Mesna: Drug information

(For additional information see "Mesna: Patient drug information" and see "Mesna: Pediatric drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

Brand Names: US

Mesnex

Brand Names: Canada

Mesna for injection; Uromitexan

Pharmacologic Category

Antidote; Chemoprotective Agent

Dosing: Adult

Note: Mesna dosing schedule should be repeated each day ifosfamide is received. If ifosfamide dose is adjusted (decreased or increased), the mesna dose should also be modified to maintain the mesna-to-ifosfamide ratio.

Prevention of ifosfamide-induced hemorrhagic cystitis:

Standard-dose ifosfamide (manufacturer's labeling): IV: Mesna dose is equal to 20% of the ifosfamide dose given for 3 doses: With the ifosfamide dose, hour 4, and at hour 8 after the ifosfamide dose (total daily mesna dose is 60% of the ifosfamide dose)

Oral mesna (following IV mesna; for ifosfamide doses ≤2 g/m^2/day): Mesna dose (IV) is equal to 20% of the ifosfamide dose at hour 0, followed by mesna dose (orally) equal to 40% of the ifosfamide dose given 2 and 6 hours after the ifosfamide dose (total daily mesna dose is 100% of the ifosfamide dose). **Note:** If the oral mesna dose is vomited within 2 hours of administration, repeat the dose or administer IV mesna.

Short infusion standard-dose ifosfamide (<2.5 g/m^2/day): ASCO guidelines: IV: Total mesna dose is equal to 60% of the ifosfamide dose, in 3 divided doses (each mesna dose as 20% of ifosfamide dose), given 15 minutes before the ifosfamide dose, and 4 and 8 hours after each dose of ifosfamide (Hensley, 2009)

Continuous infusion standard-dose ifosfamide (<2.5 g/m^2/day): ASCO guidelines: IV: Mesna dose (as a bolus) is equal to 20% of the ifosfamide dose, followed by a continuous infusion of mesna at 40% of the ifosfamide dose; continue mesna infusion for 12-24 hours after completion of ifosfamide infusion (Hensley, 2009)

High-dose ifosfamide (>2.5 g/m^2/day): ASCO guidelines: Evidence for use is inadequate; more frequent and prolonged mesna administration regimens may be required (Hensley, 2009)

Other dosing strategies used in combination with ifosfamide (off-label dosing):

Mesna continuous infusion: IV: 1.8 g/m^2/day to 5 g/m^2/day as a continuous infusion (100% of the ifosfamide dose), repeated each day ifosfamide is received; see protocols for specific

details (Bacci, 2003; Kolb, 2003; Moskowitz, 2011)

Mesna bolus followed by continuous infusion: IV: 1000 mg/m^2 1 hour prior to ifosfamide on day 1, followed by 3000 mg/m^2/day continuous infusion (continuous infusion is 100% of the ifosfamide dose) on days 1, 2, and 3 (with sufficient hydration) every 3 weeks for 6 courses (Juergens, 2006)

Prevention of cyclophosphamide-induced hemorrhagic cystitis (off-label use):

HDCAV/IE regimen for Ewing sarcoma: Children ≥4 years and Adults <40 years: IV: 2100 mg/m^2/day continuous infusion (mesna dose is equivalent to the cyclophosphamide dose) for 2 days with cyclophosphamide infusion during cycles 1, 2, 3, and 6 (Kolb, 2003)

Hyper-CVAD regimen for ALL: Adults: IV: 600 mg/m^2/day continuous infusion (mesna continuous infusion is same total dose as cyclophosphamide) on days 1, 2, and 3, beginning with cyclophosphamide and ending 6 hours after the last cyclophosphamide dose during odd-numbered cycles (cycles 1, 3, 5, 7) of an 8-cycle phase (Kantarjian, 2000)

Dosing: Pediatric

(For additional information see "Mesna: Pediatric drug information")

Prevention of ifosfamide-induced hemorrhagic cystitis (off-label use):

Short infusion standard-dose ifosfamide (<2.5 g/m^2/day): ASCO guidelines: Refer to adult dosing.

Continuous infusion standard-dose ifosfamide (<2.5 g/m^2/day): ASCO guidelines: Refer to adult dosing.

