Electronic Records: One Small Step for a Physician

BY JOYCE FRIEDEN Associate Editor, Practice Trends

WASHINGTON — Physicians who are too nervous to completely convert their offices to electronic health records can start the process with a few "baby steps" to make it less intimidating, Dr. Daniel Sands said at a health care congress sponsored by the Wall Street Journal and CNBC.

Physicians are often reluctant to leap into an EHR system because of its complexity and the expense involved, said Dr. Sands, of Harvard University, Boston. "If you're a doctor, what do you do? How do you get that [EHR] if you can't take the one big leap?"

One way to start is by using electronic communications with patients and with office staff, he said. "Why don't you get rid of those stupid yellow Post-It notes you use for phone messages? A simple step like that is a good way to get people engaged with technology."

Electronic prescribing is another way to bridge the gap, said Dr. Sands, who is also chief medical officer of ZixCorp, a Newton, Mass., company that sells electronic prescribing software. Medications can be prescribed using various electronic devices, including desktop and laptop computers, handhelds, and even mobile phones. Since studies have shown that electronic prescribing can reduce medication errors substantially, "this should be the standard of care," he said.

Another baby step to take is by using online clinical reference materials, Dr. Sands continued. "We have lots of data showing that physicians are often faced with questions when taking care of patients, and they can't find the answers because they don't have time, so they just move on. And that's really scary."

Rather than looking for answers "in a book that's out of date as soon as it's printed, maybe looking online would be a great place to start," Dr. Sands said.

(zolpidem tartrate extended of e tablets) BRIEF SUMMARY INDICATIONS AND USAGE

INUICALIUNS AND USAGE Ambien CR (zolpidem tartrate extended-relaxes tablets) is indicated for the treatment of insomnia, characterized by difficulties with sleep onset and/or sleep maintenance (as measured by wake time after sleep onset). (See Clinical Pharmacology: Controlled trials supporting safety and efficacy). The clinical trials performed in support of efficacy were both 3 weeks in dura-tion, although the final formal assessments of sleep latency and maintenance were performed after 2 weeks of treatment.

bien CR is contraindicated in patients with known hypersensitivity pidem tartrate or to any of the inactive ingredients in the formulation.

dem tartrate or to any of the inactive ingredents in the formulation. WARNINGS e sleep disturbances may be the presenting manifestation of a physical or psychiatric disorder, symptomatic treatment of insomnia should be ted only after a careful evaluation of the patient. The failure of insomnia to ta differ 7 to 10 days of treatment may indicate the presence of a primary hitaric and/or medical illness which should be evaluated. Worsening of main or the emergence of new thinking or behavior abnormalities may be consequence of an unrecognized psychiatric or physical disorder. Such ngs have emerged during the course of treatment with sedative/hypontic s, including zolpidem. Because some of the important adverse effects of dem appear to be dose related (see *Precautions* and *Dosage and* instration), it is important to use the smallest possible effective dose, cally in the elderly.

eably in the elderly: variety of abnormal thinking and behavior changes have been reported to ur in association with the use of sedative/hypnotics. Some of these changes be characterized by decreased inhibition (e.g., aggressiveness and extro-sion that seemed out of character), similar to effects produced by alcohol other CNS depressants. Visual and auditory hallucinations have been orded as well as behavioral changes such as bizarre behavior, aglitation, and ersonalization. Amnesia, anxiety and other neuro-psychiatric symptoms occur unpredictably. In primarily depressed patients, worsening of depres-n, including suicidal thinking, has been reported in association with the use edative/hyponotics.

inon, including suicidiar immining, has been reported in association with the use is deative/hypotoics. It can rarely be determined with certainty whether a particular instance of the bhormal behaviors listed above is drug induced, spontaneous in origin, or a esult of an underlying psychiatric or physical disorder. Nonetheless, the emer-pence of any new behavioral sign or symptom of concern requires careful and mmediate evaluation.

evaluation. g the rapid dose decrease or abrupt discontinuation of sedative/ there have been reports of signs and symptoms similar to those with withdrawal from other CNS-depressant drugs (see *Drug Abuse*

iated with withdrawal from other CNS-depressant drugs (see *Lrug number bependence*). ipidem, like other sedative/hypnotic drugs, has CNS-depressant effects. to the rapid onset of action, Ambien CR should only be ingested immedi-prior to going to bed. Patients should be cautioned against engaging in drous occupations requiring complete mental alertness or motor coordina-uch as operating machinery or driving a motor vehice after ingesting the including potential impairment of the performance of such activities that discur the day following ingestion of Ambien CR. Zolpidem showed addi-fifects when combined with alcohol and should not be taken with alcohol. In should also be cautioned about possible combined effects with other depressant drugs. Dosage adjustments may be necessary when Ambien administered with such agents because of the potentially additive effects. **PECAUTIONS** PRECAUTIONS

