HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Mesna Injection safely and effectively. See full prescribing information for Mesna Injection.

Mesna Injection, for intravenous use
Initial U.S. Approval: 1988

INDICATIONS AND USAGE

Mesna injection is a cytoprotective agent indicated as a prophylactic agent in reducing the incidence of ifosfamide-induced hemorrhagic cystitis. (1)

Limitation of Use:
Mesna injection is not indicated to reduce the risk of hematuria due to other pathological conditions such as thrombocytopenia. (1)

DOSAGE AND ADMINISTRATION

Mesna injection may be given on a fractionated dosing schedule of three bolus intravenous injections or a single bolus injection followed by two oral administrations of mesna tablets as outlined below. The dosing schedule should be repeated on each day that ifosfamide is administered. When the dosage of ifosfamide is adjusted, the ratio of mesna to ifosfamide should be maintained. (2)

Intravenous Dosing Schedule:

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

Intravenous and Oral Dosing Schedule:

	0 Hours	2 Hours	6 Hours
Ifosfamide	1.2 g/m^2	-	-
Mesna Injection	240 mg/m^2	-	-
Mesna Tablets	-	480 mg/m^2	480 mg/m^2

Maintain sufficient urinary output, as required for ifosfamide treatment, and monitor urine for the presence of hematuria. (2.3)

DOSAGE FORMS AND STRENGTHS

- 1 gram per 10 mL (100 mg per mL) Multiple Dose Vial (3)

CONTRAINDICATIONS

- Known hypersensitivity to mesna or to any of the excipients, including benzyl alcohol. (4)

WARNINGS AND PRECAUTIONS

- Hypersensitivity reactions: Anaphylactic reactions have been reported. Less severe hypersensitivity reactions may also occur. Monitor patients. If a reaction occurs, discontinue mesna and provide supportive care. (5.1)
- Dermatologic toxicity: Skin rash with eosinophilia and systemic symptoms, Stevens-Johnson syndrome, and toxic epidermal necrolysis have occurred. Skin rash, urticaria, and angioedema have also been seen. Monitor patients. If a reaction occurs, discontinue mesna and provide supportive care. (5.2)
- Benzyl alcohol toxicity: The preservative benzyl alcohol has been associated with serious adverse reactions and death in neonates and premature infants. Avoid use in neonates, premature, and low-birth weight infants. (5.3)
- Laboratory test alterations: False positive tests for urinary ketones and interference with enzymatic CPK activity tests have been seen. (5.4)

ADVERSE REACTIONS

The most common adverse reactions (>10%) when mesna is given with ifosfamide are nausea, vomiting, constipation, leukopenia, fatigue, fever, anorexia, thrombocytopenia, anemia, granulocytopenia, diarrhea, asthenia, abdominal pain, headache, alopecia, and somnolence. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

- Pregnancy: Use only if clearly needed. (8.1)
- Nursing mothers: Women should not breastfeed during therapy. (8.3)
- Geriatric use: Dose selection should be cautious. (8.5)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 12/2016

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Mesna injection is indicated as a prophylactic agent in reducing the incidence of ifosfamide-induced hemorrhagic cystitis.

Limitation of Use:
Mesna injection is not indicated to reduce the risk of hematuria due to other pathological conditions such as thrombocytopenia.

2 DOSAGE AND ADMINISTRATION

2.1 Intravenous Dosing

Mesna injection may be given on a fractionated dosing schedule of three bolus intravenous injections as outlined below.

Mesna injection is given as intravenous bolus injections in a dosage equal to 20% of the ifosfamide dosage weight by weight (w/w) at the time of ifosfamide administration and 4 and 8 hours after each dose of ifosfamide. The total daily dose of mesna injection is 60% of the ifosfamide dose. The recommended dosing schedule is outlined below in Table 1.

Table 1: Recommended Intravenous Dosing Schedule

	0 Hours	4 Hours	8 Hours
Ifosfamide	1.2 g/m^2	-	-
Mesna Injection[1]	240 mg/m^2	240 mg/m^2	240 mg/m^2

[1]The dosing schedule should be repeated on each day that ifosfamide is administered. When the dosage of ifosfamide is increased or decreased, the ratio of mesna injection to ifosfamide should be maintained.

2.2 Intravenous and Oral Dosing

Mesna injection may be given on a fractionated dosing schedule of a single bolus injection followed by two oral administrations of mesna tablets as outlined below.

