

Weeklong Fair's Cost-Effective Patient Education

BY ANNE SCHECK
Contributing Writer

SAN FRANCISCO — Want to provide a low-cost, king-sized dose of patient education? Just invite your entire town to a weeklong, food-filled health fair. That's what Thomas Weida, M.D., did. And to hear him tell it, the effort not only succeeded in bringing a big portion of the local population past his portals, "it was just a whole lot of fun, too."

Though some family physicians might consider back-to-back days of health presentations, information booths, and refreshment provisions a tall order, Dr. Weida said it was "a piece of cake." The health fair was a simple-to-assemble community service that got him a whole lot more patients and a huge load of professional satisfaction. "And I am an introvert," he asserted. Dr. Weida, professor of family and community medicine at the Pennsylvania

State College of Medicine in Hershey, shared his health-fair experience during a conference on patient education sponsored by the Society of Teachers of Family Medicine. The fair was held several years ago, when he had a successful practice in Rothsville, Pa., a town of about 2,000. In his corner of Pennsylvania, Dr. Weida became concerned about lifestyle factors—obesity and smoking, in particular—and decided to tackle the problem in a out-

reach program that would entice everyone. "What we need to do is hold a fair for a whole week," he announced to his office manager, who looked like she was going to faint. "I resuscitated her, and then I explained it," he joked. He sought out other local health care professionals—pharmacists, dentists, opticians, and others—and asked them to contribute to the cost of putting on the fair. "We got almost total buy-in," he said. Then he wrote a letter to the five major insurers in the area, suggesting that each become an event partner by contributing \$1,000. Two sent a check, one wanted to provide ice cream instead of

cash, and another suggested the company do on-site cholesterol screening during the fair. "That was fine with me," Dr. Weida said. "You have to be flexible in these things."

Next he told about 20 pharmaceutical representatives they could rent a booth at the fair for \$300, and to guarantee foot traffic, he would "let" them occupy a food station, where they could dole out edible treats right along with their product information. "I sort of felt sorry for the guy at the coffee urn. He didn't get that many people," Dr. Weida recalled. "But when I told him I felt badly, he said, 'I wanted to be here to support this.'"

Each day, a different event unfolded, thanks to volunteerism from local professionals. One night, a lawyer offered advice on living wills. Another evening, a physical therapist lectured on injury-preventing exercise. One weekend morning was devoted to cholesterol awareness, with serologic screenings and a low-fat breakfast.

"A local restaurant chef did the breakfast—the best of its kind I ever had: French toast made with egg whites and baked apple mixture on top," Dr. Weida recalled at the conference, also sponsored by the American Academy of Family Physicians. The weekend also featured a stand-up comedian (laughter as good medicine); a psychologist who had a device to detect anxiety—it worked on the same principle as the "mood ring," explained Dr. Weida—and an appearance by the crime-fighting canine McGruff (who held forth on the importance of bike helmets).

The health fair was such a success that Dr. Weida found himself congratulated throughout town, the recipient of honks and hand waves. The phone nearly rang off the hook with patients making new appointments, he said. Best of all, the health fair cost him little, except in the substantial time he took to help organize it. "It was tremendous bang for our buck," he said.

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References: 1. Data on file, Sanofi-Synthelabo Inc. 2. IMS Health, National Prescription Audit Plus, MAT May 2004.



BRIEF SUMMARY

INDICATIONS AND USAGE
Ambien (zolpidem tartrate) is indicated for the short-term treatment of insomnia. Ambien has been shown to decrease sleep latency and increase the duration of sleep for up to 35 days in controlled clinical studies.

CONTRAINDICATIONS
None known.

WARNINGS
Since sleep disturbances may be the presenting manifestation of a physical and/or psychiatric disorder, symptomatic treatment of insomnia should be initiated only after a careful evaluation of the patient. The use of Ambien to treat insomnia after 7 to 10 days of treatment may indicate the presence of a primary psychiatric and/or medical illness which should be evaluated. Worsening of insomnia or the emergence of new thinking or behavior abnormalities may be the consequence of an unrecognized psychiatric or physical disorder. Such findings have emerged during the course of treatment with sedative/hypnotic drugs, including Ambien. Because some of the important adverse effects of Ambien appear to be dose related (see Precautions and Dosage Administration), it is important to use the smallest possible effective dose, especially in the elderly.

A variety of abnormal thinking and behavior changes have been reported to occur in association with the use of Ambien. Some of these changes may be characterized by decreased inhibition (eg, aggressiveness and overexcitability that seemed out of character), similar to effects produced by alcohol and other CNS depressants. Other reported changes have included bizarre behavior, agitation, hallucinations, and depersonalization. Amnesia and other neuropsychiatric symptoms may occur unpredictably. In primarily depressed patients, including suicidal thinking, has been reported in association with the use of sedative/hypnotics.

