SOUTH AFRICAN PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S5

PROPRIETARY NAME AND DOSAGE FORM

THADEN-25 (hard-gelatin capsule)

THADEN-75 (film-coated tablet)

COMPOSITION

Each hard-gelatin capsule of THADEN-25 contains 25 mg dothiepin hydrochloride.

Excipients:

Gelatin, lactose monohydrate, magnesium stearate, ponceau 4R (C.I. 16255), starch maize, titanium dioxide (C.I. 77891), yellow oxide (C.I. 77492)

Contains sugar: Lactose monohydrate 130 mg

Each film-coated tablet of THADEN-75 contains 75 mg dothiepin hydrochloride.

Excipients:

FD&C blue no.2 (C.I. 73015), FD&C yellow no. 6 (C.I. 15985), lecithin (soya), macrogol, magnesium stearate, polyvinyl alcohol, ponceau 4R aluminium lake (C.I. 16255), povidone, starch maize, talc purified, titanium dioxide (C.I. 77891), tricalcium phosphate

Sugar free

CATEGORY AND CLASS

A 1.2 Psychoanaleptics (antidepressants)

PHARMACOLOGICAL ACTION

Dothiepin hydrochloride is a tricyclic antidepressant.

INDICATIONS

For the treatment of depression in adults.

CONTRAINDICATIONS

The acute phase of myocardial infarction, and in patients with heart block.

Administration is not advised during the first trimester of pregnancy (see HUMAN REPRODUCTION).

WARNINGS AND SPECIAL PRECAUTIONS

SPECIAL WARNING:

This medicine should at all times be kept out of the reach of children, as even small doses may be fatal to them.

Special precautions:

a) Caution should be observed with patients suffering from a depressive phase of manic depressive psychosis, as occasionally hypomania or mania can be precipitated in such

patients. Withdraw the medicine if the depression turns into a manic phase. Patients with suicidal tendencies should be carefully supervised during treatment.

b) In elderly male patients suffering from prostatism, urinary retention may be precipitated.

c) In patients suffering from cardiac disease, special caution should be observed because of the occasional problems of tachycardia, dysrhythmias, orthostatic hypotension and other unwanted effects on blood pressure, aggravation of conduction disturbances, and electro-cardiograph abnormalities. Regular cardiological and electrocardiographic examination is advised.

d) Use with caution in patients with hyperthyroidism or with impaired liver function and in those with a history of epilepsy, untreated narrow-angle glaucoma, urinary retention, prostatic hypertrophy or constipation.

e) In diabetic patients, as blood sugar concentrations may be altered.

f) Withdraw the medicine if allergic skin reactions appear.

Effects on ability to drive and use machines

At the time of initiation of therapy, patients should be advised not to drive a motor vehicle, climb dangerous heights or operate dangerous machinery, for at least seven days. In these situations, impaired decision making could lead to accidents.

Porphyria

Use of THADEN is generally considered to be unsafe in porphyria.

Excipients

THADEN-25 contains lactose monohydrate which may have an effect on the glycaemic control of patients with diabetes mellitus. Patients with the rare hereditary conditions of

galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take THADEN-25.

INTERACTIONS

The medicine should not usually be given to patients receiving other central nervous system depressants, e.g. barbiturates. It should not be given to patients receiving monoamine oxidase inhibitors or within 14 days of stopping such treatment. The pressor effects of the direct acting sympathomimetic agents, adrenaline or noradrenaline, are enhanced, and the use of local anaesthetics containing these vasoconstrictors should be avoided as hypertensive reactions may occur. The simultaneous administration of anticholinergic agents may be dangerous. The hypotensive effect of certain antihypertensive agents may be reduced. The effects of tricyclic antidepressants are influenced by medicine that affect their metabolism. Barbiturates and other enzyme inducers such as anti-epileptics increase their metabolism while neuroleptics, cimetidine, methylphenidate, and possibly oestrogens and oral contraceptives reduce it. Hyperthyroid patients or those taking thyroid preparations may show an enhanced response to tricyclic antidepressants. The effects of bethanidine, debrisoquine, guanethidine and possibly of clonidine are reduced by tricyclic antidepressants.

HUMAN REPRODUCTION

Administration is not advised during the first trimester of pregnancy (see CONTRAINDICATIONS).

DOSAGE AND DIRECTIONS FOR USE

Adults: Dosage may vary widely depending on the individual patient and conditions. It is preferable to use the smaller dose for the first few days.