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. Mesna tablets are given orally in a dosage equal to 40% of the ifosfamide dose 2 and 6 hours after each dose of ifosfamide. The total daily dose of mesna is 100% of the ifosfamide dose. The recommended dosing schedule is outlined in Table 2.

Table 2: Recommended Intravenous and Oral Dosing Schedule

	0 Hours	2 Hours	6 Hours
Ifosfamide	1.2 g/m^2	-	-
Mesna Injection[1]	240 mg/m^2	-	-
Mesna Tablets	-	480 mg/m^2	480 mg/m^2

[1]The dosing schedule should be repeated on each day that ifosfamide is administered. When the dosage of ifosfamide is increased or decreased, the ratio of mesna to ifosfamide should be maintained.

The efficacy and safety of this ratio of intravenous and oral mesna has not been established as being effective for daily doses of ifosfamide higher than 2 g/m^2.

Patients who vomit within two hours of taking oral mesna should repeat the dose or receive intravenous mesna injection.

2.3 Monitoring for Hematuria

Maintain adequate hydration and sufficient urinary output, as required for ifosfamide treatment, and monitor urine for the presence of hematuria. If severe hematuria develops when mesna injection is given according to the recommended dosage schedule, dosage reductions or discontinuation of ifosfamide therapy may be required.

2.4 Preparation for Intravenous Administration and Stability

Preparation
Determine the volume of mesna injection for the intended dose.

Dilute the volume of mesna injection for the dose in any of the following fluids to obtain a final concentration of 20 mg/mL:

- 5% Dextrose Injection, USP
- 5% Dextrose and 0.2% Sodium Chloride Injection, USP
- 5% Dextrose and 0.33% Sodium Chloride Injection, USP
- 5% Dextrose and 0.45% Sodium Chloride Injection, USP
- 0.9% Sodium Chloride Injection, USP
- Lactated Ringer's Injection, USP

Stability
The mesna injection multiple dose vials may be stored and used for up to 8 days after initial puncture.

Store diluted solutions at 25°C (77°F). Use diluted solutions within 24 hours.

Do not mix mesna injection with epirubicin, cyclophosphamide, cisplatin, carboplatin, and nitrogen mustard.

The benzyl alcohol contained in mesna injection vials can reduce the stability of ifosfamide. Ifosfamide and mesna injection may be mixed in the same bag provided the final concentration of ifosfamide does not exceed 50 mg/mL. Higher concentrations of ifosfamide may not be compatible with mesna injection and may reduce the stability of ifosfamide.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Any solutions which are discolored, hazy, or contain visible particulate matter should not be used.

3 DOSAGE FORMS AND STRENGTHS

- Mesna injection: 1 gram per 10 mL (100 mg per mL) Multiple Dose Vial

4 CONTRAINDICATIONS

Mesna injection is contraindicated in patients known to be hypersensitive to mesna or to any of the excipients *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Mesna may cause systemic hypersensitivity reactions, including anaphylaxis. These reactions may include fever, cardiovascular symptoms (hypotension, tachycardia), acute renal impairment, hypoxia, respiratory distress, urticaria, angioedema, laboratory signs of disseminated intravascular coagulation, hematological abnormalities, increased liver enzymes, nausea, vomiting, arthralgia, and myalgia. These reactions may occur with the first exposure or after several months of exposure. Monitor for signs or symptoms. Discontinue mesna and provide supportive care.

5.2 Dermatologic Toxicity

Drug rash with eosinophilia and systemic symptoms and bullous and ulcerative skin and mucosal reactions, consistent with Stevens-Johnson syndrome or toxic epidermal necrolysis have occurred. Mesna may cause skin and mucosal reactions characterized by urticaria, rash, erythema, pruritus, burning sensation, angioedema, periorbital edema, flushing and stomatitis. These reactions may occur with the first exposure or after several months of exposure. Discontinue mesna and provide supportive care.

5.3 Benzyl Alcohol Toxicity

Benzyl alcohol, a preservative in mesna injection, has been associated with serious adverse reactions and death (including gasping syndrome) in neonates, premature, and low-birth weight infants. The minimum amount of benzyl alcohol at which toxicity may occur is not known. Consider the combined daily metabolic load of benzyl alcohol from all sources when prescribing mesna injection (10.4 mg benzyl alcohol per mL). Neonates, premature, and low-birth weight infants, as well as patients receiving high dosages, may be more likely to develop toxicity. Monitor patients for signs or symptoms of toxicity. Avoid use in neonates, premature, and low-birth weight infants *[see Use in Specific Populations (8.4)]*.

