

# **AUSTRALIAN PRODUCT INFORMATION - SINEQUAN<sup>®</sup> (doxepin (as hydrochloride)) capsules**

## **1 NAME OF THE MEDICINE**

Doxepin (as hydrochloride)

## **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

SINEQUAN capsules contain doxepin hydrochloride equivalent to 10 mg and 25 mg of doxepin.

### **Excipient with known effect**

Each 10 mg and 25 mg capsule contains lactose monohydrate. For the full list of excipients, see Section 6.1 List of excipients.

## **3 PHARMACEUTICAL FORM**

Capsule, hard

SINEQUAN 10 mg capsules are supplied as natural, size #4 capsules printed with “Sinequan 10” and the Pfizer logo. The capsules contain a white, homogenous powder free from foreign matter.

SINEQUAN 25 mg capsules are supplied as natural, size #4 capsules printed with “Sinequan 25” and the Pfizer logo. The capsules contain a white, homogenous powder free from foreign matter.

## **4 CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

Treatment of major depression

### **4.2 Dose and method of administration**

The optimum oral dose depends on the severity of the condition and the individual patient's response. The dose varies from 30 to 300 mg daily.

The daily dose is usually administered on t.i.d. 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 whose presenting symptoms are mild in nature, 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 dose 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, the dose 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.

When 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 if daytime drowsiness is experienced as a side effect of treatment, Sinequan may be administered by this regimen, or the dose may be reduced (see Section 4.4 Special warnings and precautions for use).

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

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

Anti-anxiety effect is apparent before the antidepressant effect. Optimal antidepressant effect may not be evident for two to three weeks.

### **4.3 Contraindications**

Sinequan (doxepin hydrochloride) is contraindicated in individuals who have shown hypersensitivity to TCAs (tricyclic antidepressants), doxepin, or any of the inactive ingredients.

Sinequan is contraindicated in patients with glaucoma or a tendency to urinary retention. These disorders should be ruled out, particularly in older patients.

### **4.4 Special warnings and precautions for use**

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 Sinequan in patients with cardiac disease.

The dosage of Sinequan 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 Section 4.8 Adverse effects).

Patients should be warned that drowsiness may occur with the use of this drug (see Section 4.7 Effects on Ability to Drive and Use Machines and Section 4.2 Dose and method of administration).

Combined use with other antidepressants, alcohol or anti-anxiety agents should be undertaken with due recognition of the possibility of potentiation (see Section 4.5 Interactions with other medicines and other forms of interactions). It is known, for example, that monoamine oxidase inhibitors may potentiate other drug effects; therefore, patients who have been receiving MAO inhibitors should have that therapy discontinued two weeks prior to receiving Sinequan.

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 behaviours (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.

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 initial treatment period (generally the first one to two months) in those receiving antidepressants. The average risk of such events in patients treated with an antidepressant was 4% compared with 2% of patients with 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 adolescents 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 trials of antidepressant medicines (SSRIs and others) showed the increased risk of suicidal thinking and behaviour (suicidality) during the initial treatment period (generally the first one to two months) extends to young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. These studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 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 Sinequan should be written for the smallest quantity of 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

Overdosage with tricyclic antidepressants, including Sinequan, may lead to severe morbidity, requiring aggressive supportive therapy, and carries a significant risk of fatal outcome (see Section 4.9 Overdose). In view of this risk, before prescribing any tricyclic antidepressant, including Sinequan, clinicians 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 Sinequan, prescriptions should be written for the smallest feasible amount and patients should be supervised closely during the early course of treatment.

### Use in Renal and Hepatic Impairment

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

## Use in the Elderly

The dose of Sinequan in elderly patients should be adjusted carefully, based on the patient's condition (see also Section 4.3 Contraindications).

## Paediatric Use

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

## 4.5 Interactions with other medicines and other forms of interactions

### MAO 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 two weeks prior to the cautious initiation of therapy with Sinequan. The exact length of time may vary and is dependent on 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 7-10%). 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.

### 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 5 weeks may be necessary).

## **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.

## **Sympathomimetic Agents**

The cardiovascular effect of sympathomimetic agents such as adrenaline, nonadrenaline 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, discontinuation of cimetidine has been reported to decrease established steady-state tricyclic antidepressant levels and compromise their therapeutic effects.

## **Alcohol**

Patients should be cautioned that their response to alcohol may be potentiated. It should be borne in mind that alcohol ingestion may increase the danger inherent in any intentional or unintentional Sinequan overdose. 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 Section 5 Pharmacological properties).

## **Tolazamide**

A case of severe hypoglycaemia has been reported in a type II diabetic patient maintained on tolazamide (1 g/day) 11 days after the addition of doxepin (75 mg/day).

## **4.6 Fertility, pregnancy and lactation**

### **Effects on Fertility**

No data available

### **Use in Pregnancy – 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.

### **Use in Lactation**

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 Sinequan. Because of potential for adverse effects to the nursing infant, breast-feeding is not recommended during doxepin therapy.

