

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use SINEQUAN® safely and effectively. See full prescribing information for SINEQUAN.

SINEQUAN (doxepin hydrochloride) capsules, for oral use

SINEQUAN (doxepin hydrochloride) oral solution

Initial U.S. Approval: 1969

### WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

See full prescribing information for complete boxed warning.

- **Increased risk of suicidal thoughts and behaviors in pediatric and young adults taking antidepressants. Closely monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors (5.1)**
- **SINEQUAN is not approved for use in pediatric patients (8.4)**

### RECENT MAJOR CHANGES

Dosage and Administration (2.4, 2.5, 2.6, 2.7, 2.8) 7/2025

Warnings and Precautions (5.2, 5.5) 7/2025

### INDICATIONS AND USAGE

SINEQUAN is a tricyclic antidepressant (TCA) indicated for the treatment of major depressive disorder (MDD) in adults (1).

### DOSAGE AND ADMINISTRATION

- Prior to initiating treatment with SINEQUAN, screen patients for a personal or family history of bipolar disorder, mania, or hypomania. (2.1)
- Recommended starting oral dosage is 25 mg three times daily or 75 mg once daily. (2.2)
- Recommended target total dosage range is between 75 mg/day and 150 mg/day (may be given once daily or in divided doses). (2.2)
- Maximum recommended dosage is 100 mg three times daily. (2.2)
- Wait at least 14 days after discontinuation of a monoamine oxidase inhibitor (MAOI) before initiating therapy with SINEQUAN. (2.3)
- See the Full Prescribing Information for dosage modifications intended to reduce the risk of anticholinergic effects, for strong CYP2D6 inhibitors, and in known CYP2D6 and CYP2C19 poor metabolizers. (2.4, 2.5, 2.6).
- When discontinuing SINEQUAN, gradually reduce the dosage until discontinued. (2.7)
- See Full Prescribing Information for recommended preparation instructions for the oral solution. (2.8)

### DOSAGE FORMS AND STRENGTHS

- Capsules: 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, and 150 mg (3)
- Oral solution: 10 mg per mL (3)

### CONTRAINDICATIONS

- Hypersensitivity to doxepin (4)
- Glaucoma (4)
- Current or past urinary retention (4)
- Taking MAOIs, or within 14 days of stopping MAOIs (4)

### WARNINGS AND PRECAUTIONS

- **Suicidal Thoughts and Behaviors:** Monitor for clinical worsening and suicide thoughts and behaviors. Consider changing the therapeutic regimen,

including possibly discontinuing SINEQUAN, in patients who are experiencing emergent suicidal thoughts or behaviors. (5.1)

- **Serotonin Syndrome:** Risk increases with concomitant use of other serotonergic drugs. Monitor all patients taking SINEQUAN for the emergence of serotonin syndrome. Discontinue SINEQUAN and any concomitant serotonergic agents immediately and initiate supportive treatment if serotonin syndrome occurs. (5.2, 7)
- **Angle-Closure Glaucoma:** Avoid use of SINEQUAN in patients with untreated anatomically narrow angles. (5.3)
- **Sedation and Driving Risks:** Because SINEQUAN can cause sedation, warn patients against driving a car or operating dangerous machinery while taking SINEQUAN. (5.4)
- **Activation of Mania or Hypomania:** Prior to initiating antidepressant therapy, screen for bipolar disorder. SINEQUAN is not approved for use in treating bipolar depression. (5.5)

### ADVERSE REACTIONS

Most common adverse reactions (incidence  $\geq$  5%) are somnolence, dry mouth, dizziness, constipation and fatigue. (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

- **Serotonergic Drugs:** Monitor patients for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increases. If serotonin syndrome occurs, consider discontinuation of SINEQUAN and/or concomitant serotonergic drugs. (5.2, 7)
- **Strong CYP2D6 Inhibitors:** Concomitant use of TCAs with drugs that can inhibit CYP2D6 may require lower dosages for the TCA or the other drug, and monitor TCA plasma levels. (7)
- **Carbamazepine:** Monitor doxepin plasma concentrations and increase SINEQUAN dosage in patients taking carbamazepine. (7)
- **Cimetidine:** Monitor doxepin plasma concentrations and consider reducing the SINEQUAN dosage in patients taking cimetidine. (7)
- **Alcohol:** Avoid concomitant use. (7)
- **CNS Depressants:** Dosage reduction may be needed based on clinical response and tolerability. (7)
- **Tolazamide:** Monitor glucose levels and reduce the SINEQUAN dosage as appropriate. (7)

### USE IN SPECIFIC POPULATIONS

- **Pregnancy:** Neonates exposed to TCAs, including SINEQUAN, late in the third trimester have developed poor adaptation (respiratory distress, temperature instability, feeding difficulty, hypotonia, irritability). Monitor neonates who were exposed to SINEQUAN in the third trimester of pregnancy for poor neonatal adaptation syndrome. (8.1)
- **Lactation:** Breastfeeding not recommended. (8.2)
- **Geriatric Use:** May cause confusion and oversedation. (8.5)
- **CYP2C19 and CYP2D6 Poor Metabolizers:** Increased risk of SINEQUAN-associated adverse reactions. (8.7)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 7/2025

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## FULL PRESCRIBING INFORMATION

### WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

**Antidepressants increase the risk of suicidal thoughts and behavior in pediatric and young adult patients in short-term studies. Closely monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors [see Warnings and Precautions (5.1)]. SINEQUAN is not approved for use in pediatric patients [see Use in Specific Populations (8.4)].**

## 1 INDICATIONS AND USAGE

SINEQUAN is indicated for the treatment of major depressive disorder (MDD) in adults.

## 2 DOSAGE AND ADMINISTRATION

### 2.1 Screen for Bipolar Disorder Prior to Starting SINEQUAN

Prior to initiating treatment with SINEQUAN, screen patients for a personal or family history of bipolar disorder, mania, or hypomania [see Warnings and Precautions (5.5)].

### 2.2 Recommended Dosage

The recommended starting oral dosage for SINEQUAN is 25 mg three times daily or 75 mg once daily. The recommended target total oral dosage range for SINEQUAN is between 75 mg/day and 150 mg/day (may be given once daily or in divided doses). The maximum recommended oral dosage for SINEQUAN is 100 mg three times daily.