Chers administered wini such agents because of the potentially additive effects. **PRECAUTIONS General Use in the elderly and/or debilitated patients:** Impaired motor and/or cogni-tive performance after repeated exposure or unusual sensitivity to sedative/hyponic drugs is a concern in the treatment of elderly and/or debil-tated patients. Therefore, the recommended Ambien CR dosage is 6.25 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 liness:** Clinical experience with zolpidem in patients with concomitant systemic illness is limited. Caution is advisable in using Ambien CR in patients with diseases or conditions that could affect metabolism or hemodynamic responses. Although studies did not reval respi-ratory depressant effects at hypnotic doses of zolpidem tartate in normals or in patients with concomitate responses. Although studies did not reval respi-ratory depressant effects at hypnotic doses of zolpidem tartate in normals or sito xygen stutration and increase in the times of oxygen desaturation below 80% and 90% was observed in patients with mild-to-moderate sleep apnea when treated with a immediate-release formulation of zolpidem tartrate (10 mg) when compared to placebo. However, precautions should be observed (11 mg) when compared to placebo. However, precautions should be observed (12 mg) when compared to platents with compromised respiratory function, since sedative/hypnotics have the capacity to depress respiratory drive. Post-marketing reports of respiratory insufficiency in patients evelving immediate-release zolpidem tartate, most of which involved patients with pre-existing mediate-release zolpidem tartate did not patients should be closely monitored. A study in subjects with hepatic impair ment did reveal prolonged elimination in his group, therefore, treatment should be initiated with Ambien of 2.52 mg in patients with hepatic

It at any one time. nation for patients: Patient information is printed at the end of this insert. sure safe and effective use of Ambien CR, this information and instructions did in the patient information section should be discussed with patients. atory tests: There are no specific laboratory tests recommended.

boratory tests: There are no specific laboratory tests recommended. IS active drugs: An immediate-release formulation of zolpidem tartrate was auated in healthy voluntees: in single-dose interaction studies for several S drugs. A study involving haloperidol and zolpidem tartrate revealed effect of haloperidol on the pharmacokinetics or pharmacokinetics or pharma cokinetics or pharmacine in combination with zolpidem tartrate produced no phar-tockinetic interaction other than a 20% decrease in peak levels of pipern. Impramine in combination with zolpidem tartrate produced no phar-tockinetic interaction other than a 20% decrease in peak levels of pipernmine, but there was an additive effect of decreased alertness. Similarly, lorpromazine in combination with zolpidem tartrate produced no pharmaco-elic interaction, but there was an additive effect of decreased alertness. An additive effect on psychomotor performance between alcohol and pidem tartate was demonstrated. A single-dose interaction study with zolpidem tartrate 10 mg and fluxettie mically significant pharmacokinetic or pharmacodynamic interactions. When hitple doses of zolpidem tartrate and fluxette at stady state concentra-ns were evaluated in healthy females, the only significant change was a 17% rease in the zolpidem half-like. There was no evidence of an additive effect promonance. The latter and fluxetten at tarta 10 mg and fluxetten in comonor performance.

chomotor performance. oliowing five consecutive nightly doses of zolpidem tartrate 10 mg in the sence of sertraline 50 mg (17 consecutive daily doses, at 7:00 am, in healthy ale volunteers). Zolpidem C_{max} was significantly higher (43%) and T_{max} s significantly decreased (53%). Pharmacokinetics of sertraline and semethvisertraline were unaffected by zoloidem.

