PRODUCT INFORMATION

Deptran

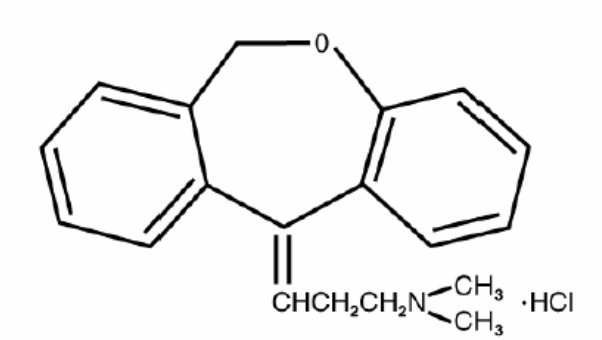
Doxepin (as hydrochloride)

NAME OF THE MEDICINE

Active ingredient : Doxepin hydrochloride

Chemical name : 11-[3-dimethylaminopropylidene]-6H-dibenz[b,e]oxepin hydrochloride

Structural formula :



Molecular formula : $C_{19}H_{21}NO.HCl$

Molecular weight : 315.8

CAS Registry no. : 1229-29-4

DESCRIPTION

Doxepin hydrochloride, a dibenzoxepin derivative, consists of a mixture of the *cis*- and *trans*- isomers in a constant ratio (13 to 18.5% *cis*; 87 to 81.5% *trans*). It is a white, crystalline powder, with a slight and amine-like odour. It is soluble in 1.5 parts of water, in 1 part of ethanol (96%) and in 2 parts of chloroform, and has a melting point of 185°-191°.

Deptran 10 mg and 25 mg capsules. Both strengths contain the following inactive ingredients: lactose, sodium starch glycollate, purified talc, magnesium stearate, sodium lauryl sulfate, colloidal anhydrous silica, gelatin, titanium dioxide. The 25 mg capsules also contain brilliant blue FCF CI42090 and erythrosine CI45430.

Deptran 50 mg and 75 mg tablets. Both strengths contain the following inactive ingredients: lactose, microcrystalline cellulose, povidone, purified talc, sodium starch glycollate, magnesium stearate, carnauba wax, hypromellose and titanium dioxide. The 50 mg tablets also contain: diethyl phthalate, erythrosine CI45430 and indigo carmine CI73015. The 75 mg tablets contain macrogol 400.

PHARMACOLOGY

Deptran is a dibenzoxepin psychotherapeutic agent. The mechanism of action of doxepin is not definitely known. It is not a CNS stimulant nor a monoamine oxidase (MAO) inhibitor. The current theory is that the clinical effects are due, at least in part, to influences on the adrenergic activity at the synapses so that deactivation of noradrenaline by reuptake into the nerve terminals is prevented.

Animal studies suggest that doxepin hydrochloride does not appreciably antagonise the antihypertensive action of guanethidine. In animal studies, anticholinergic, antiserotonin and antihistamine effects on smooth muscle have been demonstrated. At higher than usual clinical doses, noradrenaline response was potentiated in animals. This effect was not demonstrated in humans.

At clinical dosages up to 150 mg/day, Deptran can be given to man concomitantly with guanethidine and related compounds without blocking the antihypertensive effect. At dosages above 150 mg/day, blocking of the antihypertensive effect of these compounds has been reported.

Pharmacokinetics

Doxepin is readily absorbed from the gastrointestinal tract, and extensively demethylated by first-pass metabolism in the liver, to its primary active metabolite, desmethyldoxepin. Since doxepin slows gastrointestinal transit time, absorption can be delayed, particularly in overdosage.

Paths of metabolism of both doxepin and desmethyldoxepin include hydroxylation, N-oxidation, and conjugation with glucuronic acid.

Doxepin is excreted in the urine, mainly in the form of its metabolites, either free or in conjugated form.

Doxepin and desmethyldoxepin are widely distributed throughout the body and are extensively bound to plasma and tissue protein.

