Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Uromitexan 400 mg Injection
	Injection containing MESNA (2- mercaptoethanesulphonate sodium) 100 mg/ml

PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE

Uromitexan 400 mg injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Per 1 ml:

Mesna (sodium-2-mercaptoethane sulphonate) 100 mg.

3. PHARMACEUTICAL FORM

Solution for injection

Clear, colourless liquid in a 5 ml clear glass ampoule with a blue one point cut (OPC) and a 2 colour ring code: upper ring blue; lower ring green.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

UROMITEXAN (Mesna) is an aid in the reduction of toxicity in the urinary passages caused by oxazaphosphorines (cyclophosphamide, ifosfamide).

4.2 Posology and method of administration

Posology

Unless otherwise prescribed, UROMITEXAN (Mesna) should be injected intravenously at a dosage of 20 percent of the oxazaphosphorine doses, at the times 0 hours (i.e. concurrently with the oxazaphosphorines), four hours and eight hours thereafter.

UROMITEXAN dosing is dependent on the dose of concomitant oxazaphosphorine medicine that a patient receives.

The UROMITEXAN dosing schedule should be repeated each day that the oxazaphosphorine medicine is received.

If the oxazaphosphorine dose is adjusted, the UROMITEXAN dose should also be modified to maintain the mesna-to-oxazaphosphorine ratio.

Paediatric use:

Safety and effectiveness of UROMITEXAN in paediatric patients (<16 years of age) have not been established (see section 4.4).

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 concomitant disease or other medicine therapy. However, the ratio of UROMITEXAN to oxazaphosphorines should remain unchanged (see section 4.4).

Method of administration

UROMITEXAN is administered by means of intravenous injection.

Parenteral medicinal products should be inspected visually for particulate matter and discoloration prior to administration.

Any solutions which are discoloured, hazy, or contain visible particulate matter should not be used.

4.3 Contraindications

Known hypersensitivity to UROMITEXAN, other thiol containing compounds or any of the inactive ingredients.

Pregnancy and Lactation (see section 4.6).

4.4 Special warnings and precaution for use

Warnings

The protective effect of UROMITEXAN is restricted to the urinary passages. All other prophylactic measures and concomitant therapy recommended for oxazaphosphorine treatment are not affected and should be continued as before.

Hypersensitivity

Hypersensitivity reactions (hyperergic reactions) following UROMITEXAN therapy may occur. Therefore, it should be ensured that adequate emergency medication is available when UROMITEXAN is used.

Hypersensitivity reactions to UROMITEXAN may have been reported following administration of UROMITEXAN as an uroprotectant. These include various skin and subcutaneous tissue symptoms (see section 4.8).

In addition, cases of severe bullous and ulcerative skin and mucosal reactions were reported. Some reactions were considered to be consistent with Stevens-Johnson Syndrome, toxic epidermal necrolysis, or erythema exudativum multiforme.

In some cases, skin reactions were accompanied by one or more other symptoms, such as:

- fever,

- cardiovascular symptoms (hypotension, in some cases reported as fluid refractory, tachycardia, ECG signs consistent with perimyocarditis, hypertension) (see section 4.8),
- signs consistent with acute renal impairment,
- pulmonary symptoms (hypoxia, respiratory distress, bronchospasm, tachypnea, cough, bloody sputum (see section 4.8),
- haematological abnormalities (laboratory signs of disseminated intravascular coagulation, leukopaenia, eosinophilia, lymphopaenia, thrombocytopaenia, pancytopaenia (see section 4.8),
- increased liver enzymes,
- nausea, vomiting,
- pain in the extremities, arthralgia, myalgia, malaise,
- stomatitis, and
- conjunctivitis.

Some reactions have presented as anaphylaxis.

Fever accompanied by, e.g., hypotension, but no skin manifestations has also been reported.

Severe as well as minor reactions were reported with the use of UROMITEXAN in regimens to treat both severe systemic autoimmune disorders and malignancy.

In most cases, reactions occurred during or after a first treatment occasion or after several weeks of UROMITEXAN exposure. In other cases, the initial reaction was observed only after several months of exposure.

Patients with autoimmune disease who were treated with cyclophosphamide and UROMITEXAN appeared to have a higher incidence of hypersensitivity reactions.

