DRUG NAME: Mesna

SYNONYM(S): sodium 2-mercaptoethanesulfonate[1-4]

COMMON TRADE NAME(S): UROMITEXAN®, MESNEX® (USA)

CLASSIFICATION: cytoprotective agent, non-cytotoxic[5]

Special pediatric considerations are noted when applicable, otherwise adult provisions apply.

MECHANISM OF ACTION:

Mesna is a synthetic compound that protects the bladder from the urotoxic metabolites of oxazaphosphorine derivatives (e.g., ifosfamide, cyclophosphamide) by chemically interacting with them and their metabolites as a sulfhydryl donor in urine.[1-3]

PHARMACOKINETICS:

Oral Absorption	unaffected by food; (urinary) bioavailability 45-79%; time to peak plasma concentration: 2-4 hours[1,4]	
Distribution	intravascular	
	cross blood brain barrier?	no
	volume of distribution	0.65 L/kg
	plasma protein binding	69-75%
Metabolism	rapidly oxidized to dimesna (mesna disulfide) in circulation; no hepatic metabolism	
	active metabolite(s)	none[1,3]
	inactive metabolite(s)	dimesna
Excretion	dimesna is rapidly filtered and eliminated by the kidneys, where ~30% is reduced back to the active drug, mesna, by the glutathione system	
	urine	>60% (mesna and dimesna)[1-3]
	feces	none[1,3]
	terminal half life	IV[1-4]: 0.36-1.08h PO[1-3]: 1.15-8.3h
	clearance	no information found

Adapted from standard reference[1] unless specified otherwise.

USES:

Primary uses:
*Reduction and prevention of urinary tract toxicity (hemorrhagic cystitis) of oxazaphosphorines

*Health Canada approved indication

Other uses:

SPECIAL PRECAUTIONS:

Contraindicated in patients with a history of hypersensitivity reaction to mesna[2,3] or other sulfhydryl (thiol) compounds[1,4]

Autoimmune disorders (e.g., rheumatoid arthritis, systemic lupus erythematosus, nephritis) may put patients at increased risk of developing hypersensitivity reactions to mesna.[1,4]

Limited place in therapy: Mesna does not prevent nephrotoxicity or non-urologic toxicities associated with oxazaphosphorine derivatives.[1] Mesna does not prevent hematuria associated with other conditions such as thrombocytopenia.[1] Mesna is not a replacement for adequate hydration (i.e., at least 1 L of oral or IV fluid daily, prior to and during ifosfamide therapy).[1]

Special populations: Safety and efficacy of mesna in **children** have not been established; however, mesna has been used for prophylaxis of ifosfamide-induced hemorrhagic cystitis in infants and children 4 months to 16 years of age and for prophylaxis of cyclophosphamide-induced hemorrhagic cystitis in children ≥5 months without unusual adverse effects.[1] **Neonates** may potentially be at risk from benzyl alcohol preservative; toxicity has been associated with large amounts (i.e., 100-400 mg/kg daily). Avoid use in neonates if possible, although the American Academy of Pediatrics states that the presence of small amounts of the preservative in a commercially available injection should not preclude its use when indicated. Each mL of mesna in multidose vials contains 10.4 mg of benzyl alcohol as a preservative.[1]

Carcinogenicity: not carcinogenic in rats.[2,3]

Mutagenicity: not mutagenic in Ames test.[1-3] Non-clastogenic in mammalian *in vitro* and *in vivo* chromosome tests.[1]

Fertility: no information found.

Pregnancy: FDA Pregnancy Category B. Animal-reproduction studies have not shown a fetal risk but there are no controlled studies in pregnant women.[1-4]

Breastfeeding: Not recommended due to the potential secretion into breast milk.[1,4]

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important.[6] When placebo-controlled trials are available, adverse events are included if the incidence is ≥5% higher in the treatment group.

At recommended doses, side effects are not usually observed.[3]

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
cardiovascular (arrhythmia)	tachycardia (≤8%[1,4]), with high doses
cardiovascular (general)	hypotension (≤8%[1]); with high doses, transient
dermatology/skin	*extravasation hazard: irritant*[7]
gastrointestinal	*emetogenic potential: low to low-moderate*[8]
	diarrhea; with high doses
	unpleasant taste (100%)[1,4]; see **Dosage Guidelines** for management suggestions
musculoskeletal	arthralgia; with high doses
neurology	somnolence (3-11%)[1,6]
pain	abdominal pain (3-18% IV; 5-16% PO[1]), with high doses
	headache (3-11%[1]), with high doses
	limb pain (<1%[4]), with high doses

Adapted from standard reference[3] unless specified otherwise.

INTERACTIONS:

AGENT	EFFECT	MECHANISM	MANAGEMENT
cyclophosphamide[1]	no effect		
doxorubicin[1]	no effect		
ifosfamide[1]	no effect		
methotrexate[1]	no effect		
sodium nitroprusside tests for urinary ketones[1] (e.g., CHEMSTRIP®, MULTISTIX®, LABSTIX®)[4]	false positive result	the sulfonate group in mesna is presumed to interact with the sodium nitroprusside reagent	interpret results accordingly
vincristine[1]	no effect		

SUPPLY AND STORAGE:

Tablets: not available in Canada

Injection: Baxter supplies mesna for injection as a 100 mg/mL solution, in 4 mL and 10 mL ampoules.

