1 UROMITEXAN (100mg/mL solution for injection)

100mg/mL solution for injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient

Uromitexan solution for injections contains 100mg/mL mesna.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Appearance

Uromitexan is a sterile preservative-free aqueous solution of clear and colourless appearance in clear glass ampoules for intravenous administration.

The solution has a pH range of 6.5 - 8.5.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Uromitexan injection is indicated for the prophylaxis of haematuria and haemorrhagic cystitis in patients treated with cyclophosphamide or ifosfamide in doses considered to be urotoxic.

Uromitexan is also indicated in at risk patients even though these patients may be receiving relatively low doses of oxazaphosphorines. At risk patients include those that have experienced previous irradiation of the small pelvis, cystitis with earlier oxazaphosphorine therapy, and/or a case history of urinary tract disease.

4.2 Dose and method of administration

Sufficient mesna must be given to protect the patient adequately from the urotoxic toxic effects of the oxazaphosphorine. When calculating the dose of mesna, the quantity should be rounded up to the nearest whole ampoule.

Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. Any solutions which are discoloured or contain visible particulate matter should not be used.

In the treatment of children and particularly when administering very high doses - such as required when conditioning patients for bone-marrow transplantations - the **Uromitexan** doses should be increased or time intervals reduced, and additional administration of **Uromitexan** is advisable.

Where ifosfamide is used as a 24 hour infusion

Uromitexan is given as an intravenous bolus at a total dose of 60% of the ifosfamide dose, in 7 divided doses every 4 hours from 0 - 24 hours, then 3 further intravenous boluses of the same dose at 28, 32 and 36 hours.

It can be used as an infusion, with an initial bolus of 20% of the dose of ifosfamide at 0 hours, and a continuous infusion of 60 - 100% of the dose of ifosfamide throughout the 24 hours, with a further 3 intravenous boluses of 20% at 28, 32 and 36 hours.

There is evidence that the dose necessary for urothelial protection in children is 40% of the dose of the oxazaphosphorine given at 0, 3, 6 and 9 hours.

It has been shown at some centres that **Uromitexan** is effective when taken orally. The dose is 40% of the dose of the oxazaphosphorine at 0, 3, 6 and 9 hours. It should be taken immediately the ampoule is opened in a soft drink (e.g orange juice).

Uromitexan can be given in the same "giving set" as the oxazaphosphorine.

If necessary the dose of **Uromitexan** given as a bolus, can be increased from 30% given 3 times at 4 hourly intervals, to 40% given 4 times at 3 hourly intervals. This dose is recommended in patients who may have damaged urothelium from previous treatment with oxazaphosphorines or pelvic irradiation, or who are not adequately protected by **Uromitexan** given at the standard dose.

Urinary output should be kept above 100mL/hour. A diuretic may be used if necessary and the urine should be monitored for haematuria.

Preparation

For intravenous administration. The medicine can be diluted by adding the contents of a **Uromitexan** ampoule to any of the following fluids obtaining final concentrations of 1.5 to 3mg mesna/mL fluid:

- Glucose Injection 5%,
- Sodium Chloride Injection 0.9%,
- Sodium Chloride and Glucose Injection, with concentrations ranging from 0 - 0.9% Sodium Chloride, and 0 - 5% Glucose,
- Lactated Ringer's Injection.

Solutions of mesna when diluted in the solutions nominated above may be prepared and, if necessary, stored for short periods under refrigeration. However, the diluted solutions do not contain an antimicrobial preservative, and in order to reduce microbial hazards it is recommended that dilution should be effected as soon as practicable prior to use, and infusion commenced as soon as practicable thereafter.

Infusion should be started within 6 to 8 hours of preparation of the admixture and completed within 24 hours, with any residue discarded.

Diluted solutions should be inspected visually before use. Any solutions which are discoloured, hazy or contain visible particulate matter should not be used.

4.3 Contraindications

Uromitexan is contraindicated in individuals with a known hypersensitivity to mesna or any of the excipients (see section 6.1) and other thiols.