In many cases, symptoms appeared on the day of exposure, with a tendency to shorter intervals following subsequent exposures.

In some patients, the occurrence and/or severity of reaction appeared to vary with the dose administered.

Recurrence of reactions, in some cases with increasing severity, has been reported with re-exposure. However, in some cases, a reaction did not recur with re-exposure.

Some patients with a history of a reaction have shown positive delayed-type skin test results. However, a negative delayed reaction does not exclude hypersensitivity to mesna. Positive immediate-type skin test reactions have occurred in patients regardless of previous mesna exposure or history of hypersensitivity reactions, and may be related to the concentration of the UROMITEXAN solution used for testing

Prescribers should

- be aware of the potential for such reactions and that reactions may worsen with re-exposure and may in some cases be life-threatening,
- be aware that hypersensitivity reactions to UROMITEXAN were interpreted to resemble the clinical picture of sepsis and, in patients with autoimmune disorders, resemble an exacerbation of the underlying disease.

UROMITEXAN will not prevent or alleviate any of the other adverse reactions or toxicities associated with oxazaphosphorine therapy**.**

A morning specimen of urine should always be examined for the presence of haematuria (microscopic evidence of red blood cells) each day prior to oxazaphosphorine therapy. If haematuria develops when UROMITEXAN is given with oxazaphosphorines according to the

recommended dosage schedule, depending on the severity of the haematuria, dosage reduction or discontinuation of oxazaphosphorine therapy may be initiated**.**

Thiol Compounds

UROMITEXAN is a thiol compound, i.e., a sulfhydryl (SH) group-containing organic compound. Thiol compounds show some similarities in their adverse reaction profiles, including a potential to elicit severe skin reactions. Examples of medicines that are thiol compounds include amifostine, penicillamine and captopril.

It is not clear whether patients who experienced an adverse reaction to such a medicine are at increased risk for any reactions, or similar reactions, to another thiol compound. However, when considering subsequent use of another thiol compound in such patients, the possibility of an increased risk should be taken into account.

Precautions

UROMITEXAN does not prevent haemorrhagic cystitis in all patients. Patients should be monitored accordingly.

Sufficient urinary output should be maintained, as required for oxazaphosphorine treatment.

Laboratory test interferences

UROMITEXAN treatment may cause false positive reactions in nitroprusside sodium-based urine tests (including dipstick tests) for ketone bodies and false positive or false negative reactions in the dipstick tests for erythrocytes in the urine. The addition of glacial acetic acid can be used to differentiate between a false positive result (cherry-red colour that fades) and a true positive result (red-violet colour that intensifies).

UROMITEXAN treatment may cause false positive reactions in Tillman's reagent-based urine screening tests for ascorbic acid.

In pharmacokinetic studies in healthy volunteers, serum creatine phosphokinase (CPK) values were lower in samples taken 24 hours after mesna dosing than in pre-dosing samples. While available data are insufficient to determine the cause of this phenomenon, it might be considered to represent a significant interference with thiol (e.g., N-acetylcysteine) dependent enzymatic CPK tests.

Paediatric use

Safety and effectiveness of UROMITEXAN in paediatric patients (<16 years of age) have not been established in clinical studies performed by Baxter (see section 4.2).

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 pharmaceutical therapy. The ratio of oxazaphosphorines to UROMITEXAN should remain unchanged.

Sodium content

UROMITEXAN contains approximately 59 mg of sodium per 400 mg mesna.

4.5 Interaction with other medicines and other forms of interaction

The systemic effects of oxazaphosphorines are not affected by UROMITEXAN.

UROMITEXAN is incompatible *in vitro* with cisplatin, carboplatin and nitrogen mustard. *In vivo* compatibility has not been demonstrated.

Mixing UROMITEXAN with epirubicin leads to inactivation of epirubicin and should be avoided.

UROMITEXAN neither affects the antineoplastic efficacy of cytostatics such as doxorubicin, carmustine (BCNU), methotrexate, vincristine, nor the therapeutic effect of other medicines such as digitalis glycosides.

4.6 Fertility, pregnancy and lactation

The safety of UROMITEXAN in pregnant and lactating women has not been established. UROMITEXAN should not be used during pregnancy and lactation (see section 4.3).