Other dosing strategies used in combination with ifosfamide (off-label dosing):

Mesna continuous infusion: IV: 1.8 g/m^2/day to 5 g/m^2/day as a continuous infusion (100% of the ifosfamide dose), repeated each day ifosfamide is received; see protocols for specific details (Bacci, 2003; Kolb, 2003; Moskowitz, 2011)

Mesna bolus followed by continuous infusion: IV: 1000 mg/m^2 1 hour prior to ifosfamide on day 1, followed by 3000 mg/m^2/day continuous infusion (continuous infusion is 100% of the ifosfamide dose) on days 1, 2, and 3 (with sufficient hydration) every 3 weeks for 6 courses (Juergens, 2006)

Mesna (20% higher than ifosfamide) continuous infusion: IV: 3600 mg/m^2/day continuous infusion for 4 days (mesna dose is 20% higher than ifosfamide), with hydration, during weeks 4 and 9 (3 additional postop courses were administered in good responders) (Le Deley, 2007)

Prevention of cyclophosphamide-induced hemorrhagic cystitis (off-label use): HDCAV/IE regimen for Ewing sarcoma: Children ≥4 years and Adults <40 years: IV: 2100 mg/m^2/day continuous infusion (mesna dose is equivalent to the cyclophosphamide dose) for 2 days with cyclophosphamide infusion during cycles 1, 2, 3, and 6 (Kolb, 2003)

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

There are no dosage adjustments provided in the manufacturer's

labeling (has not been studied)

Dosing: Hepatic Impairment There are no dosage adjustments provided in the manufacturer's labeling (has not been studied)

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Intravenous:

Mesnex: 100 mg/mL (10 mL) [contains benzyl alcohol, edetate disodium]

Generic: 100 mg/mL (10 mL)

Tablet, Oral:

Mesnex: 400 mg [scored]

Generic Equivalent Available (US) May be product dependent

Dosage Forms: Canada Information with regard to form, strength, and availability of products uniquely available in Canada but currently not available in the US. Refer also to Dosage forms.

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Intravenous:

Mesna for injection: 100 mg/mL (10 mL) [contains benzyl alcohol, edetate disodium]

Uromitexan: 100 mg/mL (4 mL, 10 mL) [contains edetate disodium]

Uromitexan: 100 mg/mL (10 mL, 50 mL) [contains benzyl alcohol, edetate disodium]

Administration Maintain adequate hydration and urinary output during ifosfamide treatment

IV: Administer as an IV bolus (per manufacturer); may also be administered by short infusion or continuous infusion (maintain continuous infusion for 12-24 hours after completion of ifosfamide infusion) (Hensley, 2009); refer to specific protocol for administration rate/details

Oral: Administer orally in tablet formulation; patients who vomit within 2 hours after taking oral mesna should repeat the dose or receive IV mesna. A solution may be prepared from solution for injection by dilution in syrup, juice, carbonate beverages, or milk (Goren, 1991); see Extemporaneously Prepared section.

Use

Prevention of ifosfamide-induced hemorrhagic cystitis: Preventive agent to reduce the incidence of ifosfamide-induced hemorrhagic cystitis

Limitations of use: Mesna is not indicted to reduce the risk of hematuria due to other conditions such as thrombocytopenia

Use: Off-Label

Prevention of cyclophosphamide-induced hemorrhagic cystitis (with high-dose cyclophosphamide)

Adverse Reactions

Mesna alone (frequency not defined):

Cardiovascular: Flushing

Central nervous system: Dizziness, drowsiness, headache, hyperesthesia, rigors

Dermatologic: Skin rash

Gastrointestinal: Anorexia, constipation, diarrhea, dysgeusia (with oral administration), flatulence, nausea, unpleasant taste (with oral administration), vomiting

Local: Injection site reaction

Neuromuscular & skeletal: Arthralgia, back pain

Ophthalmic: Conjunctivitis

Respiratory: Cough, flu-like symptoms, pharyngitis, rhinitis

Miscellaneous: Fever

<1%, postmarketing and/or case reports (mesna alone or in combination): Anaphylaxis, erythema at injection site, hypersensitivity reaction, hypertension, hypotension, increased serum transaminases, increased ST segment on ECG, limb pain, malaise, myalgia, pain at injection site, tachycardia, tachypnea, thrombocytopenia

Contraindications

Hypersensitivity to mesna or any component of the formulation

Warnings/Precautions

Concerns related to adverse effects:

• Anaphylaxis/hypersensitivity reactions: Hypersensitivity reactions have been reported; symptoms ranged from mild hypersensitivity to systemic anaphylactic reactions and may include fever, hypotension, tachycardia, acute renal impairment, hypoxia, respiratory distress, urticaria, angioedema, signs of disseminated intravascular coagulation, hematologic abnormalities, increased liver enzymes, nausea, vomiting, arthralgia, and myalgia. Reactions may occur with the first exposure, or after several months of treatment. Monitor for signs/symptoms of reactions. May require discontinuation. Patients with autoimmune disorders receiving cyclophosphamide and mesna may be at increased risk. Mesna is a thiol compound; it is unknown if the risk for reaction is increased in patients who have had a reaction to other thiol compounds (eg, amifostine).

