rapidly oxidized to its major metabolite, Mesna disulfide (diMesna). Mesna disulfide remains in the intravascular compartment and is rapidly eliminated by the kidneys. In the kidney, the Mesna disulfide is reduced to the free thiol compound, Mesna, which reacts chemically with the urotoxic ifosfamide metabolites (acrolein and 4-hydroxy-ifosfamide) resulting in their detoxification. The first step in the detoxification process is the binding of Mesna to 4-hydroxy-ifosfamide forming a nonurotoxic 4-sulfoethylthioifosfamide. Mesna also binds to the double bonds of acrolein and to other urotoxic metabolites. In multiple human xenograft or rodent tumor model studies of limited scope, using IV or IP routes of administration, Mesna in combination with ifosfamide (at dose ratios of up to 20-fold as single or multiple course) failed to demonstrate interference with antitumor efficacy.

Pharmacokinetics

At doses of 2-4 g/m^2, the terminal elimination half-life of ifosfamide is about 4-8 hours. As a result, in order to maintain adequate lavels of Mesna in the urinary bladder during the course of elimination of the urotoxic ifosfamide metabolites, repeated doses of Mesna are requried. The urinary bioavailability of oral Mesna ranged from 45-79% of intravenously administered Mesna. Food dose not affect the urinary availability of orally administered Mesna. Approximately 18-26% of the combined intravenous and oral Mesna dose appears as free Mesna in the urine. When compared to intravenously administered Mesna, the intravenous plus oral dosing regimen increases systemic exposures (150%) and provides more sustained excretion of Mesna in the urine over a 24-hour period. Approximately 5% of the Mesna dose is excreted during the 12-24 hour interval, as compared to negligible amounts in patients give the IV regimen. The fraction of the administered dose of Mesna excreted in the urine is independent of dose. Protein binding of Mesna is in a moderate Range (69-75%).

Indications: It is indicated as a prophylactic agent in preventing ifosfamide-induced hemorrhagic cystitis (syndrome of bleeding and irritation of the bladder). It is also indicated in preventing high dose cyclophospamide-induced hemorrhagic cystitis.

Dosage and Administration: For the prophylaxis of ifosfamide induced hemorrhagic cystitis, Mesna may be given on a fractionated dosing schedule of three bolus intravenous injections or a single bolus injection followed by IV administration of mesna as outlined below.

Intravenous schedule: Mesna is given as intravenous bolus injection in a dosage equal to 20% of the ifosfamide dosage (w/w) at the time of ifosfamide administration and 4 and 8 hours after each dose of Ifosfamide. The total daily dose of Mesna is 60% of the ifosfamide dose. The recommended dosing schedule is outlined below:

	0 Hours	4 Hours	8 Hours
Ifosfamide	1.2g/m^2	-	-
Mesna	240 mg/m^2	240 mg/m^2	240 mg/m^2

Intravenous Dosing: Mesna Injection is given as intravenous bolus injections in a dosage equal to 20% of the Ifosfamide dosage (w/w) at the time of Ifosfamide administration. The recommended dosing schedule is outlined below:

	0 Hours	2 Hours	6 Hours
Ifosfamide	1.2g/m^2	-	-
Mesna	240 mg/m^2	240 mg/m^2	240 mg/m^2

Preparation of Intravenous Solutions/Stability: For IV administration the drug can be diluted by adding the Mesna Injection solution to any of the following fluids obtaining final concentrations of 20 mg Mesna/ml: 5% Dextrose Injection, 5% Dextrose and 0.2% Sodium Chloride Injection, 5% Dextrose and 0.33% Sodium Chloride Injection, 5% Dextrose and 0.45% Sodium Chloride Injection, 0.92% Sodium Chloride Injection, Lactated Ringer's Injection.

For example: One ml of Mesna Injection multidose vial 100 mg/ml may be added to 4 ml of any of the solutions listed above to crate a final concentration of 20mg Mesna/ml. Diluted solutions are chemically and physically stable for 24 hours at 25° C (77° F). Mesna is not compatible with cisplatin or carboplatin. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

Side effects : The common side effects are colic, depression, diarrhea, fatigue, headache, hypotension, irritability, joint pains, limb pains, nausea, rash, tachycardia, vomiting.

Contraindication: It is contraindicated in patients with known hypersensitivity to Mesna or to any of the excipients of this product.

Use in pregnancy and lactation: Pregancy Category B. There are no adequate and well-controlled studies in pregnant women. **Nursing Mother-**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 Mesna, 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: No clinical drug interaction studies have been conducted with Mesna.

Precautions:

Allergic reactions to Mesna ranging from mild hypersensitivity to systemic anaphylactic reactions have been reported. Patients with automimmune disorders who were treated with cyclophosphamide and mesna appeared to have a higher incidence of allergic reactions. The majority of these patients received Mesna orally. Mesna has been developed as an agent to reduce the risk of ifosfamide induced hemorrhagic cystitis. It will not prevent or alleviate any of the other adverse reactions or toxicities associated with ifosfamide therapy. Mesna does not prevent hemorrhagic cystitis in all patients. Up to 6% of patients treated with Mesna have developed hematuria (>50 RBC/hpf or Who grade 2 and above). As a result, a morning specimen of urine should be examined for the presence of hematuria (microscopic evidence of red blood cells) each day prior to Ifasfamide therapy. If hematuria develops when Mesna is given with Ifosamide according to the recommended dosage schedule, depending on the severity of the hematuria, dosage reductions or discontinuation of Ifosfamide therapy may be initiated. In order to reduce the risk of hematuria, Mesna must be administered with each dose of Ifosfamide as outlined in the DOSAGE AND ADMINISTRATION section. Mesna is not effective in reducing the risk of hematuria due to other pathological conditions such as thrombocytopenia. Because of the benzyl alcohol content, the multidose vial should not be used in neonates or infants and should be used with caution in older pediatric patients.

Overdose: There is no known antidote for Mesna. Oral doses of 6.1 and 4.3 g/kg were lethal to mice and rats, respectively. These doses are approximately 15 and 22 times the maximum recommended human dose on a body surface area basis. Death was preceded by diarrhea, tremor, convulsions, dyspnea, and cyanosis.

Storage: Store in the original carton at 20°-25°C. Protect from light. Keep out of the reach of children.

Packing: Mes-D: Each box contains 1 Vial of Mesna BP 400mg injection.

DRUG INTERNATIONAL LTD.
UNIT-2
TONGI, GAZIPUR