4.7 Effects on ability to drive and use machines

Patients undergoing treatment with UROMITEXAN may experience undesirable effects (including, syncope, light-headedness, lethargy/drowsiness, dizziness and blurred vision), which could affect the ability to drive or use machines. The decision to drive or operate machinery should be made on an individual basis.

4.8 Undesirable effects

The most frequently occurring adverse reactions (> 10 %) associated with use of UROMITEXAN, per subject are: headache (36,05 %), infusion site reactions (25,32 %), abdominal pain/colic (22,09 %), light-headedness (16,28 %), lethargy/drowsiness (12,79 %), pyrexia (12,79 %), rash (12,79 %), diarrhoea (11,63 %), nausea (11,63 %), flushing (10,47 %), and influenza-like illness (10,47 %).

The most frequently occurring adverse reactions (> 1 %) associated with use of UROMITEXAN, per administration are: infusion site reactions (15,35 %), headache (5,24 %), abdominal pain/colic (4,39 %), nausea (1,72 %), diarrhoea (1,53 %), rash (1,72 %), flushing (1,33 %), light-headedness (1,33 %), lethargy/drowsiness (1,33 %), and pyrexia (1,149 %).

The most severe adverse reactions associated with use of UROMITEXAN are: toxic epidermal necrolysis, Stevens-Johnson syndrome, anaphylaxis, and medicinal rash with eosinophilia and systemic symptoms (DRESS).

Because UROMITEXAN is used in combination with oxazaphosphorines or oxazaphosphorine-containing combination chemotherapy, it is difficult to distinguish the adverse reactions, which may be due to UROMITEXAN from those caused by concomitantly administered cytotoxic agents.

Adverse Reactions from Clinical Trials:

The following information is based on data from pharmacokinetic studies in healthy volunteers who received no concomitant medications.

The adverse reactions from clinical trials were identified from 6 UROMITEXAN pharmacokinetic studies in healthy volunteers, who were administered UROMITEXAN without concurrent chemotherapy. In these studies, a total of 86 subjects received oral doses of UROMITEXAN. Of these 86 subjects, 79 subjects also received intravenously administered UROMITEXAN. A total of 1049 UROMITEXAN doses were administered.

Four studies administered single oral doses (tablets or solution) of 600 mg to 2400 mg; with three of these studies also administering single intravenous doses of 600 mg to 1200 mg. Two studies were multiple-dose studies that administered mesna three times daily for 5 days. In these studies, total daily doses of mesna tablets ranged from 1200 mg to 2400 mg, and total daily doses of intravenous mesna infusions ranged from 334 mg to 1800 mg.

Incidences are as follows: Very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1 000, < 1/100); rare (≥ 1/10 000, < 1/1 000) and very rare (< 1/10 000), including isolated reports.

Clinical Trial Adverse Reactions					
		Per subject N = 86		**Per administration N = 1049**	
System Organ Class (SOC)	**Adverse Reaction**	**Frequency**	**Frequency Ratio (Percentage)**	**Frequency**	**Frequency Ratio (Percentage)**
BLOOD AND LYMPHATIC SYSTEM DISORDERS	**Lymphadenopathy**	Common	3/86 (3,49 %)	Uncommon	3/1049 (0,29 %)
METABOLISM AND NUTRITION DISORDERS	**Decreased appetite**	Common	7/86 (8,14 %)	Uncommon	7/1049 (0,67 %)
	Feeling of dehydration	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)
PSYCHIATRIC DISORDERS	**Insomnia**	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)
	Nightmare	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)
NERVOUS SYSTEM DISORDERS	**Headache**	Very common	31/86 (36,05 %)	Common	55/1049 (5,24 %)
	Light-headedness	Very common	14/86 (16,28 %)	Common	14/1049 (1,33 %)
	Lethargy/ Drowsiness	Very common	11/86 (12,79 %)	Common	14/1049 (1,33 %)
	Dizziness	Common	5/86 (5,81 %)	Uncommon	5/1049 (0,48 %)
	Paraesthesia	Common	4/86 (4,65 %)	Uncommon	4/1049 (0,38 %)
	Hyperaesthesia	Common	2/86 (2,33 %)	Uncommon	2/1049 (0,19 %)

