

# DOXEPIN HYDROCHLORIDE- doxepin hydrochloride capsule

## PD-Rx Pharmaceuticals, Inc.

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### HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use DOXEPIN HYDROCHLORIDE CAPSULES safely and effectively. See full prescribing information for DOXEPIN HYDROCHLORIDE CAPSULES.

DOXEPIN HYDROCHLORIDE capsules, for oral use  
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)
- Doxepin hydrochloride capsules are not approved for use in pediatric patients ( 8.4)

#### RECENT MAJOR CHANGES

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

Warnings and Precautions ( 5.2, 5.5) 7/2025

#### INDICATIONS AND USAGE

Doxepin hydrochloride capsules are a tricyclic antidepressant (TCA) indicated for the treatment of major depressive disorder (MDD) in adults ( 1).

#### DOSAGE AND ADMINISTRATION

- Prior to initiating treatment with doxepin hydrochloride capsules, 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 doxepin hydrochloride capsules. ( 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 doxepin hydrochloride capsules, gradually reduce the dosage until discontinued. ( 2.7)

#### DOSAGE FORMS AND STRENGTHS

- Capsules: 10 mg, 25 mg, 50 mg, 75 mg and 100 mg ( 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 doxepin hydrochloride capsules, 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 doxepin hydrochloride capsules for the emergence of serotonin syndrome. Discontinue doxepin hydrochloride capsules and any concomitant serotonergic agents immediately and initiate supportive treatment if serotonin syndrome occurs. ( 5.2, 7)
- Angle-Closure Glaucoma: Avoid use of doxepin hydrochloride capsules in patients with untreated

anatomically narrow angles. ( 5.3)

- **Sedation and Driving Risks:** Because doxepin hydrochloride capsules can cause sedation, warn patients against driving a car or operating dangerous machinery while taking doxepin hydrochloride capsules. ( 5.4)
- **Activation of Mania or Hypomania:** Prior to initiating antidepressant therapy, screen for bipolar disorder. Doxepin hydrochloride capsules are not approved for use in treating bipolar depression. ( 5.5)

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#### ADVERSE REACTIONS

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

**To report SUSPECTED ADVERSE REACTIONS, contact Mylan at 1-877-446-3679 (1-877-4-INFO-RX) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

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#### DRUG INTERACTIONS

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- **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 doxepin hydrochloride capsules 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 doxepin hydrochloride capsules dosage in patients taking carbamazepine. ( 7)
- **Cimetidine:** Monitor doxepin plasma concentrations and consider reducing the doxepin hydrochloride capsules 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 doxepin hydrochloride capsules dosage as appropriate. ( 7)

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#### USE IN SPECIFIC POPULATIONS

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- **Pregnancy:** Neonates exposed to TCAs, including doxepin hydrochloride capsules, late in the third trimester have developed poor adaptation (respiratory distress, temperature instability, feeding difficulty, hypotonia, irritability). Monitor neonates who were exposed to doxepin hydrochloride capsules 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 doxepin hydrochloride capsule-associated adverse reactions. ( 8.7)

**See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.**

**Revised: 10/2025**

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## FULL PRESCRIBING INFORMATION: CONTENTS\*

### WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

### 1 INDICATIONS AND USAGE

### 2 DOSAGE AND ADMINISTRATION

- 2.1 Screen for Bipolar Disorder Prior to Starting Doxepin Hydrochloride Capsules
- 2.2 Recommended Dosage
- 2.3 Switching Patients to or from a Monoamine Oxidase Inhibitor
- 2.4 Dosage Modifications Intended to Reduce the Risk of Anticholinergic Effects
- 2.5 Dosage Modifications for Strong CYP2D6 Inhibitors
- 2.6 Dosage Modifications in Known CYP2D6 and CYP2C19 Poor Metabolizers
- 2.7 Discontinuation of Doxepin Hydrochloride Capsules Treatment