Since the systematic evaluations of Ambien CR in combination with other CNS-active drugs have been limited, careful consideration should be given to the pharmacology of any CNS-active drug to be used with zolpidem. Any drug with CNS-depressant effects could potentially enhance the CNS-depressant effects of zoloidem.

with CNS-depressant effects could potentially enhance the UNS-depressant effects of zolpidem. **Drugs that affect drug metabolism via cytochrome P450:** A randomized, double-blind, crossover interaction study in ten healthy volunteers between irraconazole (200 mg once daily for 4 days) and a single dose of an immediate-release formulation of zolpidem tartrate (10 mg) given five hours after the last dose of irraconazole resulted in a 34% increase in AUC_{0-xxx} of zolpidem. There were no significant pharmacodynamic effects of zolpidem on subjective drowsiness, postural sway, or psychomotor performance. A randomized, placebo-controlled, crossover interaction study in eight healthy female volunteers between five consecutive daily doses of rifampin (600 mg) given 17 hours after the last dose or frifampin showed significant reductions of the AUC (-73%), C_{max} (-58%), and T_{1/2} (-36%) of zolpidem together with significant reductions in the pharmacodynamic effects of zolpidem.

of zöpidem. Other drugs: A study involving cimetidine/zolpidem tartrate and ranitidine/zolpidem tartrate combinations revealed no effect of either drug or the pharmacoknietics or pharmacodynamics of zolpidem. Al or effect on digoxin kinetics and did not affect prothrombin time when given with warratin in normal subjects. Zolpidem's sedative/hypnotic effect was reverses by flumazenit; however, no significant alterations in zolpidem pharmacoknietics: were found.

Weitsellt in normal subjects. Zolpidem's sedative/hypnotic effect was reversed by flumazenii; however, no significant alterations in zolpidem pharmackinetics were found.
 DrgJLaboratory 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: Zolpidem tatrate was administered to CD-1 mice and Sprague-Dawley ratis for two years at dietary dosages of 4, 18, and 80 mg/kg/day. No evidence of carcinogenic potential was observed in either mice or rats at doses up to 80 mg base/kg/day (40 and 80 times the maximum recommended human dose [MHRD] of Ambien CR 12.5 mg [10 mg zolpidem dasa], erspectively, on a mg/m² basis).
 Mutagenesis: Zolpidem did not have mutagenic activity in several tests including an *in vitro* bacterial reverse mutation (Anee) assay, an *in vitro* marmalian per forward mutation assay in nouse lymphoma cells, and an *in vitro* unscheduled DMA synthesis in rat hepatocytes. Zolpidem was not clastogenic in an *in vitro* chromosomal aberration assay in human lymphocytes or in an *in vitro* chromosomal aberration assay in human lymphocytes or in an *in vitro* marmalian dividence of the stat doses of 4, 20, or 100 mg base/kg/day. Treatment of Sprague-Dawley rats at doses of a 40, or not main gad continued through mating, gestation, and weaning which occurred on post parture By 25. Zolpidem administered by cal gavage to Sprague-Dawley rats at doses of a 40, or not ong base/kg/day. Treatment of fendles began 14 days prior to mating and continued through mating.
 Metagenedic definition data as a dose of a 40, or not ong base/kg/day. Treatment of and by base/kg was associated with irregular estrus cycles and prolonged pre-coital intervis, but did not produce a decline in ferility. The no-effect dose

Internationable of the secretion of milk. The robertect tools for material and off basis). There are no adequate and well-controlled studies in pregnant women. Ambien CR should be used during pregnancy only if the potential benefit justi-fies the potential risk to the fetus. **Ronteratogenic effects:** Studies to assess the effects on children whose moth-sers took zolpidem during pregnancy have not been conducted. However, chil-dren born of mothers taking sedative/hyponotic drugs may be at some risk for withdrawal symptoms from the drug during the postnatal period. In addition, neonatal flaccidity has been reported in infants born of mothers who received sedative/hyponotic drugs during pregnancy. **Labor and delivery:** Ambien CR has no established use in labor and delivery. (See also **Pregnancy.**) **Nursing Mothers:** Studies in lactating mothers indicate that the half-life of zolpidem is similar to that in young normal volunteers (2.6: 0.3 hr). Between 0.004% and 0.019% of the total administered dose is excreted into milk, but the effect of zolpidem on the infant is unknown. In addition, in a rat study, zolpi dem inhibited the secretion of milk. The no-effect dose was 4 mg base/kg or 6 times the recommended human dose in mg/m². The use of Ambien CR in a 3-week placebo-controlled study. The adverse of 25 mg Ambien CR in a 3-week placebo-controlled study. The adverse of 18 have not been established. CRIENCE Studies of 99 elderly (≥65 years of age). Dizziness was of 2.5 mg Ambien CR in a 3-week placebo-controlled study. The adverse of 2.5 mg Ambien CR in a 3-week placebo-controlled study. Solpi Ambien CR 12.5 mg in younger adults (≤64 years of age). Dizziness was treported in Ry of Ambien CR-Lereated patients compared with 3% of those treated with placebo.

