

American Osteopathic Association
Continuing Medical Education

CERTIFICATION OF HOME STUDY

This is to certify that I, _____ completed the following
activity for AOA CME credits. Please print

Type of activity (such as reading or listening) _____

Name of journal(s) or audio-tape and date(s) of issue(s): _____

(One-half CREDIT may be granted for each issue or tape)

AOA number

D.O.'s signature

College and year of graduation

Current address (including zip code)

MAIL TO: AOA Division of CME, 212 East Ohio Street, Chicago, Illinois 60611

KEEP A DUPLICATE FOR YOUR RECORDS!

The **Home Study** form is intended to document individual reading of recognized scientific journals, listening to approved audio-tapes, and other approved home study courses and programs under the criteria described for Category **2-B**.

Only one type of home study, such as reading, should be indicated on a single form, though multiple issues of scientific journals may be listed.

This form should **not** be used, however, when CME quiz cards for the AOA Journal are submitted separately.

FOR OFFICE USE ONLY

Cat. **2-B** Credits _____

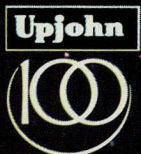
Date _____

Program # _____

Doctor # _____

Doctor's Name _____

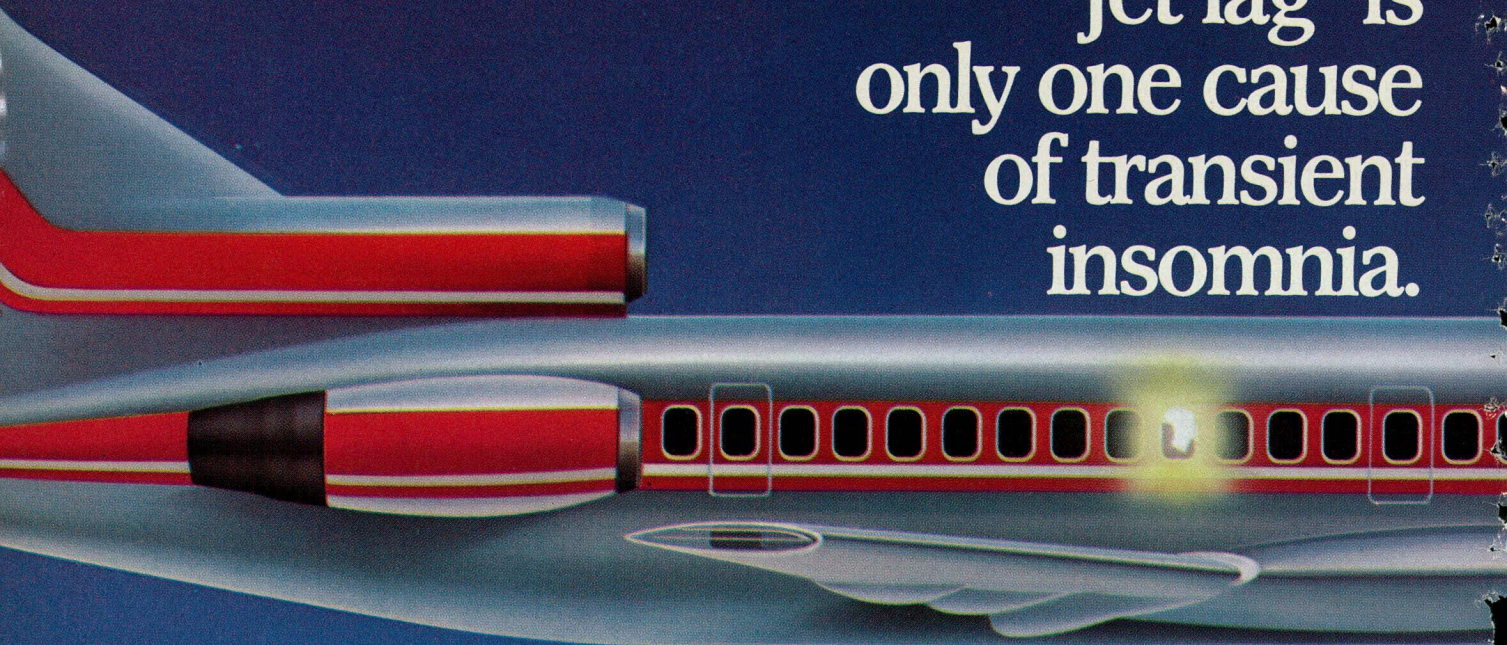
Please refer to the revised CME GUIDE for additional information.