### 3 DOSAGE FORMS AND STRENGTHS

### 4 CONTRAINDICATIONS

## **5 WARNINGS AND PRECAUTIONS**

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

## **6 ADVERSE REACTIONS**

- 6.1 Clinical Trials Experience
- 6.2 Postmarketing Experience

## **7 DRUG INTERACTIONS**

## **8 USE IN SPECIFIC POPULATIONS**

- 8.1 Pregnancy
- 8.2 Lactation
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Hepatic Impairment
- 8.7 Use in Genomic Subgroups

## **9 DRUG ABUSE AND DEPENDENCE**

- 9.1 Controlled Substance
- 9.2 Abuse
- 9.3 Dependence

## **10 OVERDOSAGE**

## **11 DESCRIPTION**

## **12 CLINICAL PHARMACOLOGY**

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

## **13 NONCLINICAL TOXICOLOGY**

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

## **16 HOW SUPPLIED/STORAGE AND HANDLING**

## **17 PATIENT COUNSELING INFORMATION**

\* Sections or subsections omitted from the full prescribing information are not listed.

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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)]. Doxepin hydrochloride capsules are not approved for use in pediatric patients [see Use in Specific Populations (8.4)].**

## **1 INDICATIONS AND USAGE**

Doxepin hydrochloride capsules are indicated for the treatment of major depressive disorder (MDD) in adults.

## **2 DOSAGE AND ADMINISTRATION**

### **2.1 Screen for Bipolar Disorder Prior to Starting Doxepin Hydrochloride Capsules**

Prior to initiating treatment with doxepin hydrochloride capsules, 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 doxepin hydrochloride capsules is 25 mg three times daily or 75 mg once daily. The recommended target total oral dosage range for doxepin hydrochloride capsules is between 75 mg/day and 150 mg/day (may be given once daily or in divided doses). The maximum recommended oral dosage for doxepin hydrochloride capsules 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 doxepin hydrochloride capsules [see *Contraindications (4)*, *Warnings and Precautions (5.2)*, and *Drug Interactions (7)*].

Wait at least 14 days after discontinuation of doxepin hydrochloride capsules before initiating therapy with an MAOI [see *Contraindications (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 doxepin hydrochloride capsules dosage [see *Adverse Reactions (6.1)*].

### **2.5 Dosage Modifications for Strong CYP2D6 Inhibitors**

Reduce the doxepin hydrochloride capsules 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 doxepin hydrochloride capsules 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 Doxepin Hydrochloride Capsules Treatment**

When discontinuing doxepin hydrochloride capsules, gradually reduce the dosage until

[discontinued [see Adverse Reactions (6)] .

### 3 DOSAGE FORMS AND STRENGTHS

Doxepin Hydrochloride Capsules, USP are available containing doxepin hydrochloride, USP equivalent to 10 mg, 25 mg, 50 mg, 75 mg or 100 mg of doxepin.

- The 10 mg capsules are hard-shell, gelatin capsules with a buff opaque cap and buff opaque body axially printed with **MYLAN** over **1049** in black ink on both the cap and the body.
- The 25 mg capsules are hard-shell, gelatin capsules with an ivory opaque cap and white opaque body axially printed with **MYLAN** over **3125** in black ink on both the cap and the body.
- The 50 mg capsules are hard-shell, gelatin capsules with an ivory opaque cap and ivory opaque body axially printed with **MYLAN** over **4250** in black ink on both the cap and the body.
- The 75 mg capsules are hard-shell, gelatin capsules with a brite lite green opaque cap and brite lite green opaque body axially printed with **MYLAN** over **5375** in black ink on both the cap and the body.
- The 100 mg capsules are hard-shell, gelatin capsules with a brite lite green opaque cap and white opaque body axially printed with **MYLAN** over **6410** in black ink on both the cap and the body.

### 4 CONTRAINDICATIONS

Doxepin hydrochloride capsules are 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 (doxepin hydrochloride capsules are 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 doxepin hydrochloride capsules-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of doxepin hydrochloride capsules 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 doxepin hydrochloride capsules, in patients who are experiencing emergent suicidal thoughts or behaviors.

