Drug Monograph

A - Drug Name

mesna

SYNONYM(S): Sodium 2-mercaptoethane sulfonate

COMMON TRADE NAME(S): Uromitexan® (multiple brands available)

back to top

B - Mechanism of Action and Pharmacokinetics

Mesna reacts with acrolein and other urotoxic metabolites of oxazaphosphorines (cyclophosphamide or ifosfamide) in the urine to form stable, non-urotoxic compounds. Mesna does not have any antitumour activity, nor does it appear to interfere with the antitumour activity of antineoplastic drugs

Absorption	Bioavailability	oral: 50% (i.e., oral dose usually 2 x IV dose); provides lower but more prolonged urinary levels and higher systemic exposure, with total urinary recovery comparable to IV. Urinary bioavailability not affected by food.
Distribution	Hydrophilic, does not enter most cells (i.e., remains in intravascular space).	
	Cross blood brain barrier?	no
	PPB	69-75 %
Metabolism	Rapidly oxidized in plasma to dimesna (mesna disulfide). No hepatic metabolism.	
	Active metabolites	no

	Inactive metabolites	Dimesna (only metabolite)
Elimination	Rapidly cleared from plasma, filtered by glomerulus and partially (33%) reduced by the glutathione system back to mesna in renal tubules, then secreted into urine as a free thiol.	
	Urine	IV: 32% mesna and 33% dimesna within 24 hours
	Half-life	± 1 hr (up to 8 hours with PO)

back to top

C - Indications and Status

Health Canada Approvals:

- Prevention and reduction of hemorrhagic cystitis secondary to cyclophosphamide or ifosfamide (oxazaphosphorines)

back to top

D - Adverse Effects

Emetogenic Potential: Not applicable

Extravasation Potential: Irritant (undiluted)

The following adverse effects were observed in healthy patients who received IV/PO mesna without concurrent chemotherapy.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	Flushing (11%)	I
	Hypotension (rare, may be fluid refractory)	I
	Palpitations (1%)	I
Dermatological	Rash (may be severe)	I E
Gastrointestinal	Abdominal pain (22%) (more frequent with oral use)	I E

	Anorexia (8%)	I
	Constipation (2%)	E
	Diarrhea (12%) (more frequent with oral use)	I E
	Dry mouth (2%)	I E
	Flatulence (9%)	E
	Nausea, vomiting (12%) (mild, more frequent with oral use)	I
	Other (4%) (GI pain - epigastric)	I
General	Fatigue (4%)	E
	Flu-like symptoms (11%)	I
Hematological	Lymphopenia (may be severe, generally reversible)	I
Hepatobiliary	↑ LFTs (1%)	E
Hypersensitivity	Hypersensitivity (rare)	I
Injection site	Injection site reaction (25%) (venous irritation- rare, when undiluted)	I
Metabolic / Endocrine	Other (↑ PO4; moderate, transient)	E
Musculoskeletal	Musculoskeletal pain (8%)	E
Nervous System	Cognitive disturbance (1%)	E
	Dizziness (16%)	I
	Dysgeusia (100%) (unpleasant taste)	I
	Headache (36%)	I
	Paresthesia (5%)	E
Ophthalmic	Blurred vision (1%)	I E
	Conjunctivitis (6%)	I
	Photophobia (4%)	I E
Respiratory	Cough, dyspnea (4%)	I

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.
"*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.
Dose-limiting side effects are underlined.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
D = *delayed* (weeks to months) L = *late* (months to years)

No **venous irritation** was observed when mesna was diluted with water 1:3.

Hypersensitivity reactions, from mild allergic reactions to anaphylactic reactions, have occurred in patients receiving mesna. The incidence of hypersensitivity reactions appeared to be higher in

patients with autoimmune disorders who were treated with cyclophosphamide; most of these patients received oral mesna. Reactions may occur during or after a first treatment or may be delayed until after several weeks or months of mesna exposure. Recurrence of reactions, in some cases with increased severity, has been reported with re-exposure. **Skin** reactions include local or generalized rashes, and may be severe in some cases (e.g. Stevens-Johnson syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms (DRESS) syndrome). Some skin reactions were accompanied by flu-like or systemic symptoms (e.g. cardiovascular, pulmonary symptoms, prolonged prothrombin time, hematological changes, ↑LFTs or conjunctivitis, etc). Photodistribution of a rash has also been reported.

back to top

E - Dosing

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response and concomitant therapy. Various mesna dosages have been used; optimum dosages and methods of administration have been established. Total daily IV dosage of mesna generally is equivalent to 60-160% of the total daily dosage of the oxazaphosphorine derivative (e.g. cyclophosphamide or ifosfamide); however, doses greater than 120% of oxazaphosphorine dose may be associated with increased gastrointestinal toxicity.

