CONTRIIBUTIONS

- Lovenkredensen humanely to one of the reciprocity, including benzyl alcohol.
- ADVERSE EVENTS

The most common adverse reactions (> 1%) when mesna is given with ifosfamide are nausea, vomiting, constipation, leukopenia, fatigue, fever, anorexia, thrombocytopenia, anemia, granulocytopenia, diarrhea, anemia, abdominal pain, headache, anorexia, and vomiting.

In patients with a history of renal failure or concurrent drug therapy, monitor the urine for prolongation of antecedent urine output.

4.2 By May's Test

The May's test provides a qualitative indication of the purity of mesna injection.

The following tests are recommended to assess the purity of mesna injection:

- Visual inspection: Check the color, clarity, and absence of particulate matter.
- Densitometry: Use densitometry to verify the concentration of mesna.
- pH measurement: Determine the pH to ensure it falls within the specified range.
- Specific gravity: Measure the specific gravity to confirm the correct concentration.

If any of these tests fail, the mesna injection should be discarded.

5.2 Dermatologic Toxicity

Drug rash with eosinophilia and systemic symptoms and bullae and ulcerative skin and mucosal reactions, consistent with Stevens-Johnson syndrome or toxic epidermal necrolysis, have occurred. Malignant skin and mucosal reactions characterized by acanthosis, keratosis, erythema, pruritus, burning sensation, exfoliation, paronychia, edema, flushing and/or stomatitis. These reactions may occur with the first exposure or after several months of exposure. Discontinue mesna and provide supportive care.

5.3 Bursal Alcohol Toxicity

Benzyl alcohol, a preservative in mesna, has been associated with various adverse reactions and death (including gasping syndrome) in neonates, prematures, 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 (15.4 mg/kg benzyl alcohol/m). Neonates, prematures, and low-birth weight infants, as well as patients receiving high doses, may be more likely to develop toxicity. Monitor patients for signs or symptoms of toxicity. Avoid use in neonates, prematures, and low-birth weight infants. Use in Specific Populations (4.4).

6.4 Laboratory Test Interferences

False-Positive Tests for Eugonic CPM Activity

Mesna may interfere with electrolyte concentration phosphatase (CPM) activity tests that use a third component (i.e., Na-acetylcysteine) for CPM normalization. This may result in a falsely low CPM level.

False-Positive Tests for Acetic Acid

Mesna may cause false-positive reactions in Timens's reagent-based urine screening tests for acetic acid.

6.5 Use in Patients with a History of Adverse Reactions to Third Components

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

ADVERSE REACTIONS

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

- Hypersensitivity Reactions (see Warnings and Precautions (5.1))
- Dermatologic 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 Third Components (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.

Adverse reaction data are available from four Phase I studies in which single intravenous doses of 600 to 1200 mg of mesna injection without concurrent chemotherapy were administered to a total of 53 healthy volunteers. The most frequently reported side effects (observed in three or more healthy volunteers) for healthy volunteers receiving single doses of mesna injection alone were headache, injection site reactions, flushing, diaphoresis, nausea, vomiting, somnolence, dizziness, anorexia, fever, pharyngitis, hypertension, influenza-like symptoms, and coughing. In two Phase III multiple-dose studies where healthy volunteers received mesna tablets or intravenous mesna followed by repeated doses of mesna tablets, fatigue and chills were reported. In addition, condensation was reported by healthy volunteers who had received repeated doses of intravenous mesna.

Adverse reactions in healthy volunteers receiving mesna alone included injection site reactions, abdominal pain, epigastric pain, gingival hyperplasia, mucosal irritation, lightheadedness, back pain, arthralgia, myalgia, conjunctivitis, nasal congestion, rhinorrhea, photophobia, fatigue, lightheadedness, chest pain, dysuria, plasmatic pain, dry mouth, dryness, drowsiness, and hypothermia. In healthy volunteers, mesna was commonly associated with a rapid (within 24 hours) increase 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 concurrently administered cisplatin agents.

Adverse reactions reasonably associated with mesna administration intravenously and orally are four controlled studies in which patients received ifosfamide or ifosfamide-containing regimens are presented in Table 3. 6.1 Clinical Trials Experience

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Additional adverse reactions in healthy volunteers receiving mesna alone included injection site reactions, abdominal pain, epigastric pain, gingival hyperplasia, mucosal irritation, lightheadedness, back pain, arthralgia, myalgia, conjunctivitis, nasal congestion, rhinorrhea, photophobia, fatigue, lightheadedness, chest pain, dysuria, plasmatic pain, dry mouth, dryness, drowsiness, and hypothermia. In healthy volunteers, mesna was commonly associated with a rapid (within 24 hours) increase in lymphocyte count, which was generally reversible within one week of administration.

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Adverse reactions reasonably associated with mesna administration intravenously and orally are four controlled studies in which patients received ifosfamide or ifosfamide-containing regimens are presented in Table 3.
Safety and effectiveness of mesna in pediatric patients has not been established. Mesna contains benzyl alcohol (10.4 mg benzyl alcohol per mL), which has been associated with serious adverse reactions and death in pediatric patients. The "gassing syndrome", characterized by central nervous system depression, metabolic acidosis and respiratory depression, has been associated with benzyl alcohol doses of 200 mg/kg in neonates, premature, and low-birth weight infants.