5.4 Laboratory Test Interferences

False-Positive Urine Tests for Ketone Bodies
A false positive test for urinary ketones may arise in patients treated with mesna when using nitroprusside sodium-based urine tests (including dipstick tests). The addition of glacial acetic acid can be used to differentiate between a false positive result (cherry-red color that fades) and a true positive result (red-violet color that intensifies).

False-Negative Tests for Enzymatic CPK Activity
Mesna may interfere with enzymatic creatinine phosphokinase (CPK) activity tests that use a thiol compound (e.g., N-acetylcysteine) for CPK reactivation. This may result in a falsely low CPK level.

False-Positive Tests for Ascorbic Acid
Mesna may cause false-positive reactions in Tillman's reagent-based urine screening tests for ascorbic acid.

5.5 Use in Patients with a History of Adverse Reactions to Thiol Compounds

Mesna is a thiol compound, i.e., a sulfhydryl (SH) group-containing organic compound. Hypersensitivity reactions to mesna and to amifostine, another thiol compound, have been reported. It is not clear whether patients who experienced an adverse reaction to a thiol compound are at increased risk for a hypersensitivity reaction to mesna injection.

6 ADVERSE REACTIONS

The following are discussed in more detail in other sections of the labeling.

- Hypersensitivity Reactions *[see Warnings and Precautions (5.1)]*
- Dermatological Toxicity *[see Warnings and Precautions (5.2)]*
- Benzyl Alcohol Toxicity *[see Warnings and Precautions (5.3)]*
- Laboratory Test Interferences *[see Warnings and Precautions (5.4)]*
- Use in Patients with a History of Adverse Reactions to Thiol Compounds *[see Warnings and Precautions (5.5)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Mesna adverse reaction data are available from four Phase 1 studies in which single intravenous doses of 600 to 1,200 mg mesna injection without concurrent chemotherapy were administered to a total of 53 healthy volunteers and single oral doses of 600 to 2,400 mg of mesna tablets were administered to a total of 82 healthy volunteers. The most frequently reported side effects (observed in two or more healthy volunteers) for healthy volunteers receiving single doses of mesna injection alone were headache, injection site reactions, flushing, dizziness, nausea, vomiting, somnolence, diarrhea, anorexia, fever, pharyngitis, hyperesthesia, influenza-like symptoms, and coughing. In two Phase 1 multiple-dose studies where healthy volunteers received mesna tablets alone or intravenous mesna injection followed by repeated doses of mesna tablets, flatulence and rhinitis were reported. In addition, constipation was reported by healthy volunteers who had received repeated doses of intravenous mesna injection.

Additional adverse reactions in healthy volunteers receiving mesna alone included injection site reactions, abdominal pain/colic, epigastric pain/burning, mucosal irritation, lightheadedness, back pain, arthralgia, myalgia, conjunctivitis, nasal congestion, rigors, paresthesia, photophobia, fatigue, lymphadenopathy, extremity pain, malaise, chest pain, dysuria, pleuritic pain, dry mouth, dyspnea, and hyperhidrosis. In healthy volunteers, mesna was commonly associated with a rapid (within 24 hours) decrease in lymphocyte count, which was generally reversible within one week of administration.

Because mesna is used in combination with ifosfamide or ifosfamide-containing chemotherapy regimens, it is difficult to distinguish the adverse reactions which may be due to mesna from those caused by the concomitantly administered cytotoxic agents.

Adverse reactions reasonably associated with mesna administered intravenously and orally in four controlled studies in which patients received ifosfamide or ifosfamide-containing regimens are presented in Table 3.