Adults:

Dosage expressed as percentage of oxazaphosphorine dose given. Note: 0 hr indicates start of the infusion. The mesna dosing schedule should be repeated on each day that the oxazaphosphorine is administered. If the oxazaphosphorine dose is adjusted, the mesna dose should also be modified to maintain the mesna-to-oxazaphosphorine drug ratio.
IV Bolus: 20% of the oxazaphosphorine dose at 0 hr, 4 hrs and 8 hrs

Oral: 20% IV at 0 hr, 40% p.o at 4 hrs and 8 hrs OR 40% p.o and 0, 4 and 8 hrs.
Vomiting within 2 hours of oral mesna should be reported to the physician so that IV mesna can be given.

Note: Higher doses and more frequent administration are required when used for myeloablation. May be given as a continuous infusion when used with continuous infusion ifosfamide (load-20%, then 40% as a continuous infusion continuing for 8-24 hrs after completion of ifosfamide)

Dosage with Toxicity:

Dosage in myelosuppression: No adjustment required.

Dosage with Hepatic Impairment:

No adjustment required.

Dosage with Renal Impairment:

No adjustment required.

Dosage in the elderly:

No dose adjustment required. Maintain ratio between ifosfamide and mesna doses.

Children:

Consult protocol being used. Generally use higher doses or more frequent administration.

back to top

F - Administration Guidelines

- May be diluted in 50-100mL of diluent (D5W, NS) up to final concentration of 1 mg/mL to 20 mg/mL and given IV over 15-30 minutes.
- May be diluted in larger volumes (1 mg/mL to 20 mg/mL) for continuous infusion over 3-24 hours.
- May be infused concurrently with ifosfamide. Note: Benzyl alcohol in multi-dose vials can reduce the stability of ifosfamide and cyclophosphamide.
- Incompatible in solution with cisplatin or carboplatin, nitrogen mustard. Admixtures with epirubicin lead to inactivation of epirubicin.
- In addition to mesna use, sufficient hydration and urine output should still be maintained.
- IV solution may be given PO; may be mixed with juice, cola or milk to mask unpleasant taste. The manufacturer (for Uromitexan®) reccomends that multi-dose vials should not be used for PO doses.
- Store ampoules and multi-dose vials at 15-25°C.

back to top

G - Special Precautions

Other:

Mesna is contraindicated in patients with known hypersensitivity to the drug. Use with caution in patients with hypersensitivity to other thiols. Formulations containing benzyl alcohol should not be used in pediatric patients who are 12 years old and younger.

Mesna does not prevent ifosfamide-induced nephrotoxicity nor prevent / decrease the incidence of non-urologic toxicities (i.e. myelosuppression, neurotoxicity) associated with oxazaphosphorines. Mesna does not replace hydration and other prophylactic or supportive measures used in oxazaphosphorines treatment. The half-life of mesna is shorter than the half-life of ifosfamide or cyclophosphamide, therefore **multiple doses or continuous infusion of mesna**, for 8-24 hours beyond the end of the oxazaphosphorine infusion is required to prevent urotoxicity.

Although mesna has not been shown to be fetotoxic, carcinogenic, or mutagenic in animal or *in vitro* studies, it is able to cross the placenta. However, its safety in **pregnancy** and effect on **fertility** have not been established. **Breast feeding** is not recommended due to the potential secretion into breast milk.

back to top

H - Interactions

AGENT	EFFECT	MECHANISM	MANAGEMENT
Test for ketones in urine	False positive, colour is reddish purple rather than purple	Sulfonate group in mesna presumed to interact with the sodium nitroprusside reagent	Caution
Serum CPK testing	Lower values were observed in samples taken 24 h after mesna than pre-mesna samples	Possibly due to significant interference with thiol dependent enzymatic CPK tests	Caution
Urine screening tests for ascorbic acid	False positive reactions in Tillman's reagent-based tests	Unknown	Caution

back to top

I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

Monitor Type	Monitor Frequency
Clinical assessment of rash, GI symptoms, infusion site reactions and hypersensitivity	
Also refer to monitoring parameters for other drugs used in the regimen	

Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

back to top

K - References

McEvoy GK, editor. AHFS Drug Information 2013. Bethesda, Maryland: American Society of Health-System Pharmacists, p. 3772-6.

Medeffect Health Professional Information: Mesna (Uromitexan®), multi-dose vials - association with fatal gasping syndrome in neonates and infants. Health Canada, September 6, 2011

Product Monograph: Mesna. Pharmaceutical Partners of Canada, January 15, 2008.

Product Monograph: Uromitexan® (mesna): Baxter Corp., August 6, 2013.

November 2017 republished to enable search by "cancer type" filter

back to top

L - Disclaimer

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

While care has been taken in the preparation of the information contained in the Formulary, such information is provided on an “as-is” basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information’s quality, accuracy, currency, completeness, or reliability.

CCO and the Formulary’s content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person’s use of the information in the Formulary.

back to top