## **4.7 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 Sinequan treatment should be borne in mind.

## **4.8 Adverse effects (undesirable effects)**

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

### **Anticholinergic Effects**

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

### **Central Nervous System Effects**

Drowsiness is the most commonly noticed side effect. This tends to disappear as therapy is continued. Insomnia and nightmares have also been reported. Other infrequently reported CNS side effects are confusion, agitation, numbness, paraesthesia, ataxia, extrapyramidal symptoms, seizures, tremor, 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 and tachycardia have been reported occasionally. Changes in ECG parameters (widening of the QRS and PR interval) very rarely.

#### Allergic

Skin rash, pruritus and hyperhidrosis have occasionally occurred.

#### Haematologic

Haemolytic anaemia has been reported.

#### Gastrointestinal

Nausea, vomiting, indigestion, dyspepsia, taste disturbances, diarrhoea and anorexia have been reported (see Anticholinergic Effects above).

#### Endocrine

Raised or lowered libido, enlargement of breasts (in females) and lowering of blood sugar levels have been reported with tricyclic administration.

#### Others

Dizziness, tinnitus, weight gain, sweating, chills, fatigue, asthenia, weakness, flushing, headache, and exacerbation of asthma have been occasionally observed as adverse effects. Hepatitis, hepatic abnormalities, increased appetite rarely.

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 as agranulocytosis, leukopenia, thrombocytopenia and purpura.

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 Sinequan should not cause these symptoms.



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

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at <http://www.tga.gov.au/reporting-problems>.

## 4.9. Overdose

Deaths may occur from overdosage with tricyclic antidepressants including doxepin, with the ingestion of 15-20 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. For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

### 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, hypertension, 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  $\geq 0.10$  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 may

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 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 reversed by use of intravenous hypertonic sodium bicarbonate to maintain the serum pH at 7.45 - 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<sub>2</sub> <20 mm Hg is avoided.

All class 1a and 1c antiarrhythmic drugs are contraindicated, whilst class 1b drugs may 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 of 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 Poison 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.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

#### Mechanism of action

The mechanism of action of doxepin hydrochloride is not definitely known. It is not a central nervous system stimulant nor a monoamine oxidase inhibitor. The current hypothesis 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 terminal is prevented.

Animal studies suggest that doxepin hydrochloride does not appreciably antagonize 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.

### **Clinical trials**

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

## **5.2 Pharmacokinetic properties**

No data available

## **5.3 Preclinical safety data**

### **Genotoxicity**

No data available

### **Carcinogenicity**

No data available

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

The 10 mg capsules contain Maize starch; Lactose monohydrate; Magnesium stearate; Sodium lauryl sulfate; Gelatin and TekPrint SW-9008 Black Ink (PI 2328)..

The 25 mg capsules contain Maize starch; Lactose monohydrate; Magnesium stearate; Sodium lauryl sulfate; Gelatin and TekPrint SW-9008 Black Ink (PI 2328)..

### **6.2 Incompatibilities**

Incompatibilities were not assessed or not identified as part of the registration of this medicine.

### 6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

### 6.4 Special precautions for storage

Store below 25°C. Protect from light.

### 6.5 Nature and contents of container

Capsules, 10 mg and 25 mg in blister packs composed of clear PVC film with aluminium foil backing containing 50 capsules.

### 6.6 Special precautions for disposal

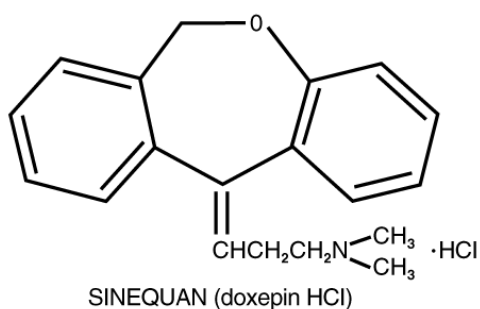
In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

### 6.7 Physicochemical properties

Doxepin hydrochloride is a dibenzoxepin derivative, and consists of a mixture of the *cis* and *trans* isomers in a constant ratio (82-85% *trans*: 15-18% *cis*). It is a white crystalline solid, readily soluble in water, lower alcohols and chloroform.

Chemical structure

The structural formula is shown below:



CAS number: 1229-29-4

## 7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 (Prescription Only Medicine)

## 8 SPONSOR

Pfizer Australia Pty Ltd  
Level 17, 151 Clarence Street  
Sydney NSW 2000  
Toll Free Number: 1800 675 229  
[www.pfizer.com.au](http://www.pfizer.com.au)

## 9 DATE OF FIRST APPROVAL

19 July 1991.

## 10 DATE OF REVISION

29 August 2019

® Registered trademark.

### Summary Table of Changes

Section changes	Summary of new information
8	Update to sponsor address