### 2.3 Switching Patients to or from a Monoamine Oxidase Inhibitor

Wait at least 14 days after discontinuation of a monoamine oxidase inhibitor (MAOI) before initiating therapy with SINEQUAN [see Contraindications (4), Warnings and Precautions (5.2), and Drug Interactions (7)].

Wait at least 14 days after discontinuation of SINEQUAN before initiating therapy with an MAOI [see Contraindications (4.4), Warnings and Precautions (5.2), and Drug Interactions (7)].

### 2.4 Dosage Modifications Intended to Reduce the Risk of Anticholinergic Effects

If anticholinergic effects (e.g., dry mouth, blurred vision, constipation) develop, reduce the SINEQUAN dosage [see Adverse Reactions (6.1)].

### 2.5 Dosage Modifications for Strong CYP2D6 Inhibitors

Reduce the SINEQUAN dosage based on doxepin plasma concentrations when used concomitantly with strong CYP2D6 inhibitors [see Drug Interactions (7)].

### 2.6 Dosage Modifications in Known CYP2D6 and CYP2C19 Poor Metabolizers

Reduce the SINEQUAN dosage based on doxepin plasma concentrations in patients who are known CYP2D6 and CYP2C19 poor metabolizers [see

*Use in Specific Populations (8.7)].*

## 2.7 Discontinuation of SINEQUAN Treatment

When discontinuing SINEQUAN, gradually reduce the dosage until discontinued [see *Adverse Reactions (6)*].

## 2.8 Preparation of SINEQUAN Oral Solution

Recommended preparation instructions for the SINEQUAN oral solution are as follows:

- Use the supplied calibrated dropper to measure the amount of SINEQUAN oral solution needed. The calibrated dropper has markings at 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg.
- Just prior to administration, mix SINEQUAN with 120 mL of water, whole or skimmed milk, or orange, grapefruit, tomato, prune, or pineapple juice. Do not mix with other liquids.
- Administer the dose immediately after mixing.

## 3 DOSAGE FORMS AND STRENGTHS

Capsules:

- 10 mg, scarlet opaque top, pink opaque body, imprinted in black with “Roerig 534” and “SINEQUAN”
- 25 mg, blue opaque top, pink opaque body, imprinted in black with “Roerig 535” and “SINEQUAN”
- 50 mg, pink opaque top, flesh opaque body, imprinted in black with "Roerig 536" and “SINEQUAN”
- 75 mg, flesh opaque top, flesh opaque body, imprinted in black with "Roerig 539" and “SINEQUAN”
- 100 mg, blue opaque top, flesh opaque body, imprinted in black with “Roerig 538” and “SINEQUAN”
- 150 mg, blue opaque top, blue opaque body, imprinted in black with “Roerig 537” and “SINEQUAN”

Active ingredients in the capsules include: 10 mg, 25, mg, 50 mg, 75 mg, 100 mg, and 150 mg of doxepin.

Oral solution: Each mL of oral solution contains 10 mg of doxepin as a clear, colorless solution for dilution prior to administration [see *Dosage and Administration (2.8)*]. Supplied as a 120 mL bottle with accompanying calibrated dropper with 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg markings.

## 4 CONTRAINDICATIONS

SINEQUAN is contraindicated in patients:

- With hypersensitivity to doxepin (hypersensitivity reactions have included tongue edema and urticaria). The possibility of cross sensitivity with other dibenzoxepines should be kept in mind.
- With glaucoma [see *Warnings and Precautions (5.3)*].

- With current or past urinary retention [see *Adverse Reactions (6.1)*].
- Taking MAOIs, or within 14 days of stopping MAOIs (including the MAOIs linezolid or intravenous methylene blue) because of an increased risk of serotonin syndrome [see *Warnings and Precautions (5.2) and Drug Interactions (7)*].

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Suicidal Thoughts and Behaviors in Adolescents and Young Adults

In pooled analyses of placebo-controlled trials of antidepressant drugs including tricyclic antidepressants and other antidepressant classes that included approximately 77,000 adult patients and 4,500 pediatric patients (SINEQUAN is not approved for use in pediatric patients), the incidence of suicidal thoughts and behaviors in antidepressant-treated patients age 24 years and younger was greater than in placebo-treated patients. There was considerable variation in risk of suicidal thoughts and behaviors among drugs, but there was an increased risk identified in young patients for most drugs studied. The drug-placebo differences in the number of cases of suicidal thoughts and behaviors per 1,000 patients treated are provided in Table 1.

**Table 1: Risk Differences of the Number of Patients of Suicidal Thoughts and Behaviors in the Pooled Placebo-Controlled Trials of Antidepressants in Pediatric and Adult Patients**

Age Range	Drug-Placebo Difference in Number of Patients of Suicidal Thoughts or Behaviors per 1,000 Patients Treated
	<b>Increases Compared to Placebo</b>
< 18 years old	14 additional patients
18-24 years old	5 additional patients
	<b>Decreases Compared to Placebo</b>
25-64 years old	1 fewer patient
≥ 65 years old	6 fewer patients

It is unknown whether the risk of suicidal thoughts and behaviors in pediatric and young adults extends to longer-term use, i.e., beyond four months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with MDD that antidepressants delay the recurrence of depression.

Monitor all SINEQUAN-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of SINEQUAN therapy, and at times of dosage changes. Counsel family members or caregivers of patients to monitor for changes in behavior and to alert the health care provider. Consider changing the therapeutic regimen, including possibly discontinuing SINEQUAN, in patients who are experiencing emergent suicidal thoughts or behaviors.

### 5.2 Serotonin Syndrome

Tricyclic antidepressants, including SINEQUAN, can precipitate serotonin syndrome, a potentially life-threatening condition. This risk is increased with concomitant use of other serotonergic drugs (e.g., other tricyclic antidepressants, SSRIs, serotonin norepinephrine reuptake inhibitors, triptans, tetracyclic antidepressants, opioids), lithium, tryptophan, buspirone,

and St. John's Wort) and with drugs that impair metabolism of serotonin (e.g., MAOIs intended to treat psychiatric disorders and others, such as linezolid or intravenous methylene blue) [see *Drug Interactions (7)*].

