Hematuria (Einhorn, b). In two randomized studies, (Fukuoka, Scheef), higher doses of 1.2 g/m² ifosfamide administered daily for 5 days, 16-26% of the patients developed hematuria (Table 1). At a dose of 2-4 g/m², the terminal elimination half-life of ifosfamide is about 4-8 hours. Ifosfamide-induced hemorrhagic cystitis is dose dependent (Table 1). At a dose of 2-4 g/m², the terminal elimination half-life of ifosfamide is about 4-8 hours. Ifosfamide-induced hemorrhagic cystitis is dose dependent (Table 1).

In the kidney, the mesna is drained into the free-tissue component, mesna, which is removed from the systemic circulation via the renal route of elimination. The first step in the metabolism of mesna is the formation of a mesna sulfonic acid (sulfamic acid), which is eliminated in the urine. Mesna also binds to the double bonds of acrolein and other urotoxic metabolites.

In multiple human xenograft or rodent tumor models of limited-stage small cell lung cancer administered with ifosfamide at doses of up to 2-3 mg/dL as single or multiple courses failed to demonstrate interference with antitumor efficacy.

Pharmacokinetics
At doses of 2-4 g/m², the terminal elimination half-life of ifosfamide is about 4-8 hours. As a result, it is important that the regimen be administered in the morning. At doses of mesna injection are required. Intravenous IV-IV Regimens
After intravenous administration of an 80-mg dose, the half-life of ifosfamide and mesna is 5.8 ± 2.6 hours, and approximately 90% of the dose recovered is eliminated within 4 hours. Mesna has a plasma clearance of 1.5 L/h/kg.

Special Populations
Gender Effect
An analysis was conducted in four male and four female volunteers; no differences in plasma pharmacokinetics were detected.

Pediatric and Geriatrics
Ifosfamide 1.2 g/m²

INDICATIONS AND USAGE
Mesna injection is contraindicated in patients known to be hypersensitive to mesna or other tar component.

Warnings
Anaphylactic reactions, decreased blood pressure, and cardiac arrhythmia have been reported. Patients with adenocarcinoma who were treated with cyclophosphamide and mesna appear to have a higher incidence of allergic reactions. The majority of the patients receiving mesna developed hematuria (Einhorn, b). In two randomized studies, (Fukuoka, Scheef), higher doses of 1.2 g/m² ifosfamide administered daily for 5 days, 16-26% of the patients developed hematuria (Table 1). At a dose of 2-4 g/m², the terminal elimination half-life of ifosfamide is about 4-8 hours. Ifosfamide-induced hemorrhagic cystitis is dose dependent (Table 1). At a dose of 2-4 g/m², the terminal elimination half-life of ifosfamide is about 4-8 hours. Ifosfamide-induced hemorrhagic cystitis is dose dependent (Table 1).

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Pediatric and Geriatrics
Ifosfamide 1.2 g/m²
**Normal Text**

**DESCRIPTION**

Mesna Injection is a denaturing agent to inhibit the formation of ifosfamide metabolites. The active ingredient mesna is a synthetic sulfhydryl compound designated as sodium-2-mercaptopropanesulfonate with a molecular formula of C6H16O3NS, and a molecular weight of 164.18. Its structural formula is as follows:

**CLINICAL PHARMACOLOGY**

**Mechanism of Action**

Mesna injection was developed as a prophylactic agent to reduce the risk of toxic effects caused by ifosfamide-induced hematuria.

**Antihematuria**

Mesna injection is a sulphydryl reagent that can react with toxic ifosfamide metabolites to produce non-toxic compounds. During ifosfamide metabolism, acrolein and other urotoxic metabolites are produced. Mesna injection reduces these metabolites by reacting with them, thereby preventing their toxic effects on the kidneys.

**Pharmacokinetics**

**Absorption**

Mesna injection is rapidly absorbed following IV administration, with peak concentrations achieved within 1 hour.

**Distribution**

Mesna distribution is primarily in the intracellular compartment and is rapidly eliminated by the kidneys.

**Metabolism**

In the kidney, the mesna disulfide is reduced to the free thiol compound, mesna, which undergoes further metabolism to form mercapturic acids. Mesna also binds to the thiol groups of proteins and other substances to detoxify them.

**Excretion**

Mesna is primarily excreted unchanged through the urine within 24 hours of administration.

**Pharmacokinetic Data**

**Special Populations**

**Pediatrics**

No clinical studies were conducted to evaluate the effect of hepatic impairment or renal insufficiency on the pharmacokinetics of mesna injection.

**Geriatric Patients**

An analysis was conducted in four male and four female volunteers; no differences in pharmacokinetic parameters were observed.

**Hepatic Impairment**

No studies on male or female fertility were conducted. No signs of male or female infertility were observed in rats or mice treated with mesna injection.

**Mutagenesis**

Mesna injection was not genotoxic in the following in vitro assays:

- Ames bacterial mutagenicity assay
- Micronucleus assay
- In vitro mammalian chromosomal aberration assay
- In vitro mammalian sister chromatid exchange assay
- In vitro Chinese hamster ovary cell survival assay
- In vitro and in vivo mammalian preneoplastic assay
- In vivo mouse lung tumor bioassay

**Carcinogenesis**

Mesna injection has been evaluated in long-term studies in rodents, but there is no evidence of carcinogenic potential in humans.

**Drug Interactions**

Mesna injection is not compatible with cisplatin or carboplatin. It is also not compatible with 5% dextrose injection, USP, or 0.9% sodium chloride injection, USP.

**Adverse Reactions**

**Adverse Reactions in Clinical Trials**

The most frequently reported adverse events observed in clinical studies include:

- Hematuria
- Nausea
- Vomiting
- Diarrhea
- Constipation
- Rash
- Pruritus
- Pyrexia
- Injection site reactions
- Headache
- Asthenia
- Fatigue
- Myalgia

**Adverse Reactions in Postmarketing Surveillance**

Adverse reactions reported during postmarketing surveillance include:

- Hematuria
- Nausea
- Vomiting
- Diarrhea
- Constipation
- Rash
- Pruritus
- Pyrexia
- Headache
- Asthenia
- Myalgia
- Anemia
- Leukopenia
- Neutropenia
- Thrombocytopenia

**Overdosage**

There is no known antidote for mesna injection. Overdosage may be managed by supporting life functions and treating any complications that arise.

**Preparation of Intravenous Solutions/Stability**

Mesna injection may be administered immediately after reconstitution with one of the following fluids:

- 0.9% Sodium Chloride Injection, USP
- 5% Dextrose Injection, USP
- 0.92% Sodium Chloride Injection, USP

The mesna injection multidose vials may be stored and used for up to 8 days.

**HOW SUPPLIED**

Mesna injection is supplied as a clear glass multidose vial containing 100 mg/ml of mesna injection in a hydrophilic plastic container. Each mL of mesna injection contains 10.4 mg as a preservative; 10.4 mg as sodium-2-mercaptoethane sulfonate with a molecular formula of C6H16O3NS, and a molecular weight of 164.18. Its structural formula is as follows:

**REFERENCES**

1. Fukuoka M, Scheef GR. Higher doses of ifosfamide: the incidence of hematuria was less than 7%.
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3. IV Mesna injection was designed to reduce the risk of toxic effects caused by ifosfamide-induced hematuria.
4. When mesna injection was administered together with these doses of ifosfamide, the incidence of hematuria was less than 7%.
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**REVIEWED FEBRUARY 2013**

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