1.5.5.1 Proposed Professional Information-CLEAN

UNAT® RANGE PACKAGE INSERT

Scheduling status:

Schedule 3

Proprietary name and dosage form:

UNAT® 2,5 Tablets

UNAT® 5 Tablets

UNAT® 10 Tablets

Composition :

UNAT 2,5: Each tablet contains 2,5 mg torasemide

UNAT 5: Each tablet contains 5,0 mg torasemide

UNAT 10: Each tablet contains 10,0 mg torasemide

Torasemide = 1-Isopropyl-3-[(4-m-toluidino-3-pyridyl) sulfonyl] urea.

Pharmacological classification:

A 18.1 Diuretics

Pharmacological action:

Torasemide acts as a salidiuretic through inhibition of renal sodium and chloride re-absorption in the ascending limb of Henlé. After oral administration the onset of action is within the first hour and peak action within 2 to 3 hours. The action may last up to 12 hours. An increase in

dose results in a corresponding linear increase in urine excretion (high ceiling activity) in healthy subjects in the 5 mg to 100 mg dose range.

After oral administration the blood pressure lowering effect of torasemide starts within the first week of treatment, the maximum effect being achieved after about 12 weeks. The exact mechanism of action of anti-hypertensive treatment with diuretics has not been established.

Torasemide is absorbed rapidly and almost completely after oral administration and peak serum levels are reached after 1 to 2 hours. More than 99,0 % of torasemide is bound to plasma proteins. The apparent distribution volume is 16 litres. Bioavailability is 80 % to 90 %. The terminal half-life of torasemide is 3 to 4 hours in healthy subjects. Total clearance is 40 ml/min and renal clearance about 10 ml/min. In patients with congestive heart failure or disorder of liver function the elimination half-life of torasemide is prolonged compared with healthy volunteers, but quantities excreted in the urine correspond to those in healthy subjects. In the presence of renal failure the elimination half-life of torasemide is unchanged.

Pharmacodynamic behaviour is not affected and the duration of action is not influenced by the severity of renal failure.

Indications:

Essential hypertension.

Oedema of cardiac and hepatic origin.

Pulmonary oedema due to acute cardiac insufficienty.

Contra-Indications:

- Renal failure with absence of urine production (anuria)
- Hepatic precoma and coma
- During pregnancy and lactation

- Patients with known hypersensitivity to sulfonylureas
- Hypovolaemia
- Hyponatraemia, hypokalaemia
- Severe disorders of micturition (e.g. prostate hypertrophy)

For lack of clinical experience, torasemide should not be used in children of 12 years or younger.

Dosage and directions for use:

Essential hypertension:

Treatment is initiated with 2,5 mg torasemide per day. The usual maintenance dose is 2,5 mg per day.

If this is insufficiently effective, the dose can be doubled to 5,0 mg per day. Higher doses will not lead to a further reduction of blood pressure.

Oedema of cardiac, hepatic and renal origin:

Treatment is initiated with 5,0 mg torasemide per day. The usual maintenance dose is 5,0 mg per day. If this is insufficiently effective, the dose can be increased up to 20 mg per day depending on the severity of the disease. In individual cases as much as 40 mg torasemide per day has been administered. Oral torasemide may be taken with some liquid on an empty stomach or at at any time in relation to a meal, as convenient.

Side effects and special precautions:

Depending on the dosage and duration of treatment, disturbances of water and electrolyte balance may occur, especially with limited salt in-take.

Signs of electrolyte and volume deficiency such as headache, dizziness, feelings of weakness, loss of appetite and cramps may occur, if diuresis is marked, especially at the start of treatment and in elderly patients.

Due to haemoconcentration after marked diuresis, hypotension and confusional states may occur.

Cases of thromboembolic complications and cardiac or cerebral ischaemia may occur.

These side-effects are generally abolished by adjusting the dosage to the individual needs. Gastrointestinal symptoms (nausea, vomiting, diarrhoea, constipation) may also occur.

