

Misuse of Meth Decreased

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the highest rate of nonmedical use (2.1%), followed by tranquilizers (0.8%), stimulants (0.5%), and sedatives (0.1%).

Of those who misused prescription-type pain relievers, 55% of people 12 years or older got prescription-type pain relievers from a friend or relative for free. More than 17% got their pain relievers from one doctor, 5% got them from a dealer or stranger, and 0.4%

bought them on the Internet.

The rate of illicit drug use also rose among U.S. residents aged 50-59 years, from 2.7% in 2002 to 6.2% in 2009 during the month prior to the survey.

The trend, according to the survey, reflects the growing aging population.

The rate of misuse decreased for just two drugs – cocaine and methamphetamine.

Misuse of cocaine decreased from 2.0% in 2008 to 1.4% in 2009 and the rate for methamphetamine decreased from 0.6% to 0.2% over the same period. The rates of alcohol and tobacco use remained relatively stable between 2008 and 2009, according to the survey.

Federal officials called for more community collaboration to increase awareness about the dangers of illicit drug use.

Dr. J. Calvin Chatlos said in an interview that he thinks it is notable that the increase in illicit drug use mostly occurred among those in the 12-17 and 18-25 age groups. The key focus among

those groups was on marijuana and psychotherapeutics, mostly pain relievers, he pointed out.

“We must ask ourselves to what degree is this related to increased acceptability of medical marijuana and the overall increase nationally in prescribing pain relievers to adults,” said Dr. Chatlos, a child and adolescent addiction psychiatrist who serves as associate clinical professor of psychiatry at the University of Medicine and Dentistry of New Jersey, New Brunswick. “This is supported in the survey results that show a decreased perceived risk of marijuana use for the past 2 years.”

Dr. Chatlos also found the increase in past month illicit drug use among people aged 50-54 to be fascinating. “Are these the parents of those in the 18-25 age group that shows increased tolerance or promotion of use?” ■

Silenor®

(doxepin) tablets for oral administration

Brief summary of Prescribing Information. For complete Prescribing Information, consult official package insert.

INDICATIONS AND USAGE

Silenor is indicated for the treatment of insomnia characterized by difficulty with sleep maintenance. The clinical trials performed in support of efficacy were up to 3 months in duration.

CONTRAINDICATIONS

Hypersensitivity:

Silenor is contraindicated in individuals who have shown hypersensitivity to doxepin HCl, any of its inactive ingredients, or other dibenzoxepines.

Co-administration With Monoamine Oxidase Inhibitors (MAOIs):

Serious side effects and even death have been reported following the concomitant use of certain drugs with MAO inhibitors. Do not administer Silenor if patient is currently on MAOIs or has used MAOIs within the past two weeks. The exact length of time may vary depending on the particular MAOI dosage and duration of treatment.

Glaucoma and Urinary Retention:

Silenor is contraindicated in individuals with untreated narrow angle glaucoma or severe urinary retention.

WARNINGS AND PRECAUTIONS

Need to Evaluate for Comorbid Diagnoses:

Because sleep disturbances may be the presenting manifestation of a physical and/or psychiatric disorder, symptomatic treatment of insomnia should be initiated only after careful evaluation of the patient. The failure of insomnia to remit after 7 to 10 days of treatment may indicate the presence of a primary psychiatric and/or medical illness that should be evaluated. Exacerbation of insomnia or the emergence of new cognitive or behavioral abnormalities may be the consequence of an unrecognized psychiatric or physical disorder. Such findings have emerged during the course of treatment with hypnotic drugs.