The estimated plasma half-life of doxepin ranges from 8 to 24 hours, and may be considerably extended in overdosage. The half-life of desmethyldoxepin is longer.

Doxepin crosses the blood-brain barrier and the placental barrier.

INDICATIONS

For the treatment of major depression.

The 50 mg and 75 mg tablets are indicated only for the maintenance treatment of major depression (see Precautions).

CONTRAINDICATIONS

Hypersensitivity to tricyclic antidepressants (TCAs), doxepin, or any of the inactive ingredients.

Glaucoma or a tendency to urinary retention, particularly in older patients.

PRECAUTIONS

Therapeutic doses of tricyclic antidepressants have the potential to cause cardiac arrhythmias, and effects on cardiac conduction are dose related. Caution should be exercised in the use of Deptran in patients with cardiac disease.

The dosage of Deptran in patients with intercurrent illness or those taking other medications should be carefully adjusted. This is especially important in patients receiving other medications with anticholinergic effects (see **ADVERSE EFFECTS**).

Impairment of motor coordination.

Patients should be warned of the possibility of drowsiness or motor incoordination occurring with the use of this drug and should therefore be cautioned against driving a car or operating dangerous machinery while taking this drug (see **PRECAUTIONS**, **Effect on Ability to Drive and Use Machines** and **DOSAGE AND ADMINISTRATION**).

Combined use with other antidepressants, alcohol or antianxiety agents should be undertaken with due recognition of the possibility of potentiation (see **INTERACTIONS WITH OTHER MEDICINES**). It is known, for example, that monoamine oxidase (MAO) inhibitors may potentiate other drug effects; therefore,

patients who have been receiving MAO inhibitors should discontinue that therapy for two weeks prior to starting on Deptran.

Should increased symptoms of psychosis or shift to manic symptomatology occur, it may be necessary to reduce dosage or add a major tranquilliser to the dosage regimen.

Bipolar Disorder and Activation of Mania/Hypomania.

A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed that treating such an episode with an antidepressant alone can increase the likelihood of precipitation of a mixed/manic episode in patients at risk of bipolar disorder. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder and depression.

Clinical Worsening and Suicide Risk associated with Psychiatric Disorders.

The risk of suicide attempt is inherent in depression and may persist until significant remission occurs. This risk must be considered in all depressed patients.

Patients with depression may experience worsening of their depressive symptoms and/or the emergence of suicidal ideation and behaviour (suicidality) whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored for clinical worsening and suicidality, especially at the beginning of a course of treatment, or at the time of dose changes, either increases or decreases. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse or whose emergent suicidality is severe, abrupt in onset, or was not part of the patient's presenting symptoms.

Patients (and caregivers of patients) should be alerted about the need to monitor for any worsening of their condition and/or the emergence of suicidal ideation/behaviour or thoughts of harming themselves and to seek medical advice immediately if these symptoms present. Patients with co-morbid depression associated with other psychiatric disorders being treated with antidepressants should be similarly observed for clinical worsening and suicidality.

Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment, are at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment.

Pooled analyses of 24 short-term (4 to 16 weeks), placebo-controlled trials of nine antidepressant medicines (SSRIs and others) in 4400 children and adolescents with major depressive disorder (16 trials), obsessive compulsive disorder (4 trials), or other psychiatric disorders (4 trials) have revealed a greater risk of adverse events representing suicidal behaviour or thinking (suicidality) during the first few months of treatment in those receiving antidepressants. The average risk of such events in patients treated with an antidepressant was 4%, compared with 2% of patients given placebo. There was considerable variation in risk among the antidepressants, but there was a tendency towards an increase for almost all antidepressants studied. The risk of suicidality was most consistently observed in the major depressive disorder trials, but there were signals of risk arising from trials in other psychiatric indications (obsessive compulsive disorder and social anxiety disorder) as well. No suicides occurred in these trials. It is unknown whether the suicidality risk in children and adolescent patients extends to use beyond several months. The nine antidepressant medicines in the pooled analyses included five SSRIs (citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline) and four non-SSRIs (bupropion, mirtazapine, nefazodone, venlafaxine).