ADVERSE REACTIONS ADVERSE REACTIONS ASsociated with discontinuation of treatment: In clinical trials with Ambien CR, 3.5% of 201 patients receiving 6.25-mg or 12.5-mg of Ambien CR discon-tinued treatment because of an adverse event. Events most commonly associ-ated with discontinuation were somnolence (1.0%), and dizziness (1.0%). Data from a clinical study in which selective serotonic reuptake inhibitor (SSRI)-treated patients were given immediate-release zolpidem tartrate revealed that four of the seven discontinuations during double-bild retartemt with zolpi-dem (n=95) were associated with impaired concentration, continuing or aggra-vated depression, and maric 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 treat-ment with Ambien CR in adults and elderly at daily doses of 12.5 mg and 6.25 mg, respectively, each for three weeks, the most commonly observed adverse events associated with the use of Ambien CR were headache, somno-lence, and diziness.

Adverse events observed at an incidence of ≥1% in controlled trials of Ambien CR: The following enumerates treatment-emergent adverse event fre-quencies that were observed at an incidence equal to 1% or greater among patients with insomnia who received Ambien CR in placebo-controlled trials. Events reported by investigators were classified utilizing the MedDRA diction-ary for the purpose of establishing event frequencies. The prescriber should be aware that these figures cannot be used to predicit the incidence of side effects in the course of usual medical practice in which patient characteristics and other factors differ from those that prevailed in these clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other proup of drug trials is conducted under a different set of conditions. However, the cited frequencies provide the physician with a basis for estimating the relative contribution of drug and nondrug factors to the incidence of side effects in the population studied.

clinical investigators involving related drug products and uses, since each group of drug trials is conducted under a different set of conditions. However, the cited figures provide the physician with a basis for estimating the relative contribution of drug and nondrug factors to the incidence of side effects in the population studied.
The following was derived from results of two placebo-controlled efficiacy trians involving Ambien CR. These trials involved patients with primary insomnia how over treated for 3 weeks with Ambien CR at doess of 125. mg (Table 1) or 0.25 mg (Table 2), respectively, included are only adverse events occurring at an incidence of a least 1% of Ambien CR patients and with an incidence greater than that seen in the placebo patients.
Incidences of Textment-Emergent Adverse Events in a 3-Week Placebo-fortaled (Dinical Trial in Advits (events reported by at least 1% of patients for adverse traguency than in the placebo patients.
Incidences of Textment-Emergent Adverse Events in a 3-Week Placebo-fixed with Ambien CR 1.25 mg (Table 2), respectively.
Networks 11% vs 0%), Europhone and infestations: Influenza (3%, vs 0%), Europhone (1% vs 0%), Psychiatric disorders: Halucinations (14% vs 0%), Europhone (1% vs 0%), Psychiatric disorders: Halucinations (14% vs 0%), Europhone (15% vs 0%), Europhone (15% vs 0%), Psychiatric 10% vs 0%), Provide Systam disorders: Hadvence 10% vs 0%), Psychiatric 10% vs 0%), Europhone (15% vs 0%), Provide Systam disorders: Hadvence 10% vs 0%), Psychiatric 10% vs 0%

ison trials suggesting a dose relationship for many of the adverse events asso-ciated with zolpidem use, particularly for certain CNS and gastrointestinal adverse events. **Other Adverse Events Observed During the Premarketing Evaluation of Ambien CR:** Uther treatment-emergent adverse events associated with partici-ation in Ambien CR studies (those reported at frequencies of <1%) were not obtigent attrates, which are listed below. **Adverse Events Observed During the Premarketing Evaluation of Immediate-Release Zolpidem Tartrate:** Immediate-release zolpidem tartrate, was administered to 3,660 subjects in clinical trias throughout the U.S. Canada, and Europe. Treatment-emergent adverse events associated with clin-cal triap articulation are used to subject in clinical trias throughout the U.S. Canada, and Europe. Treatment-emergent adverse events associated with clin-cal triap articipation were recorded by clinical trias throughout the U.S. Canada, and Europe. Treatment-emergent adverse events, similar types of untoward events were grouped into a smaller number of standardized event the proportions of the 3,660 Individuals exposed to zolpidem the proportions of the 3,660 Individuals exposed to zolpidem tartese, who experienced an event of the type cled on at least one occasion while receiving immediate-release zolpidem, they were not necessarily caused by it. Adverse events are further classified within body system categories and formative and those events where a drug cause was remote. It is important to immediate-release zolpidem, they were not necessarily caused by it. Adverse events are torther classified within body system categories and strengent adverse events are torse occurring in 1700 publicits; infrequent adverse event are torse occurring in 1700 publicits; infrequent adverse event are torse occurring in greater than 17100 publicits; infrequent adverse event are torse occurring in the following definitions; fuent adverse events are torse occurring in greater than 17100