It can rarely be determined with certainty whether a particular instance of the abnormal behaviors listed above is 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.

Following the rapid dose decrease or abrupt discontinuation of sedative/hypnotics, there have been reports of signs and symptoms similar to those associated with withdrawal from other CNS depressant drugs (ie, Drug Abuse and Dependence).

Ambien, like other sedative/hypnotic drugs, may be ingested intravenously. Due to the rapid onset of action, Ambien should only be ingested orally. Patients going to bed should be cautioned against engaging in hazardous occupations requiring complete mental alertness or motor coordination such as operating machinery or driving a motor vehicle after ingesting the drug, including potential impairment of the performance of such activities that may occur the day following ingestion of Ambien. Ambien showed additive effects when combined with alcohol and should not be used with alcohol. Patients should be cautioned about possible combined effects with other CNS-depressant drugs. Dosage adjustments may be necessary when Ambien is administered with such agents because of the potential for additive effects.

PRECAUTIONS
General
Use in the elderly and/or debilitated patients: Impaired motor and/or cognitive performance or altered sensation to sedative/hypnotic drugs is a concern in the treatment of elderly and/or debilitated patients. Therefore, the recommended Ambien dosage is 5 mg in such patients (see Dosage and Administration) to decrease the possibility of side effects. These patients should be closely monitored.

Use in patients with concomitant illness: Clinical experience with Ambien in patients with concurrent systemic illness is limited. Caution is advised in using Ambien in patients with diseases or conditions that could affect metabolism or hemodynamic responses. Although studies do not reveal respiratory depressant effects at hypnotic doses of Ambien in normal patients, a reduction in mild to moderate chronic obstructive pulmonary disease (COPD), a reduction in the Total Arousal Index together with a reduction in lowest oxygen saturation and increase in the times of oxygen desaturation below 80% and 90% were observed in patients with mild-to-moderate sleep apnea when treated with Ambien (10 mg) when compared to placebo. However, precautions should be observed if Ambien is prescribed to patients with compromised respiratory function, since sedative/hypnotics have the capacity to depress respiratory function. Post-marketing reports of respiratory insufficiency, most of which involved patients with pre-existing respiratory impairment, have been received. Data in end-stage renal failure patients repeatedly treated with Ambien did not demonstrate drug accumulation or alterations in pharmacokinetic parameters. No dosage adjustment is normally required in patients with hepatic impairment, but treatment should be initiated with 5 mg in patients with hepatic compromise, and they should be closely monitored.

Use in depression: As with other sedative/hypnotic drugs, Ambien should be administered with caution to patients exhibiting signs or symptoms of depression. Suicidal tendencies may be present and patients should be closely monitored. A study in subjects with hepatic impairment did reveal prolonged elimination in this group; therefore, treatment should be initiated with 5 mg in patients with hepatic compromise, and they should be closely monitored.

Information for patients: Patient information is printed in the complete prescribing information.

Laboratory tests: There are no specific laboratory tests recommended.

Drug interactions
CNS-active drugs: Ambien was evaluated in healthy volunteers in single-dose interaction studies for several CNS drugs. A study involving haloperidol and zolpidem revealed no effect of haloperidol on the pharmacokinetics or pharmacodynamics of zolpidem. Imipramine in combination with zolpidem produced no pharmacokinetic interaction other than a decrease in peak levels of imipramine, but there was an additive effect of decreased alertness. Similarly, chlorpromazine in combination with zolpidem produced no pharmacokinetic interaction, but there was an additive effect of decreased alertness and psychomotor performance. The lack of a drug interaction following single-dose administration does not preclude a lack of following chronic administration.

An additive effect on psychomotor performance between alcohol and zolpidem was demonstrated. A single-dose interaction study with zolpidem 10 mg and fluoxetine 20 mg at steady-state levels in male volunteers did not demonstrate any significant pharmacokinetic or pharmacodynamic interactions. When multiple doses of zolpidem and fluoxetine at steady-state concentrations were evaluated in healthy females, the only significant change was a 17% increase in zolpidem half-life. There was no evidence of an additive effect in psychomotor performance.

Drugs that affect drug metabolism via cytochrome P450: A randomized, double-blind, crossover interaction study in healthy volunteers between tramadol (200 mg once daily for 4 days) and a single dose of zolpidem 10 mg given 5 hours after the last dose of tramadol in a 24% case in AUG... of zolpidem. There were no significant pharmacodynamic effects of zolpidem on subjective drowsiness, postural sway, or psychomotor performance.