## 5.2 Serotonin Syndrome

Tricyclic antidepressants, including doxepin hydrochloride capsules, 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 doxepin hydrochloride capsules with MAOIs is contraindicated. The use of doxepin hydrochloride capsules within 14 days of discontinuing treatment with an MAOI intended to treat psychiatric disorders is contraindicated. Starting doxepin hydrochloride capsules 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 doxepin hydrochloride capsules, discontinue doxepin hydrochloride capsules before initiating treatment with the MAOI [see *Dosage and Administration (2.4) and Drug Interactions (7)*].

Monitor all patients taking doxepin hydrochloride capsules for the emergence of serotonin syndrome. Discontinue doxepin hydrochloride capsules treatment and any concomitant serotonergic agents immediately if the above symptoms occur, and initiate supportive symptomatic treatment. If concomitant use of doxepin hydrochloride capsules 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 doxepin hydrochloride capsules 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.

Doxepin hydrochloride capsules are contraindicated in patients with glaucoma. Avoid use of doxepin hydrochloride capsules in patients with untreated anatomically narrow angles.

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

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

Sedating drugs, including doxepin hydrochloride capsules, may cause oversedation in geriatric patients.

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

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

### **5.6 Risk of Seizures**

Caution should be used when doxepin hydrochloride capsules are 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 doxepin hydrochloride capsules use to identify recurrence of seizures or increase in frequency of seizures.

### **5.7 Psychosis**

In patients with schizophrenia, treatment with doxepin hydrochloride capsules for MDD may activate psychosis. If this occurs, stop doxepin hydrochloride capsules 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 doxepin-treated patients) in 1,635 doxepin-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 doxepin 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 doxepin. 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 doxepin [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 doxepin hydrochloride capsules with other drugs or classes.

**Table 2: Clinically Significant Drug Interactions with Doxepin Hydrochloride Capsules**

<b>Monoamine Oxidase Inhibitors</b>	
<i>Prevention or Management</i>	Doxepin hydrochloride capsules are contraindicated in patients taking monoamine oxidase inhibitors (MAOIs), including MAOIs such as linezolid or intravenous methylene blue. The use of doxepin hydrochloride capsules within 14 days of discontinuation of an MAOI or the use of MAOI within 14 days of discontinuation of doxepin hydrochloride capsules is contraindicated .Starting doxepin hydrochloride capsules in a patient who is being treated with an MAOI is contraindicated .
<i>Clinical Effect(s)</i>	Concomitant use of doxepin hydrochloride capsules 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 doxepin hydrochloride capsules and/or concomitant serotonergic drugs [see <i>Warnings and Precautions (5.2)</i> ].

<i>Mechanism and Clinical Effect(s)</i>	Concomitant use of doxepin hydrochloride capsules with other serotonergic drugs increases the risk of serotonin syndrome [see <i>Warnings and Precautions (5.2)</i> ].
<b>Strong CYP2D6 Inhibitors</b>	
<i>Prevention or Management</i>	Monitor doxepin plasma concentrations and reduce the doxepin hydrochloride capsules dosage or the strong CYP2D6 inhibitor as appropriate [see <i>Dosage and Administration (2.5)</i> ].
<i>Mechanism and Clinical Effect(s)</i>	Concomitant use of doxepin hydrochloride capsules with strong CYP2D6 inhibitors may increase the exposures of doxepin [see <i>Clinical Pharmacology (12.3)</i> ] which may increase the risk of doxepin hydrochloride capsules related adverse reactions [see <i>Warnings and Precautions (5)</i> and <i>Adverse Reactions (6)</i> ].
<i>Examples</i>	See <a href="http://www.fda.gov/CYPandTransporter/InteractingDrugs">www.fda.gov/CYPandTransporter/InteractingDrugs</a> for examples of strong CYP2D6 Inhibitors.
<b>Carbamazepine</b>	
<i>Prevention or Management</i>	Monitor doxepin plasma concentrations and consider increasing the doxepin hydrochloride capsules dosage in patients taking carbamazepine.
<i>Mechanism and Clinical Effect(s)</i>	Concomitant use of carbamazepine with doxepin hydrochloride capsules decreases the exposure of doxepin [see <i>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 doxepin hydrochloride capsules dosage in patients taking cimetidine.
<i>Mechanism and Clinical Effect(s)</i>	Concomitant use of doxepin hydrochloride capsules with cimetidine may increase the exposures of doxepin [see <i>Clinical Pharmacology (12.3)</i> ] which may increase the risk of doxepin hydrochloride capsules-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>	Doxepin hydrochloride capsules 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 doxepin hydrochloride capsules 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 doxepin hydrochloride capsules, 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 doxepin hydrochloride capsules dosage as appropriate.
<i>Clinical Effect(s)</i>	Doxepin hydrochloride capsules 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 doxepin hydrochloride capsules, 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-researchprograms/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 doxepin hydrochloride capsules 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 doxepin hydrochloride capsules, 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 doxepin drugs during pregnancy and the postpartum period.

