Baxter

Baxter Oncology GmbH
Frankfurt am Main
Germany · Allemagne · Alemania

Patient Information Leaflet
Please read carefully!

Uromitexan® 400 mg

Active substance: Mesna

Uroprotector®

Composition: 4 ml injection solution contains mesna 400 mg
Other constituents: sodium edetate, sodium hydroxide, water for injections

Indications: Prevention of urothelial toxicity due to oxazaphosphorines (Holoxan®, Endoxan®, Ixoten®). Uromitexan should always be given in tumour therapy with Holoxan. Where Endoxan or Ixoten are being used for tumour therapy, Uromitexan should always be given with bolus doses (over 10 mg/kg) of the cytotoxic agent and in all patients at special risk. The principle risk factors are: previous pelvic radiotherapy, cystitis with previous Holoxan, Endoxan or Ixoten therapy or a history of disorders of the urinary tract.

Contraindications: Known hypersensitivity to mesna or other thiol containing compounds.

Warnings:
The occurence of hypersensitivity reactions (hyperergic reactions) following Uromitexan therapy has been reported more frequently in patients with autoimmune disorders than in tumour patients. Skin and mucosal reactions have been observed (rash, urticaria, exanthema, enanthema), a rise in liver transaminases and non-specific common symptoms like fever, exhaustion, nausea and vomiting. Isolated circulatory reactions with hypotension and tachycardia have been observed as well. Protection of the urinary tract with Uromitexan should therefore only be undertaken in such patients following careful risk-benefit analysis and under medical supervision.
As Uromitexan is used as a Uroprotector® in the context of cytostatic treatment with oxazaphosphorines, its use during pregnancy and lactation is governed by the criteria for this type of cytostatic therapy. Animal studies have shown no evidence of embryotoxic or teratogenic effects of Uromitexan.
The protective action of Uromitexan applies only to the urinary tract. All other recommended precautions are unaffected by its use and recommendations relating to them remain in force.

Side-effects: Isolated cases of partially organ-related hypersensitivity reactions (hyperergic reactions), e.g. skin and mucosal reactions of varying extent and severity (itching, redness, vesiculation), local tissue swelling (urticarial oedema), rare cases of drop in blood pressure and increased pulse rate above 100/min (tachycardia) due to severe acute hypersensitivity reactions (anaphylactoid reactions), and also a transient rise in certain liver function tests (transaminases) have been reported. There have been rare cases of venous irritation at the injection site. In a tolerability study using high intravenous and oral doses of mesna, single doses of 60 mg/kg body weight and above were associated with nausea, vomiting, diarrhoea, headache, pain in the limbs, drop in blood pressure, tachycardia, skin reactions, exhaustion and weakness. During treatment, the above side-effects cannot always be clearly differentiated from those caused by oxazaphosphorines (Holoxan®, Endoxan®, Ixoten®), or other concomitant medication.

Interactions with other drugs: Mesna is incompatible in vitro with cisplatin, carboplatin, and nitrogen mustard.

Dosage instructions and mode of use: Unless otherwise prescribed, Uromitexan is normally administered intravenously to adults at a dose of 20 % of the oxazaphosphorine dose at time zero (the time of administration of the oxazaphosphorine), and then at 4 and 8 hours.

Example of Uromitexan administration with oxazaphosphorine injection:

Hour (Time)	0 (8.00h)	4 (12.00h)	8 (16.00h)
Oxazaphosphorine dose	40 mg/kg BW	–	–
Uromitexan® dose	8 mg/kg BW	8 mg/kg BW	8 mg/kg BW

Clinical experience with children has shown that it is beneficial in individual cases to give Uromitexan at shorter intervals (e.g. every three hours, total Uromitexan dose = 60 % of oxazaphosphorine dose). With very high-dose oxazaphosphorine cytostatic therapy (e.g. before bone marrow transplantation), the total Uromitexan dose can be increased to between 120 and 160% of the oxazaphosphorine dose. It is recommended that after administration of 20% Uromitexan (related to the total dose of oxazaphosphorine) at time zero the remaining calculated dose should be given continuously i.v. over a period of 24 hours with a perfusor. Alternatively an intermittent bolus injection is possible: For adults 3 x 40% (at times 0, 4, 8 hours) or 4 x 40% (at times 0, 3, 6, 9 hours) respectively. For children due to more frequent micturition, the bolus injections should always be given in 3-hour intervals (e.g. 20% at times 0, 1, 3, 6, 9, 12 hours). Instead of a bolus injection, short infusions of 15 minutes duration are possible.
With continuous infusions of ifosfamide (Holoxan®), it has been shown to be of benefit to give Uromitexan at time zero following the initial 20 % bolus injection (start of infusion, time 0), followed by infusion to up to 100 % of the ifosfamide dose, and to continue uroprotection for a further 6 to 12 hours after termination of the ifosfamide infusion.

Example of Uromitexan administration with a 24-hour ifosfamide infusion:

Hours (time)	0	24 30 36
Ifosfamide dose	5 g/m² body surface (= 125 mg/kg BW)	
Uromitexan bolus dose	1 g/m² body surface (= 25 mg/kg BW)	
Uromitexan infusion	Up to 5g/m² body surface (= 125 mg/kg BW) Addition to ifosfamide infusion	Up to 2.5g/m² body surface (= 62.5 mg/kg BW)

Store drugs out of children's reach !

Name and permanent address of the manufacturer and the holder of the marketing authorization
Baxter Oncology GmbH · Daimlerstraße 40 · 60314 Frankfurt, Germany · Phone: +49 69-9686 60 00

Date of last revision of the text
January 2002

Stability note: Uromitexan should not be used beyond the expiry date indicated on the package.

Attention: The protective effect of Mesna is restricted to the urinary passages. All other prophylactic measures recommended for oxazaphosphorine treatment are not affected and should continue to be used. Treatment with Uromitexan can give rise to a false-positive test for ketone bodies.

Presentation: 15 ampoules of 4 ml

Uromitexan® is available on prescription only.