PROPOSED PACKAGE INSERT

SCHEDULING STATUS:

S3

PROPRIETARY NAMES AND DOSAGE FORMS:

TORSINAT 2,5 mg (tablets)

TORSINAT 5 mg (tablets)

TORSINAT 10 mg (tablets)

COMPOSITION:

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

Torsinat 5 mg: Each tablet contains 5,0 mg torasemide

Torsinat 10 mg: Each tablet contains 10,0 mg torasemide

PHARMACOLOGICAL CLASSIFICATION:

A 18.1 Diuretics

PHARMACOLOGICAL ACTION:

Torasemide inhibits the reabsorption of sodium and chloride in the ascending limb of the loop of Henlé in the kidney. Following oral administration the onset of action is achieved within 1 hour, with peak action within 2 to 3 hours. The action may last up to twelve hours. Dosage increase results in a corresponding linear increase in urine excretion in healthy subjects in the 5 mg to 100 mg dose range.

Following oral administration, the blood pressure lowering effect of torasemide starts within the first week of treatment. The maximum effect is achieved after about 12 weeks. The exact mechanism of action of antihypertensive treatment with torasemide has not been established.

Pharmacokinetics:

Torasemide is well-absorbed and almost completely after oral administration. Peak serum concentrations are achieved within 1 to 2 hours. More than 99 % of torasemide is bound to plasma proteins. The apparent distribution volume is 16 litres. Bioavailability is 80 % to 90 %. The elimination half-life of torasemide is approximately 3 – 4 hours in healthy subjects. Total clearance is 40 ml/min and renal clearance about 10ml/min. In patients with congestive heart failure or hepatic dysfunction 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 patients with 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 insufficiency.

CONTRA-INDICATIONS:

TORSINAT must not be used:

During pregnancy and lactation

In renal failure with anuria

Hepatic precoma and coma

In patients with known hypersensitivity to sulfonylureas

Hypovolaemia

Hyponatraemia, hypokalaemia

Severe disorders of micturition (e.g. prostate hypertrophy)

Children of 12 years or younger

WARNINGS:

Missed dose must be taken as soon as possible, but do not take if almost time for next dose. Do not double dose.

May increase blood sugar levels, diabetics to take care.

Interactions:

Simultaneous use with cardiac glycosides, may result in a potassium and / or magnesium deficiency which may increase the sensitivity of the cardiac muscle to digitalis.

It may potentiate the potassium lowering effect and gluco-corticosteroids and laxatives.

Potentiation of the effect of antihypertensive medicines may occur.

Co-medication with an ACE-inhibitor may result in an excessive fall in blood pressure.

The action of anti-diabetic medicines may be reduced.

The effect of **TORSINAT** may be reduced by nonsteroidal anti–inflammatory agents.

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

TORSINAT may decrease arterial responsiveness to pressor agents e.g. epinephrine (adrenaline) and nor-epinephrine (nor-adrenaline).

The damaging effects of aminoglycoside antibiotics, cisplatin preparations and cephalosporins on the ear and kidney especially at high dose therapy may be potentiated by **TORSINAT**

Salicylate toxicity may be increased in patients receiving high doses of salicylates.

During concomitant administration with cholestyramine, bioavailability and thus the effectiveness of **TORSINAT** may be reduced.

Incompatibilities:

TORSINAT should not be mixed with other medicines in the same syringe before injection.

Pregnancy and lactation:

Safety and efficacy of **TORSINAT** in pregnancy and lactation have not been established.

DOSAGE AND DIRECTIONS FOR USE:

Essential Hypertension:

Treatment is initiated with one 2,5 mg tablet per day. The usual maintenance dose is 2,5 mg per day. If this is not sufficiently effective, the dose can be doubled to two tablets (5,0 mg) **TORSINAT** 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 one 5,0 mg tablet **TORSINAT** per day. The usual maintenance dose is 5,0 mg per day. If this is not sufficiently effective, the dose can be increased up to 4 tablets (20,0 mg) per day depending on the severity of the disease. In individual cases as much as 40 mg **TORSINAT** per day has been administered. Oral **TORSINAT** may be taken with some liquid on an empty stomach or at any time in relation to a meal, as convenient.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Nervous system disorders:

Have been reported but frequency unknown:

Dizziness, confusional states (due to marked diuresis especially at the start of treatment and in elderly patients), headache, cerebral ischaemia.

Musculoskeletal and connective tissue disorders:

Have been reported but frequency unknown:

Feelings of weakness, cramps, paraesthesia in the limbs.

Gastrointestinal disorders:

Have been reported but frequency unknown:

Nausea, vomiting, diarrhoea, constipation.

Cardiac disorders:

Have been reported but frequency unknown:

Cardiac ischaemia.

Metabolism and nutrition disorders:

Have been reported but frequency unknown:

Water and electrolyte imbalances (especially with limited salt intake), loss of appetite, increases in Gamma-GT and lipid metabolism and a raise in the uric acid level.

Less frequent: Dryness of the mouth.

Skin and subcutaneous tissue disorders:

Have been reported but frequency unknown:

Allergic skin reactions e.g. pruritus and exanthema or photosensitization.

Blood and lymphatic system disorders:

Have been reported but frequency unknown:

Decrease in the corpuscular constituents of the blood (erythrocytes, leucocytes and platelets), alterations in the blood glucose, thromboembolic complications, reduced blood, especially in patients consuming a low potassium diet, increase in blood urea and creatinine, hypotension as a result of haemoconcentration after marked diuresis.

Renal and urinary disorders:

Have been reported but frequency unknown:

An increase in urine production in patients with urinary obstructions (e.g. prostate hypertrophy) can lead to urine retention resulting in distension of the bladder.

Eye disorders:

Have been reported but frequency unknown:

Visual disturbances.

Hepato-biliary disorders:

Have been reported but frequency unknown:

Low potassium levels in patients with chronic liver function disorders.

These side-effects are generally abolished by adjusting the dosage to the individual needs.

Special precautions:

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

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

An increase in blood glucose may occur, thus careful monitoring of the carbohydrate metabolism in patients with latent or manifest diabetes mellitus is recommended.

Potential effects on alertness:

Alertness may be impaired (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 conjuction with alcohol.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

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

IDENTIFICATION:

TORSINAT 2,5 mg: White to off-white, round tablet without break notch.

TORSINAT 5 mg: White to off-white, round tablet with break notch.

TORSINAT 10 mg: White to off-white, round tablet with cross break notch.

PRESENTATION:

Aluminium/Aluminium or colourless PVC/PVDC/Aluminium blister packs containing 30 tablets.

STORAGE INSTRUCTIONS:

Store at or below 25 °C.

KEEP OUT OF THE REACH OF CHILDREN.

REGISTRATION NUMBERS:

TORSINAT 2,5 mg: A39/18.1/0192

TORSINAT 5 mg**:** A39/18.1/0193

TORSINAT 10 mg**:** A39/18.1/0194

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATES OF REGISTRATION:

Austell Laboratories (Pty) Ltd

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