A Century
of Caring
1886-1986



“Jet lag” is
only one cause
of transient
insomnia.



Hospitalization for elective surgery, job loss, and bereavement are other possible causes. In fact, according to a panel of sleep experts convened by the National Institute of Mental Health (NIMH), transient insomnia may be caused by acute situational stress lasting several days, whereas short-term insomnia is usually related to excessive stress associated with work or family life and may last up to three weeks.

HALCION provides the recommended therapeutic profile. When drug therapy is elected as appropriate in the total management of transient or short-term insomnia, the NIMH panel stated that benzodiazepines are preferred; they recommended a small dose of a rapidly eliminated hypnotic for the shortest clinically necessary period of time. HALCION, with a 2.6-hour mean elimination half-life, meets the panel's recommendations.

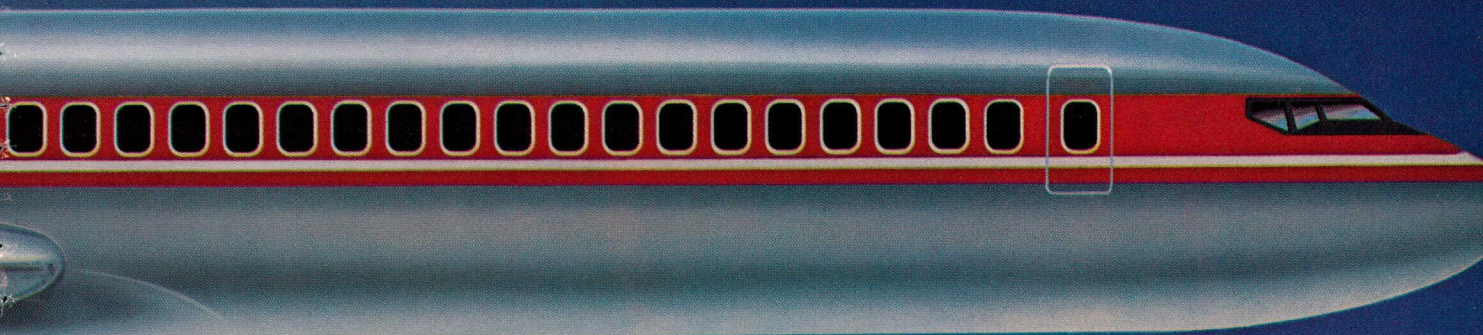
HALCION provides a full duration of sleep... In a double-blind, crossover study¹ comparing the effects of HALCION 0.5 mg tablets with placebo in ten healthy volunteers whose sleep was shifted to daytime hours, HALCION significantly ($P < 0.01$) improved the total sleep time (+50.6 minutes).

...and better alertness after awakening. In another study,² the effects of HALCION 0.5 mg and flurazepam 30 mg on alertness after a 12-hour shift in sleep-wake schedule were compared in normal sleepers. Subjects taking HALCION did not show an increase in sleep tendency during the awake period of the study, while the flurazepam subjects demonstrated a significant increase in sleepiness compared with baseline. This difference was statistically significant ($P < 0.05$).

Patients should be cautioned against engaging in hazardous tasks that require mental alertness (operating machinery or driving a motor vehicle) while taking benzodiazepines.

Halcion 0.25 MG TABLETS[®]
triazolam[®] IV

**Helps meet both goals
of insomnia therapy**



Halcion®

Tablets (triazolam) ©

INDICATIONS AND USAGE: HALCION Tablets are indicated in the short-term management of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings, and/or early morning awakenings.