Clinical Trial Adverse Reactions					
		Per subject N = 86		**Per administration N = 1049**	
System Organ Class (SOC)	**Adverse Reaction**	**Frequency**	**Frequency Ratio (Percentage)**	**Frequency**	**Frequency Ratio (Percentage)**
	Syncope	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)
	Hypoaesthesia	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)
	Disturbance in attention	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)
EYE DISORDERS	**Conjunctivitis**	Common	5/86 (5,81 %)	Uncommon	5/1049 (0,48 %)
	Photophobia	Common	3/86 (3,49 %)	Uncommon	5/1049 (0,48 %)
	Vision blurred	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)
CARDIAC DISORDERS	**Palpitations**	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)
VASCULAR DISORDERS	**Flushing**	Very common	9/86 (10,47 %)	Common	14/1049 (1,33 %)
RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS	**Nasal congestion**	Common	5/86 (5,81 %)	Uncommon	5/1049 (0,48 %)
	Cough	Common	3/86 (3,49 %)	Uncommon	3/1049 (0,28 %)
	Pleuritic pain	Common	2/86 (2,33 %)	Uncommon	3/1049 (0,29 %)
	Dry mouth	Common	2/86 (2,33 %)	Uncommon	2/1049 (0,19 %)

Clinical Trial Adverse Reactions					
		Per subject N = 86		**Per administration N = 1049**	
System Organ Class (SOC)	**Adverse Reaction**	**Frequency**	**Frequency Ratio (Percentage)**	**Frequency**	**Frequency Ratio (Percentage)**
	Bronchospasm	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)
	Dyspnoea	Common	2/86 (2,33 %)	Uncommon	2/1049 (0,19 %)
	Laryngeal discomfort	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)
	Epistaxis	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)
GASTRO-INTESTINAL DISORDERS	**Abdominal pain/colic**	Very common	19/86 (22,09 %)	Common	46/1049 (4,39 %)
	Nausea	Very common	10/86 (11,63 %)	Common	18/1049 (1,72 %)
	Diarrhoea	Very common	10/86 (11,63 %)	Common	16/1049 (1,53 %)
	Mucosal irritation[1]	Common	7/86 (8,14 %)	Uncommon	7/1049 (0,67 %)
	Flatulence	Common	8/86 (9,30 %)	Uncommon	9/1049 (0,86 %)
	Vomiting	Common	3/86 (3,49 %)	Uncommon	6/1049 (0,57 %)
	Burning pain (substernal / epigastric)	Common	3/86 (3,49 %)	Uncommon	4/1049 (0,38 %)

Clinical Trial Adverse Reactions					
		Per subject N = 86		**Per administration N = 1049**	
System Organ Class (SOC)	**Adverse Reaction**	**Frequency**	**Frequency Ratio (Percentage)**	**Frequency**	**Frequency Ratio (Percentage)**
	Constipation	Common	2/86 (2,33 %)	Uncommon	2/1049 (0,19 %)
	Gingival bleeding	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)
HEPATOBILIARY DISORDERS	**Transaminases increased**	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	**Rash[2]**	Very common	11/86 (12,79 %)	Common	18/1049 (1,72 %)
	Pruritus	Common	4/86 (4,65 %)	Uncommon	6/1049 (0,57 %)
	Hyperhidrosis	Common	2/86 (2,33 %)	Uncommon	3/1049 (0,29 %)
MUSCULO-SKELETAL AND CONNECTIVE TISSUE DISORDERS	**Arthralgia**	Common	6/86 (6,98 %)	Uncommon	7/1049 (0,67 %)
	Back pain	Common	7/86 (8,14 %)	Uncommon	9/1049 (0,86 %)
	Myalgia	Common	6/86 (6,98 %)	Uncommon	7/1049 (0,67 %)
	Pain in extremity	Common	3/86 (3,49 %)	Uncommon	3/1049 (0,29 %)
	Pain in jaw	Common	1/86 (1,16 %)	Uncommon	1/1049 (0,10 %)

