Baxter

**Instruction for use**
**Read carefully!**

# UROMITEXAN 400 mg

**Active substance:**

## Mesna 100 mg/ml

**UROPROTECTOR**

**Composition:**

Each ml injection solution contains mesna 100 mg

Other constituents:
sodium edetate, sodium hydroxide, water for injections

**Mode of action:**

Mesna is sulphydril containing compound which is excreted in the urine. Co-administration with oxazaphosphorine alkylating agents such as ifosfamide (HOLOXAN) and cyclophosphamide (ENDOXAN) significantly reduces their urotoxic effects by reacting with the causal metabolites, including acrolein, in the urinary system. No reduction in the anti-tumour activity of these oxazaphosphorine compounds has been detected.

**Indications:**

Prevention of urothelial toxicity due to oxazaphosphorines (HOLOXAN, ENDOXAN).
UROMITEXAN should always be given in tumour therapy with Holoxan. Where ENDOXAN is 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 therapy or a history of disorders of the urinary tract.

**Contraindications:**

Known hypersensitivity to mesna or other thiol containing compounds.

**Warnings and precautions :**

The occurrence 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 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.

**Geriatric Use:**

In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of Concomitant disease or other drug therapy. The ratio of oxazaphosphorines to mesna should remain unchanged.

**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, joint pain, drop in blood pressure, tachycardia, skin reactions, exhaustion and weakness. During treatment, the above side-effects can not always be clearly differentiated from those caused by oxazaphosphorines (HOLOXAN, ENDOXAN), 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 (8.00 h) | 4 (12.00 h) | 8 (16.00 h) |
|---|---|---|---|
| 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 cystostatic 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 time 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-hours Ifosfamide infusion:**

| Hours (time) | 0 | 24 30 36 |
|---|---|---|
| Ifosfamide dose | 5 g/m$^2$ body surface (≈ 125 mg/kg BW) | |
| UROMITEXAN bolus dose | 1 g/m$^2$ body surface (≈ 25 mg/kg BW) | |
| UROMITEXAN infusion | Up to 5 g/m$^2$ body surface (≈ 125 mg/kg BW) Addition to Ifosfamide infusion | Up to 2.5 g/m$^2$ body surface (≈ 62.5 mg/kg BW) |

**Store below 30°C**

**Store drugs out of children's reach!**

**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 Reg. No.: DKI 1005000543A1

**UROMITEXAN is available on prescription only**
**HARUS DENGAN RESEP DOKTER**

**Manufactured by:**

**Baxter Oncology GmbH**
Kantstrasse 2
D-33790 Halle/Westfalen
Germany

**Imported by:**

**PT. Menarini Indria Laboratories,**
Bekasi, Indonesia