Abnormal Thinking and Behavioral Changes:

Complex behaviors such as “sleep-driving” (i.e., driving while not fully awake after ingestion of a hypnotic, with amnesia for the event) have been reported with hypnotics. These events can occur in hypnotic-naïve as well as in hypnotic-experienced persons. Although behaviors such as “sleep-driving” may occur with hypnotics alone at therapeutic doses, the use of alcohol and other CNS depressants with hypnotics appears to increase the risk of such behaviors, as does the use of hypnotics at doses exceeding the maximum recommended dose. Due to the risk to the patient and the community, discontinuation of Silenor should be strongly considered for patients who report a “sleep-driving” episode. Other complex behaviors (e.g., preparing and eating food, making phone calls, or having sex) have been reported in patients who are not fully awake after taking a hypnotic. As with “sleep-driving”, patients usually do not remember these events. Amnesia, anxiety and other neuro-psychiatric symptoms may occur unpredictably.

Suicide Risk and Worsening of Depression:

In primarily depressed patients, worsening of depression, including suicidal thoughts and actions (including completed suicides), has been reported in association with the use of hypnotics. Doxepin, the active ingredient in Silenor, is an antidepressant at doses 10- to 100-fold higher than in Silenor. Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Risk from the lower dose of doxepin in Silenor cannot be excluded. It can rarely be determined with certainty whether a particular instance of the abnormal behaviors listed above is drug induced, spontaneous in origin, or a result of an underlying psychiatric or physical disorder. Nonetheless, the emergence of any new behavioral sign or symptom of concern requires careful and immediate evaluation.

CNS Depressant Effects:

After taking Silenor, patients should confine their activities to those necessary to prepare for bed. Patients should avoid engaging in hazardous activities, such as operating a motor vehicle or heavy machinery, at night after taking Silenor, and should be cautioned about potential impairment in the performance of such activities that may occur the day following ingestion. When taken with Silenor, the sedative effects of alcoholic beverages, sedating antihistamines, and other CNS depressants may be potentiated. Patients should not consume alcohol with Silenor. Patients should be cautioned about potential additive effects of Silenor used in combination with CNS depressants or sedating antihistamines.

ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of labeling:

- Abnormal thinking and behavioral changes.
- Suicide risk and worsening of depression.
- CNS Depressant effects.

Clinical Trials Experience:

The pre-marketing development program for Silenor included doxepin HCl exposures in 1017 subjects (580 insomnia patients and 437 healthy subjects) from 12 studies conducted in the United States. 863 of these subjects (580 insomnia patients

and 283 healthy subjects) participated in six randomized, placebo-controlled efficacy studies with Silenor doses of 1mg, 3 mg, and 6 mg for up to 3-months in duration. Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice. However, data from the Silenor studies provide the physician with a basis for estimating the relative contributions of drug and non-drug factors to adverse reaction incidence rates in the populations studied.

Associated with Discontinuation of Treatment:

The percentage of subjects discontinuing Phase 1, 2, and 3 trials for an adverse reaction was 0.6% in the placebo group compared to 0.4%, 1.0%, and 0.7% in the Silenor 1 mg, 3 mg, and 6 mg groups, respectively. No reaction that resulted in discontinuation occurred at a rate greater than 0.5%.

Adverse Reactions Observed at an Incidence of ≥2% in Controlled Trials:

Table 1 shows the incidence of treatment-emergent adverse reactions from three long-term (29 to 85 days) placebo-controlled studies of Silenor in adult (N=221) and elderly (N=494) subjects with chronic insomnia. Reactions reported by investigators were classified using a modified MedDRA dictionary of preferred terms for the purposes of establishing incidence. The table includes only reactions that occurred in 2% or more of subjects who received Silenor 3 mg or 6 mg in which the incidence in subjects treated with Silenor was greater than the incidence in placebo-treated subjects.

Incidence (%) of Treatment-Emergent Adverse Reactions in Long-term Placebo-Controlled Clinical Trials

System Organ Class Preferred Term*	Placebo (N=278)	Silenor 3 mg (N=157)	Silenor 6 mg (N=203)
Nervous System Disorders			
Somnolence/Sedation	4	6	9
Infections and Infestations			
Upper Respiratory Tract Infection/Nasopharyngitis	2	4	2
Gastroenteritis	0	2	0
Gastrointestinal Disorders			
Nausea	1	2	2
Vascular Disorders			
Hypertension	0	3	<1

*Includes reactions that occurred at a rate of ≥2% in any Silenor-treated group and at a higher rate than placebo.