It is recommended that HALCION not be prescribed in quantities exceeding a one-month supply.

CONTRAINDICATIONS: Patients with known hypersensitivity to this drug or other benzodiazepines.

HALCION is contraindicated in pregnant women due to potential fetal damage. Patients likely to become pregnant while receiving HALCION should be warned of the potential risk to the fetus.

WARNINGS: Overdosage may occur at four times the maximum recommended therapeutic dose. Patients should be cautioned not to exceed prescribed dosage.

Because of its depressant CNS effects, patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness and also about the simultaneous ingestion of alcohol and other CNS depressant drugs.

Anterograde amnesia and paradoxical reactions have been reported with HALCION and some other benzodiazepines.

PRECAUTIONS: General: In elderly and/or debilitated patients, treatment should be initiated at 0.125 mg to decrease the possibility of development of oversedation, dizziness, or impaired coordination. Caution should be exercised in patients with signs or symptoms of depression which could be intensified by hypnotic drugs. Suicidal tendencies and intentional overdosage is more common in these patients. The usual precautions should be observed in patients with impaired renal or hepatic function and chronic pulmonary insufficiency. Information for Patients: Alert patients about: (a) consumption of alcohol and drugs, (b) possible fetal abnormalities, (c) operating machinery or driving, (d) not increasing prescribed dosage, (e) possible worsening of sleep after discontinuing HALCION. Laboratory Tests: Not ordinarily required in otherwise healthy patients. Drug Interactions: Additive CNS depressant effects with other psychotropics, anticonvulsants, antihistaminics, ethanol, and other CNS depressants. Pharmacokinetic interactions of benzodiazepines with other drugs have been reported. Carcinogenesis, Mutagenesis, Impairment of Fertility: No evidence of carcinogenic potential was observed in mice during a 24-month study with HALCION in doses up to 4000 times the human dose. Pregnancy: Benzodiazepines may cause fetal damage if administered during pregnancy. The child born of a mother who is on benzodiazepines may be at some risk for withdrawal symptoms and neonatal flaccidity during the postnatal period. Nursing Mothers: Administration to nursing mothers is not recommended. Pediatric Use: Safety and efficacy in children below the age of 18 have not been established.

ADVERSE REACTIONS: During placebo-controlled clinical studies in which 1003 patients received HALCION Tablets, the most troublesome side effects were extensions of the pharmacologic activity of HALCION, e.g. drowsiness, dizziness, or light-headedness.

	HALCION 1003	Placebo 997
Number of Patients		
% of Patients Reporting:		
Central Nervous System		
Drowsiness	14.0	6.4
Headache	9.7	8.4
Dizziness	7.8	3.1
Nervousness	5.2	4.5
Lightheadedness	4.9	0.9
Coordination Disorder/Ataxia	4.6	0.8
Gastrointestinal		
Nausea/Vomiting	4.6	3.7

In addition, the following adverse events have been reported less frequently (i.e., 0.9-0.5%): euphoria, tachycardia, tiredness, confusional states/memory impairment, cramps/pain, depression, visual disturbances.

Rare (i.e., less than 0.5%) adverse reactions included constipation, taste alterations, diarrhea, dry mouth, dermatitis/allergy, dreaming/nightmares, insomnia, paresthesia, tinnitus, dysesthesia, weakness, congestion, death from hepatic failure in a patient also receiving diuretic drugs.

The following adverse events have been reported in association with the use of benzodiazepines: dystonia, irritability, anorexia, fatigue, sedation, slurred speech, jaundice, pruritus, dysarthria, changes in libido, menstrual irregularities, incontinence and urinary retention.

As with all benzodiazepines, paradoxical reactions such as stimulation, agitation, increased muscle spasticity, sleep disturbances, hallucinations and other adverse behavioral effects may occur rarely and in a random fashion. Should these occur, use of the drug should be discontinued.

No laboratory changes were considered to be of physiological significance.

When treatment is protracted, periodic blood counts, urinalysis and blood chemistry analyses are advisable.