A further pooled analysis of short-term placebo-controlled studies of antidepressant medications (SSRIs and others) showed the increased risk of suicidal thinking and behaviour, known as suicidality, in the initial treatment (generally the first one to two months) extends to young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short term studies did now show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond the age of 24 years; there was a reduction with antidepressants compared to placebo in adults aged 65 years and older.

Symptoms of anxiety, agitation, panic attacks, insomnia, irritability, hostility (aggressiveness), impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adults, adolescents and children being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and non-psychiatric. Although a causal link between the emergence of such symptoms and either worsening of depression and/or emergence of suicidal impulses has not been established, there is concern that such symptoms may be precursors of emerging suicidality.

Families and caregivers of children and adolescents being treated with antidepressants for major depressive disorder or for any other condition (psychiatric or non-psychiatric) should be informed about the need to monitor these patients for the emergence of agitation, irritability, unusual changes in behaviour, and other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. It is particularly important that monitoring be undertaken during the initial few months of antidepressant treatment or at times of dose increase or decrease.

Prescriptions for Deptran should be written for the smallest quantity of tablets or capsules consistent with good patient management, in order to reduce the risk of overdose.

Angle Closure Glaucoma

The pupillary dilation that occurs following use of many antidepressant drugs including doxepin may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy.

Severe Morbidity following Overdosage

Major depression carries an inherent and predictable risk of suicide, frequently involving drug overdose. Overdosage with tricyclic antidepressants, including Deptran, may lead to severe morbidity, requiring aggressive supportive therapy, and carries a significant risk of fatal outcome (see **OVERDOSAGE**). In view of this risk, before prescribing any tricyclic antidepressant, including Deptran, doctors should give serious consideration to the use of an antidepressant of a class with less potential for serious morbidity or mortality in the event of overdose. If the decision is made to prescribe Deptran, prescriptions should be written for the smallest feasible amount and patients should be supervised closely during the early course of treatment.

Deptran 50 mg and 75 mg Tablets.

The 50 mg and 75 mg tablets are indicated only for the maintenance treatment of major depression. The 50 mg and 75 mg tablets should not be used in acutely ill patients where there is a risk of suicide. There is an increased risk of completed suicide by overdose with the 50 mg and 75 mg tablets compared with the 10 mg and 25 mg capsules.

The possibility of development of withdrawal symptoms on abrupt cessation of treatment after prolonged doxepin treatment should be borne in mind.

Use in Pregnancy (Category: C)

Tricyclic antidepressants have not been shown to be associated with an increased incidence of birth defects. However there is evidence of interference with central monoamine neurotransmission in rats. Care should be taken to ensure that there are sound reasons for the use of these antidepressants in pregnancy.

Withdrawal symptoms in newborn infants have been reported with prolonged maternal use of this class of drugs.

Use in Lactation

Tricyclic antidepressants have been found in small amounts in breast milk in an approximate milk to plasma ratio of 0.4:1.5. Limited data indicate that doxepin and its active metabolite desmethyldoxepin are excreted in breast milk. There has been a report of apnoea and drowsiness in a nursing infant whose mother was taking doxepin. Because of the potential for adverse effects to the nursing infant, breast-feeding is not recommended during doxepin therapy.

Paediatric Use

The safety and efficacy of Deptran for the treatment of depression or other psychiatric disorders in children and adolescents aged less than 18 years has not been satisfactorily established. Deptran should not be used in this age group for the treatment of depression or other psychiatric disorders.

Use in the Elderly

The dose of Deptran in elderly patients should be adjusted carefully, based on the patient's condition (see also CONTRAINDICATIONS).