##### *Fetal/Neonatal Adverse Reactions*

Neonates previously exposed to TCAs, including doxepin hydrochloride capsules, 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 doxepin hydrochloride capsules in the third trimester of pregnancy for poor neonatal adaptation syndrome.

## Data

### *Human Data*

Published epidemiological studies of pregnant women exposed to TCAs, including doxepin hydrochloride capsules, 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 doxepin hydrochloride capsules treatment.

## **8.4 Pediatric Use**

The safety and effectiveness of doxepin hydrochloride capsules 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 doxepin 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 doxepin hydrochloride capsules, may cause confusion and oversedation in geriatric patients. The recommended starting doxepin hydrochloride capsules 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. Doxepin hydrochloride capsules-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 doxepin hydrochloride capsules 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 doxepin hydrochloride capsules in CYP2D6 and/or CYP2C19 poor metabolizers will likely result in higher doxepin exposures and an increased risk of doxepin hydrochloride capsule-associated adverse reactions.

## **9 DRUG ABUSE AND DEPENDENCE**

### **9.1 Controlled Substance**

Doxepin hydrochloride capsules contain doxepin, which is not a controlled substance.

### **9.2 Abuse**

Doxepin hydrochloride capsules are 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 doxepin hydrochloride capsules after prolonged administration can result in withdrawal symptoms, which is indicative of physical dependence.

## **10 OVERDOSAGE**

### Signs, Symptoms, and Complications of Doxepin Hydrochloride Capsules Overdose

Serious manifestations of tricyclic antidepressant (TCA) overdose include cardiac dysrhythmias, severe hypotension, convulsions, and CNS depression, including coma. Deaths may occur from overdosage with TCAs, including doxepin hydrochloride capsules. 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 doxepin hydrochloride capsules overdose. Contact the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

With a doxepin hydrochloride capsules 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 doxepin hydrochloride capsules overdose management.

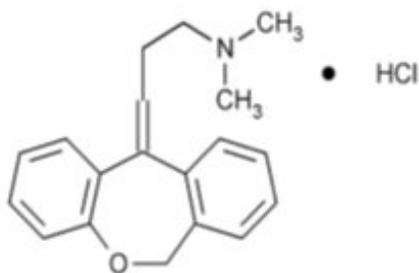
*Cardiovascular Toxicity Management:* Intravenous sodium bicarbonate should be administered to maintain the serum pH in the range of 7.45 to 7.55. If the pH response is inadequate to intravenous sodium bicarbonate therapy, hyperventilation may also be used. With concomitant use of hyperventilation and 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<sub>19</sub>H<sub>21</sub>NO • HCl with a molecular weight of 315.84. It is a white crystalline powder freely soluble in water, in ethanol (96%), and methylene chloride. 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.



Doxepin hydrochloride capsules are for oral administration.

Active ingredients for the capsules include: 10 mg, 25, mg, 50 mg, 75 mg and 100 mg of doxepin (equivalent to 11.4 mg, 28.5 mg, 57 mg, 85.5 mg and 114 mg of doxepin

hydrochloride, respectively).

Capsule inactive ingredients: colloidal silicon dioxide, magnesium stearate, microcrystalline cellulose, pregelatinized starch (corn) and sodium lauryl sulfate. The empty gelatin capsule shells contain D&C Yellow No. 10, gelatin, sodium lauryl sulfate and titanium dioxide. In addition, the 10 mg, 25 mg and 50 mg empty gelatin capsule shells contain FD&C Yellow No. 6 and the 75 mg and 100 mg empty gelatin capsule shells contain FD&C Green No. 3.