Minor changes in EEG patterns, usually low-voltage fast activity have been observed in patients during HALCION therapy and are of no known significance.

DRUG ABUSE AND DEPENDENCE: Controlled Substance: HALCION Tablets are a Controlled Substance in Schedule IV. Abuse and Dependence: Withdrawal symptoms have occurred following abrupt discontinuance of benzodiazepines. Patients with a history of seizures are at particular risk. Addiction-prone patients should be closely monitored. Repeat prescriptions should be limited to those under medical supervision.

OVERDOSAGE: Because of the potency of triazolam, overdosage may occur at 2 mg, four times the maximum recommended therapeutic dose (0.5 mg). Manifestations of overdosage include somnolence, confusion, impaired coordination, slurred speech, and ultimately, coma. Respiration, pulse, and blood pressure should be monitored and supported by general measures when necessary. Immediate gastric lavage should be performed. Multiple agents may have been ingested.

Store at controlled room temperature 15°-30°C (59°-86°F).

Caution: Federal law prohibits dispensing without prescription.

B-2-S

References:

- Walsh JK, Muehlbach MJ, Schweitzer PK: Acute administration of triazolam for the daytime sleep of rotating shift workers. *Sleep* 1984;7:223-229.
- Seidel WF, Dement WC, Roth T, et al: Treatment of a 12-hour shift of sleep schedule with benzodiazepines. *Science* 1984;224:1261-1264.

"prompt use of glucocorticoids in the emergency treatment of severe asthma can prevent significant morbidity, reduce the number of hospitalizations, and effect substantial savings in health care costs."

Littenberg, B., and Gluck, E.H.: A controlled trial of methylprednisolone in the emergency treatment of acute asthma. *N Engl J Med* 314:150-2, 16 Jan 86

Nonsteroidal anti-inflammatory drugs and renal failure

The present report concerns itself with 17 patients who presented with renal failure associated with the use of nonsteroidal anti-inflammatory drugs (NSAID).

Four patients with acute tubular necrosis and 3 patients with acute interstitial nephritis presented with acute renal failure. Four other patients presented with symptomless renal impairment that was discovered during routine follow-up in a rheumatology clinic. All 11 patients recovered when NSAID treatment was discontinued. The 6 remaining patients presented with chronic renal failure, a disease that up to now has not been associated with NSAID therapy.

The authors hypothesize that renal disease associated with NSAID may be more extensive than previously recognized. Patients who develop dyspnea, edema, proteinuria, diarrhea and vomiting, and unexplainable fatigue should probably be advised to discontinue the intake of NSAID until it is determined whether or not renal impairment is involved. Adams and associates also note that drugs with shorter half lives (for example, indomethacin and ibuprofen) are not implicated in renal failure as often as medications with long half lives (naproxen and piroxicam, for example).

Adams, D.H., et al.: Non-steroidal anti-inflammatory drugs and renal failure. *Lancet* 1:57-9, 11 Jan 86