Serotonin syndrome symptoms may include mental status changes (e.g., confusion, agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia, diaphoresis, and flushing), neuromuscular abnormalities (e.g., tremor, rigidity, clonus, and hyperreflexia), seizures and gastrointestinal signs and symptoms (e.g., nausea, vomiting, diarrhea). Patients should be monitored for the emergence of serotonin syndrome.

The concomitant use of SINEQUAN with MAOIs is contraindicated. The use of SINEQUAN within 14 days of discontinuing treatment with an MAOI intended to treat psychiatric disorders is contraindicated. Starting SINEQUAN in a patient who is being treated with an MAOI such as linezolid or intravenous methylene blue is contraindicated. No reports involved the administration of methylene blue by other routes (such as oral or local tissue injection). If it is necessary to initiate treatment with a MAOI such as linezolid or intravenous methylene blue in a patient taking SINEQUAN, discontinue SINEQUAN before initiating treatment with the MAOI [see *Dosage and Administration (2.4)* and *Drug Interactions (7.1)*].

Monitor all patients taking SINEQUAN for the emergence of serotonin syndrome. Discontinue SINEQUAN treatment and any concomitant serotonergic agents immediately if the above symptoms occur, and initiate supportive symptomatic treatment. If concomitant use of SINEQUAN with other serotonergic drugs (besides MAOIs which are contraindicated) is clinically warranted, inform patients of the increased risk for serotonin syndrome and monitor for symptoms.

### **5.3 Angle-Closure Glaucoma**

The pupillary dilation that occurs following use of many antidepressant drugs including SINEQUAN may trigger an angle closure glaucoma attack in a patient with anatomically narrow angles who does not have a patent iridectomy. Patients may wish to be examined to determine whether they are susceptible to angle closure, and have a prophylactic procedure (e.g., iridectomy), if they are susceptible.

SINEQUAN is contraindicated in patients with glaucoma. Avoid use of SINEQUAN in patients with untreated anatomically narrow angles.

### **5.4 Sedation and Driving Risks**

Because SINEQUAN can cause sedation, warn patients of the risk of sedation and caution patients against driving a car or operating dangerous machinery while taking SINEQUAN. Also caution patients that their response to alcohol may be potentiated.

Sedating drugs, including SINEQUAN, may cause oversedation in geriatric patients.

### **5.5 Activation of Mania or Hypomania**

In patients with bipolar disorder, treating MDD with SINEQUAN may precipitate a mixed/manic episode. Prior to initiating treatment with SINEQUAN, screen patients for any personal or family history of bipolar disorder, mania, or hypomania. SINEQUAN is not approved for use in treating bipolar depression.

### 5.6 Risk of Seizures

Caution should be used when SINEQUAN is given to patients with a history of seizure disorder, because this drug may lower the seizure threshold. Patients with a history of seizures should be monitored during SINEQUAN use to identify recurrence of seizures or increase in frequency of seizures.

### 5.7 Psychosis

In patients with schizophrenia, treatment with SINEQUAN for MDD may activate psychosis. If this occurs, stop SINEQUAN and consider alternative treatment options.

## 6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Suicidal Thoughts and Behaviors in Adolescents and Young Adults [*see Warnings and Precautions (5.1)*]
- Serotonin Syndrome [*see Warnings and Precautions (5.2)*]
- Angle-Closure Glaucoma [*see Warnings and Precautions (5.3)*]
- Sedation and Driving Risks [*see Warnings and Precautions (5.4)*]
- Activation of Mania or Hypomania [*see Warnings and Precautions (5.5)*]
- Risk of Seizures [*see Warnings and Precautions (5.6)*]
- Psychosis [*see Warnings and Precautions (5.7)*]

### 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adverse reactions ( $\geq 2\%$  of SINEQUAN-treated patients) in 1,635 SINEQUAN-treated patients with MDD in clinical trials included somnolence (17%), dry mouth (15%), dizziness (6%), constipation (5%), fatigue (5%), blurred vision (3%), tachycardia (3%), hypotension (3%), insomnia (2%), tremor (2%), nausea (2%), hyperhidrosis (2%), and increased weight (2%).

#### Other Adverse Reactions Observed in Clinical Trials

Other adverse reactions that occurred at an incidence of  $< 2\%$  in patients treated with SINEQUAN in clinical trials were:

- *Ear and Labyrinth Disorders*: Tinnitus.
- *Gastrointestinal Disorders*: Diarrhea, dyspepsia, vomiting.
- *General Disorders and Administration Site Conditions*: Asthenia, edema, chills.
- *Metabolism and Nutrition Disorders*: Decreased appetite.
- *Nervous System Disorders*: Ataxia, paresthesia, headache, extrapyramidal disorder.

- *Psychiatric Disorders*: Agitation, confusional state, libido decreased.
- *Pulmonary Disorders*: Asthma exacerbation.
- *Renal and Urinary Disorders*: Urinary retention.
- *Reproductive System and Breast Disorders*: Breast enlargement.
- *Skin & Subcutaneous Tissue Disorders*: Rash, pruritus.
- *Vascular Disorders*: Flushing.

## 6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of SINEQUAN. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- *Blood and Lymphatic System Disorders*: Agranulocytosis, leukopenia, thrombocytopenia, eosinophilia, purpura.
- *Cardiac Disorders*: Conduction disorder, arrhythmia.
- *Endocrine Disorders*: Inappropriate antidiuretic hormone secretion.
- *Eye Disorders*: Angle-closure glaucoma, mydriasis.
- *Gastrointestinal Disorders*: Aphthous stomatitis, abdominal pain upper.
- *General Disorders and Administration Site Conditions*: Facial edema, hyperpyrexia.
- *Hepatobiliary Disorders*: Jaundice.
- *Investigations*: Blood glucose increased.
- *Nervous System Disorders*: Hypoesthesia, dysgeusia, convulsion, tardive dyskinesia, serotonin syndrome.
- *Psychiatric Disorders*: Hallucination, disorientation.
- *Reproductive System and Breast Disorders*: Testicular swelling, gynecomastia, galactorrhea.
- *Skin and Subcutaneous Tissue Disorders*: Photosensitivity reaction, tongue edema, alopecia, urticaria.
- *Vascular Disorders*: Hypertension.

