PACKAGE LEAFLET: INFORMATION FOR THE PATIENT

UROMITEXAN
400 mg and 600 mg Tablets
Mesna

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

Throughout this leaflet, UROMITEXAN 400 mg and 600 mg Tablets will be called UROMITEXAN Tablets.

What is in this leaflet:

1 What UROMITEXAN Tablets are and what they are used for

UROMITEXAN Tablets contain a medicine called 'mesna'.

UROMITEXAN Tablets are used to help reduce and prevent bleeding in the bladder (haemorrhagic cystitis) caused by cyclophosphamide and ifosfamide. UROMITEXAN Tablets help to protect the lining of the bladder from damage caused by these two drugs. The body breaks down these two drugs to form products that can harm the bladder. UROMITEXAN Tablets work by helping to make these breakdown products less harmful. Mesna Tablets should only be taken when you are also taking cyclophosphamide or ifosfamide.

The damage to your bladder may show up as blood in your urine. Very small amounts of blood may not be seen, so your doctor or nurse will test your urine with a 'dipstick' or microscope to check for blood. If a larger amount of blood is in your urine, you will notice that it is red and very occasionally you may be able to see blood clots in it.

2 What you need to know before you are given UROMITEXAN Tablets

Do not take UROMITEXAN Tablets if:
- you are allergic (hypersensitive) to UROMITEXAN or any of the other ingredients (listed in section 6). An allergic reaction can include shortness of breath, wheezing, rash, itching or swelling of the face and lips.

If you are not sure if you are allergic talk to your doctor, nurse or pharmacist before taking UROMITEXAN Tablets.

Warnings and precautions

Talk to your doctor, nurse or pharmacist before using UROMITEXAN Tablets if:
- you have any problems with your immune systems called 'autoimmune' disease, such as

rheumatoid arthritis or lupus, where your body's immune system attacks itself. Patients with an autoimmune disease treated with cyclophosphamide and UROMITEXAN could have an increased risk of allergic (hypersensitivity) reactions.

- you have experienced any side effects in the past when given a thiol-containing compound as there could be an increased risk of experiencing side-effects with UROMITEXAN. Examples of thiol-containing medicines are amifostine (used to reduce the toxicity of some chemotherapy products), penicillamine (used to treat rheumatoid arthritis) and captopril (used to treat hypertension or heart failure).

If any of these applies to you your doctor will only give you UROMITEXAN following careful consideration of the risks and benefits to you.

Using other medicines
UROMITEXAN Tablets are taken with ifosfamide and cyclophosphamide. They do not react with these medicines, and are not known to react with any others.

However, always tell your doctor, nurse or pharmacist if you are taking or have recently taken any other medicines. This includes medicines you have obtained without a prescription.

Pregnancy, breast-feeding and fertility
UROMITEXAN Tablets are only taken with ifosfamide and cyclophosphamide. If you are pregnant and your doctor thinks that you need treatment with these medicines, you will also need to have UROMITEXAN. Discuss pregnancy with your doctor before having this medicine.

Do not breast-feed while being treated with these medicines.

Tests while you are taking UROMITEXAN Tablets
UROMITEXAN does not prevent the damage to the lining of the bladder in all patients. Your doctor or nurse will want to check your urine regularly for blood with a special 'dipstick' or look at it under a microscope.

Tell your doctor, nurse or pharmacist if you are having any other urine tests because your medicines can affect the results. 'Dipstick' and other types of tests frequently used to monitor diabetes can be used to detect 'ketones' or Vitamin C levels in your urine. UROMITEXAN can interfere with these types of urine tests.

UROMITEXAN can also interfere with the results of laboratory blood tests for the creatine phosphokinase (CPK) enzyme. Your doctor or nurse are aware of this interference and different test methods will be used while you are receiving UROMITEXAN.

UROMITEXAN with food, drink and alcohol
Food does not affect the absorption and urinary elimination of UROMITEXAN.

Driving and using machines
Some of the side effects of treatment with UROMITEXAN might affect your ability to drive and use machines safely. Your doctor will decide if it is safe for you to do so.

Important information about some of the ingredients of UROMITEXAN Tablets
This medicine contains lactose, which is a type of sugar. If you have ever been told by a doctor that you have an intolerance to some sugars, talk to your doctor before taking this medicine.

