**DOXEPIN HYDROCHLORIDE ORAL SOLUTION USP (Concentrate)**

**DESCRIPTION**

Doxepin hydrochloride is a class of psychotherapeutic agents known as dibenzoxepin tricyclic compounds. It is a white crystalline solid readily soluble in water, alcohol, and chloroform.

**MECHANISM OF ACTION**

The mechanism of action of doxepin hydrochloride is not definitely known. It is not a central nervous system stimulant or sedative except at large doses. Doxepin produces a variety of effects on the brain which would be expected to be of potential therapeutic importance. These effects include: increases in cerebral glucose utilization; increases in cerebral blood flow; decreases in brain protein breakdown; increases in cerebral uptake of tritiated water; increases in brain norepinephrine uptake; decreases in plasma corticotropin levels; and decreases in plasma prolactin levels. The mechanism of action of doxepin hydrochloride is not definitely known. It is not a central nervous system stimulant or sedative except at large doses. Doxepin produces a variety of effects on the brain which would be expected to be of potential therapeutic importance. These effects include: increases in cerebral glucose utilization; increases in cerebral blood flow; decreases in brain protein breakdown; increases in cerebral uptake of tritiated water; increases in brain norepinephrine uptake; decreases in plasma corticotropin levels; and decreases in plasma prolactin levels.

**INDICATIONS AND USAGE**

Doxepin hydrochloride is recommended for the treatment of:

1. Psychotic depressive disorders with and without anxiety
2. Depression and/or anxiety associated with alcoholism (not to be taken concomitantly with alcohol).

In addition, doxepin hydrochloride oral solution USP is a colorless liquid, is available in 120 mL glass containers.

**CONTRAINDICATIONS**

Patients who have recently received monoamine oxidase inhibitors (MAOIs) or have received an over-the-counter phenylephrine or pseudoephedrine within the past 14 days should not receive doxepin hydrochloride. The peak effect of these drugs last up to 14 days after the last dose. Doxepin hydrochloride is not recommended for use in patients with a history of trigeminal neuralgia or other severe neuropathic pain.

**WARNINGS**

**Clinical Monitoring and Suicide Risk**

Patients with a history of depression or bipolar disorder (unipolar or bipolar) may have an increased risk of suicide during the early phases of treatment. Patients should be closely monitored for the emergence of suicidal thoughts or behavior.

**Endocrine and Laboratory Tests**

Doxepin hydrochloride may cause a decrease in thyroid function, but the clinical significance of this effect is uncertain. Doxepin hydrochloride may have an effect on the level of thyroid hormone or thyroid-stimulating hormone. Clinical significance of this effect is uncertain.

**Adverse Reactions**

Some of the adverse reactions noted below have not been specifically reported with doxepin use. Doxepin hydrochloride may cause a decrease in thyroid function, but the clinical significance of this effect is uncertain. Doxepin hydrochloride may have an effect on the level of thyroid hormone or thyroid-stimulating hormone. Clinical significance of this effect is uncertain.

**DOSAGE AND ADMINISTRATION**

Doxepin hydrochloride oral solution USP is a colorless liquid, is available in 120 mL glass containers.

**DISPOSITION**

Human studies have shown that doxepin is distributed into breast milk. However, it is unknown if doxepin is excreted in human milk. Doxepin hydrochloride is not recommended for use in breastfed infants.

**REFERENCES**

The safety and effectiveness of doxepin hydrochloride in the pediatric population have not been established. Doxepin hydrochloride is not recommended for use in children under 12 years of age.