The imprinting ink contains black iron oxide, D&C Yellow No. 10 Aluminum Lake, FD&C Blue No. 1 Aluminum Lake, FD&C Blue No. 2 Aluminum Lake, FD&C Red No. 40 Aluminum Lake, propylene glycol and shellac glaze.

## **12 CLINICAL PHARMACOLOGY**

### **12.1 Mechanism of Action**

The mechanism of action of the doxepin hydrochloride capsules 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 doxepin hydrochloride capsule 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 doxepin hydrochloride capsules 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 doxepin hydrochloride capsules 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 doxepin 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 doxepin 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 doxepin alone [see *Drug Interactions (7)*].

#### *Strong CYP2D6 Inhibitors*

CYP2D6 contributes to the metabolism of doxepin and concomitant use of doxepin 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 doxepin 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

Doxepin Hydrochloride Capsules, USP are available containing doxepin hydrochloride, USP equivalent to 25 mg of doxepin.

The 25 mg capsules are hard-shell, gelatin capsules with an ivory opaque cap and white opaque body axially printed with **MYLAN** over **3125** in black ink on both the cap and the body. They are available as follows:

NDC 55289-370-30  
bottles of 30 capsules

NDC 55289-370-90  
bottles of 90 capsules

**Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]**

**Protect from light.**

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure.

**PHARMACIST:** Dispense a Medication Guide with each prescription.

## **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 doxepin hydrochloride capsules 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 doxepin hydrochloride capsules 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 doxepin hydrochloride capsules 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 doxepin hydrochloride capsules can cause sedation and caution them against driving a car or operating dangerous machinery while taking doxepin hydrochloride capsules [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 doxepin hydrochloride capsules and certain other drugs increases the risk of doxepin hydrochloride capsule-associated adverse reactions or alternatively lower doxepin hydrochloride capsules effectiveness. Instruct patients to inform their healthcare provider about all the drugs that they are taking before taking doxepin hydrochloride capsules.

#### Alcohol Use

Advise patients to avoid the use of alcohol while taking doxepin hydrochloride capsules [see *Drug Interactions (7)*].

#### Pregnancy

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

Advise pregnant women that doxepin hydrochloride capsules 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 doxepin hydrochloride capsules treatment [see *Use in Specific Populations (8.2)*].

## **Medication Guide**

<p><b>Doxepin Hydrochloride Capsules, USP</b> <b>(dox' e pin hye" droe klor' ide)</b> <b>for oral use</b></p>
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## **What is the most important information I should know about doxepin hydrochloride capsules?**

**Doxepin hydrochloride capsules can cause serious side effects, including: Increased risk of suicidal thoughts and actions.** Doxepin hydrochloride capsules 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. Doxepin hydrochloride capsules are 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
- acting aggressive, being angry, or violent
- new or worse depression
- panic attacks
- new or worse irritability
- an extreme increase in activity or talking (mania)
- thoughts about suicide or dying
- acting on dangerous impulses
- new or worse anxiety
- feeling very agitated or restless
- trouble sleeping
- other unusual changes in behavior or mood

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

## **What are doxepin hydrochloride capsules?**

Doxepin hydrochloride capsules are a prescription medicine used to treat adults with a certain type of depression called major depressive disorder (MDD).

It is not known if doxepin hydrochloride capsules are safe and effective for use in children.