4.4 Special warnings and precautions for use

The protective effect of mesna applies only to the urothelial toxic effect of oxazaphosphorines (*viz.* ifosfamide or cyclophosphamide) not to their renal and other toxic effects. Additional prophylactic or accompanying measures recommended during treatment with oxazaphosphorines are thus not affected and should not be discontinued.

Severe allergic symptoms, such as systemic anaphylactic reactions, have occurred with mesna, especially in patients suffering from autoimmune diseases.

Due to the possibility of anaphylactoid reactions, it should be ensured that adequate emergency medication is available.

Patients with autoimmune diseases who were treated with cyclophosphamide and **Uromitexan** appeared to have a higher incidence of hypersensitivity reactions: Skin and mucosal reactions of varying extent and severity (rash, itching, redness, severe bullous and ulcerative skin, vesiculation, Lyell Syndrome, Stevens-Johnson Syndrome), toxic epidermal necrolysis, erythema exudative multiforme), localised or generalised urticarial or other forms of exanthema, pruritus, burning, local tissue swelling (urticarial oedema), angioedema and/or flushing. Some reactions appeared to be consistent with a diagnosis of fixed drug eruption. Skin reactions were accompanied by one or more other symptoms (see section 4.8) such as:

- fever,
- conjunctivitis,
- cardiovascular symptoms (hypotension, in some cases reported as fluid refractory, associated with circulatory reactions and increased pulse rate above 100/min (tachycardia) hypertension, ST-segment elevation, ECG signs consistent with perimyocarditis),
- signs consistent with acute renal failure,
- pulmonary symptoms (hypoxia, respiratory distress, bronchospasm, cough, bloody sputum and increased respiration rate (tachypnoea) due to severe acute hypersensitivity reactions,
- prolonged prothrombin time and partial prothrombin time, laboratory signs of disseminated intravascular coagulopathy,
- haematological abnormalities (leukopaenia, eosinophilia, lymphopaenia, thrombocytopaenia, pancytopaenia,
- pain in the extremities, arthralgia, myalgia, malaise,
- transient rise in certain liver function tests (e.g. transaminases),
- nausea, vomiting, stomatitis.

Photodistribution of a rash has also been reported. 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 mesna 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 mesna exposure. In other cases, the initial reaction was observed only after several months of exposure. 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 mesna solution used for testing.

Protection of the urinary tract with mesna should therefore only be undertaken in such patients with autoimmune diseases following careful risk-benefit analysis and under medical supervision. 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 mesna were interpreted to resemble the clinical picture of sepsis and, in patients with autoimmune disorders, resemble an exacerbation of the underlying disease.

Thiol compounds

Mesna is a thiol compound, i.e. a sulfhydryl group-containing organic compound. Thiol compounds show some similarities in their adverse reaction profile, 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.

Uromitexan does not prevent haemorrhagic cystitis in all patients. As a result, a morning specimen of urine should be examined for the presence of haematuria (microscopic evidence of red blood cells) and proteinuria 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 indicated.

Urinary output should be maintained at 100mL/hr (as required for oxazaphosphorine treatment). The urine should be monitored for haematuria and proteinuria throughout the treatment period.

Paediatric use

Safety and effectiveness of mesna in paediatric patients (< 16 years of age) have not been established in formal clinical studies but its use in paediatric patients is referenced in the medical literature.

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.

Effects on laboratory tests

A false positive test in nitroprusside sodium-based urine tests (including dipstick tests) for urinary ketones may arise in patients treated with **Uromitexan**. In this test, a red-violet (rather than purple) colour develops which is less stable, e.g. with the addition of glacial acetic acid, will return to violet.

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

Mesna may cause false positive or false negative reactions in the dipstick test for erythrocytes in urine. To exactly determine erythrocytes in the urine, urinary microscopy is recommended.

In pharmacokinetics 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.

4.5 Interaction with other medicines and other forms of interaction

In vitro and *in vivo* animal tumour models have shown that mesna does not have any effect on the antitumour efficacy of concomitantly administered cytotoxic agents. See also section 6.2.

