doxepin (dox-e-pin)
Silenor, SINEquan, Zonalon

**Classification**

Therapeutic: antidistress agents, antidepressants, antihistamines (topical), sedative/hypnotics
Pharmacologic: tricyclic antidepressants

**Pregnancy Category C**

**Indications**


**Action**

Prevents the reuptake of norepinephrine and serotonin by presynaptic neurons; resultant accumulation of neurotransmitters potentiates their activity. Also possesses significant anticholinergic properties. Topical: Antipruritic action due to antihistaminic properties.

**Therapeutic Effects:**

PO: Relief of depression. Decreased anxiety. Sedation and improved sleep maintenance. Topical: Decreased pruritus.

**Pharmacokinetics**

Absorption: Well absorbed from the GI tract, although much is metabolized on first pass through the liver. Some systemic absorption follows topical application.
Distribution: Widely distributed. Enters breast milk; probably crosses the placenta.

Metabolism and Excretion: Metabolized by the liver by the CYP2C19 and CYP2D6 isoenzymes; the CYP2C19 enzyme system exhibits genetic polymorphism; 15–20% of Asian patients and 5–5% of Caucasian and Black patients may be poor metabolizers of CYP2C19 and may have significantly higher doxepin concentrations and an increased risk of adverse effects; the CYP2D6 enzyme system also exhibits genetic polymorphism; 7% of population may be poor metabolizers of CYP2D6 and may have significantly higher doxepin concentrations and an increased risk of adverse effects. Some conversion to active antidepressant compound. May re-enter gastric juice via secretion from enterohepatic circulation, where more absorption may occur.

**Half-life:** 6–25 hr.

**TIME/ACTION PROFILE (antidepressant activity)**

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<td>PO</td>
<td>2–3 wk</td>
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**Contraindications/Precautions**

Contraindicated in: Hypersensitivity; Concurrent use of MAO inhibitors; Some products contain bisulfites and should be avoided in patients with known intolerance; Untreated angle-closure glaucoma; Severe urinary retention; Period immediately after myocardial infarction; History of QTc prolongation, heart failure, cardiac arrhythmia.

**Use Cautiously in:**

Geri: Pre-existing cardiovascular disease (risk of adverse reactions); Prostatic enlargement (more susceptible to urinary retention); Seizures; OB: Use only if potential maternal benefit outweighs risks to fetus; Lactation: Use during lactation may result in neonatal sedation. Recommend discontinuing drug or bottle-feed; Pedi: May; risk of suicide attempt/ideation especially during dose-early treatment or dose adjustment; risk may be greater in children or adolescents; safety not established; Geriatric patients should have initial dosage.

**Adverse Reactions/Side Effects**


**Interactions**

Apply to both topical and oral use.

Drug: Doxepin is metabolized in the liver by the cytochrome P450 2D6 enzyme and its action may be affected by drugs that compete for metabolism by this enzyme including other antidepressants, phenothiazines, carbamazepine, propranolol, flurbiprofen. When used concurrently, dosage of one or the other or both may be necessary. Concurrent use of other drugs that inhibit the activity of the cytochrome P450 2D6 enzyme may require dosage adjustments.

**Overdosage:**

PO, IM, IV:

- Supportive measures indicated. Induced vomiting and activated charcoal if given within 1 hour; do not give if patient is comatose.
- Hemodialysis, if available.

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PO (Adults): Antidepressant/antianxiety—25 mg 3 times daily, may be increased up to 150 mg/day in outpatients or 300 mg/day in inpatients; some patients may require only 25–50 mg/day. Once stabilized, entire daily dose may be given at bedtime. Antihistaminic—10 mg at bedtime initially, may be increased up to 25 mg. Antivertigo—6 mg at bedtime (should not exceed 3 mg/day if concurrently taking cimetidine).

PO (Geriatric Patients): Antidepressant/antianxiety—25–50 mg initially, may be increased up to 60 mg at bedtime (should not exceed 3 mg/day if concurrently taking cimetidine).

Topical (Adults): Antipruritic—as needed to 6 mg at bedtime. May require only 25–50 mg/day. Once stabilized, entire daily dose may be given at bedtime.