Table 3: Adverse Reactions in ≥5% of Patients Receiving Mesna in Combination with Ifosfamide-Containing Regimens

Mesna Regimen	Intravenous-Intravenous-Intravenous[1]	Intravenous-Oral-Oral[1]
N exposed	119 (100%)	119 (100%)
Incidence of AEs	101 (84.9%)	106 (89.1%)
Nausea	65 (54.6)	64 (53.8)
Vomiting	35 (29.4)	45 (37.8)
Constipation	28 (23.5)	21 (17.6)
Leukopenia	25 (21)	21 (17.6)
Fatigue	24 (20.2)	24 (20.2)
Fever	24 (20.2)	18 (15.1)
Anorexia	21 (17.6)	19 (16)
Thrombocytopenia	21 (17.6)	16 (13.4)
Anemia	20 (16.8)	21 (17.6)
Granulocytopenia	16 (13.4)	15 (12.6)
Asthenia	15 (12.6)	21 (17.6)
Abdominal Pain	14 (11.8)	18 (15.1)
Alopecia	12 (10.1)	13 (10.9)
Dyspnea	11 (9.2)	11 (9.2)
Chest Pain	10 (8.4)	11 (9.2)
Hypokalemia	10 (8.4)	11 (9.2)
Diarrhea	9 (7.6)	17 (14.3)
Dizziness	9 (7.6)	5 (4.2)
Headache	9 (7.6)	13 (10.9)
Pain	9 (7.6)	10 (8.4)
Sweating Increased	9 (7.6)	2 (1.7)
Back Pain	8 (6.7)	6 (5)
Hematuria	8 (6.7)	7 (5.9)
Injection Site Reaction	8 (6.7)	10 (8.4)
Edema	8 (6.7)	9 (7.6)
Edema Peripheral	8 (6.7)	8 (6.7)
Somnolence	8 (6.7)	12 (10.1)
Anxiety	7 (5.9)	4 (3.4)
Confusion	7 (5.9)	6 (5)
Face Edema	6 (5)	5 (4.2)
Insomnia	6 (5)	11 (9.2)
Coughing	5 (4.2)	10 (8.4)
Dyspepsia	4 (3.4)	6 (5)
Hypotension	4 (3.4)	6 (5)
Pallor	4 (3.4)	6 (5)
Dehydration	3 (2.5)	7 (5.9)
Pneumonia	2 (1.7)	8 (6.7)
Tachycardia	1 (0.8)	7 (5.9)
Flushing	1 (0.8)	6 (5)

[1]Intravenous dosing of ifosfamide and mesna injection followed by either intravenous or oral doses of mesna according to the applicable dosage schedule *[see Dosage and Administration (2)]*.

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Mesna
Injection

6.2 Postmarketing Experience

The following adverse reactions have been reported in the postmarketing experience of patients receiving mesna in combination with ifosfamide or similar drugs, making it difficult to distinguish the adverse reactions which may be due to mesna from those caused by the concomitantly administered cytotoxic agents. Because these reactions are reported from a population of unknown size, precise estimates of frequency cannot be made.

Cardiovascular: Hypertension

Gastrointestinal: Dysgeusia

Hepatobiliary: Hepatitis

Nervous System: Convulsion

Respiratory: Hemoptysis

7 DRUG INTERACTIONS

No clinical drug interaction studies have been conducted with mesna.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B.

Risk Summary

There are no studies of mesna in pregnant women. Reproduction studies performed in rats and rabbits at oral doses approximately 10 times the maximum recommended total daily intravenous-oral-oral human dose on a body surface area basis (1,000 mg/kg in rabbits and 2,000 mg/kg in rats) revealed no evidence of harm to the fetus due to mesna. The incidence of malformations in human pregnancies has not been established for mesna. All pregnancies, regardless of drug exposure, have a background rate of 2 to 4% for major malformations and 15 to 20% for pregnancy loss. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

8.3 Nursing Mothers

It is not known whether mesna or dimesna is excreted in human milk. Benzyl alcohol present in maternal serum is likely to cross into human milk and may be orally absorbed by a nursing infant. Because many drugs are excreted in human milk and because of the potential for adverse reactions in nursing infants from mesna, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

Safety and effectiveness of mesna in pediatric patients have not been established. Mesna injection contains benzyl alcohol (10.4 mg benzyl alcohol per mL) which has been associated with serious adverse reactions and death in pediatric patients. The "gasping syndrome," (characterized by central nervous system depression, metabolic acidosis and gasping respirations) has been associated with benzyl alcohol dosages >99 mg/kg/day in neonates, premature, and low-birth weight infants. Additional symptoms may include gradual neurological deterioration, seizures, intracranial hemorrhage, hematologic abnormalities, skin breakdown, hepatic and renal failure, hypotension, bradycardia, and cardiovascular collapse. The minimum amount of benzyl alcohol at which toxicity may occur is not known. Neonates, premature, and low-birth weight infants, as well as patients receiving high dosages, may be more likely to develop toxicity. Practitioners administering this and other medications containing benzyl alcohol should consider the combined daily metabolic load of benzyl alcohol from all sources *[see Warnings and Precautions (5.3)]*.