Other drugs: A study involving zolpidem/zolpidem and ramelteon/zolpidem combinations revealed no effect of either drug on the pharmacokinetics or pharmacodynamics of zolpidem. Zolpidem had no effect on digoxin kinetics and did not affect prothrombin time when given with warfarin in normal subjects. Zolpidem's sedative/hypnotic effects were not affected by fumarate, however, no significant alterations in zolpidem pharmacokinetics were found.

Drug/Laboratory test interactions: Zolpidem is not known to interfere with commonly employed clinical laboratory tests. In addition, clinical data indicate that zolpidem does not cross-react with benzodiazepines, opiates, barbiturates, cocaine, cannabinoids, or amphetamines in two standard urine drug screens.

Carcinogenesis, mutagenesis, impairment of fertility
Carcinogenesis: Zolpidem was administered to rats and mice for 2 years at dietary dosages of 4, 15, and 50 mg/kg/day. In mice, these doses are 20 to 25 times or 2 to 35 times the maximum 10-mg human dose on a mg/kg or mg/m² basis, respectively. In rats these doses are 43 to 376 times or 1.5 to 11.5 times the maximum 10-mg human dose on a mg/kg or mg/m² basis, respectively. No evidence of carcinogenic potential was observed in mice. Renal liposarcomas were seen in 4/100 rats (3 males, 1 female) receiving 80 mg/kg/day and a renal lipoma was observed in one male rat at the 100 mg/kg/day dose. Incidence rates of lipoma and liposarcoma for zolpidem were comparable to those seen in historical controls and the tumor findings are thought to be spontaneous occurrences.

Mutagenesis: Zolpidem did not have mutagenic activity in several tests including the Ames test, genotoxicity in mouse lymphoma cells *in vitro*, chromosomal aberrations in cultured human lymphocytes, unscheduled DNA synthesis in rat hepatocytes *in vivo*, and the micronucleus test in mice.

Impairment of fertility: In rat reproductive study, the high dose (100 mg/kg/day) of zolpidem resulted in irregular estrus cycles and prolonged progestational intervals, but there was no effect on male or female fertility after oral dosing of 4 to 100 mg/kg/day. At the high dose, incidence rates of fetal loss and stillbirths were increased. In mice, there was no effect on male or female fertility parameters. No effects on any other fertility parameters were noted.

Pregnancy
Teratogenic effects: Category B. Studies to assess the effects of zolpidem on human reproduction are being conducted.

Teratology studies: were conducted in rats and rabbits. In rats, adverse maternal and fetal effects occurred at 20 and 100 mg/kg bask and no adverse effects were observed in the offspring. In rabbits, dose-related maternal sedation and decreased weight gain occurred at all oral doses. At the high dose (100 mg/kg), there was an increase in postimplantation fetal loss and underfertilization of spermata in viable fetuses.

Use during pregnancy: should be used during pregnancy only if clearly needed.

Nonteratogenic effects: Studies to assess the effects on children whose mothers took zolpidem during pregnancy have not been conducted. However, children born of mothers taking sedative/hypnotic drugs may be at some risk for withdrawal symptoms from the drug during the perinatal period. In addition, neonatal fatality has been reported in infants born of mothers who received sedative/hypnotic drugs during pregnancy.

Labor and delivery: Ambien has no established use in labor and delivery.

Nursing mothers: Studies in lactating women indicated that between 0.04 and 0.24% of the total administered dose is secreted into milk, but the effect of zolpidem on the infant is unknown.

Use of Safety in nursing mothers: is not recommended.

Geriatric use: A total of 154 patients in U.S. controlled clinical trials and 897 patients in non-U.S. clinical trials who received zolpidem were ≥60 years of age. For a total of 105 patients receiving zolpidem at doses of ≤10 mg of placebo, there were three adverse events occurring at an incidence of at least 3% for zolpidem and for which the zolpidem incidence was at least twice the placebo incidence (ie, they could be considered drug related).

| Adverse Event | Zolpidem | Placebo |
|---------------|----------|---------|
| Dizziness | 3% | 0% |
| Drowsiness | 5% | 2% |
| Diarrhea | 3% | 1% |

A total of 301,959 (1.5%) non-U.S. patients receiving zolpidem reported falls, including 20,020 (3%) who were ≥70 years of age. Of these 28 patients, 22 (82%) were receiving zolpidem doses >10 mg. A total of 241,959 (1.2%) non-U.S. patients receiving zolpidem reported confusion, including 18,274 (7%) who were ≥70 years of age. Of these 18 patients, 14 (78%) were receiving zolpidem doses >10 mg.