Withdrawal syndrome occurred after stopping SINEQUAN [*see Drug Abuse and Dependence (9.3)*].

The following adverse reaction has been reported with use with other tricyclic antidepressants: decreased blood glucose.

## 7 DRUG INTERACTIONS

Table 2 describe the clinically significant drug interactions of SINEQUAN with other drugs or classes.

**Table 2: Clinically Significant Drug Interactions with SINEQUAN**

<b>Monoamine Oxidase Inhibitors</b>	
<i>Prevention or Management</i>	SINEQUAN is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs), including MAOIs such as linezolid or intravenous methylene blue. The use of SINEQUAN within 14 days of discontinuation of an MAOI or the use of MAOI within 14 days of discontinuation of SINEQUAN is contraindicated. Starting SINEQUAN in a patient who is being treated with an MAOI is contraindicated.
<i>Clinical Effect(s)</i>	Concomitant use of SINEQUAN and MAOIs increases the risk of serotonin syndrome [ <i>Warnings and Precautions (5.2)</i> ].
<b>Other Serotonergic Drugs (Besides MAOIs)</b>	
<i>Prevention or Management</i>	Monitor patients for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increases. If serotonin syndrome occurs, consider discontinuation of SINEQUAN and/or concomitant serotonergic drugs [ <i>see Warnings and Precautions (5.2)</i> ].
<i>Mechanism and Clinical Effect(s)</i>	Concomitant use of SINEQUAN with other serotonergic drugs increases the risk of serotonin syndrome [ <i>see Warnings and Precautions (5.2)</i> ].
<b>Strong CYP2D6 Inhibitors</b>	
<i>Prevention or Management</i>	Monitor doxepin plasma concentrations and reduce the SINEQUAN dosage or the strong CYP2D6 inhibitor as appropriate [ <i>see Dosage and Administration (2.5)</i> ].
<i>Mechanism and Clinical Effect(s)</i>	Concomitant use of SINEQUAN with strong CYP2D6 inhibitors may increase the exposures of doxepin [ <i>see Clinical Pharmacology (12.3)</i> ] which may increase the risk of SINEQUAN related adverse reactions [ <i>see Warnings and Precautions (5) and Adverse Reactions (6)</i> ].
<i>Examples</i>	See <a href="http://www.fda.gov/CYPandTransporterInteractingDrugs">www.fda.gov/CYPandTransporterInteractingDrugs</a> for examples of strong CYP2D6 Inhibitors.
<b>Carbamazepine</b>	
<i>Prevention or Management</i>	Monitor doxepin plasma concentrations and consider increasing the SINEQUAN dosage in patients taking carbamazepine.
<i>Mechanism and Clinical Effect(s)</i>	Concomitant use of carbamazepine with SINEQUAN decreases the exposure of doxepin [ <i>see Clinical Pharmacology (12.3)</i> ] which could lead to reduced treatment effect.

<b>Cimetidine</b>	
<i>Prevention or Management</i>	Monitor doxepin plasma concentrations and consider reducing the SINEQUAN dosage in patients taking cimetidine.
<i>Mechanism and Clinical Effect(s)</i>	Concomitant use of SINEQUAN with cimetidine may increase the exposures of doxepin [see <i>Clinical Pharmacology (12.3)</i> ] which may increase the risk of SINEQUAN-related anticholinergic effects (e.g., dry mouth, blurred vision, constipation) [see <i>Adverse Reactions (6.1)</i> ].
<b>Alcohol</b>	
<i>Prevention or Management</i>	Avoid concomitant use with alcohol.
<i>Mechanism and Clinical Effect(s)</i>	SINEQUAN may potentiate the sedative effects of alcohol [see <i>Warnings and Precautions (5.4)</i> ].
<b>CNS Depressants</b>	
<i>Prevention or Management</i>	Dosage reduction of SINEQUAN and/or the CNS depressant may be needed based on clinical response and tolerability.
<i>Mechanism and Clinical Effect(s)</i>	When concomitantly administered with SINEQUAN, the sedative effects of CNS depressant may be potentiated [see <i>Warnings and Precautions (5.4)</i> ].
<b>Tolazamide</b>	
<i>Prevention or Management</i>	Monitor glucose levels and reduce the SINEQUAN dosage as appropriate.
<i>Clinical Effect(s)</i>	SINEQUAN may cause severe hypoglycemia when concomitantly used with tolazamide.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to antidepressants, including SINEQUAN, during pregnancy. Health care providers are encouraged to advise patients to register by calling the National Pregnancy Registry for Antidepressants 1-866-961-2388 or visiting online at <https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/antidepressants>.

#### Risk Summary

Available data from published epidemiological studies and postmarketing reports have not established an increased risk for major birth defects or miscarriage with SINEQUAN use (see *Data*). There are risks (see *Clinical Considerations*):

- To the mother associated with untreated depression in pregnancy.
- Poor neonate adaptation from exposure to tricyclic antidepressants (TCAs), including SINEQUAN, during the third trimester of pregnancy.

Animal reproduction toxicity of doxepin has not been fully characterized.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of major birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

### Clinical Considerations

#### *Disease-associated Maternal and/or Embryofetal Risk*

Women who discontinue antidepressants during pregnancy are more likely to experience a relapse of MDD than women who continue antidepressants. This finding is from a prospective longitudinal study of 201 pregnant women with a history of MDD who were euthymic and taking antidepressants at the beginning of pregnancy. Consider the risk of untreated MDD when considering discontinuation of SINEQUAN drugs during pregnancy and the postpartum period.

#### *Fetal/Neonatal Adverse Reactions*

Neonates previously exposed to TCAs, including SINEQUAN, late in the third trimester during pregnancy have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These findings are consistent with either direct toxic effects of TCAs or possibly a drug discontinuation syndrome. Monitor neonates who were exposed to SINEQUAN in the third trimester of pregnancy for poor neonatal adaptation syndrome.

### Data

*Human Data:* Published epidemiological studies of pregnant women exposed to TCAs, including SINEQUAN, have not established an association with major birth defects, miscarriage, or adverse maternal outcomes. Methodological limitations of these observational studies include small sample size and lack of adequate controls.

