APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

PROPRIETARY NAME (and dosage form)

RISAT 5 mg (Tablet)

RISAT 10 mg (Tablet)

COMPOSITION

RISAT 5 mg:

Each uncoated tablet contains torasemide anhydrous 5 mg. Contains lactose.

RISAT 10 mg:

Each uncoated tablet contains torasemide anhydrous 10 mg. Contains lactose.

The other ingredients of **RISAT** are cellulose, microcrystalline, crospovidone, lactose monohydrate, magnesium stearate, and povidone.

PHARMACOLOGICAL CLASSIFICATION

A 18.1 Diuretics.

PHARMACOLOGICAL ACTION

Torasemide is a salidiuretic. It inhibits renal sodium and chloride re-absorption in the ascending limb of Henlé. 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 antihypertensive treatment with torasemide has not been established.

Pharmacokinetics:

After oral administration, torasemide is absorbed rapidly and almost completely 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 %. In healthy subjects, the terminal half-life of torasemide is 3 to 4 hours. Total clearance is 40 ml/min and renal clearance about 10 ml/min.

Special populations:

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. The elimination half-life of torasemide is unchanged in the presence of renal failure. The duration of action is not influenced and pharmacodynamic behaviour is not affected by the severity of renal failure.

INDICATIONS

RISAT tablets are indicated in:

- Essential hypertension.
- Oedema of cardiac and hepatic origin.
- Pulmonary oedema due to acute cardiac insufficiency.

CONTRA-INDICATIONS

RISAT tablets are contra-indicated in:

- hypersensitivity to torasemide or any of the ingredients of **RISAT**
- renal failure with absence of urine production (anuria)
- hepatic failure.
- during pregnancy and lactation
- patients with known hypersensitivity to sulfonylureas
- hypovolaemia
- hyponatraemia, hypokalaemia
- severe disorders of micturition (e.g. prostate hypertrophy)

Due to lack of clinical experience, **RISAT** should not be used in children of 12 years or younger.

WARNINGS

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

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

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.

In patients receiving high doses of salicylates, salicylate-toxicity may be increased.

INTERACTIONS

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

The effect of **RISAT** may be reduced by nonsteroidal anti-inflammatory medicines (NSAIDs).

The action of antidiabetic medicines may be reduced.

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

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

The arterial responsiveness to pressor agents, e.g. epinephrine (adrenaline) and norepinephrine (noradrenaline) may be decreased by torasemide.

On concomitant treatment with cholestyramine, bioavailability and therefore the effectiveness of **RISAT** may be reduced.

Concurrent use with antidysrhythmic medicines may lead to an increased risk of dysrhythmias associated with hypokalaemia.

When **RISAT** and anticoagulants are used concurrently, the effects of the anticoagulants may be decreased.

Because of reduced renal clearance, concomitant use with lithium may promote lithium toxicity.

Probenecid may decrease the activity of torasemide.

PREGNANCY AND LACTATION

RISAT is contra-indicated in pregnancy and lactation.

DOSAGE AND DIRECTIONS FOR USE

Essential hypertension:

Treatment is initiated with 2,5 mg **RISAT** 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. **RISAT** may be taken with or without meals.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS

Side-effects:

Metabolic and nutrition disorders:

Less frequent:

Disturbances of water and electrolyte balance, especially with limited salt intake.

Hypokalaemia, hyponatraemia and hypochloraemic alkalosis.

Blood and lymphatic system disorders:

Less frequent:

A decrease in the erythrocyte, leucocyte, and platelet counts.

Vascular disorders:

Less frequent:

Hypotension

The following side-effects have been reported and frequencies are unknown:

Thromboembolic complications

Cardiac disorders:

The following side-effects have been reported and frequencies are unknown:

Cardiac or cerebral ischaemia.

Gastrointestinal disorders:

Frequent:

Constipation, nausea, vomiting

Less frequent:

Gastrointestinal haemorrhage, dry mouth.

The following side-effects have been reported and frequencies are unknown:

Diarrhoea.

Renal and urinary disorders:

The following side-effects have been reported and frequencies are unknown:

Increase in blood urea and creatinine, even in clinically healthy kidneys or in the presence of damaged kidneys.

Skin and subcutaneous tissue disorders:

Less frequent:

Allergic skin reactions, e.g. pruritus and exanthema or photosensitisation.

Nervous system disorders:

Frequent:

Dizziness, headache

Less frequent:

Paraesthesia in the limbs.

The following side-effects have been reported and frequencies are unknown:

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

Eye disorders:

Less frequent:

Visual disturbances.

Ear and labyrinth disorders:

Less frequent:

Ototoxicity.

Investigations:

The following side-effects have been reported and frequencies are unknown:

Increases in Gamma-GT, alteration in the blood glucose and lipid metabolism and a rise in the uric acid level.

Special Precautions:

Regular monitoring of the electrolyte balance, glucose, uric acid, creatinine and lipid levels is required with long-term treatment with **RISAT**.

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.

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

RISAT contains lactose and should not be given to patients with rare hereditary problems or a history of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.

Ability to drive and use of machinery:

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

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. There is no known specific antidote.

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

RISAT 5 mg:

White to off-white, oval shaped, biconvex, uncoated tablets debossed with ‘C’ on one side and with a score line in between ‘4’ and ‘1’ on the other side.

RISAT 10 mg:

White to off-white, oval shaped, biconvex, uncoated tablets debossed with 'C' on one side and with a score line in between '4' and '2' on the other side.

PRESENTATION

RISAT 5 mg AND RISAT 10 mg:

1. **Blister Packs:**

   Tablets are packed in blister packs (composed of clear PVC film and silver coloured aluminium lidding foil). Each blister contains 10 tablets.

   Pack size 30's: Each carton contains 3 blisters of 10 tablets each.

2. **HDPE Container Pack:**

   a. Tablets are packed in white 40 ml opaque, round, wide-mouth HDPE containers with a 33 mm neck finish, closed with a white opaque polypropylene stock ribbed closure with an induction sealing wad.
   b. Tablets are packed in white 200 ml opaque, round, wide-mouth HDPE containers with a 38 mm neck finish, closed with a white opaque polypropylene stock ribbed closure with an induction sealing wad.

   Pack size: 30's: One HDPE container of 30 tablets.

   Pack size: 500's: One HDPE container of 500 tablets.

STORAGE INSTRUCTIONS

Store at or below 25 °C.

Do not remove the blisters from the carton until required. Keep the bottle tightly closed.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

RISAT 5 mg: 43/18.1/1042

RISAT 10 mg: 43/18.1/1043

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Aurogen South Africa (Pty) Ltd

Woodhill Office Park, Building 1, 53 Phillip Engelbrecht Avenue

Meyersdal, Ext. 12, 1448

Johannesburg

South Africa

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