ADVERSE REACTIONS
Associated with discontinuation of treatment: Approximately 4% of 1,301 patients who received zolpidem discontinued treatment because of an adverse clinical event. Events most commonly associated with discontinuation from U.S. trials were daytime drowsiness (0.5%), dizziness (0.4%), and fatigue (0.4%).

Approximately 4% of 1,369 patients who received zolpidem at all doses (1 to 50 mg) in the foreign trial discontinued treatment because of an adverse event. Events most commonly associated with discontinuation from these trials were daytime drowsiness (1.1%), dizziness/vertigo (0.8%), amnesia (0.5%), nausea (0.5%), headache (0.4%), and falls (0.4%).

Data from a clinical study in which selective serotonin reuptake inhibitor (SSRI) treated patients were given zolpidem revealed that four of the seven discontinuations during double-blind treatment with zolpidem (n=59) were associated with impaired concentration, continuing or aggravated depression, and manic reaction; one patient treated with placebo (n=97) was discontinued after an attempted suicide.

Incidence in controlled clinical trials
Most commonly observed adverse events in controlled trials: During short-term treatment (up to 10 nights) with Ambien at doses up to 10 mg, the most commonly observed adverse events associated with the use of zolpidem and seen at statistically significant differences from placebo-treated patients were drowsiness (reported by 2% of zolpidem patients), dizziness (1%), and diarrhea (1%). During longer-term treatment (26 to 35 nights) with zolpidem (up to 10 mg), the most commonly observed adverse events associated with the use of zolpidem and seen at statistically significant differences from placebo-treated patients were dizziness (5%) and drug-related feelings (2%).

Treatment-emergent adverse experiences in placebo-controlled clinical trials: The following are treatment-emergent adverse events from U.S. placebo-controlled trials. Data limited to data from doses up to and including 10 mg. In short-term trials, events seen in zolpidem patients (n=88) at an incidence equal to 1% or greater compared to placebo (n=73) were: headache (17% vs 8%), dizziness (15% vs 11%), fatigue (15% vs 11%), and myalgia (11% vs 9%). In long-term clinical trials, events seen in zolpidem patients (n=182) at an incidence of 1% or greater compared to placebo (n=161) were: dry mouth (3% vs 1% for placebo), allergy (4% vs 1%),

back pain (3% vs 2%), influenza-like symptoms (2% vs 0%), chest pain (1% vs 0%), fatigue (1% vs 2%), palpitation (2% vs 0%), headache (19% vs 22%), drowsiness (8% vs 5%), dizziness (15% vs 1%), lethargy (3% vs 1%), drug-related feelings (3% vs 1%), lightheadedness (2% vs 1%), depression (2% vs 1%), abnormal dreams (1% vs 0%), amnesia (1% vs 0%), anxiety (1% vs 0%), nervousness (1% vs 3%), sleep disorder (1% vs 0%), nausea (6% vs 6%), dyspepsia (5% vs 6%), diarrhea (2% vs 2%), abdominal pain (2% vs 2%), constipation (2% vs 1%), anorexia (1% vs 1%), vomiting (1% vs 1%), infection (1% vs 1%), myalgia (7% vs 7%), arthralgia (4% vs 4%), upper respiratory infection (5% vs 6%), sinusitis (4% vs 2%), pharyngitis (5% vs 1%), rhinitis (1% vs 3%), rash (2% vs 1%), and urinary tract infection (2% vs 2%).

Dose relationship for adverse events: There is evidence from dose comparison trials suggesting a dose relationship for many of the adverse events associated with zolpidem use, particularly for certain CNS and gastrointestinal adverse events.

Adverse events are further classified and enumerated in order of decreasing frequency using the following definitions: frequent adverse events are defined as those occurring in greater than 1/100 subjects; infrequent adverse events are those occurring in 1/100 to 1/1,000 patients; rare events are those occurring in less than 1/1,000 patients.

Frequent: abdominal pain, abnormal dreams, allergy, amnesia, anorexia, anxiety, arthralgia, asthenia, ataxia, back pain, chest pain, confusion, constipation, depression, diarrhea, diplopia, dizziness, drowsiness, drug-related feelings, dry mouth, dyspepsia, euphoria, fatigue, headache, hiccups, infection, influenza-like symptoms, insomnia, lethargy, lightheadedness, myalgia, nausea, nervousness, palpitation, sleep disorder, vertigo, vision abnormal, vomiting.