In the treatment of depression, THADEN is given in doses of 25 mg three times daily initially, gradually increased to 50 mg three times daily if necessary; alternatively, 75 mg or 150 mg may be given as a single night-time dose. Higher doses of up to 225 mg daily have been given in severely depressed patients. The recommended initial dose for the elderly is 50 mg to 75 mg daily. Half the normal maintenance dose may be adequate in the elderly.

SIDE EFFECTS

Many side effects are caused by its anti-muscarinic actions. These include dry mouth, sour or metallic taste, constipation which can lead to paralytic ileus, urinary retention, blurred vision and disturbances in accommodation, palpitations, tachycardia, and impotence. When anticholinergic effects are severe the medicine should be discontinued or reduced.

Other adverse effects include drowsiness (but nervousness and insomnia may occur), headache, peripheral neuropathy, tremor, orthostatic hypotension, hypertension, dizziness, sweating, weakness and fatigue, ataxia, epileptiform seizures, extrapyramidal symptoms including speech difficulties, tinnitus, stomatitis and gastric irritation with nausea and vomiting. Confusion or delirium may occur, particularly in the elderly. Anorexia with weight loss, or weight gain, sometimes with inappropriate appetite (carbohydrate craving) may occur. Allergic skin reactions and photosensitisation have been reported, as well as cholestatic jaundice and blood disorders, including eosinophilia, bone-marrow depression, thrombocytopenia, leucopenia, and agranulocytosis. The tricyclic antidepressants have an

adverse effect on the myocardium and can cause conduction defects and cardiac arrhythmias; an increased risk of sudden death has been suspected in cardiac patients receiving tricyclic antidepressants.

Endocrine effects associated with tricyclic antidepressant therapy include changes in libido, interference with sexual function, gynaecomastia and breast enlargement, and galactorrhoea. Changes in blood sugar concentrations may also occur, as well as inappropriate secretion of antidiuretic hormone.

NOTE: Elderly patients are more prone to all these effects, and therapy should be initiated at lower standard doses in the elderly.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENTS

Symptoms

Overdosage and poisoning may be characterised by central nervous system depression or excitation, severe anti-cholinergic effects and cardiotoxicity. The following symptoms and signs are characteristic of acute overdosage: drowsiness, restlessness, ataxia, stupor, coma, pyrexia, palpitations, tachycardia, cardiac arrhythmias, hypotension and in severe cases, respiratory depression. Epileptiform seizures may occur.

Treatment

The stomach should be emptied by emesis or aspiration and lavage. In particular, the patient should be monitored for cardiac arrhythmias and anti-arrhythmic measures instituted if cardiac output is jeopardised.

IDENTIFICATION

THADEN-25: A white powder encapsulated within a size “3” hard-gelatin capsule with opaque red body and cap.

THADEN-75: A round, red, film-coated, bevelled-edged, biconvex tablet.

PRESENTATION

THADEN-25:

100 hard-gelatin capsules are packed in a white, polypropylene securitainer, together with a leaflet, and sealed with a white, low density polyethylene cap.

100 hard-gelatin capsules are packed in a clear polyvinyl chloride film and sealed with an aluminium foil backing. The blister strips are packed, together with a leaflet, into an outer pre-printed cardboard carton.

100 hard-gelatin capsules are packed in a white high density polyethylene container, together with a leaflet, and sealed with a white high density polyethylene screw cap with an induction seal liner.

THADEN-75:

28 film-coated tablets are packed in a clear polyvinyl chloride film and sealed with an aluminium foil backing. The blister strips are packed together with a leaflet, into an outer pre-printed cardboard carton.

28 film-coated tablets are packed in a white, polypropylene securitainer, together with a leaflet, silica gel sachet and white foam insert, and sealed with a white, low density polyethylene cap.

28 film-coated tablets are packed in a white, polyethylene minigrip bag or metallised low-density polyethylene layflat bag sealed with a zip layflat.

Not all packs or pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS

Store at or below 25 °C.

Protect from light.

Keep in original packaging until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

THADEN-25: Z/1.2/171

THADEN-75: Z/1.2/301

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

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

Dates of registration:

THADEN-25: 24 November 1992

THADEN-75: 02 February 1993

Date of the most recent amendment to the professional information as approved by the Authority: 02 February 1993

Namibia:	NS3
25 mg:	04/1.2/0171
75 mg:	04/1.2/0170

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