Clinical Trial Adverse Reactions					
		Per subject N = 86		**Per administration N = 1049**	
System Organ Class (SOC)	**Adverse Reaction**	**Frequency**	**Frequency Ratio (Percentage)**	**Frequency**	**Frequency Ratio (Percentage)**
RENAL AND URINARY DISORDERS	**Dysuria**	Common	2/86 (2,33 %)	Uncommon	2/1049 (0,19 %)
GENERAL DISORDERS AND ADMINISTRATIVE SITE CONDITIONS	**Infusion site reactions**	Very common	20/79 (25,32 %)	Very common	68/443 (15,35 %)
	- Infusion site Pruritus	Very common	15/79 (18,99 %)	Common	35/443 (7,90 %)
	- Infusion site rash	Very common	11/79 (13,92 %)	Common	20/443 (4,51 %)
	- Infusion site pain	Common	5/79 (6,33 %)	Common	5/443 (1,13 %)
	- Infusion site erythema	Common	3/79 (3,80 %)	Uncommon	3/443 (0,68 %)
	- Infusion site urticaria	Common	2/79 (2,53 %)	Uncommon	3/443 (0,68 %)
	- Infusion site swelling	Common	1/79 (1,27 %)	Uncommon	1/443 (0,23 %)
	Pyrexia	Very common	11/86 (12,79 %)	Common	12/1049 (1,14 %)
	Influenza-like illness[3]	Very common	9/86 (10,47 %)	Unknown	Unknown
	Rigors	Common	4/86 (4,65 %)	Uncommon	5/1049 (0,48 %)

Clinical Trial Adverse Reactions					
		Per subject N = 86		**Per administration N = 1049**	
System Organ Class (SOC)	**Adverse Reaction**	**Frequency**	**Frequency Ratio (Percentage)**	**Frequency**	**Frequency Ratio (Percentage)**
	Fatigue	Common	3/86 (3,49 %)	Uncommon	3/1049 (0,29 %)
	Chest pain	Common	2/86 (2,33 %)	Uncommon	2/1049 (0,19 %)
	Malaise	Common	2/86 (2,33 %)	Uncommon	3/1049 (0,29 %)

[1] Oral, rectal.

[2] Including nonpruritic, pruritic, erythema/erythematous, eczematous, papular, and/or macular rashes.

[3] The per administration frequency cannot be determined from the data reviewed.

Time to onset and experience with re-exposure

Some subjects experienced their events on first exposure to mesna and others after the second or third exposure. In general, the complete spectrum of symptoms experienced by a subject developed over a period of several hours. Some subjects experienced no further reactions after their initial event while others experienced an exacerbation of events upon repeated dosing.

Infusion site reactions

In some subjects experiencing local cutaneous infusion site reactions, subsequent exposure to UROMITEXAN resulted in a cutaneous event in other areas.

Cutaneous/mucosal reactions

Cutaneous and mucosal reactions were reported to occur after both intravenous and oral mesna. These reactions included rashes, pruritus, flushing, mucosal irritation, pleuritic pain, and conjunctivitis. Approximately one-quarter of subjects with any event experienced cutaneous/mucosal reactions in conjunction with other adverse symptoms, which included, dyspnoea, fever, headache, gastrointestinal symptoms, drowsiness, malaise, myalgia, and influenza-like symptoms.

Gastrointestinal reactions

Gastrointestinal reactions reported in healthy subjects included nausea, vomiting, diarrhoea, abdominal pain/colic, epigastric pain/burning, constipation, and flatulence and were reported to occur after intravenous and oral mesna administration.

In-vivo effect on lymphocyte counts

In pharmacokinetics studies in healthy volunteers, administration of single doses of mesna was commonly associated with a rapid (within 24 hours) and in some cases marked decrease in lymphocyte count, which was generally reversible within 1 week of administration. Data from studies with repeated dosing over several days are insufficient to characterize the time course of lymphocyte count changes under such conditions.

In-vivo effect on serum phosphorus levels

In pharmacokinetics studies in healthy volunteers, administration of mesna on single or multiple days was in some cases associated with moderate transient increases in serum phosphorus concentration.

These phenomena should be considered when interpreting laboratory results.

Post-Marketing Side Effects:

The following side effects have been reported in the post-marketing experience, listed by MedDRA System Organ Class (SOC), then by Preferred Term in order of severity, as appropriate.

Because UROMITEXAN is used in combination with oxazaphosphorines or oxazaphosphorine-containing combination chemotherapy, it is often difficult to distinguish adverse reactions that may be due to UROMITEXAN from those caused by concomitantly administered cytotoxic agents.

The following side effects have been identified from post-marketing reports of patients receiving UROMITEXAN in combination with oxazaphosphorine cytostatics and other medications.