The most common treatment-emergent adverse reaction in the placebo and each of the Silenor dose groups was somnolence/sedation.

Studies Pertinent to Safety Concerns for Sleep-promoting Drugs:

Residual Pharmacological Effect in Insomnia Trials: Five randomized, placebo-controlled studies in adults and the elderly assessed next-day psychomotor function within 1 hour of awakening utilizing the digit-symbol substitution test (DSST), symbol copying test (SCT), and visual analog scale (VAS) for sleepiness, following night time administration of Silenor. In a one-night, double-blind study conducted in 565 healthy adult subjects experiencing transient insomnia, Silenor 6 mg showed modest negative changes in SCT and VAS. In a 35-day, double-blind, placebo-controlled, parallel group study of Silenor 3 and 6 mg in 221 adults with chronic insomnia, small decreases in the DSST and SCT occurred in the 6 mg group. In a 3-month, double-blind, placebo-controlled, parallel group study in 240 elderly subjects with chronic insomnia, Silenor 1 mg and 3 mg was comparable to placebo on DSST, SCT, and VAS.

DRUG INTERACTIONS

Cytochrome P450 Isozymes:

Silenor is primarily metabolized by hepatic cytochrome P450 isozymes CYP2C19 and CYP2D6, and to a lesser extent, by CYP1A2 and CYP2C9. Inhibitors of these isozymes may increase the exposure of doxepin. Silenor is not an inhibitor of any CYP isozymes at therapeutically relevant concentrations. The ability of Silenor to induce CYP isozymes is not known.

Cimetidine:

Silenor exposure is doubled with concomitant administration of cimetidine, a nonspecific inhibitor of CYP isozymes. A maximum dose of 3 mg is recommended in adults and elderly when cimetidine is co-administered with Silenor.

Alcohol:

When taken with Silenor, the sedative effects of alcohol may be potentiated.

CNS Depressants and Sedating Antihistamines:

When taken with Silenor, the sedative effects of sedating antihistamines and CNS depressants may be potentiated.

Tolazamide:

A case of severe hypoglycemia has been reported in a type II diabetic patient maintained on tolazamide (1 g/day) 11 days after the addition of oral doxepin (75 mg/day).

USE IN SPECIFIC POPULATIONS

Pregnancy:

Pregnancy Category C:

There are no adequate and well-controlled studies of Silenor in pregnant women. Silenor should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Administration of doxepin to pregnant animals resulted in adverse effects on offspring development at doses greater than the maximum recommended human dose (MRHD) of 6 mg/day. When doxepin (30, 100, and 150 mg/kg/day) was administered orally to pregnant rats during the period of organogenesis, developmental toxicity (increased incidences of fetal structural abnormalities and decreased fetal body weights) was noted at ≥100 mg/kg/day. The plasma exposures (AUC) at the no-effect dose for embryo-fetal developmental toxicity in rats (30 mg/kg/day) are approximately 6 and 3 times the plasma AUCs for doxepin and nordoxepin (the primary metabolite in humans), respectively, at the MRHD. When administered orally to pregnant rabbits (10, 30, and 60 mg/kg/day) during the period of organogenesis, fetal body weights were reduced at the highest dose in the absence of maternal toxicity. The plasma exposures (AUC) at the no-effect dose for developmental effects (30 mg/kg/day) are approximately 6 and 18 times the plasma AUCs for doxepin and nordoxepin, respectively, at the MRHD. Oral administration of doxepin (10, 30, and 100 mg/kg/day) to rats throughout the pregnancy and lactation periods resulted in decreased pup survival and transient growth delay at the highest dose. The plasma exposures (AUC) at the no-effect dose for adverse effects on pre- and postnatal development in rats (30 mg/kg/day) are approximately 3 and 2 times the plasma AUCs for doxepin and nordoxepin, respectively, at the MRHD.