## **Do not take doxepin hydrochloride capsules if you:**

- are allergic to doxepin, or any of the ingredients in doxepin hydrochloride capsules. See the end of this Medication Guide for a complete list of ingredients in doxepin hydrochloride capsules
- 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 doxepin hydrochloride capsules**

**Before taking doxepin hydrochloride capsules, 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 doxepin hydrochloride capsules 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 doxepin hydrochloride capsules
  - Babies born to mothers who take certain medicines, including doxepin hydrochloride capsules, 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 doxepin hydrochloride capsules during pregnancy
  - There is a pregnancy registry for women who are exposed to doxepin hydrochloride capsules during pregnancy. The purpose of this registry is to collect information about the health of women exposed to doxepin hydrochloride capsules and their babies. If you become pregnant during treatment with doxepin hydrochloride capsules, 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. Doxepin hydrochloride can pass into your breast milk and harm your baby. Do not breastfeed during treatment with doxepin hydrochloride capsules. Talk to your health care provider about the best way to feed your baby during treatment with doxepin hydrochloride capsules

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

Doxepin hydrochloride capsules and other medicines may affect each other causing possible serious side effects. Doxepin hydrochloride capsules may affect the way other medicines work and other medicines may affect the way doxepin hydrochloride capsules work.

**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 doxepin hydrochloride capsules with your other medicines.

Do not start or stop any other medicines during treatment with doxepin hydrochloride capsules 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 doxepin hydrochloride capsules?**

- Take doxepin hydrochloride capsules exactly as your health care provider tells you to take them. Do not change your dose or stop taking doxepin hydrochloride capsules without first talking to your healthcare provider.
- Your health care provider may need to change the dose of doxepin hydrochloride capsules until it is the right dose for you.
- If you miss a dose of doxepin hydrochloride capsules, 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 doxepin hydrochloride capsules at the same time.
- If you take too many doxepin hydrochloride capsules, 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 doxepin hydrochloride capsules?**

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

### **What are the possible side effects of doxepin hydrochloride capsules?**

**Doxepin hydrochloride capsules can cause serious side effects, including:**

- See “**What is the most important information I should know about doxepin hydrochloride capsules?**”
- **Serotonin syndrome.** Taking doxepin hydrochloride capsules can cause a potentially life-threatening problem called serotonin syndrome. The risk of developing serotonin syndrome is increased when doxepin hydrochloride capsules are taken with certain other medicines. See “ **Do not take doxepin hydrochloride**

**capsules if you:**” Stop taking doxepin hydrochloride capsules 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).** Doxepin hydrochloride capsules 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 doxepin hydrochloride capsules. 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 doxepin hydrochloride capsules include:**

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

These are not all the possible side effects of doxepin hydrochloride capsules. Call your health care provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA1088.

**How should I store doxepin hydrochloride capsules?**

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

**General Information about the safe and effective use of doxepin hydrochloride capsules.**

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not take doxepin hydrochloride capsules for a condition for which they were not prescribed. Do not give doxepin hydrochloride capsules to other people, even if they have the same symptoms that you have. They may harm them. You can ask your pharmacist or healthcare provider for information about doxepin hydrochloride

capsules that is written for health professionals.

**What are the ingredients in doxepin hydrochloride capsules?**

*Active Ingredient:*doxepin hydrochloride

*Inactive Ingredients for Doxepin Hydrochloride Capsules:*colloidal silicon dioxide, magnesium stearate, microcrystalline cellulose, pregelatinized starch (corn) and sodium lauryl sulfate. The empty gelatin capsule shells contain D&C Yellow No. 10, gelatin, sodium lauryl sulfate and titanium dioxide. In addition, the 10 mg, 25 mg and 50 mg empty gelatin capsule shells contain FD&C Yellow No. 6 and the 75 mg and 100 mg empty gelatin capsule shells contain FD&C Green No. 3.

The imprinting ink contains black iron oxide, D&C Yellow No. 10 Aluminum Lake, FD&C Blue No. 1 Aluminum Lake, FD&C Blue No. 2 Aluminum Lake, FD&C Red No. 40 Aluminum Lake, propylene glycol and shellac glaze.

For more information, contact Mylan at 1-877-446-3679 (1-877-4-INFO-RX).

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

Manufactured for:

**Mylan Pharmaceuticals Inc.**

Morgantown, WV 26505 U.S.A.