In patients with urinary obstructions e.g. prostate hypertrophy, increased urine production can lead to urine retention resulting in distension of the bladder.

In rare cases treatment with torasemide may cause a decrease in the corpuscular constituents of the blood (erythrocytes, leucocytes, platelets).

Lowered potassium levels may occur in the blood especially if a low potassium diet is followed or in patients with vomiting, diarrhoea, excessive use of laxatives or in chronic disorders of liver function.

During treatment with torasemide there may be a rise in blood urea and creatinine, even in clinically healthy kidneys or in the presence of damaged kidneys.

Increases in Gamma-GT, alteration in blood glucose and lipid metabolism and a rise in the uric acid level may occur. Allergic skin reactions e.g. pruritus and xanthema or photosensitisation have been reported in isolated cases. Acute hypersensitivity reactions (which may be life-threatening) may occur in isolated cases after intravenous administration.

Rarely, dryness of the mouth and paraetsthesia in the limbs and visual disturbances have been reported.

Special precautions

Long-term treatment with torasemide requires regular monitoring of the electrolyte balance, glucose, uric acid, creatinine and lipid levels.

In patients with a tendency to hyperuricaemia and gout, careful monitoring is required.

As a rise in blood glucose may occur, careful monitoring of the carbohydrate metabolism in patients with latent or manifest diabetes mellitus is recommended.

Potential effects of alertness

Individually varying reactions can impair alertness (e.g. patient's ability to drive vehicles or to operate machinery). This applies particularly when beginning treatment, switching from another medicine or starting a new co-medication and in conjunction with alcohol.

Interactions

When used simultaneously with cardiac glycosides a potassium and/or magnesium deficiency may increase the sensitivity of the cardiac muscle to digitalis.

The kalidiuretic effect of mineralo- and glucocorticosteroids and laxatives may be increased.

Nonsteroidal anti-inflammatory medicines may reduce the effect of torasemide.

The effect of antihypertensive medicines may be potentiated. Consecutive treatment or start of a new co-medication with an ACE-inhibitor may result in an excessive fall in blood pressure.

The action of antidiabetic medicines may be reduced.

Torasemide may potentiate the damaging effects of aminoglycocide antibiotics, cisplatin, preparations and cephalosporins on the ear and kidney especially at high dose therapy.

The action of curare containing muscle relaxants and of theophylline can be potentiated.

Torasemide may decrease arterial responsiveness to pressor agents e.g. epinephrine and nor-epinephrine.

In patients receiving high doses of salicylates, salicylate-toxicity may be increased. On concomitant treatment with cholestyramine, bioavailability and thus the effectiveness of torasemide may be reduced.

Known symptoms of overdosage and particulars of its treatment :

If overdosage occurs there may be a marked diuresis with the danger of loss of liquids and electrolytes which may lead to somnolence and confusion, hypotension, circulatory collapse and gastrointestinal symptoms, No specific antidote is known. Symptoms of overdosage generally disappear on reduction of the dose or withdrawal of the medicament and simultaneous replacement of fluid and electrolytes (to be monitored).

Identification

UNAT 2,5 : White to off-white round tablet, embossed with T 2.5 on one side.

UNAT 5 : White to off-white round tablet with a T-break mark and 5.0 embossed on one side.

UNAT 10 : White to off-white round tablet with a T-break mark and 10.0 embossed on one side.

Presentation:

UNAT 2,5: Blister packs containing 30 tablets.

UNAT 5: Blister packs containing 30 tablets.

UNAT 10: Blister packs containing 30 tablets.

Storage instructions:

Store at or below 25 °C.

KEEP OUT OF REACH OF CHILDREN.

Registration number(s):

UNAT 2,5 – A28/18.1/0292

UNAT 5 – A28/18.1/0293

UNAT 10 – A28/18.1/0294

Name and business address of the holder of the certificate of registration:

Viatris South Africa (Pty) Ltd

4 Brewery Street

Isando, Johannesburg

1609

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