4.6 Fertility, pregnancy and lactation

Effects on fertility

Animal studies of potential toxicity in a fertility and general reproductive screen have not been carried out. It is not known whether Uromitexan can affect reproductive capacity.

Pregnancy (Category B1)

Teratology studies with oral doses of mesna to rabbits at up to 1000mg/kg/day and to rats at up to 2000mg/kg/day have revealed no harm to the foetus. Animal studies of potential toxicity in a peri-/post-natal screen have not been carried out. It is not known whether **Uromitexan** can cause foetal harm when administered to a pregnant woman. **Uromitexan** should be given to a pregnant woman only if the benefits clearly outweigh any possible risks.

Breast-feeding

It is not known whether mesna or dimesna are excreted in human milk. Because many medicines are excreted in human milk and because of the potential for adverse reactions in breast-fed infants, a decision should be made whether to discontinue breast-feeding or discontinue the medicine, taking into account the importance of the medicine to the mother.

4.7 Effects on ability to drive and use machines

Patients undergoing treatment with mesna may experience undesirable effects (including, e.g. syncope, lightheadedness, 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

As **Uromitexan** is used in combination with oxazaphosphorine alkylating agents and other chemotherapeutic agents with documented toxicities, it is difficult to distinguish the adverse reactions which may be due to **Uromitexan** from those caused by the concomitantly administered cytotoxic agents.

As a result, the adverse reaction profile of **Uromitexan** was determined in three Phase 1 studies (16 subjects) utilising intravenous and oral administration and 2 controlled studies in which ifosfamide and **Uromitexan** were compared to ifosfamide and standard prophylaxis.

In Phase 1 studies in which intravenous bolus doses of 0.8 - 1.6g/m^2 **Uromitexan** were administered as a single or three repeated doses to a total of 10 subjects, a bad taste in the mouth (100%) and soft stools (70%) were reported. At intravenous and oral bolus doses of 2.4g/m^2, headache (50%), fatigue (33%), nausea (33%), diarrhoea (83%), limb pain (50%), hypotension (17%) and allergy (17%) were reported in the 6 subjects who participated in this study.

Frequently reported side effects from clinical studies and/or spontaneous reporting are nausea, vomiting, flatulence, diarrhoea, constipation, colic (e.g. abdominal pain), anorexia, influenza-like reactions, fever, rigors, flushing, cough, pharyngitis, lightheadedness/dizziness, lethargy/ somnolence, headache, back pain, arthralgia.

Venous irritation may occur in rare instances. This reaction may be attributed to the physical properties of mesna (i.e. pH 6, and hypertonic solution). No venous complications were observed

when the solution was given diluted with Sterile Water for Injection BP (1 part mesna solution to 3 parts water).

Isolated cases of partially organ-related hypersensitivity reactions have been reported, e.g. in some cases associated with decreased platelet counts (thrombocytopenia), skin and mucosal reactions of varying extent and severity (rash, itching, redness, vesiculation, Lyell syndrome, Stevens-Johnson syndrome), local tissue swelling (urticarial oedema), conjunctivitis. Very rare cases of hypotension associated with circulatory reactions and increased pulse rate above 100/min (tachycardia), as well as increased respiration rate (tachypnoea) due to severe acute hypersensitivity reactions (anaphylactoid reactions), hypertension, ST-segment elevation, myalgia, and also a transient rise in certain liver function tests (e.g. transaminases) have been reported.

The most severe adverse reactions associated with use of mesna are: toxic epidermal necrolysis, Stevens-Johnson syndrome, anaphylaxis, and drug rash with eosinophilia and systemic symptoms (DRESS). The occurrence of hypersensitivity reactions (hyperergic reactions) following **Uromitexan** has been reported more frequently in patients with autoimmune disorders than in tumour patients (see sections 4.3 and 4.4).