Revised: 10/2025

VPL:DXPN:RX

**PRINCIPAL DISPLAY PANEL - 25 mg**

**Doxepin HCl**

**Capsules, USP**

**25 mg\***

**PHARMACIST: Dispense the accompanying Medication Guide to each patient.**

**Rx only**

MAY CAUSE DROWSINESS. USE CAUTION WHILE DRIVING OR PERFORMING TASKS REQUIRING MENTAL ALERTNESS. AVOID ALCOHOL WHILE TAKING THIS MEDICATION.

**R only** WARNING: KEEP THIS OUT OF THE REACH OF CHILDREN  
**DOSAGE and STORAGE: SEE PACKAGE INSERT**

55289-370-30	55289-370-30	55289-370-30
DOXEPIN	DOXEPIN	DOXEPIN
HCL USP	HCL USP	HCL USP
25 MG	25 MG	25 MG
30 CAPSULES	30 CAPSULES	30 CAPSULES
ReOrder # 103450	ReOrder # 103450	ReOrder # 103450
LOT H22C56	LOT H22C56	LOT H22C56
EXP 05/2024	EXP 05/2024	EXP 05/2024

CALL YOUR DOCTOR FOR MEDICAL ADVICE ABOUT SIDE EFFECTS. YOU MAY REPORT SIDE EFFECTS TO THE FDA AT 1-800-FDA-1088

TAKE \_\_\_\_\_ CAPSULE(S) \_\_\_\_\_ TIMES A DAY.  
 TOME \_\_\_\_\_ CAPSULA(S) \_\_\_\_\_ VECES AL DIA.

Each CAPSULE Contains: DOXEPIN HYDROCHLORIDE USP EQUIVALENT TO 25 MG OF DOXEPIN

NDC: 55289-370-30



DOXEPIN  
 HCL USP

25 MG

30 CAPSULES



GTIN: 00355289370307  
 SNO: H22C56000001  
 EXP: 05/2024  
 LOT: H22C56

IVORY/WHITE  
 ORGANOLEPTIC MARKINGS:  
 MAYLAN 3125  
 CAPSULE

355289370307  
 00378312501  
 MAYLAN PHARMACEUTICALS INC.  
 MORGANTOWN, WV 26505 USA  
 MADE IN PUERTO RICO

## DOXEPIN HYDROCHLORIDE

doxepin hydrochloride capsule

### Product Information

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:55289-370(NDC:0378-3125)
<b>Route of Administration</b>	ORAL		

### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
DOXEPIN HYDROCHLORIDE (UNII: 3U9A0FE9N5) (DOXEPIN - UNII:5ASJ6HUZ7D)	DOXEPIN	25 mg

### Inactive Ingredients

Ingredient Name	Strength
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
STARCH, CORN (UNII: O8232NY3SJ)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
FERROSO FERRIC OXIDE (UNII: XM0M87F357)	
D&C YELLOW NO. 10 ALUMINUM LAKE (UNII: CQ3XH3DET6)	
FD&C BLUE NO. 1 ALUMINUM LAKE (UNII: J9EQA3S2JM)	

<b>FD&amp;C BLUE NO. 2 ALUMINUM LAKE</b> (UNII: 4AQJ3LG584)	
<b>FD&amp;C RED NO. 40</b> (UNII: WZB9127XOA)	
<b>PROPYLENE GLYCOL</b> (UNII: 6DC9Q167V3)	
<b>SHELLAC</b> (UNII: 46N107B71O)	

### Product Characteristics

<b>Color</b>	white (ivory opaque) , white (white opaque)	<b>Score</b>	no score
<b>Shape</b>	CAPSULE	<b>Size</b>	16mm
<b>Flavor</b>		<b>Imprint Code</b>	MYLAN;3125
<b>Contains</b>			

### Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:55289-370-30	30 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	08/02/2007	
2	NDC:55289-370-90	90 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	03/16/2020	

### Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA070791	05/13/1986	

**Labeler** - PD-Rx Pharmaceuticals, Inc. (156893695)

**Registrant** - PD-Rx Pharmaceuticals, Inc. (156893695)

### Establishment

Name	Address	ID/FEI	Business Operations
PD-Rx Pharmaceuticals, Inc.		156893695	repack(55289-370)

Revised: 1/2026

PD-Rx Pharmaceuticals, Inc.