• Dermatologic toxicity: Drug rash with eosinophilia and systemic symptoms and bullous/ulcerative skin, and mucosal reactions consistent with Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) have been reported. The skin and mucosal reactions may be characterized by rash, pruritus, urticaria, erythema, burning sensation, angioedema, periorbital edema, flushing, and

stomatitis. Reactions may occur with the first exposure, or after several months of treatment. May require discontinuation.

• Hematuria: Monitor urine for hematuria. Severe hematuria despite utilization of mesna may require ifosfamide dose reduction or discontinuation. Examine morning urine specimen for hematuria prior to ifosfamide or cyclophosphamide treatment; if hematuria (>50 RBC/HPF) develops, reduce the ifosfamide/cyclophosphamide dose or discontinue the drug; will not prevent hemorrhagic cystitis in all patients. Mesna will not reduce the risk of hematuria related to thrombocytopenia. Patients should receive adequate hydration during treatment.

• Ifosfamide/cyclophosphamide toxicities: Mesna is intended for the prevention of hemorrhagic cystitis and will not prevent or alleviate other toxicities associated with ifosfamide or cyclophosphamide.

Dosage form specific issues:

• Benzyl alcohol and derivatives: Some dosage forms may contain benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity (“gasping syndrome”) in neonates; the “gasping syndrome” consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction (including convulsions, intracranial hemorrhage), hypotension, and cardiovascular collapse (AAP ["Inactive" 1997]; CDC, 1982); some data suggests that benzoate displaces bilirubin from protein binding sites (Ahlfors, 2001); avoid or use dosage forms containing benzyl alcohol with caution in neonates. See manufacturer’s labeling.

Metabolism/Transport Effects

None known.

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

There are no known significant interactions.

Pregnancy Risk Factor

B (show table)

Pregnancy Implications

Adverse effects were not observed in animal reproduction studies. Use during pregnancy only if clearly needed.

Breast-Feeding Considerations

It is not known if mesna is excreted in breast milk. Benzyl alcohol, a component in some formulations, does enter breast milk and may be absorbed by a nursing infant. Due to the potential for adverse reactions in the nursing infant, a decision should be made to discontinue breast-feeding or to discontinue mesna, taking into account the importance of treatment to the mother.

Monitoring Parameters

Monitor urine for hematuria; urine output and hydration status; monitor for signs/symptoms of hypersensitivity or dermatologic toxicity

Mechanism of Action

In blood, mesna is oxidized to dimesna which in turn is reduced in the kidney back to mesna, supplying a free thiol group which binds to and inactivates acrolein, the urotoxic metabolite of ifosfamide and cyclophosphamide

Pharmacodynamics/Kinetics

Distribution: 0.65 ± 0.24 L/kg; distributed to total body water

Protein binding: 69% to 75%

Metabolism: Rapidly oxidized to mesna disulfide (dimesna) in the intravascular compartment. Mesna and dimesna do not undergo hepatic metabolism.

Bioavailability: Oral: Free mesna: 58% (range: 45% to 71%); not affected by food

Half-life elimination: Mesna: ~22 minutes; Dimesna: ~70 minutes

Time to peak, plasma: Oral: Free mesna: 1.5 to 4 hours

Excretion: Urine (32% as mesna; 33% as dimesna); majority of IV dose excreted within 4 hours

Pricing: US

Solution (Mesna Intravenous)

100 mg/mL (10 mL): $39.60

Solution (Mesnex Intravenous)

100 mg/mL (10 mL): $39.60

Tablets (Mesnex Oral)

400 mg (10): $943.09

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

Delinar (AR); Ifomes (BD); Mescryo (CR, DO, GT, HN, MX, NI, PA, SV); Mesnil (MX, PE, PY); Mesodal (MX); Mistabron (KR, LU, PH, VN); Mitexan (BR); Mucofluid (ES); Novacarel (CR, DO, GT, HN, NI, PA, SV); Uromes (CR, DO, GT, HN, NI, PA, SV); Uromiteksan (UA); Uromitexan (AE, AT, AU, BE, BG, BH, CH, CL, CN, CY, CZ, DE, DK, EE, EG, ES, FI, FR, GB, GR, HK, HR, HU, ID, IE, IN, IS, IT, JO, KR, KW, LB, LT, LU, MT, NL, NO, NZ, PK, PL, PT, QA, RO, RU, SA, SE, SG, SI, SK, TH, TR, TW, UY, VN); Uroprot (MX, TH)

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