Antidepressant/antianxiety—10 mg at bedtime initially, may be increased up to 10 mg at bedtime. Once stabilized, entire daily dose may be given at bedtime.

Route/Dosage

NURSING IMPLICATIONS

Assessment

- Monitor BP and pulse rate prior to and during initial therapy. Patients taking high doses or with a history of cardiovascular disease should have EKG monitored prior to and periodically during therapy.

- Assess for sexual dysfunction (decreased libido, erectile dysfunction).

- Assess weight and BMI initially and throughout treatment. Obtain IBF and cholesterol levels in overweight obese individuals.

- Gastrointestinal disturbances: Monitor stool frequency and consistency. Asses for abdominal pain or discomfort.

- Depression: Assess suicidal ideation. Restrict amount of drug available to patient. Risk may be increased in children, adolescents, and adults. Patients with a history of depression or mania, or suicidal ideation may require close monitoring.

- Insomnia: Assess degree and manifestations of anxiety prior to and during therapy. Avoid initiating therapy in children, adolescents, and adults. Patients with a history of depression or mania, or suicidal ideation may require close monitoring.

- Pain: Assess the type, location, and severity of pain prior to and periodically during therapy. Use pain scale to assess effectiveness of therapy.

- Anxiety: Assess degree and manifestations of anxiety prior to and during therapy. Assess falls risk and institute fall prevention strategies. Assess for anticholinergic effects.

- Drug-Natural Products: Monitor for drug interactions. Patients taking high doses of doxepin are at increased risk for additive anticholinergic effects. Risk may be increased in children, adolescents, and adults. Patients with a history of depression or mania, or suicidal ideation may require close monitoring.

- Antipruritic—Monitor pruritic area prior to and periodically during therapy. Use pain scale to assess effectiveness of therapy.

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CONTINUED

doxepin

- May be given as a single dose 30 min before bedtime to minimize sedation during the day. Dose increases should be made at bedtime because of sedation. Dose titration is a slow process; may take weeks to months.
- To avoid intralethal, super 50% for 3 days, then 50% again for 3 days, then discontinue.
- PO: Administer medication with or immediately following a meal to minimize gastric irritation. Capsules may be opened and mixed with foods or fluids of patient’s choice and easily swallowed.
- Oral concentrate must be diluted at least 120 mL of water, milk, or fruit juice. Use calibrated measuring device to ensure accurate amount.
- Topical: Apply thin film of doxepin cream only to affected areas, and rub in gently. Apply only to affected skin; not for ophthalmic, oral, or intravaginal use.

Patient/Family Teaching

- Inform patient that systemic side effects may occur with oral or topical use.
- May cause drowsiness and blurred vision. Caution patient to avoid driving and other activities requiring alertness until response to the medication is known.
- Orthostatic hypotension, sedation, and confusion are common during early therapy, especially in geriatric patients. Protect patient from falls. Institute fall precautions. Advise patient to change positions slowly.
- Advise patient to avoid alcohol or other CNS depressant drugs during and for at least 3–7 days after therapy has been discontinued.
- Inform patient that urinary retention occurs or if dry mouth or constipation persists. Sugarless candy or gum may diminish dry mouth, and an increase in fluid intake or bulk may prevent constipation. Consult health care professional if dry mouth persists for more than 2 wk.
- Advise patient to notify health care professional if excessive drowsiness occurs with topical application. Number of applications per day, amount of cream applied, or area of application may be reduced. May require discontinuation of therapy.

Evaluation/Desired Outcomes

- Increased sense of well being.
- Renewed interest in surroundings.
- Increased appetite.

Note: ● = Canadian drug name. [ ] = Genetic Implication. CAPS indicates life-threatening, underlines indicate most frequent. Strikethrough indicates discontinued.
● Improved energy level.
● Improved sleep.
● Decrease in anxiety.
● Decrease in chronic pain. Patients may require 2–6 wk of oral therapy before full therapeutic effects of medication are evident.
● Decrease in pruritus associated with eczema.

Why was this drug prescribed for your patient?