## **8.2 Lactation**

### Risk Summary

Data from published literature report the presence of doxepin and nordoxepin in human milk. There are reports of excessive sedation, respiratory depression, poor suckling and swallowing and hypotonia in breastfed infants exposed to doxepin at doses used to treat MDD. There are no data on the effects of doxepin on milk production.

Because of the potential for serious adverse reactions, including excess sedation and respiratory depression in a breastfed infant, advise patients that breastfeeding is not recommended during SINEQUAN treatment.

## **8.4 Pediatric Use**

The safety and effectiveness of SINEQUAN in pediatric patients have not been established.

Antidepressants increase the risk of suicidal thoughts and behaviors in pediatric patients [see *Warnings and Precautions (5.1)*].

## 8.5 Geriatric Use

Clinical studies of SINEQUAN did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger adult patients.

Sedating drugs, including SINEQUAN, may cause confusion and oversedation in geriatric patients. The recommended starting SINEQUAN dosage in geriatric patients is generally lower than those of younger adult patients.

## 8.6 Hepatic Impairment

The effect of hepatic impairment (HI) on the pharmacokinetics of doxepin has not been studied. Doxepin is primarily metabolized in the liver. SINEQUAN-treated patients with HI may have a greater systemic doxepin exposure than those with normal liver function. Consider obtaining doxepin concentrations in patients with HI and modifying the dosage as appropriate.

## 8.7 Use in Genomic Subgroups

The recommended SINEQUAN dosage in CYP2C19 and CYP2D6 poor metabolizers is lower than the recommended dosage in CYP2C19 and CYP2D6 normal metabolizers [*see Dosage and Administration (2.6)*].

According to the literature, doxepin is primarily metabolized by CYP2D6 and/or CYP2C19; thus, the use of SINEQUAN in CYP2D6 and/or CYP2C19 poor metabolizers will likely result in higher doxepin exposures and an increased risk of SINEQUAN-associated adverse reactions.

# 9 DRUG ABUSE AND DEPENDENCE

## 9.1 Controlled Substance

SINEQUAN contains doxepin, which is not a controlled substance.

## 9.2 Abuse

SINEQUAN is not associated with abuse.

## 9.3 Dependence

Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, manifested by withdrawal signs and symptoms after abrupt discontinuation or a significant dose reduction of a drug. Abrupt cessation of SINEQUAN after prolonged administration can result in withdrawal symptoms, which is indicative of physical dependence.

# 10 OVERDOSAGE

## Signs, Symptoms, and Complications of SINEQUAN Overdose

Serious manifestations of tricyclic antidepressant (TCA) overdose include cardiac dysrhythmias, severe hypotension, convulsions, and CNS depression, including coma. Deaths may occur from overdose with TCAs, including SINEQUAN. Changes in the electrocardiogram, particularly in QRS axis or width, are clinically significant indicators of TCA toxicity. A maximal limb-lead QRS duration of  $\geq 0.1$  seconds may be the best indication of the TCA overdose severity.

Signs and symptoms of TCA toxicity develop rapidly after TCA overdose. Other signs of TCA overdose may include confusion, disturbed concentration, transient visual hallucinations, dilated pupils, agitation, hyperactive reflexes, stupor, drowsiness, muscle rigidity, vomiting, hypothermia, or hyperpyrexia. There are reports of patients succumbing to fatal dysrhythmia late after TCA overdose.

### Management of Overdose

The following are recommendations for the management of a SINEQUAN overdose. Contact the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

With a SINEQUAN overdose, obtain an ECG and immediately initiate cardiac monitoring in the hospital. A minimum of six hours of observation with cardiac monitoring and observation for signs of CNS depression, respiratory depression, hypotension, cardiac dysrhythmias, conduction blocks, and seizures is recommended. If signs of toxicity occur during this period, extended monitoring is recommended.

Monitoring of plasma doxepin levels should not guide SINEQUAN overdose management.

*Cardiovascular Toxicity Management:* Intravenous sodium bicarbonate should be administered to maintain the serum pH in the range of 7.45 to 7.55. If the pH response is inadequate to intravenous sodium bicarbonate therapy, hyperventilation may also be used. With concomitant use of hyperventilation and sodium bicarbonate therapy frequently monitor pH and pCO<sub>2</sub>. A pH > 7.6 or a pCO<sub>2</sub> < 20 mm Hg is undesirable. Dysrhythmias unresponsive to intravenous sodium bicarbonate therapy/hyperventilation may respond to lidocaine therapy. Type 1A and 1C antiarrhythmics are generally contraindicated (e.g., quinidine, disopyramide, and procainamide) in the setting of TCA overdose. Hemodialysis, peritoneal dialysis, exchange transfusions, and forced diuresis generally have been reported as ineffective in TCA overdose due to high tissue and protein binding of doxepin.

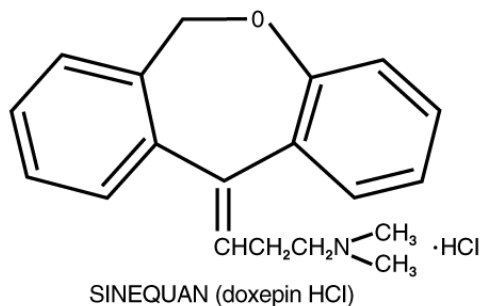
*CNS Toxicity Management:* In patients with TCA overdose who have CNS depression, early intubation is recommended because of the potential for abrupt deterioration. Seizures should be controlled with benzodiazepines, or if these are ineffective, other anticonvulsants (e.g., phenobarbital, propofol). Avoid use of physostigmine to treat TCA overdose.

## **11 DESCRIPTION**

Doxepin is a tricyclic antidepressant.

The molecular formula of doxepin hydrochloride is  $C_{19}H_{21}NO \cdot HCl$  with a molecular weight of 315.84. It is a white crystalline solid soluble in water, lower alcohols and chloroform. Doxepin is a dibenzoxepin derivative. Specifically, it is an isomeric mixture of:

1-Propanamine, 3-dibenz[*b,e*]oxepin-11(6*H*)ylidene-*N,N*-dimethyl-, hydrochloride. The structural formula of doxepin is shown below.