Use in Renal and Hepatic Impairment

Deptran should be used with caution in patients with hepatic or renal impairment.

Effects on Ability to Drive and Use Machines

Since drowsiness or motor in-coordination may occur with the use of this drug, patients should be warned of the possibility and cautioned against driving a car or operating dangerous machinery while taking this drug.

Patients should also be cautioned that their response to alcohol may be potentiated.

The possibility of development of withdrawal symptoms on abrupt cessation of treatment after prolonged Deptran treatment should be borne in mind.

INTERACTIONS WITH OTHER MEDICINES

Monoamine oxidase inhibitors.

Serious side effects and even death have been reported following the concomitant use of certain drugs with MAO inhibitors. Therefore, MAO inhibitors should be discontinued at least 2 weeks prior to the cautious initiation of Deptran therapy. The exact length of time may vary and is dependent upon the particular MAO inhibitor being used, the length of time it has been administered, and the dosage involved.

Drugs metabolised by cytochrome P450 2D6.

The biochemical activity of the cytochrome P450 metabolising isoenzyme 2D6 (debrisoquin hydroxylase) is reduced in a subset of the Caucasian population (about 7 to 10%). Such individuals are called poor metabolisers and may have higher than expected plasma concentrations of tricyclic antidepressants when given usual doses.

Cytochrome P450 2D6 inhibitors.

Normal metabolisers may resemble poor metabolisers when given compounds that inhibit cytochrome P450 2D6. The drugs that inhibit cytochrome P450 2D6 include some that are not metabolised by the enzyme (quinidine, cimetidine) and many that are substrates for P450 2D6 (many other antidepressants, phenothiazines and the Type 1C antiarrhythmics propafenone and flecainide). Concomitant use of tricyclic antidepressants with drugs that inhibit cytochrome P450 2D6 may require lower doses than usually prescribed for either the tricyclic antidepressant (TCA) or the other drug. Whenever one of these other drugs is withdrawn from co-therapy, an increased dose of tricyclic antidepressant may be required. It is desirable to monitor TCA plasma levels whenever a TCA is co-administered with a known inhibitor of P450 2D6.

Hepatic enzyme inducers.

Substances that activate the hepatic monooxygenase enzyme system (e.g. barbiturates, phenytoin, carbamazepine) may lower the plasma concentration of tricyclic antidepressants and so reduce their effect. In addition, concomitant administration of a tricyclic antidepressant with phenytoin or carbamazepine may lead to elevated serum phenytoin or carbamazepine concentrations. If necessary, the doses of these drugs should be adjusted.

Selective serotonin reuptake inhibitors.

The selective serotonin reuptake inhibitors (SSRIs), e.g. fluoxetine, sertraline and paroxetine, inhibit P450 2D6 and can elevate tricyclic antidepressant blood levels. The extent to which SSRI-TCA interactions may pose clinical problems will depend on the degree of inhibition and the pharmacokinetics of the SSRI involved. Caution is indicated in the co-administration of tricyclic antidepressants with any of the SSRIs and in switching from one class to the other. Sufficient time must elapse before initiating tricyclic antidepressant treatment in a patient being withdrawn from fluoxetine, given the long half-life of the parent and active metabolite (at least five weeks may be necessary).

Sympathomimetic agents.

The cardiovascular effect of sympathomimetic agents such as adrenaline, noradrenaline and amphetamine (as well as nasal drops and local anaesthetics containing sympathomimetics) may be potentiated by tricyclic antidepressants.

Anticholinergic agents.

Tricyclic antidepressants may have an additive anticholinergic effect when given in combination with anticholinergics or neuroleptics with an anticholinergic action (e.g. phenothiazines); hyperexcitation states or delirium may occur, as well as attacks of glaucoma, urinary retention or paralytic ileus.

Cimetidine.