Additional symptoms may include gradual neurological deterioration, seizures, intracranial hemorrhage, hemorrhagic abcesses, skin necrosis, respiratory failure, and death. Ifosfamide patients should not be given a minimum amount of benzyl alcohol at which toxicity may occur is not known. Neonates, preterm, and low-birth weight infants, as well as preterm neonates receiving high doses, may be more likely to develop toxicity. Providers 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 [5.4]).

4.4 Pediatric Use

Safety and effectiveness of mesna in pediatric patients has not been established. Mesna contains benzyl alcohol (10.4 mg benzyl alcohol per mL), which has been associated with serious adverse reactions and death in pediatric patients. The "gassing syndrome", characterized by central nervous system depression, metabolic acidosis and respiratory depression, has been associated with benzyl alcohol doses of 200 mg/kg in neonates, premature, and low-birth weight infants.

Additional symptoms may include gradual neurological deterioration, seizures, intracranial hemorrhage, hemorrhagic abcesses, skin necrosis, respiratory failure, and death. Ifosfamide patients should not be given a minimum amount of benzyl alcohol at which toxicity may occur is not known. Neonates, preterm, and low-birth weight infants, as well as preterm neonates receiving high doses, may be more likely to develop toxicity. Providers 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 [5.4]).

4.5 Genetic Use

Clinical studies of mesna did not include sufficient numbers of subjects aged 65 or 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 renal, renal, or cardiac function, and of concomitant disease or other drug therapy. The risk of toxicity to mesna should remain unchanged.

6.2 Precautions

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 concurrently administered cytotoxic agents. Because these reactions are reported from a population of unknown size, precise estimates of frequency cannot be made.

Cardiovascular: Hypertension
Gastrointestinal: Diarrhea
Hepatobiliary: Hepatitis
Nervous System: Somnolence
Respiratory: Hypersensitivity
Systemic: Anaphylaxis

7. DRUG INTERACTIONS

7.1 Concomitant Use

In clinical trials with ifosfamide, mesna has been administered to patients together with other anticancer agents. The concomitant use of mesna with other antineoplastic agents has been associated with increased incidences of some adverse reactions.

7.2 Postmarketing Experience

8.1 Pregnancy

8.2 Use in Specific Populations

8.3 Pediatric Use

8.4 Nursing Mothers

8.5 Interaction with Other Drugs

9.1 General Information

9.2 Administration

9.3 Dosage

9.4 Storage and Stabilization

9.5 Stability

9.6 Overdosage

10.1 OVERDOSAGE

10.2 Exceeding the Maximum Recommended Human Dose

10.3 Hemorrhagic Cystitis

11. DESCRIPTION

11.1 Mechanism of Action

11.2 Pharmacokinetics

11.3 Excretion

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

12.2 Pharmacokinetics

12.3 Excretion

13. ADVERSE REACTIONS

13.1 Hemorrhagic Cystitis

13.2 Nausea, Vomiting

13.3 Other Adverse Reactions

14. CLINICAL STUDIES

14.1 Intravenous Mesna

14.2 Oral Mesna

14.3 Intravenous Versus Oral Mesna

14.4 Other Mesna Regimens

15. PATIENT COUNSELING INFORMATION

15.1 General Information

15.2 Nausea, Vomiting

15.3 Other Adverse Reactions

15.4 Drug Interactions

15.5 Contraindications

15.6 Precautions

15.7 Adverse Reactions

15.8 Overdosage

15.9 Patient Counseling Information

16. HOW SUPPLIED/STORAGE AND HANDLING

16.1 Storage and Stabilization

16.2 Stability

16.3 Overdosage

16.4 Other Information

17. PATIENT COUNSELING INFORMATION

17.1 General Information

17.2 Nausea, Vomiting

17.3 Other Adverse Reactions

17.4 Drug Interactions

17.5 Contraindications

17.6 Precautions

17.7 Adverse Reactions

17.8 Overdosage

17.9 Patient Counseling Information

18. HOW SUPPLIED/STORAGE AND HANDLING

18.1 Storage and Stabilization

18.2 Stability

18.3 Overdosage

18.4 Other Information

19. PATIENT COUNSELING INFORMATION

19.1 General Information

19.2 Nausea, Vomiting

19.3 Other Adverse Reactions

19.4 Drug Interactions

19.5 Contraindications

19.6 Precautions

19.7 Adverse Reactions

19.8 Overdosage

19.9 Patient Counseling Information

20. HOW SUPPLIED/STORAGE AND HANDLING

20.1 Storage and Stabilization

20.2 Stability

20.3 Overdosage

20.4 Other Information

21. PATIENT COUNSELING INFORMATION

21.1 General Information

21.2 Nausea, Vomiting

21.3 Other Adverse Reactions

21.4 Drug Interactions

21.5 Contraindications

21.6 Precautions

21.7 Adverse Reactions

21.8 Overdosage

21.9 Patient Counseling Information

22. HOW SUPPLIED/STORAGE AND HANDLING

22.1 Storage and Stabilization

22.2 Stability

22.3 Overdosage

22.4 Other Information

23. PATIENT COUNSELING INFORMATION

23.1 General Information

23.2 Nausea, Vomiting

23.3 Other Adverse Reactions

23.4 Drug Interactions

23.5 Contraindications

23.6 Precautions

23.7 Adverse Reactions

23.8 Overdosage

23.9 Patient Counseling Information

24. HOW SUPPLIED/STORAGE AND HANDLING

24.1 Storage and Stabilization

24.2 Stability

24.3 Overdosage

24.4 Other Information