Incidence of adverse effects

Primary System Organ Class (SOC)	Very common > 1/10	Common > 1/100 – < 1/10	Uncommon > 1/1000 – < 1/100	Rare > 1/10000 – < 1/1000	Very Rare < 1/10 000, incl. isolated reports
Infections and infestations		Pharyngitis			
Blood and lymphatic system disorders					Thrombocytopenia (hypersensitivity)
Immune system disorders					Hypersensitivity reactions Anaphylactoid reactions
Metabolism and nutrition disorders		Anorexia			
Nervous system disorders		Dizziness Somnolence Headache			
Eye disorders					Conjunctivitis
Cardiac disorders					ST segment elevation Tachycardia
Vascular disorders		Flushing			Circulatory reactions Hypotension Hypertension
Respiratory disorders		Coughing			Tachypnea
Gastrointestinal disorders		Nausea Vomiting Diarrhoea Constipation Colic Abdominal pain Flatulence			

Primary System Organ Class (SOC)	Very common > 1/10	Common > 1/100 – < 1/10	Uncommon > 1/1000 – < 1/100	Rare > 1/10000 – < 1/1000	Very Rare < 1/10 000, incl. isolated reports
Skin and subcutaneous tissue disorders					Skin and mucosal reactions: Rash Itching Redness Vesiculation Lyell syndrome Stevens-Johnson syndrome Urticarial edema Local tissue swelling
Musculoskeletal and connective tissue disorders		Arthralgia Back pain			Myalgia Limb and joint pain
General disorders and administration site conditions		Fever Rigors Influenza-like reactions		Injection site reactions	Weakness Mucosal reactions Lack of energy Exhaustion
Investigations					Decreased platelet counts Increased respiration rate Rise in certain liver function tests Rise in transaminases

Time to onset

In these studies, 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.

Experience with re-exposure

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 mesna 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, 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 adverse reactions
The following adverse reactions have been identified from post-marketing reports of patients receiving mesna in combination with oxazaphosphorine cytostatics and other medications.

Many of the adverse reactions listed occurred as part of a syndrome suggestive of hypersensitivity reactions (see section 4.4).

BLOOD AND LYMPHATIC SYSTEM DISORDERS: Pancytopaenia, 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 oedema, Oedema 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).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

No specific antidote for mesna is known. Overdosage should be managed with supportive measures to sustain the patient through any period of toxicity. Mesna has been administered at doses from 70 to 100mg/kg without any toxic effect on haematopoiesis, hepatic or renal function or the CNS.

Overdose may lead to the reactions observed in a tolerability study in healthy volunteers at single doses of 60 - 70mg/kg: nausea, vomiting, abdominal pain, colic, diarrhoea, headache, fatigue, paresthesia, fever, limb and joint pains, lack of energy like exhaustion and weakness, depression, irritability, rash, bronchospasm, flushing, hypotension, bradycardia and tachycardia.

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

For advice on the management of overdose please contact the National Poisons Centre on phone number: 0800 764 766 [0800 POISON] in New Zealand (or 131126 in Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

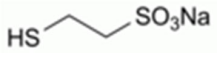
Pharmacotherapeutic group Detoxifying agents for antineoplastic treatment
ATC code V03AF

Mechanism of action

Uromitexan was developed as a prophylactic agent, used to prevent and reduce the urothelial toxicity (haemorrhagic cystitis) induced by oxazaphosphorine alkylating agents such as ifosfamide or cyclophosphamide.

The active ingredient, mesna, is a synthetic sulphydryl compound designated as sodium 2-mercapto-ethane sulphonate.

Chemical structure



Structural formula $HS\text{-}CH_2\text{-}CH_2\text{-}SO_3^-Na^+$

Molecular formula $C_2H_5NaO_3S_2$

Molecular weight 164.18

CAS number 19767-45-4

5.2 Pharmacokinetic properties

Metabolism

Analogous to the physiological cysteine-cystine system, following intravenous administration, mesna is rapidly and easily converted by autoxidation to its only metabolite, disodium 2,2'-dithio-bisethane sulphonate (mesna disulphide, dimesna) forming a disulphide link. Following intravenous injection, only a small portion of the administered dose is detected in the blood as a reduced thiol compound (mesna). Mesna disulphide remains in the intravascular space and is rapidly delivered to the kidney. In the renal tubular epithelium a considerable proportion of mesna disulphide is again reduced to a free thiol compound, presumably mediated by glutathione reductase. Acrolein or other urotoxic oxazaphosphorine metabolites are detoxified by chemical reaction with the free thiol compound i.e. mesna.