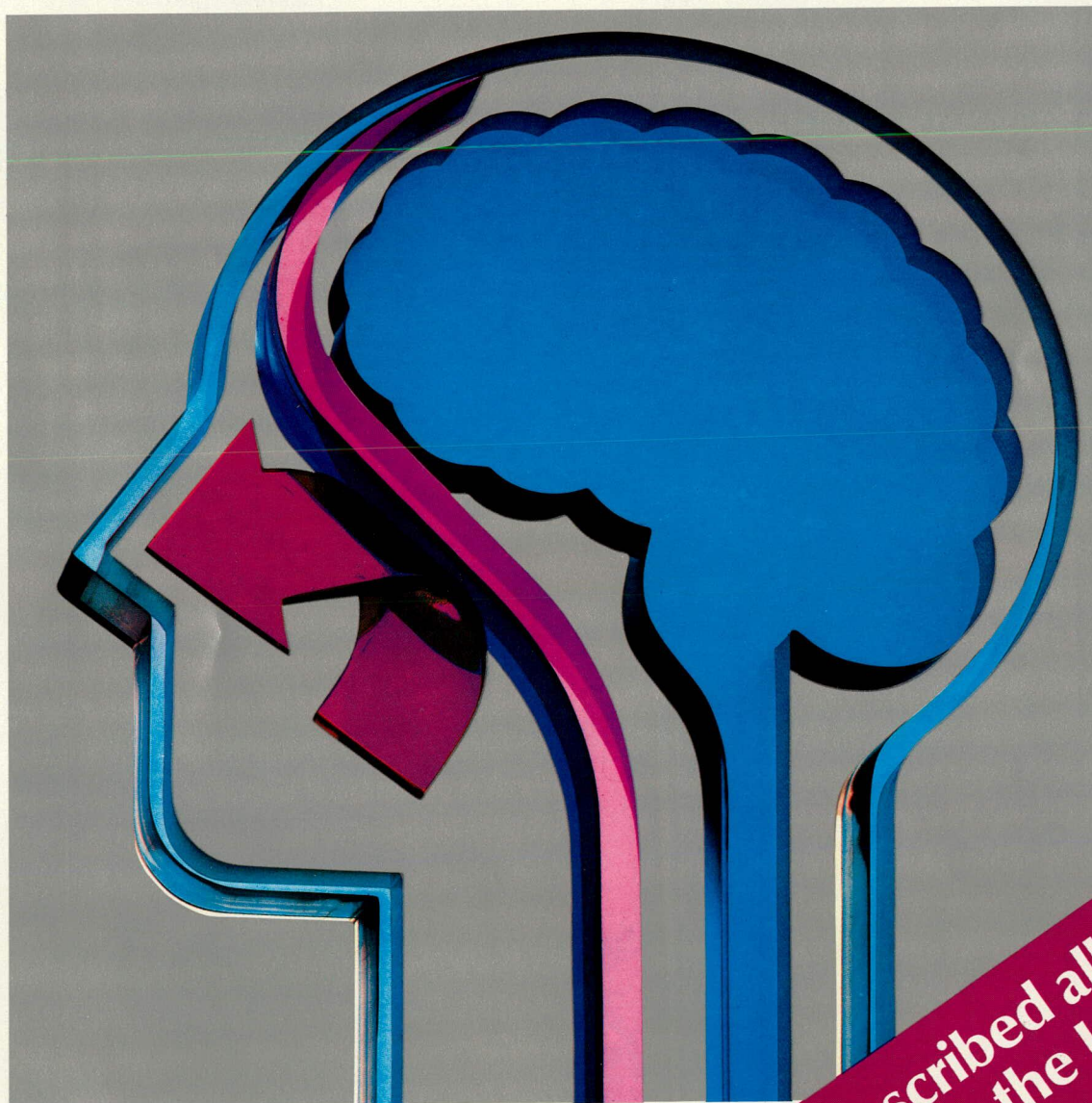
*A major turning point in seasonal
allergic rhinitis therapy*

Pharmacologically distinct

SELDANE[®]

(terfenadine) 60 mg tablets BID

Separating sedation from relief*



*The reported incidence of sedation with Seldane (9.0%) in controlled clinical studies did not differ significantly from that reported in patients receiving placebo (8.1%).

†Based on monthly prescription audits of single-entity antihistamines, combination antihistamine/decongestants, nasal steroids, and nasal cromolyn sodium.

Before prescribing Seldane, please see Brief Summary of Prescribing Information which appears on the last page.