SINEQUAN (doxepin hydrochloride) capsules and SINEQUAN (doxepin hydrochloride) oral solution are for oral administration.

Active ingredients for the capsules include: 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, and 150 mg of doxepin (equivalent to 11.31 mg, 28.26 mg, 56.53 mg, 84.79 mg, 113.05 mg, and 169.58 mg of doxepin hydrochloride, respectively).

Capsule inactive ingredients: hard gelatin capsules (which may contain Blue 1, Red 3, Red 40, Yellow 10, and other inert ingredients); magnesium stearate; sodium lauryl sulfate; starch.

Oral solution inactive ingredients: glycerin; methylparaben; peppermint oil; propylparaben; water.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

The mechanism of action of the SINEQUAN in the treatment of MDD in adult patients is not well understood.

### 12.2 Pharmacodynamics

The exposure-response relationship and time course of pharmacodynamic response for the safety and effectiveness of doxepin have not been fully characterized.

### 12.3 Pharmacokinetics

#### Absorption

In healthy volunteers, a single oral SINEQUAN dose of 75 mg resulted in peak plasma doxepin concentrations that ranged from 8.8 ng/mL to 45.8 ng/mL (mean 26.1 ng/mL). Peak levels were reached between 2 and 4 hours (mean 2.9 hours) after SINEQUAN administration. Peak levels for the primary active metabolite *N*-desmethyldoxepin (nordoxepin) ranged from 4.8 ng/mL to 14.5 ng/mL (mean 9.7 ng/mL) and were achieved between 2 and 10 hours after SINEQUAN administration.

#### Distribution

The mean apparent volume of distribution for doxepin was approximately 20 L/kg. The protein binding for doxepin was approximately 76%.

### Elimination

In healthy volunteers, the plasma elimination half-life of doxepin ranged from 8 to 24 hours (mean 17 hours). The half-life of nordoxepin ranged from 33 to 80 hours (mean 51 hours). The mean plasma clearance for doxepin was approximately 0.84 L/hour/kg.

### *Metabolism*

After oral SINEQUAN administration, approximately 55% to 87% of doxepin undergoes first-pass metabolism in the liver, forming the primary active metabolite nordoxepin. Metabolic pathways of doxepin include demethylation, N-oxidation, hydroxylation and glucuronide formation.

### *Excretion*

Doxepin is excreted primarily in the urine, mainly as its metabolites, either free or in conjugate form.

### Specific Populations

*Patients with Hepatic Impairment:* Specific clinical studies have not been performed to evaluate the pharmacokinetics of doxepin in patients with hepatic impairment. Patients with hepatic impairment may have a greater systemic doxepin exposure than those with normal liver function [see *Use in Specific Populations (8.6)*].

*Patients with Renal Impairment:* The extent of renal excretion of doxepin is unknown. Specific clinical studies have not been performed to evaluate the pharmacokinetics of doxepin in patients with renal impairment compared to those with normal renal function.

### Drug Interaction Studies

*Carbamazepine:* After concomitant use of SINEQUAN and carbamazepine, the combined exposure of doxepin and nordoxepin (12 hours after the last dose) was decreased by 55% compared to that after the use of SINEQUAN alone [see *Drug Interactions (7)*].

*Strong CYP2D6 Inhibitors:* CYP2D6 contributes to the metabolism of doxepin and concomitant use of SINEQUAN with strong CYP2D6 inhibitors may increase doxepin exposure [see *Drug Interactions (7)*].

*Cimetidine:* Cimetidine is a non-specific inhibitor of CYP1A2, 2C19, 2D6, and 3A4. When cimetidine 300 mg twice daily was administered concomitantly with a single 6 mg dose of another oral doxepin product, there was approximately a 2-fold increase in doxepin C<sub>max</sub> and AUC compared to doxepin without cimetidine [see *Drug Interactions (7)*].

*CYP2D6 Substrates:* Concomitant use of SINEQUAN and other CYP2D6 substrates may have impact on the plasma doxepin concentrations. The clinical significance of this possible impact is unknown.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

#### Carcinogenesis

The carcinogenic potential of doxepin in animals has not been fully characterized.

#### Mutagenesis

The mutagenetic potential of doxepin in animals has not been fully characterized.

#### Impairment of Fertility

Doxepin had no effect on female fertility in rats at oral doses up to 25 mg/kg/day (1.6x the human dose of 150 mg/day on a mg/m<sup>2</sup> basis for a 60 kg human).

Insemination and conception were reduced in untreated female rats mated with male rats administered doxepin at 25 mg/kg/day for a period of  $\geq 7$  months.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

#### How Supplied

See Table 3 for strengths and package configurations for SINEQUAN (doxepin hydrochloride) capsules.

**Table 3: SINEQUAN Capsule Strengths and Package Configurations**

<b>Strength*</b>	<b>Capsule Top and Body Color</b>	<b>Capsule Imprinting in Black</b>	<b>Bottle Count</b>	<b>NDC</b>
10 mg	Scarlet opaque top/pink opaque body	“Roerig 534” and “SINEQUAN”	100	NDC 0049-5340-66
25 mg	Blue opaque top/pink opaque body	“Roerig 535” and “SINEQUAN”	100	NDC 0049-5350-66
50 mg	Pink opaque top/flesh opaque body	“Roerig 536” and “SINEQUAN”	100	NDC 0049-5360-66
75 mg	Flesh opaque top/flesh opaque body	“Roerig 539” and “SINEQUAN”	100	NDC 0049-5390-66
100 mg	Blue opaque top/flesh opaque body	“Roerig 538” and “SINEQUAN”	100	NDC 0049-5380-66
150 mg	Blue opaque top/blue opaque body	“Roerig 537” and “SINEQUAN”	50	NDC 0049-5370-50

\* Strength of doxepin

SINEQUAN (doxepin hydrochloride) oral solution. Each mL of oral solution contains 10 mg of doxepin as a clear, colorless solution and is supplied in 120 mL bottles (NDC 0049-5100-47) with an accompanying dropper calibrated at 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg.

Store SINEQUAN at controlled room temperature between 20°C to 25°C (68°F to 77°F).

## 17 PATIENT COUNSELING INFORMATION

Advise patients to read FDA-approved patient labeling (Medication Guide).

