Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dothep 25mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains 25 mg of dosulepin hydrochloride.
Excipients - Contains Lactose Monohydrate 94.0mg and Ponceau 4R (E124)
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard
Brown/red hard capsule, marked ‘G DN 25’ in black ink.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Dosulepin is indicated in the treatment of symptoms of depressive illness - in particular where an anti-anxiety effect is required.

4.2 Posology and method of administration

Dothep capsules are administered orally.

Recommended dosage schedules:

Adults: Initially 75mg/day in divided doses (as capsules) or as a single dose at night, increasing to 150mg/day. In certain circumstances e.g. in hospital use, dosages up to 225mg daily have been used. Suggested dosage regimen : 25 to 50mg three times daily or, alternatively, 75 or 150mg as a single dose at night.

Elderly: 50-75 mg daily initially. As with any antidepressant, the initial dose should be increased with caution under close supervision. Half the normal adult dose may be sufficient to produce a satisfactory clinical response.

Children: Not recommended.

4.3 Contraindications

Dothep capsules are contraindicated in patients with:
Closed angle glaucoma.
Existing urinary retention.
Recent myocardial infarction.
Any degree of heart block or other cardiac arrhythmias.
Mania.
Severe liver disease.
Women who are breast-feeding.
Crrently receiving monoamine oxidase inhibitors or have received these within the previous two weeks.

4.4 Special warnings and precautions for use

Special precautions for use:

Dosulepin should not be used in the treatment of children and adolescents under the age of 18 years. Studies in depression in this age group did not show a beneficial effect for tricyclic antidepressants. Studies with other classes of antidepressants have shown a risk of suicidality, self harm and hostility related to these compounds. This risk cannot be excluded with Dosulepin. In addition, Dosulepin is associated with a risk of cardiovascular adverse events in all age groups. Furthermore, long term safety data in children and adolescents concerning growth, maturation and cognitive and behavioural development are not available (see also section 4.8 Undesirable effects and section 4.9 Overdose).

The elderly are particularly liable to experience adverse reactions to antidepressants, especially agitation, confusion and postural hypotension. Patients posing a high suicidal risk require close supervision.

Dosulepin should be given only with caution to epileptic patients and to those with cardiovascular disorders.Its use should be avoided in patients with symptoms suggestive of prostatic hypertrophy and a history of epilepsy. Tricyclic antidepressants potentiate the central nervous depressant action of alcohol. Anaesthetics given during tri/tetracyclic antidepressant therapy may increase the risk of arrhythmias and hypotension. If surgery is necessary, the anaesthetist should be informed that a patient is being so treated.

It may be two to four weeks from the start of treatment before there is an improvement in the patient's depression; the patient should be monitored closely during this period. The anxiolytic effect may be observed within a few days of commencing treatment. Initially, Dosulepin may impair alertness; patients likely to drive vehicles or operate machinery should be warned of this possibility.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Withdrawal symptoms may occur on abrupt cessation of tricyclic therapy and include insomnia, irritability and excessive perspiration. Similar symptoms in neonates whose mothers received tricyclic antidepressants during the third trimester have also been reported, although this has not been observed following treatment with Dothiepin. It is recommended that antidepressants should be withdrawn gradually.

Suicide/suicidal thoughts or clinical worsening
Depression is associated with an increased risk of suicidal thoughts, self harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.

Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment. A meta-analysis of placebo-controlled clinical trials of antidepressant drugs in adult patients with psychiatric disorders showed an increased risk of suicidal behaviour with antidepressants compared to placebo in patients less than 25 years old.

Close supervision of patients and in particular those at high risk should accompany drug therapy especially in early treatment and following dose changes. Patients (and caregivers of patients) should be alerted about the need to monitor for any clinical worsening, suicidal behaviour or thoughts and unusual changes in behaviour and to seek medical advice immediately if these symptoms present.

Special warnings:
Dependence - withdrawal symptoms may occur on abrupt cessation of treatment.
Tolerance - not applicable.

4.5 Interaction with other medicinal products and other forms of interaction

Dosulepin should not be given concurrently with monoamine oxidase inhibitors (MAOI's); nor within 14 days of stopping such treatment. Dosulepin may alter the pharmacological effects of some concurrently administered drugs including CNS depressants such as alcohol and narcotic analgesics. The effects of these will be potentiated, as will the effects of adrenaline and noradrenaline.