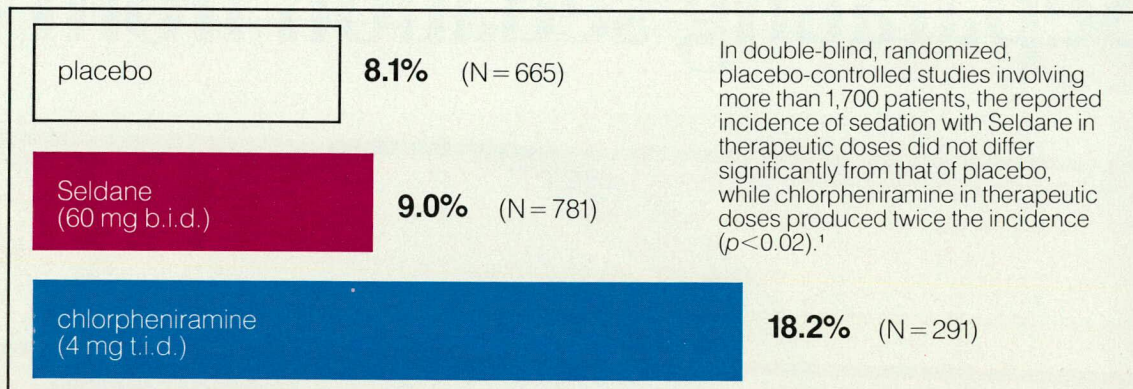
**The #1 prescribed allergy
product in the U.S.†**

Pharmacologically distinct
SELDANE[®]
(terfenadine) 60 mg tablets BID



Sedation equivalent to placebo

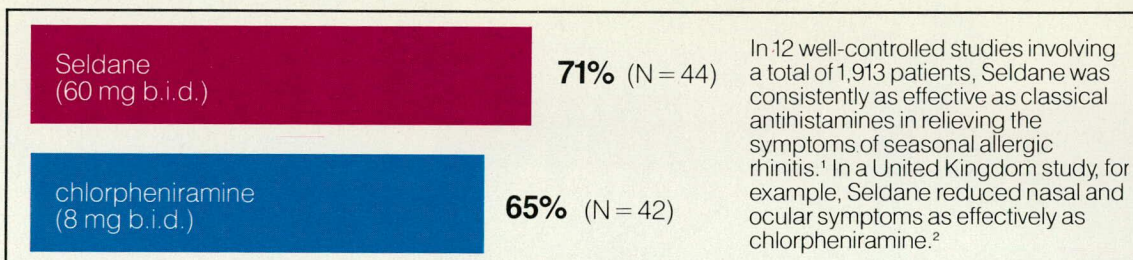
Incidence of drowsiness



Data from all controlled clinical studies in which Seldane (60 mg b.i.d.) was compared to either placebo or positive control.¹

Efficacy equal to classical therapy

Percentage relief of symptoms²



Low incidence of undesired effects

In controlled clinical studies, the incidence of reported adverse effects in patients receiving Seldane was similar to that reported in patients receiving placebo.¹

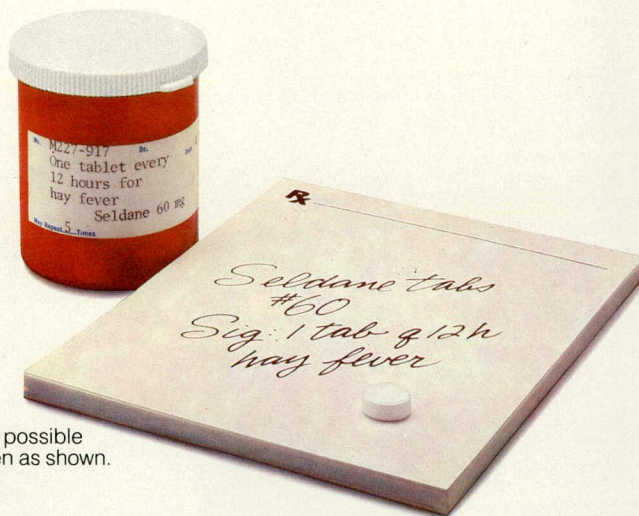
See Brief Summary for CONTRAINDICATIONS, PRECAUTIONS, and ADVERSE REACTIONS.

Extensively metabolized, with favorable half-life

Seldane® (terfenadine) is rapidly and extensively metabolized and distributed in tissues, resulting in extremely low levels of circulating unchanged drug. It has an alpha (distribution) half-life of 3.4 hours and a beta (elimination) half-life of 20.3 hours.¹

Rapid, long-lasting relief with b.i.d. dosage

Studies have shown that the antihistaminic effect of Seldane on histamine wheals begins within 1 to 2 hours, reaching maximum at 3 to 4 hours. A 60 mg tablet of Seldane shows antihistaminic action for 12 hours or more.¹



Because Seldane is a recently introduced drug, to eliminate any possible confusion with similar trademarks, prescriptions should be written as shown.