What to do if you see a different doctor, or have to go to hospital

If you see any other doctor or have to go to hospital for any reason, tell them what medicines you are taking. Do not take any other medicines unless your doctor knows you are taking UROMITEXAN.

3 How to take UROMITEXAN Tablets

Taking this medicine

- Take this medicine by mouth.
- You can take the tablets with or without food.
- While you are taking UROMITEXAN Tablets you should drink enough fluid every day to maintain a urine output of 100 ml per hour.
- This helps to dilute your urine and keeps a good flow of urine. It will help to protect your bladder.

You should pass urine (empty your bladder) as normal when you need to. Do not try to change your usual pattern.

The recommended usual dose

- Your doctor will decide how much of the medicine you will need and when you will need to take it. Always take the medicine exactly as your doctor tells you.
- The dose will depend on:
  - the dose and timing of your treatment with ifosfamide or cyclophosphamide
  - if ifosfamide or cyclophosphamide is being given to you as tablets or injection
  - if you suffer from water infections (urinary tract infections)
  - if you have ever had signs of bladder damage from ifosfamide or cyclophosphamide before
  - if you have had radiation therapy near your bladder.

Use in children

Children generally urinate more frequently than adults. For children your doctor may need to shorten the interval between doses and/or increase the number of individual doses.

If you are not sure how to take your tablets, ask your doctor, nurse or pharmacist.

If you take more UROMITEXAN Tablets than you should

If you take too many tablets, or if a child has swallowed any of your tablets, talk to a doctor or go to a hospital straight away. Always take the labelled medicine container with you whether or not there is any medicine left.

Taking too much of UROMITEXAN can cause symptoms such as nausea, vomiting, abdominal pain, diarrhoea, headache, fatigue, limb and joint pains, rash, flushing, low blood pressure, slow or irregular heartbeat, feeling of pins and needles like tingling, fever, and breathing difficulties.

A specific antidote treatment for UROMITEXAN overdose is not known.

If you forget to take UROMITEXAN Tablets

It is very important to take UROMITEXAN Tablets at the times your doctor has told you:

- these times will have been carefully worked out to make sure that your bladder is fully protected against damage.

If you do forget to take your tablets, take them as soon as you remember, and talk to your doctor or go to your nearest hospital immediately for advice.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Some of these side effects may be caused by cyclophosphamide or ifosfamide rather than UROMITEXAN, as they are always taken together.

Tell your doctor straight away, if you notice any of the following side effects, you may need urgent medical attention:

- The most severe adverse reactions associated with use of Mesna are:
  - Anaphylaxis. Signs of this would be shortness of breath, wheezing, rash, itching or swelling of the face and lips (hypersensitivity). Severe allergic reactions could lead to difficulty in breathing or shock, with a possible fatal outcome (anaphylactic shock, anaphylactic/anaphylactoid reaction).

- Stevens-Johnson syndrome or toxic epidermal necrolysis which are life threatening conditions which cause:
  - rash,
  - ulcers,
  - sore throat,
  - fever,
  - conjunctivitis,
  - blistering of the skin.

  - Drug rash with eosinophilia and systemic symptoms (DRESS) which is a life threatening hypersensitivity reaction to drugs which can cause:
    - rash,
    - fever,
    - pain and swelling of internal organs,
    - swollen and tender lymph nodes,
    - changes in blood cells (eosinophilia).

- The most frequently occurring adverse reactions associated with use of UROMITEXAN, are:
  - feeling sick, headache, diarrhoea,
  - fever, flushing, rash,
  - waves of sudden abdomen or stomach pain (colic),
  - light headedness, lack of energy, tiredness,
  - flu-like illness.

If you are actually sick (vomit) after taking UROMITEXAN Tablets, you may need to have UROMITEXAN by injection instead.

Other possible side effects include:

Blood and Lymphatic System
- swollen/enlarged lymph nodes (lymphadenopathy).
- decrease in the number of cells in your blood:
  - of red and white blood cells, as well as platelets (pancytopenia),
  - of white cells - which fight infection (leukopenia, lymphopenia),
  - of platelets - which help your blood clot (thrombocytopenia),
- abnormally high amounts of eosinophils, type of white blood cell produced in the bone
- marrow, either the blood or in body tissues (eosinophilia).

Metabolism and Nutrition
- decreased appetite,

- feeling dehydrated.