### Suicidal Thoughts and Behaviors

Advise patients and caregivers to look for the emergence of suicidal thoughts and behaviors, especially early during SINEQUAN treatment and when the dosage is increased or decreased, and instruct them to report suicidal thinking and behavior to their health care provider

*[see Warnings and Precautions (5.1)].*

### Serotonin Syndrome

Caution patients about the risk of serotonin syndrome particularly with the concomitant use of SINEQUAN and other serotonergic drugs (e.g., other TCAs, SSRIs, SNRIs, triptans, opioids), lithium, tryptophan, buspirone, and St. John's Wort and with drugs that impair metabolism of serotonin (in particular, MAOIs, both those intended to treat psychiatric disorders and also others, such as linezolid) *[see Warnings and Precautions (5.2), Drug Interactions (7)]*. Instruct patients to contact their health care provider or report to the emergency room if they experience signs or symptoms of serotonin syndrome.

### Angle-Closure Glaucoma

Advise patients that taking SINEQUAN can cause pupillary dilation, which in susceptible individuals, can trigger angle closure glaucoma. Patients may wish to be examined to determine whether they are susceptible to angle closure, and have a prophylactic procedure (e.g., iridectomy), if they are susceptible *[see Warnings and Precautions (5.3)]*.

### Effects on Driving and Operating Heavy Machinery

Inform patients that SINEQUAN can cause sedation and caution them against driving a car or operating dangerous machinery while taking SINEQUAN *[see Warnings and Precautions (5.4)]*.

### Activation of Mania or Hypomania

Advise patients to observe for signs of mania/hypomania activation and instruct them to report such symptoms to the healthcare provider.

### Drug Interactions

Inform patients that the use of SINEQUAN and certain other drugs increases the risk of SINEQUAN-associated adverse reactions or alternatively lower SINEQUAN effectiveness. Instruct patients to inform their healthcare provider about all the drugs that they are taking before taking SINEQUAN.

### Alcohol Use

Advise patients to avoid the use of alcohol while taking SINEQUAN *[see Drug Interactions (7.5)]*.

### Pregnancy

Advise patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to SINEQUAN during pregnancy. Advise women to notify their healthcare provider if they become pregnant or intend to become pregnant during SINEQUAN treatment.

Advise pregnant women that SINEQUAN use late in pregnancy may increase the risk for neonatal complications requiring prolonged hospitalization, respiratory support, or tube feeding [see *Use in Specific Populations (8.1)*].

#### Lactation

Advise patients that breastfeeding is not recommended during SINEQUAN treatment [see *Use in Specific Populations (8.2)*].

#### Important Administration Instructions for the Oral Solution

For patients prescribed SINEQUAN oral solution, tell them to:

- Use the supplied calibrated dropper to measure the amount of oral solution needed.
- Just prior to administration, mix SINEQUAN with 120 mL of water, whole or skimmed milk, or orange, grapefruit, tomato, prune or pineapple juice only. Do not mix with anything other than the liquids listed.
- Administer the dose immediately after mixing.



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This product's labeling may have been updated. For the most recent Prescribing Information, please visit [www.pfizer.com](http://www.pfizer.com).

LAB-0072-11.2

**MEDICATION GUIDE**  
**SINEQUAN® (SIN' eh-kwon)**  
**(doxepin hydrochloride) capsules**  
**for oral use**

**SINEQUAN® (SIN' eh-kwon)**  
**(doxepin hydrochloride) oral solution**

**What is the most important information I should know about SINEQUAN?**

**SINEQUAN can cause serious side effects, including:**

**Increased risk of suicidal thoughts and actions.** SINEQUAN and other antidepressant medicines may increase the risk of suicidal thoughts and actions in people 24 years of age and younger, especially within the first few months of treatment or when the dose is changed. SINEQUAN is not for use in children.

**How can I watch for and try to prevent suicidal thoughts and actions in myself or a family member?**

- Pay close attention to any changes, especially sudden changes in mood, behavior, thoughts, or feelings, or if you develop suicidal thoughts or actions. This is very important when an antidepressant medicine is started or when the dose is changed.
- Call your health care provider right away to report new or sudden changes in mood, behavior, thoughts, or feelings or if you develop suicidal thoughts or actions.
- Keep all follow-up visits with your health care provider as scheduled. Call your health care provider between visits as needed, especially if you have concerns about symptoms.

**Call your health care provider or get emergency help right away if you or a family member have any of the following symptoms, especially if they are new, worse, or worry you:**

- |  |   |
|--|---|
| ○ suicide attempts                                   | ○ thoughts about suicide or dying           |
| ○ acting aggressive, being angry, or violent         | ○ acting on dangerous impulses              |
| ○ new or worse depression                            | ○ new or worse anxiety                      |
| ○ panic attacks                                      | ○ feeling very agitated or restless         |
| ○ new or worse irritability                          | ○ trouble sleeping                          |
| ○ an extreme increase in activity or talking (mania) | ○ other unusual changes in behavior or mood |

See **“What are the possible side effects of SINEQUAN?”** for more information about side effects.

**What is SINEQUAN?**

SINEQUAN is a prescription medicine used to treat adults with a certain type of depression called major depressive disorder (MDD).

It is not known if SINEQUAN is safe and effective for use in children.

**Do not take SINEQUAN if you:**

- are allergic to doxepin, or any of the ingredients in SINEQUAN. See the end of this Medication Guide for a complete list of ingredients in SINEQUAN
- have glaucoma
- have or have had trouble urinating
- are taking, or have stopped taking within the last 14 days, a medicine called a Monoamine Oxidase Inhibitor (MAOI), including the antibiotic linezolid or intravenous methylene blue
  - Ask your health care provider or pharmacist if you are not sure if you are taking an MAOI, including the antibiotic linezolid or intravenous methylene blue
  - **Do not start taking an MAOI for at least 14 days after you stop treatment with SINEQUAN**