Cimetidine has been reported to produce clinically significant fluctuations in steady-state serum concentrations of various tricyclic antidepressants. Serious anticholinergic symptoms (i.e. severe dry mouth, urinary retention and blurred vision) have been associated with elevations in the serum levels of tricyclic antidepressants when cimetidine therapy is initiated. Additionally, higher than expected tricyclic antidepressant levels have been observed when they are begun in patients already taking cimetidine. In patients who have been reported to be well controlled on tricyclic antidepressants while receiving concurrent cimetidine therapy, discontinuation of cimetidine has been reported to decrease established steady-state serum tricyclic antidepressant levels and compromise their therapeutic effects.

Alcohol.

It should be borne in mind that alcohol ingestion may increase the danger inherent in any intentional or unintentional doxepin overdosage. This is especially important in patients who may use alcohol excessively.

Antihypertensive agents.

The antihypertensive effects of guanethidine and related agents are reduced or negated by concurrent use with TCAs (see PHARMACOLOGY).

Tolazamide.

A case of severe hypoglycaemia has been reported in a type II diabetic patient maintained on tolazamide (1 g/day) eleven days after the addition of doxepin (75 mg/day).

ADVERSE EFFECTS

Note. Some of the adverse effects noted below have not been specifically reported with doxepin use. However, due to the close pharmacological similarities among the tricyclics, the effects should be considered when prescribing doxepin.

Anticholinergic effects.

Dry mouth, blurred vision, constipation and urinary retention have been reported. If they do not subside with continued therapy, or if the symptoms become severe, it may be necessary to reduce the dose. There have been isolated cases of elevated intraocular pressure.

Central nervous system effects.

The most commonly noticed side effect is drowsiness. This tends to disappear as therapy is continued. Insomnia and nightmares have also been reported. Other infrequently reported CNS side effects are confusion, disorientation, agitation, numbness, tardive dyskinesias, tremor, hallucinations, paraesthesias, ataxia, extrapyramidal symptoms, seizures, anxiety, nervousness and aggressive reaction. An NMS-like syndrome has occurred in a patient with a history of depression with psychotic features treated with a lithium/doxepin combination.

Cardiovascular.

Cardiovascular effects including hypotension, hypertension and tachycardia have been reported occasionally. Changes in ECG parameters (widening of the QRS and PR interval) very rarely.

Allergic.

Skin rash, facial oedema, photosensitisation, urticaria and pruritus have occasionally occurred.

Haematologic.

Eosinophilia has been reported in a few patients. There have been occasional reports of bone marrow depression, manifesting as agranulocytosis, leukopenia, thrombocytopenia and purpura. Haemolytic anaemia.

Gastrointestinal.

Nausea, vomiting, indigestion, taste disturbances, diarrhoea, anorexia and aphthous stomatitis have been reported (see **Anticholinergic effects**).

Endocrine.

Raised or lowered libido, testicular swelling, gynaecomastia in males, enlargement of breasts and galactorrhoea in females, syndrome of inappropriate antidiuretic hormone secretion and raising or lowering of blood sugar levels have been reported with tricyclic administration.

Other.

Dizziness, tinnitus, headache, weight gain, sweating, chills, fatigue, weakness, flushing, jaundice alopecia, headache, exacerbation of asthma and hyperpyrexia (in association with chlorpromazine) have been occasionally observed. Rare reports of hepatitis, hepatic abnormalities and increased appetite.

The following adverse events have been identified from the post-marketing experience:

Central Nervous System Effects:

Disorientation, hallucinations, tardive dyskinesia, hypoaesthesia, dysgeusia and convulsion.

Cardiovascular:

Hypertension, conduction disorders and arrhythmias.

Allergic:

Facial oedema, photosensitisation, urticaria and tongue oedema.

Haematologic:

Eosinophilia, bone marrow depression manifesting s agranulocytosis, leukopenia, thrombocytopenia and purpure.

Gastrointestinal:

Upper abdominal pain and aphthous stomatitis.

