

UROMITEXAN 400 MG

הרכב:

MESNA 400 MG/VIAL

ההתוויה הרשומה לתכשיר בישראל:

Prevention of urinary passage toxicity of oxazaphosphorines (the active components of Holoxan: Ifosfamide, Endoxan: Cyclophosphamide, Ixoten: Trofosamide), in particular in high-risk patients with previous radiation therapy in the area of the lesser pelvis, cystitis with previous Holoxan, Endoxan or Ixoten, urinary passage diseases in anamnesis.

בהודעה זו כלולים השינויים המהותיים בלבד. בעלונים ישנם שינויים נוספים.
טקסט חדש מסומן עם קו תחתון, טקסט המהווה החמרה **מודגש בצהוב**.

להלן העדכונים העיקריים בעלון לרופא:

4.4 Special warnings and special precautions for use

Hypersensitivity

[...]

There are also case reports of serious blistering and ulceration of the skin and mucous membranes. Some reactions were consistent with Stevens-Johnson syndrome.

The skin reactions were accompanied in some cases by one or several other symptoms, including fever, cardiovascular symptoms, signs of acute renal failure, lung symptoms, hematologic abnormalities, increased levels of liver enzymes, nausea, vomiting, pain in the extremities, arthralgia, myalgia, malaise, stomatitis and conjunctivitis (see section 4.8). Some reactions have presented as anaphylaxis. Fever accompanied by (for example) hypotension but no skin manifestations has also been reported.

[...]

Reactions to mesna ranging from serious to mild have been reported with the use of mesna to treat severe systemic autoimmune disorders and malignancies. In most cases, the reactions occurred during or after a first treatment occasion or several weeks after mesna exposure. In other cases, the initial reaction was not observed until several months after the exposure. Symptoms tend to appear at shorter intervals following repeated exposure. The incidence and/or severity of reaction may vary with the dose administered. Some patients experienced reactions after re-exposure, which were of increasing severity in some cases.

Some patients with a history of a reaction showed 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.

Prescribers should

- be aware of reactions that may worsen with re-exposure and may in some cases become life-threatening
- be aware that hypersensitivity reactions to mesna might be interpreted as resembling the clinical picture of sepsis and, in patients with autoimmune disorders, as resembling an exacerbation of the underlying disease.

Thiol compounds

Mesna is a thiol compound (contains a sulfanyl-(SH-)group). Thiol compounds show some similarities in their adverse reaction profiles and may elicit severe skin reactions. Examples of drugs that are thiol compounds include amifostine, penicillamine and captopril.

It is not clear whether patients who experienced an adverse reaction to such a drug are at increased risk for reactions to another thiol compound. In these cases, special caution is required when using thiol compounds.

Mesna does not prevent hemorrhagic cystitis in all patients. Therefore, patients should be monitored accordingly.

Sufficient urinary output should be maintained, as with any oxazaphosphorine treatment.

[...]

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

[...]

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.

4.8 Undesirable effects

The most frequently occurring adverse reactions (> 10%) associated with use of mesna are headache, infusion site reactions, abdominal pain/colic, light-headedness, lethargy/drowsiness, fever, rash, diarrhea, nausea, flushing, and flu-like illness.

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).

[...]

Blood and lymphatic system disorders

Common: Lymphadenopathy

Not known: Pancytopenia, Leukopenia, Lymphopenia, Thrombocytopenia, Eosinophilia

[...]

Metabolism and nutrition disorders

Common: Appetite decreased, Feeling of dehydration

Psychiatric disorders

Common: Insomnia, Nightmares

Nervous system disorders

Very common: Headache, Light-headedness, Lethargy/drowsiness

Common: Dizziness, Paresthesia, Hyperesthesia, Syncope, Hypoesthesia, Disturbance in attention

Eye disorders

Common: Conjunctivitis, Photophobia, Blurred vision

[...]

Cardiac disorders

Common: Palpitations

Not known: Electrocardiogram abnormalities, [...]

[...]

Vascular disorders

Very common: Flushing

[...]

Respiratory, thoracic and mediastinal disorders

Common: Nasal congestion, Cough, Pleuritic pain, Xerostomia, Bronchospasm, Dyspnea, Laryngeal discomfort, Epistaxis

Not known: Difficulty breathing, Hypoxia, Reduced oxygen saturation, Hemoptysis [...]

Gastrointestinal disorders

Very common: Abdominal pain/colic, Nausea, Diarrhea

Common: Mucosal irritation, Flatulence, Burning pain (substernal/epigastric), Constipation, Gingival bleeding

Not known: Stomatitis, Dysgeusia

Hepatobiliary disorders

Common: Transaminases increased

Not known: Hepatitis, Gamma glutamyl transferase levels increased, Blood alkaline phosphatase levels increased

Skin and subcutaneous tissue disorders

Very common: Rash

Common: Pruritus, Hyperhidrosis

Not known: Toxic epidermal necrolysis, Erythema multiforme, Drug rash, Ulceration and/or bullae/blistering, Angioedema, Rash, Photosensitivity, Urticaria, Burning sensation, Erythema [...]

Musculoskeletal and connective tissue disorders

Common: Arthralgia, Back pain, Myalgia, Pain in the extremities, Jaw pain

Renal and urinary disorders

Common: Dysuria

Not known: Acute renal failure

General disorders and administration site conditions

Very common: At the infusion site: pruritus, rash, Fever, Flu-like illness

Common: At the infusion site: Pain, erythema, urticaria, swelling, Rigors, Fatigue, Chest pain, Malaise

Not Known: Facial edema, Peripheral edema, Asthenia, At the infusion site: thrombophlebitis, skin irritation

Investigations

Not known: Lab signs of disseminated intravascular coagulation, Prothrombin time prolonged,
Activated partial thromboplastin time prolonged

[...]

Onset of symptoms and re-exposure

Adverse reactions may occur after the first exposure to mesna. In some cases, symptoms are not observed until after the second or third exposure. In general, the complete spectrum of symptoms developed over a period of several hours. Following re-exposure, some patients experienced no further reactions while others experienced definite reactions.

Infusion site reactions

In some patients experiencing local cutaneous infusion site reactions after administration of the drug, subsequent exposure resulted in cutaneous reactions at other locations.

[...]

4.9 Overdose

Reports of inadvertent overdose and observations from a high-dose tolerability study in healthy subjects showed that, in adults, single doses in the range of approximately 4 g to 7 g of mesna can cause symptoms such as, but not limited to: nausea, vomiting, abdominal pain/colic, diarrhea, headache, fatigue, limb and joint pains, rash, flushing, hypotension, bradycardia, tachycardia, paresthesia, fever and bronchospasm.

Compared with patients receiving lower mesna doses or hydration treatment only, a markedly increased rate of nausea, vomiting and diarrhea has been found in oxazaphosphorine-treated patients receiving ≥ 80 mg mesna per kg per day.

[...]

העלון לרופא/לצרכן מפורסם במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על ידי פניה לבעל הרישום.

בברכה,
ד"ר דניאל ונגר
רוקח ממונה
מגאפארם בע"מ