

Mesna for Injection
100 mg/mL
Uroprotector

ACTION

Mesna is rapidly and easily converted by auto-oxidation to its only metabolite disodium 2,2-dithio-bis ethane sulfonate (mesna disulfide, dimesna), forming a disulphide link. Following intravenous injection, only a small portion of the administered dose is detected in the blood as a reactive thiol compound (mesna). Mesna disulphide remains in the intravascular space and is rapidly forwarded to the kidney. In the renal tubular epithelium, a considerable proportion of mesna disulphide is again reduced to a free thiol compound, presumably by mediation of glutathione reductase. It is then capable of chemically reacting with acrolein or other urotoxic oxazaphosphorine metabolites in the urine, thereby developing its detoxifying activity.

The first and most important step towards detoxification is the addition of mesna to the double bond of acrolein, resulting in the formation of a stable thio ether which could be detected in the urine by chromatography. In the second step, mesna reduces the speed of degradation of the 4-hydroxy metabolite in the urine. A relatively stable, non-urotoxic condensation product from 4-hydroxy cyclophosphamide or 4-hydroxy ifosfamide and mesna is formed. By such stabilization, mesna inhibits the degradation of 4-hydroxy cyclophosphamide or 4-hydroxy ifosfamide and hence the formation of acrolein. This intermediate deactivated product could also be detected by chromatographic urinalysis.

INDICATIONS

Mesna is indicated for the reduction and prevention of urinary tract toxicity (hemorrhagic cystitis) of oxazaphosphorines. (See **ADVERSE REACTIONS** sections of the CYTOXAN and Ifosfamide for Injection, USP Product Monographs.)

CONTRAINDICATIONS

Mesna is contraindicated in individuals with a known hypersensitivity to it.

WARNINGS

The protective effect of mesna applies only to the urotoxic effects of oxazaphosphorines. Additional prophylactic or accompanying measures recommended during treatment with oxazaphosphorines are thus not affected and should not be discontinued.

***In vitro*, mesna is incompatible with cisplatin.**

The combination of an oxazaphosphorine cytostatic agent with mesna and cisplatin in the same infusion solution is not stable and is not to be used.

PRECAUTIONS

Mesna treatment may cause false positive reactions in tests for ketone bodies in the urine. The colour reaction is reddish purple rather than purple. The reddish purple colour is less stable, and fades immediately by adding glacial acetic acid.

Use in Children

Mesna has been administered to patients as young as 13 years of age. Due to the presence of benzyl alcohol, the product should not be used in neonates or infants.

Use in Pregnancy

Although the use of mesna in pregnant women has not been established, animal studies have not revealed any embryotoxic or mutagenic effects. However, in view of the fact that oxazaphosphorines are not recommended during pregnancy, this would eliminate the need for mesna.

ADVERSE REACTIONS

At recommended doses, side effects are not usually observed.

The following adverse reactions have been reported in a phase I trial in healthy volunteers:

- 1) diarrhea;
- 2) abdominal pain;
- 3) headache;
- 4) pain in limbs and joints;
- 5) transient drop in blood pressure;
- 6) increase in pulse rate.

These reactions occurred at doses of 60 mg/kg or more, given as a single bolus.

Venous irritation may occur in rare instances. This reaction may be attributed to the physical properties of mesna (i.e., pH 6 and hypertonic solution). No venous complications were observed when the solution was given diluted with Sterile Water for Injection, USP (one part mesna solution to three parts water).

SYMPTOMS AND TREATMENT OF OVERDOSAGE

No specific antidote for mesna is known. Overdosage should be managed with supportive measures to sustain the patient through any period of toxicity. Mesna has been administered at doses from 70 to 100 mg/kg without any toxic effect on hematopoiesis, hepatic and renal function or the central nervous system.

DOSAGE AND ADMINISTRATION

Mesna should be administered by intravenous injection, usually at 20% of the respective oxazaphosphorine dose at times 0 (= administration of the cytostatic agent), 4 and 8 hours. In the case of Ifosfamide for Injection, USP, the usual dose of Mesna is 10-12 mg/kg i.v. at 0, 4 and 8 hours after the Ifosfamide for Injection, USP dose. (See **DOSAGE AND ADMINISTRATION** sections of the CYTOXAN and Ifosfamide for Injection, USP Product Monographs.)

In the treatment of children, and particularly when administering very high doses – such as required when conditioning patients for bone marrow transplantations – the Mesna doses should be given at 0, 1, 3, 6, 9 and 12 hours or dosage increased to 30% of the respective oxazaphosphorine dose.

Oral administration of mesna – e.g., in patients with poor veins – is also feasible. Mesna is then given either at doses of 20% of the oxazaphosphorine dose at time 0 hour by the parenteral route, followed by oral doses of 40% of the oxazaphosphorine dose after 4 and 8 hours, taken in juice or cola, or in 3 oral doses of 40% of the oxazaphosphorine dose at times 0, 4 and 8 hours.

PHARMACEUTICAL INFORMATION**Drug Substance**

Proper Name: Mesna
Chemical Name: Sodium 2-mercaptoethanesulfonate

Structural Formula: HS-CH₂-CH₂-SO₃⁻ Na⁺

Molecular Formula: C₂H₅O₃S₂Na

Molecular Weight: 164.18

Description:

Mesna is a white to slightly cream-coloured crystalline or microcrystalline powder with a characteristic odour. It is freely soluble in water, sparingly soluble in methanol and practically insoluble in the usual organic solvents.

Composition:

Each mL of Mesna for Injection contains: 100 mg Mesna, 10.4 mg Benzyl Alcohol, Edetate Disodium, Water for Injection, and Sodium Hydroxide for pH adjustment.

STABILITY AND STORAGE RECOMMENDATIONS

Store the vials between 15 and 30°C. Vials must be discarded within 28 days after initial puncture.

Solutions for IV Infusion

- 5% Dextrose Injection, USP
- 0.9% Sodium Chloride Injection, USP

Solutions for infusion should be made up at a concentration of 1 mg/mL or greater.

Stability of Solution

Storage: Solutions for infusion should be used within 24 hours, if stored below 25°C, or 48 hours if stored refrigerated (2 - 8°C), from the time of preparation.

As with all parenteral drug products, intravenous admixtures should be inspected visually for clarity, particulate matter, precipitate, discolouration and leakage prior to administration. The unused portion should be discarded.

AVAILABILITY OF DOSAGE FORMS

Mesna for Injection is available as 100 mg/mL in 10 mL multiple-dose vials as follows:

C730310 10 mL vials in packages of 10 vials.