Labor and Delivery:

The effects of Silenor on labor and delivery in pregnant women are unknown.

Nursing Mothers:

Doxepin is excreted in human milk after oral administration. There has been a report of apnea and drowsiness occurring in a nursing infant whose mother was taking the higher dose of doxepin used to treat depression. Caution should be exercised when Silenor is administered to nursing women.

Pediatric Use:

The safety and effectiveness of Silenor in pediatric patients have not been evaluated.

Geriatric Use:

A total of 362 subjects who were ≥65 years and 86 subjects who were ≥75 years received Silenor in controlled clinical studies. No overall differences in safety or effectiveness were observed between these subjects and younger adult subjects. Greater sensitivity of some older individuals cannot be ruled out. Sleep-promoting drugs may cause confusion and over-sedation in the elderly. A starting dose of 3 mg is recommended in this population and evaluation prior to considering dose escalation is recommended.

Use in Patients With Hepatic Impairment:

Patients with hepatic impairment may display higher doxepin concentrations than healthy individuals. Initiate Silenor treatment with 3 mg in patients with hepatic impairment and monitor closely for adverse daytime effects.

Use in Patients With Sleep Apnea:

Silenor has not been studied in patients with obstructive sleep apnea. Since hypnotics have the capacity to depress respiratory drive, precautions should be taken if Silenor is prescribed to patients with compromised respiratory function. In patients with severe sleep apnea, Silenor is ordinarily not recommended for use.

OVERDOSAGE

Doxepin is routinely administered for indications other than insomnia at doses 10- to 50-fold higher than the highest recommended dose of Silenor.

The signs and symptoms associated with doxepin use at doses several-fold higher than the maximum recommended dose (Excessive dose) of Silenor for the treatment of insomnia are described, as are signs and symptoms associated with higher multiples of the maximum recommended dose in the full prescribing information.

PATIENT COUNSELING INFORMATION

Prescribers or other healthcare professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with hypnotics, should counsel them in appropriate use, and should instruct them to read the Medication Guide.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

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Smoking Quit Rate Rises With Longer Therapy

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY OF ADDICTION MEDICINE

SAN FRANCISCO – An intensive smoking-cessation program helped 33% of 202 patients in drug treatment quit smoking, an intent-to-treat analysis found.

A high proportion of patients in treatment for substance use also smoke cigarettes and have a hard time quitting, with previous studies suggesting quit rates of 5%-12%, Dr. Milan Khara said at the meeting.

The study enrolled 252 patients who were in drug treatment programs in 8 weeks of group therapy for smoking cessation plus free pharmacotherapy for smoking cessation during the group therapy and for up to an additional 18 weeks, for a total program length of 26 weeks, said Dr. Khara of the University of British Columbia, Vancouver.

The overall quit-smoking rate of 33% in the intent-to-treat analysis was exceeded by a quit rate of 43% among 152 patients who completed the program.

Among these completers, the quit rate was 51% in those who attended the 8 weeks of smoking-cessation group therapy and participated in after-care, compared with 18% of completers who only attended the 8 weeks of group therapy. About 80% of people in drug treatment programs smoke tobacco. “Within addiction services, we’ve largely had a blind spot about tobacco,” Dr. Khara said. “We often believe that these patients don’t want to quit smoking,” but other studies have shown that 44%-80% of patients in drug treatment expressed interest in quitting.

—Sherry Boschert

Disclosures: Dr. Khara has received funding from or been a consultant for Pfizer and Johnson & Johnson, which make smoking-cessation medications. Johnson & Johnson and divisions of the Canadian government funded provision of medications in the study.