Pharmaceutical Partners of Canada supplies mesna for injection as a 100 mg/mL solution, in 10 mL multidose vials. Each mL of mesna in multidose vials contains 10.4 mg of benzyl alcohol as a preservative. See **Caution** section.

For basic information on the current brand used at the BC Cancer Agency, see Chemotherapy Preparation and Stability Chart in Appendix.

SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at the BC Cancer Agency, see Chemotherapy Preparation and Stability Chart in Appendix.

Compatibility of selected drugs[9]: The following are compatible via Y-site injection: allopurinol sodium, amifostine, aztreonam, cefepime HCl, cladribine, cyclophosphamide, docetaxel, doxorubicin HCl liposome, filgrastim, fludarabine phosphate, gatifloxacin, gemcitabine HCl, granisetron, ifosfamide, linezolid, melphalan HCl, methotrexate sodium, ondansetron HCl, paclitaxel, piperacillin sodium-tazobactam sodium, sargramostim, sodium bicarbonate, teniposide, thiotepa, vinorelbine tartrate.
The following are compatible in the same infusion solution: hydroxyzine, ifosfamide.

Incompatibility of selected drugs[9]: The following are incompatible via Y-site injection: amphotericin B cholesteryl sulfate complex.
The following are incompatible in the same infusion solution: carboplatin, cisplatin.

PARENTERAL ADMINISTRATION:

BCCA administration guideline noted in ***bold***, ***italics***

Subcutaneous	no information found
Intramuscular	no information found
Direct intravenous	***approved route[1]***
Intermittent infusion	***over 15-30 minutes[1,4]***
Continuous infusion	***over 24 hours[4]***

BCCA administration guideline noted in ***bold***, ***italics***

Intraperitoneal	no information found
Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical	no information found

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Various mesna dosages have been used, and optimum dosages and methods of administration have not been established.[1]

Mesna dosing is based on the dosage of the oxazaphosphorine derivative (e.g., ifosfamide or cyclophosphamide). **Dosage is expressed as a percentage of oxazaphosphorine dose given**.
Hour 0 is the time of the start of the oxazaphosphorine infusion.

***Adults*:**

BCCA usual dose noted in ***bold, italics***

Mesna dose is a percentage of the oxazaphosphorine (e.g., ifosfamide or cyclophosphamide) dose given. Hour 0 is the time of the start of the oxazaphosphorine infusion.

	Cycle Length:	
**Oral:*	N/A[2,3]	40% of the oxazaphosphorine dose at hour 0, 4, and 8 *Extemporaneous oral solutions may be prepared using the parenteral dosage form. Because the injection solution has a disagreeable taste, doses are usually prepared by dilution with syrup, milk, juice, or carbonated beverages.[1-4] If an oral dose is vomited within two hours, the dose should be repeated or IV mesna given.[4,10]
Intravenous and Oral Combination:	N/A[2,3]	20% of the oxazaphosphorine dose IV at hour 0, followed by 40% of the oxazphosphorine dose PO at hour 4 and 8
	N/A[1,4,10]	20% of the oxazaphosphorine dose IV at hour 0, followed by 40% of the oxazphosphorine dose PO at hour 2 and 6
	N/A[***11***]	***20% of the oxazaphosphorine dose IV at hour 0, followed by 40% of the oxazaphosphorine dose PO at hour 5 and 9***
	N/A[***12,13***]	***20% of the oxazaphosphorine dose IV at hour 0, followed by 48% of the oxazaphosphorine dose PO at hour 3 and 7***
Intravenous:	N/A[2,3,10]	20% of the oxazaphosphorine dose at hour 0, 4, and 8
	N/A[2,3]	10-12 mg/kg at hour 0, 4, and 8
	N/A[4]	20% of the oxazaphosphorine dose at hour 0, 3, 6, and 9

BCCA usual dose noted in ***bold, italics***

Mesna dose is a percentage of the oxazaphosphorine (e.g., ifosfamide or cyclophosphamide) dose given. Hour 0 is the time of the start of the oxazaphosphorine infusion.

	Cycle Length:	
	N/A[14]	***12% of the ifosfamide dose at hour 0, then 50% of the ifosfamide dose admixed with ifosfamide and infused over 24 hours, followed by 25% of the ifosfamide dose over 12 hours***
	N/A[11-13]	***20% of the oxazaphosphorine dose at hour 0, 5, and 9***

Concurrent radiation: results from *in vitro* test systems and clinical experience indicate that mesna may safely be used in regimens that include total body irradiation[1]

Dosage in myelosuppression: modify according to protocol by which patient is being treated; if no guidelines available, refer to Appendix 6 "Dosage Modification for Myelosuppression"

Dosage in renal failure: no adjustment required[1]

Dosage in hepatic failure: no adjustment required[1]

Dosage in dialysis: no information found

Dosage in elderly: Although geriatric individuals were included in clinical studies, it has not been determined whether geriatric patients respond differently than younger adults. The ratio of ifosfamide to mesna should remain unchanged.[1]

Children:

	Cycle Length:	
Intravenous:	N/A[2,3]	20% of the oxazaphosphorine dose at hour 0, 1, 3, 6, 9, and 12
	N/A[2,3]	30% of the oxazaphosphorine dose at hour 0, 4, and 8

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