**Before taking SINEQUAN, tell your health care provider about all your medical conditions, including if you:**

- have, or have a family history of bipolar disorder, mania, or hypomania
- have or had depression, suicidal thoughts or behavior
- have kidney or liver problems
- have or had seizures or convulsions
- are pregnant or plan to become pregnant. Taking SINEQUAN during your third trimester of pregnancy may harm your unborn baby. Tell your health care provider if you become pregnant or think you may be pregnant during treatment with SINEQUAN
  - Babies born to mothers who take certain medicines, including SINEQUAN, during the third trimester of pregnancy may have symptoms of sedation, such as breathing problems, sluggishness, low muscle tone, feeding problems, and withdrawal symptoms. Talk to your health care provider about the risks to your unborn or newborn baby if you take SINEQUAN during pregnancy
  - There is a pregnancy registry for women who are exposed to SINEQUAN during pregnancy. The purpose of this registry is to collect information about the health of women exposed to SINEQUAN and their babies. If you

become pregnant during treatment with SINEQUAN, talk to your health care provider about registering with the National Pregnancy Registry for Antidepressants. You can register by calling 1-866-961-2388 or visiting online at <https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/antidepressants/>

- are breastfeeding or plan to breastfeed. SINEQUAN can pass into your breast milk and harm your baby. Do not breastfeed during treatment with SINEQUAN. Talk to your health care provider about the best way to feed your baby during treatment with SINEQUAN

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

SINEQUAN and other medicines may affect each other causing possible serious side effects. SINEQUAN may affect the way other medicines work and other medicines may affect the way SINEQUAN works.

**Especially tell your health care provider if you take:**

- medicines used to treat mood, anxiety, psychotic, or thought disorders, including selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs)
- medicines to treat migraine headaches known as triptans
- other tricyclic antidepressants
- tetracyclic antidepressants
- opioids
- lithium
- tryptophan
- buspirone
- St. John's Wort
- carbamazepine
- cimetidine
- tolazamide
- medicines that can cause drowsiness

Ask your health care provider if you are not sure if you are taking any of these medicines. Your health care provider can tell you if it is safe to take SINEQUAN with your other medicines.

Do not start or stop any other medicines during treatment with SINEQUAN without first talking to your healthcare provider.

Know the medicines you take. Keep a list of them to show to your healthcare providers when you start to take a new medicine.

**How should I take SINEQUAN?**

- Take SINEQUAN exactly as your health care provider tells you to take it. Do not change your dose or stop taking SINEQUAN without first talking to your healthcare provider.
- Your health care provider may need to change the dose of SINEQUAN until it is the right dose for you.
- For people taking SINEQUAN oral solution:
  - Use the calibrated dropper that comes with SINEQUAN oral solution to measure the prescribed dose. The calibrated dropper has markings at 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg.
  - Mix your prescribed dose with 120 mL (4 ounces) of water, whole or skimmed milk, or orange, grapefruit, tomato, prune, or pineapple juice. Do not mix with other liquids.
  - Take the dose right away after mixing.
- If you miss a dose of SINEQUAN, take the missed dose as soon as you remember. If it is almost time for the next dose, do not take the missed dose and take your next dose at the regular time. Do not take two doses of SINEQUAN at the same time.
- If you take too much SINEQUAN, call your healthcare provider or Poison Help Line at 1-800-222-1222 or go to the nearest hospital emergency room right away.

**What should I avoid while taking SINEQUAN?**

- Do not drive a car or another motor vehicle, operate heavy machinery, or do dangerous activities while taking SINEQUAN. SINEQUAN can cause sleepiness or may affect your ability to make decisions, think clearly, or react quickly.
- Do not drink alcohol during treatment with SINEQUAN. Drinking alcohol during treatment with SINEQUAN can increase your risk of having serious side effects.

## What are the possible side effects of SINEQUAN?

### SINEQUAN can cause serious side effects, including:

- See “**What is the most important information I should know about SINEQUAN?**”
- **Serotonin syndrome.** Taking SINEQUAN can cause a potentially life-threatening problem called serotonin syndrome. The risk of developing serotonin syndrome is increased when SINEQUAN is taken with certain other medicines. See “**Do not take SINEQUAN if you:**” Stop taking SINEQUAN and **call your healthcare provider or go to the nearest hospital emergency room right away** if you have any of the following signs and symptoms of serotonin syndrome:
  - agitation
  - confusion
  - fast heartbeat
  - dizziness
  - flushing
  - shaking (tremors), stiff muscles, or muscle twitching
  - seizures
  - seeing or hearing things that are not real (hallucinations)
  - coma
  - changes in blood pressure
  - sweating
  - high body temperature (hyperthermia)
  - loss of coordination
  - nausea, vomiting, diarrhea
- **Eye problems (angle-closure glaucoma).** SINEQUAN may cause a type of eye problem called angle-closure glaucoma in people with certain eye problems. You may want to undergo an eye examination to see if you are at risk and receive preventative treatment if you are. Call your healthcare provider if you have eye pain, changes in your vision, or swelling or redness in or around the eye.
- **Manic episodes.** Manic episodes may happen in people with bipolar disorder who take SINEQUAN. Symptoms may include:
  - greatly increased energy
  - racing thoughts
  - unusually grand ideas
  - talking more or faster than usual
  - severe trouble sleeping
  - reckless behavior
  - excessive happiness or irritability
- **Seizures (convulsions)**

### The most common side effects of SINEQUAN include:

- feeling overly sleepy
- dry mouth
- dizziness
- constipation
- tiredness

These are not all the possible side effects of SINEQUAN.

Call your health care provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

## How should I store SINEQUAN?

- Store SINEQUAN at controlled room temperature between 20°C to 25°C (68°F to 77°F).
- Keep SINEQUAN and all medicines out of the reach of children.

## General Information about the safe and effective use of SINEQUAN.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not take SINEQUAN for a condition for which it was not prescribed. Do not give SINEQUAN to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about SINEQUAN that is written for health professionals.

## What are the ingredients in SINEQUAN?

*Active ingredient:* doxepin hydrochloride

*Inactive Ingredients for SINEQUAN Capsules:* hard gelatin capsules (which may contain Blue 1, Red 3, Red 40, Yellow 10, and other inert ingredients); magnesium stearate; sodium lauryl sulfate; starch.

*Inactive Ingredients for SINEQUAN Oral Solution:* glycerin; methylparaben; peppermint oil; propylparaben; water.



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For optional information about SINEQUAN call 1-800-438-1985 or go to [www.pfizer.com](http://www.pfizer.com).

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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