**DRUG INTERACTIONS**

Doxepin hydrochloride is a substrate for CYP3A4 and a competitive inhibitor of CYP2C9 and CYP2C19. Doxepin hydrochloride may increase the plasma concentrations of drugs that are metabolized by CYP3A4 and decrease the plasma concentrations of drugs that are metabolized by CYP2C19. Doxepin hydrochloride may decrease the plasma concentrations of drugs that are metabolized by CYP2C9. Doxepin hydrochloride may increase the plasma concentrations of drugs that are metabolized by CYP1A2. Doxepin hydrochloride may increase the plasma concentrations of drugs that are metabolized by CYP2C19. Doxepin hydrochloride may decrease the plasma concentrations of drugs that are metabolized by CYP2C9. Doxepin hydrochloride may increase the plasma concentrations of drugs that are metabolized by CYP1A2.

**CLINICAL PHARMACOLOGY**

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**PHARMACOKINETICS**

The pharmacokinetics of doxepin hydrochloride are not definitely known. It is not a central nervous system stimulant or sedative except at large doses. Doxepin produces a variety of effects on the brain which would be expected to be of potential therapeutic importance. These effects include: increases in cerebral glucose utilization; increases in cerebral blood flow; decreases in brain protein breakdown; increases in cerebral uptake of tritiated water; increases in brain norepinephrine uptake; decreases in plasma corticotropin levels; and decreases in plasma prolactin levels.

**RECOMMENDATIONS**

The safety and effectiveness of doxepin hydrochloride in the pediatric population have not been established. Doxepin hydrochloride is not recommended for use in children under 12 years of age.
Antidepressant Medicines, Depression and other Serious Mental Illnesses, and Suicidal Thoughts or Actions

Read the Medication Guide that comes with your or your family member’s antidepressant medicine. This Medication Guide is only about the risk of suicidal thoughts and actions with antidepressant medicines.

Talk to your, or your family member’s, healthcare provider about:

- all risks and benefits of treatment with antidepressant medicines
- all treatment choices for depression or other serious mental illness

What is the most important information I should know about antidepressant medicines, depression and other serious mental illnesses, and suicidal thoughts or actions?

1. Antidepressant medicines may increase suicidal thoughts or actions in some children, teenagers, and young adults within the first few months of treatment.

2. Depression and other serious mental illnesses are the most important causes of suicidal thoughts and actions. Some people may have a particularly high risk of having suicidal thoughts or actions. These include people who have (or have a family history of) bipolar illness (also called manic-depressive illness) or suicidal thoughts or actions.

3. 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, behaviors, thoughts, or feelings. This is very important when an antidepressant medicine is started or when the dose is changed.
   - Call the healthcare provider right away to report new or sudden changes in mood, behavior, thoughts, or feelings.
   - Keep all follow-up visits with the healthcare provider as scheduled. Call the healthcare provider between visits as needed, especially if you have concerns about symptoms.

Call a healthcare provider right away if you or your family member has any of the following symptoms, especially if they are new, worse, or worry you:

- thoughts about suicide or dying
- attempts to commit suicide
- new or worse depression
- new or worse anxiety
- feeling very agitated or restless
- panic attacks
- trouble sleeping (insomnia)
- new or worse irritability
- acting aggressive, being angry, or violent
- acting on dangerous impulses
- an extreme increase in activity and talking (mania)
- other unusual changes in behavior or mood
- Visual problems: eye pain, changes in vision, swelling or redness in or around the eye

What else do I need to know about antidepressant medicines?

- Antidepressants are medicines used to treat depression and other illnesses. It is important to discuss all the risks of treating depression and also the risks of not treating it. Patients and their families or other caregivers should discuss all treatment choices with the healthcare provider, not just the use of antidepressants.

- Antidepressant medicines have other side effects. Talk to the healthcare provider about the side effects of the medicine prescribed for you or your family member.

- Antidepressant medicines can interact with other medicines. Know all of the medicines that you or your family member takes. Keep a list of all medicines to show the healthcare provider. Do not start new medicines without first checking with your healthcare provider.

- Not all antidepressant medicines prescribed for children are FDA approved for use in children. Talk to your child’s healthcare provider for more information.

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

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

Manufactured By:

TEVA PHARMACEUTICALS USA
Sellersville, PA 18960

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