8.5 Geriatric Use

Clinical studies of mesna did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. The ratio of ifosfamide to mesna should remain unchanged.

8.6 Use in Patients with Renal Impairment

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

8.7 Use in Patients with Hepatic Impairment

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

10 OVERDOSAGE

There is no known antidote for mesna.

In a clinical trial, 11 patients received intravenous mesna injection 10 mg/kg to 66 mg/kg per day for 3 to 5 days. Patients also received ifosfamide or cyclophosphamide. Adverse reactions included nausea, vomiting, diarrhea and fever. An increased rate of these adverse reactions has also been found in oxazaphosphorine-treated patients receiving ≥80 mg mesna injection per kg per day intravenously compared with patients receiving lower doses or hydration treatment only.

Postmarketing, administration of 4.5 g to 6.9 g of mesna resulted in hypersensitivity reactions including mild hypotension, shortness of breath, asthma exacerbation, rash, and flushing.

11 DESCRIPTION

Mesna Injection is a detoxifying agent to inhibit the hemorrhagic cystitis induced by ifosfamide. The active ingredient, mesna, is a synthetic sulfhydryl compound designated as sodium-2-mercaptoethane sulfonate with a molecular formula of $C_2H_5NaO_3S_2$ and a molecular weight of 164.18. Its structural formula is as follows:

$$HS–CH_2–CH_2SO_3–Na^+$$

Mesna injection is a sterile, nonpyrogenic, aqueous solution of clear and colorless appearance in clear glass multiple dose vials for intravenous administration. Mesna injection contains 100 mg/mL mesna, 0.25 mg/mL edetate disodium and sodium hydroxide for pH adjustment. Mesna injection multiple dose vials also contain 10.4 mg/mL of benzyl alcohol as a preservative. The solution has a pH range of 6.5 to 8.5.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Mesna 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 non-urotoxic 4-sulfoethylthioifosfamide. Mesna also binds to the double bonds of acrolein and to other urotoxic metabolites and inhibits their effects on the bladder.

12.3 Pharmacokinetics

Absorption

Following oral administration, peak plasma concentrations were reached within 1.5 to 4 hours and 3 to 7 hours for free mesna and total mesna (mesna plus dimesna and mixed disulfides), respectively. Oral bioavailability averaged 58% (range 45 to 71%) for free mesna and 89% (range 74 to 104%) for total mesna based on plasma AUC data from 8 healthy volunteers who received 1,200 mg oral or intravenous doses.

Food does not affect the urinary availability of orally administered mesna.

Distribution

Mean apparent volume of distribution (V_d) for mesna is 0.652 ± 0.242 L/kg after intravenous administration which suggests distribution to total body water (plasma, extracellular fluid, and intracellular water).

Metabolism

Analogous to the physiological cysteine-cystine system, mesna is rapidly oxidized to its major metabolite, mesna disulfide (dimesna). Plasma concentrations of mesna exceed those of dimesna after oral or intravenous administration.

Excretion

Following intravenous administration of a single 800 mg dose, approximately 32% and 33% of the administered dose was eliminated in the urine in 24 hours as mesna and dimesna, respectively. Mean plasma elimination half-lives of mesna and dimesna are 0.36 hours and 1.17 hours, respectively. Mesna has a plasma clearance of 1.23 L/h/kg.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term studies in animals have been performed to evaluate the carcinogenic potential of mesna.

Mesna was not genotoxic in the *in vitro* Ames bacterial mutagenicity assay, the *in vitro* mammalian lymphocyte chromosomal aberration assay or the *in vivo* mouse micronucleus assay.

No studies on male or female fertility were conducted. No signs of male or female reproductive organ toxicity were seen in 6-month oral rat studies (≤2,000 mg/kg/day) or 29-week oral dog studies (520 mg/kg/day) at doses approximately 10-fold higher than the maximum recommended human dose on a body surface area basis.