Endocrine:

Testicular swelling, Gynaecomastia (in males), galactorrhoea (in females), syndrome of inappropriate ADH secretion and raised blood sugar level.

Withdrawal symptoms:

Abrupt cessation of treatment after prolonged administration may produce nausea, headache and malaise. These are not indicative of addiction and gradual withdrawal of Deptran should not cause these symptoms.

Other:

Jaundice, alopecia, mydriasis, angle closure glaucoma and hyperpyrexia (in association with chlorpromazine).

DOSAGE AND ADMINISTRATION

The optimum oral dose depends on the severity of the condition and the individual patient's response. The dose varies from 30 mg to 300 mg daily, and is usually administered in a three times daily regimen. When the optimum dose has been reached, it may be given as a single daily dose up to a maximum of 150 mg.

For patients where the presenting symptoms are mild, it is advisable to initiate treatment at a dose of 30 mg daily; a good clinical response is obtained in many of these patients at a daily dose of 30 to 50 mg. The dosage may be adjusted according to the individual response.

For the majority of patients with moderate or severe symptoms, it is recommended that treatment commences with an initial dose of not more than 75 mg daily in divided doses. Many of these patients will respond satisfactorily at this dose level. For patients who do not respond at this dose level, the dosage may be adjusted according to individual response. In more severely ill patients, particularly where depression is the predominant presenting symptom, it may be necessary to administer a dose of up to 300 mg a day in divided doses to obtain a clinical response. This dosage is not intended for initiation of treatment.

Where insomnia is a troublesome symptom, it is recommended that after initial titration as discussed above, the total daily dose be divided so that a higher proportion but not more than 150 mg is given for the evening dose. A single daily dose of up to 150 mg may be given in the evening once the optimum daily dose has been reached. Similarly, should daytime drowsiness be experienced as a side effect of treatment, the same routine should be adopted, or the dosage may be reduced (see **PRECAUTIONS**).

It is often possible in the individual patient to reduce the dose for maintenance therapy, having already obtained a satisfactory therapeutic response.

Dosage reduction may be required in elderly patients and in patients with hepatic impairment.

Optimal antidepressant effect may not be evident for two to three weeks whereas the antianxiety effect should be evident sooner.

OVERDOSAGE

Deaths may occur from overdosage with tricyclic antidepressants including doxepin, with the ingestion of 15 to 20 mg/kg or more being potentially fatal. Because of its rapid absorption and the onset of cardiac and central nervous system toxicity, the patient should be brought to hospital as soon as possible for immediate monitoring and treatment.

Multiple drug ingestion (including alcohol) is common in deliberate tricyclic antidepressant overdose. As the management is complex and changing, it is recommended that the physician contact the Poisons Information Centre on 131126 for current information and treatment.

Signs and Symptoms

Symptoms and signs at presentation depend upon the dose and the time since ingestion. The rapid absorption of TCAs can cause a patient with initially trivial symptoms to deteriorate and develop life threatening toxicity rapidly. Patients who are asymptomatic at three hours post ingestion do not normally develop major toxicity. Mild toxicity is commonly manifested by anticholinergic effects such as drowsiness, blurred vision and excessive dryness of mouth.

However, major toxicity can develop rapidly within 6 hours resulting in severe neurologic, anticholinergic and cardiovascular syndromes including: respiratory depression, mental status changes, delirium, convulsions, seizures, CNS depression (including coma), cardiac dysrhythmias (tachycardia is a common anticholinergic and early sympathomimetic effect, supraventricular and ventricular tachycardias, AV block, torsade de pointes and ventricular fibrillation), hypotension and ECG changes (such as QRS widening and QTc prolongation).

Other signs may also include: confusion, disturbed concentration, transient visual or auditory hallucinations, agitation, stupor, urinary retention (bladder atony), decreased gastrointestinal motility (paralytic ileus), hyperthermia or hypothermia, hyperpyrexia, dilated pupils, hyperreflexia, muscle rigidity and vomiting.