Infrequent: abnormal hepatic function, agitation, arthritis, bronchitis, cerebrovascular disorder, coughing, cystitis, decreased cognition, decreased difficulty concentrating, dysarthria, dysphagia, dyspnea, edema, emotional lability, eye irritation, eye pain, falling, fever, flatulence, gastroenteritis, hallucination, hyperkalemia, hypertension, hypoesthesia, illusion, increased SGPT, increased sweating, leg cramps, malaise, menstrual disorder, migraine, pallor, paresthesia, postural hypotension, pruritus, sciditis, sleeping habit daytime dosing, speech disorder, stupor, syncope, tachycardia, taste perversion, tinnitus, tremor, urinary incontinence, vaginitis.

Rare: abnormal body sensation, abnormal accommodation, abnormal gait, abnormal thinking, abscess, acne, acute renal failure, aggressive reaction, allergic reaction, allergy aggravated, altered saliva, anaphylactic shock, anemia, angina pectoris, apathy, appetite increased, arrhythmia, arteritis, arthrosis, bilirubinemia, breast fibroadenoma, breast neoplasm, breast pain, bronchiopneumonia, bruising, circulatory disorder, circulatory system disorder, increased libido, delusion, dematosis, depersonalization, dermatitis, dysphasia, dysuria, enteritis, epistaxis, emetion, esophageal spasms, extravasation, face edema, feeling strange, flushing, furuncles, gastritis, glaucoma, plex, glaucoma plex simplex, herpes zoster, host, hot flashes, hypercholesterolemia, hyperhemoglobinemia, hyperhidrosis, hypertension aggravated, hypokinesia, hypotension, hypotonia, hypoxia, impotence, increased alkaline phosphatase, increased BUN, increased ESR, increased saliva, increased SGOT, injection-site inflammation, intestinal obstruction, intoxicated feeling, locomotion abnormal, leukopenia, lymphadenopathy, macrocytic anemia, manic reaction, micturition frequency, muscle weakness, myocardial infarction, neuralgia, pain, neuritis, neuropathy, neurosis, nocturia, otitis externa, otitis media, pain, panic attacks, paresis, parosmia, periorbital edema, personality disorder, phlebitis, photopsia, photosensitivity reaction, pneumonia, polyuria, polyuria edema, pulmonary embolism, purpura, pyelonephritis, renal hemorrhage, renal pain, restless legs, rigors, scalds, somnambulism, suicide attempts, tendinitis, tenesmus, tetany, thrombosis, thrombosed, tooth caries, urinary retention, urticaria, varicose veins, ventricular tachycardia, weight decrease, yawning.

DRUG ABUSE AND DEPENDENCE

Controlled substance: Schedule IV.

Abuse and dependence: Studies of abuse potential in former drug abusers found that the effects of single doses of zolpidem tartrate 40 mg were similar, but not identical, to diazepam 20 mg, while zolpidem tartrate 10 mg was difficult to distinguish from placebo.

Sedative/hypnotics have produced withdrawal signs and symptoms following abrupt discontinuation. These reported symptoms range from mild dysphoria and insomnia to a withdrawal syndrome that may include abdominal and muscle cramps, vomiting, sweating, tremors, and convulsions. The U.S. clinical trial experience from zolpidem does not reveal any clear evidence for withdrawal syndrome. Nevertheless, the following adverse events included in DSM-IV criteria for uncomplicated sedative/hypnotic withdrawal were reported at an incidence of 1% during clinical trials following placebo substitution occurring within 48 hours following last zolpidem treatment: fatigue, nausea, flushing, lightheadedness, uncontrolled crying, emesis, stomach cramps, panic attack, nervousness, and abdominal discomfort. Adverse event reports of abuse, dependence and withdrawal have been received.

Individuals with a history of addiction to, or abuse of, drugs or alcohol are at increased risk of habituation and dependence; they should be under careful surveillance when receiving any hypnotic.

OVERDOSSAGE
Signs and symptoms: In European postmarketing reports of overdose with zolpidem alone, impairment of consciousness has ranged from oxycodone to light coma, with one case each of cardiovascular and respiratory compromise. Individuals have fully recovered from zolpidem tartrate overdoses up to 400 mg (40 times the maximum recommended dose). Overdose cases involving multiple CNS-depressant agents, including zolpidem, have resulted in more severe symptomatology, including fatal outcomes.

Recommended treatment: General symptomatic and supportive measures should be used along with immediate gastric lavage where appropriate. Intravenous fluids should be administered as needed. Flumazenil may be useful. Absorption of zolpidem is decreased by activated charcoal. Signs and symptoms of mild to moderate supportive measures are indicated. Sedative drugs should be withheld following zolpidem overdose. Zolpidem is not dialyzable. The possibility of multiple drug ingestion should be considered.

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