14 CLINICAL STUDIES

14.1 Intravenous Mesna Injection

Hemorrhagic cystitis produced by ifosfamide is dose dependent (Table 4). At a dose of 1.2 g/m² ifosfamide administered daily for 5 days, 16 to 26% of the patients who received conventional uroprophylaxis (high fluid intake, alkalinization of the urine, and the administration of diuretics) developed hematuria (>50 RBC per hpf or macrohematuria) (Studies 1, 2, and 3). In contrast, none of the patients who received mesna injection together with this dose of ifosfamide developed hematuria (Studies 3 and 4). In two randomized studies, (Studies 5 and 6), higher doses of ifosfamide, from 2 g/m² to 4 g/m² administered for 3 to 5 days, produced hematuria in 31 to 100% of the patients. When mesna injection was administered together with these doses of ifosfamide, the incidence of hematuria was less than 7%.

Table 4: Percent of Mesna Injection Patients Developing Hematuria (≥50 RBC/hpf or macrohematuria)

Study	Conventional Uroprophylaxis (number of patients)	Standard Mesna Injection Intravenous Regimen (number of patients)
Uncontrolled Studies*		
Study 1	16% (7/44)	-
Study 2	26% (11/43)	-
Study 3	18% (7/38)	0% (0/21)
Study 4	-	0% (0/32)
Controlled Studies†		
Study 5	31% (14/46)	6% (3/46)
Study 6	100% (7/7)	0% (0/8)

*Ifosfamide dose 1.2 g/m² d x 5

†Ifosfamide dose 2 g/m² to 4 g/m² d x 3 to 5

14.2 Oral Mesna

Clinical studies comparing recommended intravenous and oral mesna dosing regimens demonstrated incidences of grade 3 to 4 hematuria of <5%. Study 7 was an open label, randomized, two-way crossover study comparing three intravenous doses with an initial intravenous dose followed by two oral doses of mesna in patients with cancer treated with ifosfamide at a dose of 1.2 g/m² to 2 g/m² for 3 to 5 days. Study 8 was a randomized, multicenter study in cancer patients receiving ifosfamide at 2 g/m² for 5 days. In both studies, development of grade 3 or 4 hematuria was the primary efficacy endpoint. The percent of patients developing hematuria in each of these studies is presented in Table 5.

Table 5: Percent of Mesna Patients Developing Grade 3 or 4 Hematuria

	Mesna Dosing Regimen	
Study	Standard Intravenous Regimen (number of patients)	Intravenous + Oral Regimen (number of patients)
Study 7	0% (0/30)	3.6% (1/28)
Study 8	3.7% (1/27)	4.3% (1/23)

16 HOW SUPPLIED/STORAGE AND HANDLING

Mesna Injection, is available as:

Product No.	NDC No.	Strength	
730310	63323-733-10	1 gram per 10 mL (100 mg per mL)	Multiple Dose Vial, in packages of 10.
730311	63323-733-11	1 gram per 10 mL (100 mg per mL)	Multiple Dose Vial, packaged individually.

The container closure is not made with natural rubber latex.

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information).

- Advise the patient to discontinue mesna and seek immediate medical attention if any signs or symptoms of a hypersensitivity reaction, including systemic anaphylactic reactions occur *[see Warnings and Precautions (5.1)]*.
- Advise the patient to take mesna at the exact time and in the exact amount as prescribed. Advise the patient to contact their healthcare provider if they vomit within 2 hours of taking oral mesna, or if they miss a dose of oral mesna *[see Dosage and Administration (2.2)]*.
- Mesna does not prevent hemorrhagic cystitis in all patients nor does it prevent or alleviate any of the other adverse reactions or toxicities associated with ifosfamide. Advise the patient to report to their healthcare provider if his/her urine has turned a pink or red color *[see Dosage and Administration (2.3)]*.
- Advise the patient to drink 1 to 2 liters of fluid each day during mesna therapy *[see Dosage and Administration (2.3)]*.
- Advise the patient that Stevens-Johnson syndrome, toxic epidermal necrolysis, and drug rash with eosinophilia and systemic symptoms and bullous and ulcerative skin and mucosal reactions have occurred with mesna. Advise the patient to report to their healthcare provider if signs and symptoms of these syndromes occur *[see Warnings and Precautions (5.2)]*.

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Revised: December 2016