Pharmacologically distinct

SELDANE®

(terfenadine) 60 mg tablets BID

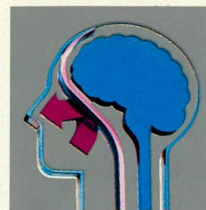
Separating sedation from relief



The only peripheral, H₁-specific antagonist available in the U.S.

Before prescribing Seldane, please see Brief Summary of Prescribing Information which appears on the last page.

Pharmacologically distinct
SELDANE[®]
 (terfenadine) 60 mg tablets BID
Separating sedation from relief



The #1 prescribed allergy product in the U.S., with more than 13 million patient-months of experience worldwide

- Sedation equivalent to placebo
- Efficacy equal to classical therapy
- Low incidence of adverse effects
- Rapid, long-lasting relief
- Convenient b.i.d. dosage

Seldane[®] (terfenadine)

60 mg Tablets

BRIEF SUMMARY

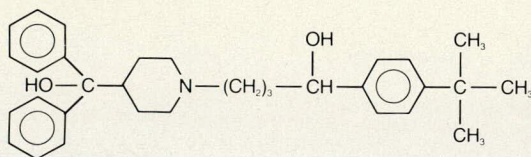
CAUTION: Federal law prohibits dispensing without prescription.

DESCRIPTION

Seldane (terfenadine) is available as tablets for oral administration. Each tablet contains 60 mg terfenadine. Tablets also contain, as inactive ingredients: corn starch, gelatin, lactose, magnesium stearate, and sodium bicarbonate.

Terfenadine is a histamine H₁-receptor antagonist with the chemical name α -[4-(1,1-Dimethylethyl) phenyl]-4-(hydroxydiphenylmethyl)-1-piperidinebutanol.

It has the following chemical structure:



Terfenadine occurs as a white to off-white crystalline powder. It is freely soluble in chloroform, soluble in ethanol, and very slightly soluble in water.

CONTRAINDICATIONS

Seldane is contraindicated in patients with a known hypersensitivity to terfenadine or any of its ingredients.

PRECAUTIONS

Information for patients

Patients taking Seldane should receive the following information and instructions. Antihistamines are prescribed to reduce allergic symptoms. Patients should be questioned about pregnancy or lactation before starting Seldane therapy, since the drug should be used in pregnancy or lactation only if the potential benefit justifies the potential risk to fetus or baby. Patients should be instructed to take Seldane only as needed and not to exceed the prescribed dose. Patients should also be instructed to store this medication in a tightly closed container in a cool, dry place, away from heat or direct sunlight, and away from children.

Carcinogenesis, mutagenesis, impairment of fertility

Oral doses of terfenadine, corresponding to 63 times the recommended human daily dose, in mice for 18 months or in rats for 24 months, revealed no evidence of tumorigenicity. Microbial and micronucleus test assays with terfenadine have revealed no evidence of mutagenesis.

Reproduction and fertility studies in rats showed no effects on male or female fertility at oral doses of up to 21 times the human daily dose. At 63 times the human daily dose there was a small but significant reduction in implants and at 125 times the human daily dose reduced implants and increased post-implantation losses were observed, which were judged to be secondary to maternal toxicity.

Pregnancy Category C

There was no evidence of animal teratogenicity. Reproduction studies have been performed in rats at doses 63 times and 125 times the human daily dose and have revealed decreased pup weight gain and survival when terfenadine was administered throughout pregnancy and lactation. There are no adequate and well-controlled studies in pregnant women. Seldane should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic effects

Seldane is not recommended for nursing women. The drug has caused decreased pup weight gain and survival in rats given doses 63 times and 125 times the human daily dose throughout pregnancy and lactation. Effects on pups exposed to Seldane only during lactation are not known, and there are no adequate and well-controlled studies in women during lactation.