Psychiatric
- insomnia,
- nightmares.

Nervous System
- dizziness,
- fainting (syncope),
- sensation of tickling, tingling, burning, pricking (paresthesia),
- increased or abnormally painful sensitivity to touch (hyperesthesia),
- reduced sensitivity to touch (hypoesthesia),
- disturbance in paying attention,
- fits (convulsions).

Eyes
- blurred sight,
- sensitivity to light,
- inflammation of the eye (conjunctivitis),
- swelling around the eyes (periorbital oedema).

Heart and Circulation
- changes in the electrical patterns of your heart seen as abnormal ECG heart tracing patterns,
- sensation that you have a “pounding” heartbeat (palpitation),
- rapid heartbeat (tachycardia),
- low or high blood pressure (hypotension, hypertension).

Lungs
- nasal congestion,
- cough,
- severe, sharp pain when breathing in (pleuritic pain),
- dry mouth,
- difficulty in breathing or wheezing (bronchospasm),
- shortness of breath (dyspnea),
- vocal cord discomfort (laryngeal discomfort),
- nosebleeds (epistaxis),
- severe difficulty breathing (respiratory distress),
- decrease levels of oxygen in your body (hypoxia, oxygen saturation decreased),
- rapid breathing (tachypnea)
- coughing up blood or bloody sputum (hemoptysis).

Digestive system
- irritation of the lining of the mouth and digestive system (mucosal irritation),
- flatulence,
- burning pain in the area of the stomach,
- constipation,
- bleeding gums,
- inflammation of the lining of your mouth including ulcers (stomatitis),
- bad taste in mouth,

Liver
- increased levels of certain proteins produced by your liver called enzymes (increased transaminases). Your doctor will do blood tests to test for these,
- inflammation of the liver which can cause jaundice, weight loss and malaise (hepatitis).

Skin and Subcutaneous Tissue
- itching (pruritus),
- excessive sweating (hyperhidrosis),
- itchy, red rash which can develop in to sores (erythema multiforme, erythema),
- ulceration or blistering,
- swelling of the deeper layers of the skin, caused by a build-up of fluid (angioedema),
- skin rash notable for pale red, raised, itchy bumps (urticaria),
- burning sensation.

Musculoskeletal and Connective Tissue
- muscle or joint pain (myalgia, arthralgia),
- back pain,
- pain in hands or feet (pain in extremity),
- jaw pain.

Renal and Urinary
- painful urination (dysuria),
- kidney failure (acute renal failure).

General Disorders and Administrative Site Conditions
- chills (rigors),
- chest pain,
- swelling of the face (face oedema),
- swelling of tissues, usually in the lower limbs, due to the accumulation of fluids (oedema peripheral),
- muscle weakness (Asthenia).

Investigations
- abnormal test results for measurements of blood clotting.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort
Terrace, IRL - Dublin 2;
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
E-mail: medsafety@hpra.ie.

By reporting side effects you can help provide more information on the safety of this medicine.

5 How to store UROMITEXAN Tablets

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the label after EXP.

The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. If you have some tablets left over, take them back to your hospital. These measures will help protect the environment.

6 Contents of the pack and other information

What UROMITEXAN Tablets contains
- The active substance is mesna and each film-coated tablet contains 400 mg or 600 mg.
- The other ingredients are: lactose monohydrate, microcrystalline cellulose, dibasic calcium

phosphate dehydrate, corn starch, povidone K25, magnesium stearate, hydroxypropylmethylcellulose, polyethylene glycol 6000, titanium dioxide (E 171), simethicone.

What UROMITEXAN Tablets looks like and contents of the pack
The tablets are white and oblong with a notch on one side and either M4 or M6 on the other. They are available in blister strips in cartons containing 10, 20 and 50 tablets.

Marketing Authorisation Holder and Manufacturer

The Marketing Authorisation holder is:
Baxter Holding B.V.
Kobaltweg 49,
3542CE Utrecht,
Netherlands

Send all enquiries to this address.

UROMITEXAN Tablets are manufactured by:
Baxter Oncology GmbH
Kantstrasse 2
33790 Halle/Westfalen
Germany

This leaflet was last revised in 11/2018.

For information about UROMITEXAN Tablets or to request this leaflet in formats such as audio or large print please contact the Marketing Authorisation Holder: Tel: 01635 206345.