The hypotensive activity of certain antihypertensive agents, e.g. bethanidine, debrisoquine, guanethidine, may be reduced by Dosulepin. Anaesthetics given during tri/tetracyclic anti-depressant therapy may increase the risk of arrhythmias and hypotension. If surgery is necessary, the anaesthetist should be informed that a patient is being so treated.

It is advisable to review all antihypertensive therapy during treatment with Dosulepin.

Barbiturates may decrease and methylphenidate may increase the serum concentration of Dosulepin and thus affect its antidepressant action.

4.6 Fertility, pregnancy and lactation

There is no evidence as to the safety of Dosulepin in human pregnancy nor is there evidence from animal work that it is free from hazard. It should only be used in pregnancy, in particular in the first and last trimesters, if there are compelling reasons.

Dosulepin is excreted in breast milk; therefore it is not recommended for use during lactation.

4.7 Effects on ability to drive and use machines

Initially, Dosulepin may impair alertness, patients likely to drive vehicles or operate machinery should be warned of this possibility.

4.8 Undesirable effects

The following adverse effects, although not all reported with Dosulepin have occurred with other tricyclic antidepressants.

Atropine-like side effects including dry mouth, disturbances of accommodation, tachycardia, constipation and hesitancy of micturition are common early in treatment, but usually diminish. Other adverse effects include drowsiness, sweating, postural hypotension, tremor and skin rashes. Interference with sexual function may occur.

Serious adverse effects are rare. These include depression of the bone marrow, agranulocytosis, cholestatic jaundice, hypomania and convulsions. Psychotic manifestations, including mania and paranoid delusions may be exacerbated during treatment with tricyclic antidepressants.

Withdrawal symptoms may occur on abrupt cessation of tricyclic therapy and include insomnia, irritability and excessive perspiration. Similar symptoms in neonates whose mothers received tricyclic antidepressants during the third trimester have also been reported, although this has not been reported following treatment with Dosulepin.

Cardiac arrhythmias and severe hypotension are likely to occur with high dosage or in deliberate overdosage. They may also occur in patients with pre-existing heart disease taking a normal dose.

Cases of suicidal ideation and suicidal behaviours have been reported during Dosulepin therapy or early after treatment discontinuation (see section 4.4).

Class effects
Epidemiological studies, mainly conducted in patients 50years of age and older, show an increased risk of bone

fractures in patients receiving SSRls and TeAs. The mechanism leading to this risk is unknown.

4.9 Overdose

There is no specific antidote for Dosulepin. Gastric lavage is recommended. When the patient is unconscious or the cough reflex depressed the lungs should be protected by a cuffed endotrachael tube.

Repeated gastric/intestinal aspiration or repeated administration of activated charcoal may remove drug and metabolites excreted into the gut via the bile. Continuous ECG monitoring is advisable. Abnormalities of cardiac rhythm and epileptic convulsions may occur and should be treated accordingly. Forced diuresis is not recommended. Bedrest is advisable, even after recovery.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Non-selective monoamine reuptake inhibitor. ATC code: N06AA16
Dosulepin HCl is a tricyclic antidepressant with actions and uses similar to those of amitriptyline.

5.2 Pharmacokinetic properties

Dosulepin HCl is readily absorbed from the gastrointestinal tract and extensively demethylated by first-pass metabolism in the liver to its primary active metabolite - desmethyldothiepin (northiaden). Dosulepin is excreted in the urine, mainly in the form of its metabolites; small amounts are also excreted in the faeces. The half life is approx. 19-33 hours.

5.3 Preclinical safety data

No further information available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents:
Lactose monohydrate
Povidone
Sodium starch glycolate Type A
Magnesium stearate
Purified talc

Capsule shells:
Gelatin
Red iron oxide (E172)
Yellow iron oxide (E172)
Black iron oxide (E172)
Titanium dioxide (E171)
Ponceau 4R (E124)

Printing ink:
Black iron oxide (E172)
Propylene glycol (E1520)
Shellac

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

4 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

PVC/A1 blisters in strips packed in cartons containing 28, 56, 60, 84, 100, 250, 500 or 1000 capsules.
Polypropylene tablet container with polyethylene cap containing 28, 56, 60, 84, 100, 250, 500 and 1000 capsules.
Not all pack sizes will be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Mc Dermott Laboratories Ltd. T/A Gerard Laboratories
35/36 Baldoyle Industrial Estate
Grange Road
Dublin 13

8 MARKETING AUTHORISATION NUMBER

PA 577/20/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12 May 2000

Date of last renewal: 12 May 2010

10 DATE OF REVISION OF THE TEXT

April 2011