Many of the side effects listed in the following SOCs occurred as part of a syndrome suggestive of hypersensitivity reactions. (See Section 4.4)

BLOOD AND LYMPHATIC SYSTEM DISORDERS: Pancytopenia, leukopaenia, lymphopaenia, thrombocytopaenia, eosinophilia.

IMMUNE SYSTEM DISORDERS: Anaphylaxis, hypersensitivity.

NERVOUS SYSTEM DISORDERS: Convulsion.

EYE DISORDERS: Periorbital oedema.

CARDIAC DISORDERS: Electrocardiogram abnormal (consistent with perimyocarditis), tachycardia.

VASCULAR DISORDERS: Hypotension (in some cases fluid refractory), hypertension.

RESPIRATORY, THORACIC, MEDIASTINAL DISORDERS: Respiratory distress, hypoxia, oxygen saturation decreased, tachypnoea, haemoptysis.

GASTROINTESTINAL DISORDERS: Stomatitis, bad taste.

HEPATOBILIARY DISORDERS: Hepatitis, gamma-glutamyl transferase increased, blood

alkaline phosphatase increased.

SKIN AND SUBCUTANEOUS TISSUE DISORDERS: Toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, drug rash with eosinophilia and systemic symptoms, ulcerations and/or bullae/blistering (mucocutaneous, mucosal, oral, vulvovaginal, anorectal), angioedema, fixed drug eruption, rash (vesicular, exfoliative, maculo-papular, morbilliform), photodistributed rash, urticaria, burning sensation, erythema.

RENAL AND URINARY DISORDERS: Acute renal failure.

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Face edema, edema peripheral, asthenia, infusion site reactions (thrombophlebitis, irritation).

INVESTIGATIONS: Laboratory signs of disseminated intravascular coagulation, prothrombin time prolonged, activated partial thromboplastin time prolonged.

INJURY, POISONING AND PROCEDURAL COMPLICATIONS: Occupational sensitization to other mesna formulations used for inhalation (manifested as eczema, papulovesicular rash, erythema, pruritus).

4.9 Overdose

A specific antidote for UROMITEXAN is not known. Due to the possibility of anaphylactoid reactions in patients with autoimmune disorders, it should be ensured that adequate emergency medication is available.

Reports of inadvertent overdose and observations from a high-dose tolerability study in healthy volunteers showed that, in adults, single doses in the range of approximately 4 g to 7 g of UROMITEXAN can cause symptoms such as nausea, vomiting, abdominal pain/colic, diarrhoea, headache, fatigue, limb and joint pains, paraesthesia, fever, bronchospasm, rash, flushing, hypotension, bradycardia and tachycardia.

A markedly increased rate of nausea, vomiting and diarrhoea has also been found in oxazaphosphorine-treated patients receiving ≥ 80 mg UROMITEXAN per kg per day intravenously compared with patients receiving lower doses or hydration treatment only.

Treatment is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

Pharmacological classification: A 18 Medicines acting on the genito-urinary system

5.1 Pharmacodynamic properties

The active ingredient, mesna, is a synthetic sulfhydryl compound designated as sodium-2-mercaptoethane sulfonate

5.2 Pharmacokinetic properties

Mesna is rapidly oxidised to its major metabolite, mesna disulfide (dimesna). Mesna disulfide remains in the intravascular compartment and is eliminated by the kidneys.

Protein binding of mesna is in a moderate range (69 - 75 %).

After intravenous administration of an 800 mg dose, the half-lives of mesna and dimesna are reported to be about 0,36 hours and 1,17 hours, respectively. Approximately 32 % and 33 % of the administered dose was eliminated in the urine in 24 hours as mesna and dimesna, respectively. The majority of the dose recovered was eliminated within 4 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Inactive ingredients: sodium edetate, sodium hydroxide and water for injections.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

60 months.

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

Ampoules:

15 x 5 ml ampoules containing 400 mg per 4 ml.

50 x 5 ml ampoules containing 400 mg per 4 ml.

6.6 Special precautions for disposal and other handling

Not Applicable.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Baxter Healthcare South Africa (Pty) Ltd

The Campus – Eden Gardens

57 Sloane Street & Cnr Main Rd

Bryanston

2021

8. REGISTRATION NUMBER

S/18/306

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23 November 1989

10. DATE OF REVISION OF THE TEXT

28 October 2022

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