Management and Treatment

Where the dose taken is known to be low (<5 mg/kg) and manifested only by mild symptoms, ECG monitoring, supportive therapy, and observation for signs of CNS or respiratory depression and cardiovascular effects for at least 6 hours may be all that is necessary. If signs of toxicity occur at any time during this period, extended monitoring is recommended.

Severe toxicity must be suspected if overdosage is unknown, complicated by intake of alcohol or multiple drugs, or when symptoms have deteriorated. A maximal limb-lead QRS duration of ≥ 0.10 seconds may be the best indication.

Management should include cardiac monitoring to detect ECG abnormalities, establishing an intravenous line (normal saline) and securing the patient's airway. Activated charcoal my reduce absorption of the drug if given within one to two hours after ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via a nasogastric tube ensuring that the airway is protected. Emesis is not indicated since rapid neurologic and haemodynamic deterioration may occur.

Cardiovascular Effects:

CV effects may be reserved by use of intravenous hypertonic sodium bicarbonate to maintain the serum pH at 7.45 to 7.55. If the pH response is inadequate, hyperventilation may also be used, but extreme caution must be taken if conducted concomitantly so that pH > 7.60 or a pCO_2 < 20 mm Hg is avoided.

All class 1a and 1c antiarrhythmic drugs are contraindicated, whilst class 1b drugs may also exacerbate arrhythmias and the sodium channel blockade.

In rare instances, haemoperfusion may be beneficial in acute refractory cardiovascular instability in patients with acute toxicity. However, haemodialysis, peritoneal dialysis, exchange transfusions and forced diuresis are of little benefit due to high tissue and protein binding to doxepin.

Cardiovascular effects may persist beyond 48 hours.

CNS Depression:

In patients with CNS depression, early intubation is advised because of the potential for abrupt deterioration. Seizures should be controlled with benzodiazepines or if ineffective, by anticonvulsants (e.g. phenobarbitone, phenytoin). Because of its potentially fatal adverse effects. physostigmine is not recommended except to treat

life-threatening symptoms that have been unresponsive to other therapies. Physostigmine should only be used in consultation with the Poisons Information Centre.

Neurologic effects may persist for 24 to 48 hours.

Follow-up:

Since overdosage is often deliberate, patients may attempt suicide by other means during the recovery phase, therefore psychiatric referral may be appropriate.

In cases of overdosage, it is advisable to contact the Poisons Information Centre (131126) for recommendation on the management and treatment of overdosage.

PRESENTATION AND STORAGE CONDITIONS

Deptran 10	10 mg doxepin capsule: white opaque; 50's in PVC/PVDC/Al blister pack. Store below 25°C
Deptran 25	25 mg doxepin capsule: white opaque body, blue cap; 10's*, 50's, 90's or 100's in PVC/PVDC/Al blister pack. Store below 25°C
Deptran 50	50 mg doxepin tablet: violet film coated, hexagonal, marked "DN" over "50" on one side, "α" on reverse; 10's*, 50's or 1000's* in PVC/PVDC/Al blister pack. Store below 30°C
Deptran 75	75 mg doxepin tablet: white film coated, hexagonal, marked "DN" break line "75" on one side, "α" on reverse; 30's in PVC/PVDC/Al blister pack. Store below 30°C

* Not marketed in Australia

NAME AND ADDRESS OF THE SPONSOR

Alphapharm Pty Limited

ABN 93 002 359 739

Level 1, 30 The Bond

30-34 Hickson Road

Millers Point NSW 2000

www.alphapharm.com.au

POISON SCHEDULE OF THE MEDICINE

S4 – Prescription Only Medicine

DATE OF FIRST INCLUSION ON THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)

Deptran 10 and 25 – 02/07/1997

Deptran 50 – 20/09/1991

Deptran 75 – 19/10/1992

DATE OF MOST RECENT AMENDMENT

05/02/2016

Deptran_ pi\Dec15/00