Excretion

The first and most important step towards detoxification is the reaction of mesna with the double bond of acrolein, resulting in the formation of a stable thioether which can be detected in the urine by chromatography. In the second step, mesna reduces the speed of degradation of the 4-hydroxy metabolite in the urine. A relatively stable, non-urotoxic condensation product from 4-hydroxy cyclophosphamide or 4-hydroxy ifosfamide and mesna is formed. As a result of this chemical interaction, mesna inhibits the degradation of 4-hydroxy cyclophosphamide or 4-hydroxy ifosfamide and hence the formation of acrolein. The presence of this intermediate chemical species can be detected by chromatographic urinalysis.

5.3 Preclinical safety data

Genotoxicity

No data available.

Carcinogenicity

No long-term animal studies have been performed to evaluate the carcinogenic potential of mesna.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium edetate dihydrate (0.2 – 0.3mg/mL) and sodium hydroxide, for pH adjustment.
Water for injections.

6.2 Incompatibilities

In vitro mesna is incompatible with cisplatin, carboplatin and nitrogen mustard. The combination of an oxazaphosphorine cytostatic agent with mesna and cisplatin in the same infusion solution is not stable and is not to be used.

Holoxan (ifosfamide, 3mg/mL) may be admixed with diluted mesna solutions 1.5 to 3.0mg/mL (0.15 to 0.3%). Admixtures of **Holoxan** 3.0mg/mL and **Uromitexan** 1.5 to 3.0mg/mL stored in PVC plastic bags and refrigerated have been shown to be chemically and physically stable for 24 hours when diluted in the following sterile solutions:

- Sodium Chloride Injection 0.9%
- Compound Sodium Lactate Injection
- Glucose Injection 5%
- Glucose 2.5% + Sodium Chloride 0.45% Injection

However, because of the risk of microbial contamination it is recommended that admixtures be administered within 6 to 8 hours of preparation.

Mixing mesna and epirubicin leads to inactivation of epirubicin and should be avoided.

6.3 Shelf life

60 months (unopened). The expiry date can be found on the packaging.

6.4 Special precautions for storage

Store at or below 30°C (unopened vials).

6.5 Nature and contents of container

Uromitexan (mesna) solution for injection 100mg/mL:

200mg Single Dose 2mL ampoule	Box of 15 ampoules of 2mL (colour-ring coding turquoise/yellow).
400mg Single Dose 4mL ampoule	Box of 15 ampoules of 4mL (colour-ring coding blue/green).
1000mg Single Dose 10mL ampoule	Box of 15 ampoules of 10mL (colour-ring coding blue/green).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE

Prescription Medicine.

8 SPONSOR

Uromitexan is distributed in New Zealand by

Baxter Healthcare Ltd
33 Vestey Drive
Mt Wellington
Auckland 1060.

Baxter Healthcare Ltd
PO Box 14 062
Panmure
Auckland 1741

Phone (09) 574 2400.

Uromitexan is distributed in Australia by

Baxter Healthcare Pty Ltd
1 Baxter Drive
Old Toongabbie, NSW 2146.

9 DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine: 9 March 2989.

10 DATE OF REVISION OF THE TEXT

17 September 2019.

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
ALL	Headings and formatting made consistent throughout document.,
3	Excipients moved to section 6.1
4.2	General dose advice aligned with wording in tablets data sheet and number of ampoules to use clarified.
4.4, 4.6, 4.8	Safety information updated.
5.1	Pharmacodynamic and carcinogenicity information relocated.
6	Excipient renamed from edetate disodium to disodium edetate. Information on incompatibilities relocated to correct section

Based on Australian PI most recent amendment 29 August 2019; and CCDS 424 2014 0307.

Please refer to the Medsafe website (www.medsafe.govt.nz) for most recent data sheet.