

Doxepin (Silenor) for Insomnia

DHIREN PATEL, PharmD, and JENNIFER D. GOLDMAN-LEVINE, PharmD
Massachusetts College of Pharmacy and Health Sciences, Boston, Massachusetts

STEPS new drug reviews cover Safety, Tolerability, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

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Silenor is a new low-dose formulation of the tricyclic antidepressant doxepin (which is typically taken as a 25- to 150-mg dose at bedtime). Low-dose doxepin is labeled for the treatment of insomnia characterized by difficulty maintaining sleep. The exact mechanism by which the medication exerts its sleep maintenance effect is unknown, but is thought to be antagonism of histamine H₁ receptors.¹

Drug	Dosage	Dose form	Monthly cost*
Doxepin (Silenor)	3 to 6 mg daily	3-mg and 6-mg tablets	\$208

*—Price for 30 3-mg or 6-mg tablets at CVS Pharmacy on May 18, 2011.

SAFETY

Doxepin is safe when used at low dosages. Antidepressants are required to have labeling that warns of an increased risk of suicide; however, there have been no reports of suicide among patients taking low-dose doxepin. Unlike higher-dose formulations of doxepin, Silenor does not have a boxed warning for suicide risk.¹ No dosage adjustments are necessary in patients with renal impairment. Doxepin should not be used in patients with severe urinary retention or in those who also take or who have recently stopped taking monoamine oxidase inhibitors. Abrupt discontinuation is not associated with a withdrawal syndrome.¹ The metabolism of doxepin is affected by cimetidine (Tagamet); patients who take both drugs should not take more than 3 mg of doxepin per day. Low-dose doxepin does not seem to be affected by other drugs that affect the cytochrome P450 system. Silenor is a U.S. Food and Drug Administration pregnancy category C drug.¹

TOLERABILITY

Silenor has an adverse effect profile comparable to that of placebo. In clinical trials

of 1,017 patients, approximately 1 percent withdrew because of adverse effects.¹ Rebound insomnia and withdrawal symptoms have not been reported. Next-day sedation, anticholinergic effects, and memory impairment do not occur at low dosages.^{2,3} The use of central nervous system depressants, alcohol, and sedating antihistamines may increase the sedative effect of doxepin and should be avoided.¹

EFFECTIVENESS

Silenor has been studied mainly in older patients with primary insomnia and difficulty falling asleep, frequent waking, or sleep duration of less than 6.5 hours. In sleep studies comparing 3-mg and 6-mg doses for two nights, total sleep duration increased 25 to 38 minutes compared with placebo.^{2,3} Time to sleep onset (sleep latency) did not decrease significantly. The benefit in younger adults does not seem to be as pronounced.¹ When given nightly for up to three months, the 3-mg dose produces consistent results without causing next-day residual effects on cognitive performance; the long-term effects of the 6-mg dose have not been studied.⁴ No research has compared Silenor with other hypnotics. ►



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PRICE

Silenor costs approximately \$208 for 30 3-mg or 6-mg tablets. Less expensive formulations of doxepin are available, such as a generic oral solution (10 mg per mL; approximately \$24 per 120-mL bottle) and a generic 10-mg capsule (approximately \$20 for 90 capsules). Pharmacists cannot substitute these products for Silenor; the generic name must be used on the prescription.

SIMPLICITY

Patients older than 65 years should begin with a 3-mg dose, and increase to 6 mg if necessary. In younger adults, the recommended starting dose is 6 mg. Patients with hepatic impairment or with a tendency for urinary retention should start with the lower dose. Doxepin should be taken within 30 minutes before bedtime, but not within three hours of a meal. Dependence has not been shown in studies, and there are no limitations on the duration or frequency of use.

Bottom Line

In older patients with primary insomnia, Silenor can increase duration of sleep without next-day effects. However, it does not significantly decrease the time to sleep onset, and it is less effective in younger adults. Less expensive options for insomnia treatment are available, including a generic oral solution of doxepin and a generic 10-mg capsule.

Address correspondence to Dhiren Patel, PharmD, at dhiren.patel1@mcphs.edu. Reprints are not available from the authors.

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