Pediatric use

Safety and effectiveness of Seldane in children below the age of 12 years have not been established.

General

Consideration should be given to potential anticholinergic (drying) effects in patients with lower airway disease, including asthma.

ADVERSE REACTIONS

Experience from clinical studies, including both controlled and uncontrolled studies involving more than 2,400 patients who received Seldane, provides information on adverse experience incidence for periods of a few days up to six months. The usual dose in these studies was 60 mg twice daily, but in a small number of patients, the dose was as low as 20 mg twice a day, or as high as 600 mg daily.

In controlled clinical studies using the recommended dose of 60 mg b.i.d., the incidence of reported adverse effects in patients receiving Seldane was similar to that reported in patients receiving placebo. (See Table below.)

ADVERSE EVENTS REPORTED IN CLINICAL TRIALS

Adverse Event	Percent of Patients Reporting			All Clinical Studies**	
	Seldane N = 781	Placebo N = 665	Control N = 626***	Seldane N = 2462	Placebo N = 1478
Central Nervous System					
Drowsiness	9.0	8.1	18.1	8.5	8.2
Headache	6.3	7.4	3.8	15.8	11.2
Fatigue	2.9	0.9	5.8	4.5	3.0
Dizziness	1.4	1.1	1.0	1.5	1.2
Nervousness	0.9	0.2	0.6	1.7	1.0
Weakness	0.9	0.6	0.2	0.6	0.5
Appetite Increase	0.6	0.0	0.0	0.5	0.0
Gastrointestinal System					
Gastrointestinal Distress (Abdominal distress, Nausea, Vomiting, Change in Bowel habits)	4.6	3.0	2.7	7.6	5.4
Eye, Ear, Nose, and Throat					
Dry Mouth/Nose/Throat	2.3	1.8	3.5	4.8	3.1
Cough	0.9	0.2	0.5	2.5	1.7
Sore Throat	0.5	0.3	0.5	3.2	1.6
Epistaxis	0.0	0.8	0.2	0.7	0.4
Skin					
Eruption or itching	1.0	1.7	1.4	1.6	2.0

*Duration of treatment in "CONTROLLED STUDIES" was usually 7-14 DAYS.

**Duration of treatment in "ALL CLINICAL STUDIES" was up to 6 months.

***CONTROL DRUGS: Chlorpheniramine (291 patients), d-Chlorpheniramine (189 patients), Clemastine (146 patients)

In addition to the more frequent side effects reported in clinical trials (See Table), adverse effects have been reported at a lower incidence in clinical trials and/or spontaneously during marketing of Seldane that warrant listing as possibly associated with drug administration. These include: alopecia, anaphylaxis, angioedema, bronchospasm, depression, galactorrhea, insomnia, menstrual disorders (including dysmenorrhea), musculoskeletal pain, nightmares, palpitation, paresthesia, sweating, tachycardia, tremor, urinary frequency, and visual disturbances. In clinical trials, several instances of mild, or in one case, moderate transaminase elevations were seen in patients receiving Seldane. Mild elevations were also seen in placebo treated patients. Foreign marketing experiences include isolated reports of jaundice, cholestatic hepatitis, and hepatitis; in most cases available information is incomplete. In neither the clinical trials nor foreign experience is a causal relationship of liver abnormalities to Seldane use clear.

OVERDOSAGE

Information concerning possible overdosage and its treatment appears in Full Prescribing Information.

Product Information as of May, 1985

MERRELL DOW PHARMACEUTICALS INC.
 Subsidiary of The Dow Chemical Company
 Cincinnati, Ohio 45215

Merrell Dow

References: 1. Data available upon request, MERRELL DOW PHARMACEUTICALS INC., Cincinnati, Ohio 45215. 2. Backhouse CI, Brewster BS, Lockhart JDF, et al: Terfenadine in allergic rhinitis. A comparative trial of a new antihistamine versus chlorpheniramine and placebo. Practitioner 226:347-348, 351, 1982.