Body as a whole: Frequent: allergy, asthenia, back pain, influenza-like symptoms. Infruenza-like symptoms. Infruenza-like symptoms. Infruenza-like symptoms. Inforenzamet. Chest pain, edema. Italling, fatigue, fever, malaise, trauma. Rare: allergic reaction, allergy aggravated, anaphylactic shock, face edema, hot flashes, increased ESR, pain, restless legs, rigors, tolerance increased, weight nernased.

eceraas. ardiovascular system: Frequent: palpitation. Infrequent: cerebrovascular dis-rder, hypertension, tachycardia. Rare: angina pectoris, arrhythmia, arteritis, irculatory failure, extrasystoles, hypertension aggravated, myocardial infarc-iro, phlebitis, pulmonary embolism, pulmonary edema, varicose veins, ven-ricular tachycardia.

tricular tachycardia. Central and peripheral nervous system: Frequent ataxia, confusion, depres sion, dizzines, drowsiness, drugged feeling, euphoria, headache, insomnia lethargy, lightheadedness, vertigo. Intrequent: abnormal dreams, agitatior amnesia, anxiety, decreased cognition, detached, difficulty concentrating dysarthria, emotional lability, haliucination, hypoesthesia, illusion, leg camps migraine, nervousness, paresthesia, sleep disorder, sieeping (after daytim dosing), speech disorder, stupor, tremor. Rare: abnormal gait, abnormal think ing, aggressive reaction, apathy, appetite increased, decreased libido, delusior

dementia, depersonalization, dysphasia, feeling strange, hypokinesia, hypoto-mia, hysteria, intoxicated feeling, manic reaction, neuralgia, neurtis, neuropa-thy, neurosis, panic attacks, paresis, personality disorder, somnambulism, suicide attempts, tetany, yawning. **Gastrointestinal system:** *Frequent* abdominal pain, diarrhea, dyspepsia, hic-cup, nausea. *Intrequent* anorexia, constipation, dysphagia, flatilence, gas-troenteritis, vomiting. *Rare:* enteritis, eructation, esophagospasm, gastritis, hemorthoids, intestinal obstruction, rectal hemorrhage, tooth caries. **Hematologic and lymphatic system:** *Rare:* anemia, hyperhemoglobinemia, leukopenia, lymphadenopathy, macrocytic anemia, purpura, thrombosis. **Immunologic system:** *Infrequent:* hadottane, Backess, herpes simplex, herpes zoster, otitis externa, otitis media. **Liver and bilirary system:** *Infrequent:* haptic function, increased SGPT. *Rare:* bilirubinemia, increased SGOT. **Metabolic and hurtifionat:** *Infrequent:* hyperglycemia, thirst. *Rare:* gout, hypercholesteremia, hyperfligidemia, increased alkaline phosphatase, increased BiUN, perioribital edema. **Musculoskeletal system:** *Frequent:* anthralgia, myalgia. *Infrequent:* arthritis. *Rare:* arthrosis, breast neoplasm, breast pain. **Respiratory system:** *Infrequent:* hardnihits. *Rare:* breast fibroadenosis, breast neoplasm, breast pain. **Respiratory system:** *Frequent:* harshrulis, sinustis, upper respiratory infec-tion. *Infrequent:* branchittis, coughing, dyspnea, rhinitis. *Rare:* breasten, bullow epistaxis, hypoxia, laryngitis, preumonia.

eruption, dermattils, fruunculosis, injection-site inflammation, photosensitivity, reaction, urticaria. Special senses: Frequent: diplopia, vision abnormal. Infrequent: eye irritation eye pain, scientiis, taste perversion, tinnitus. Rarc: conjunctivitis, corneal ulcer ation, lacrimation abnormal, parosmia, photopsia. Urogenital system: Frequent: urinary tract infection. Infrequent: cystitis, uri-nary incontinence. Rare: acute renal failure, dysuria, micturition frequency nocturia, polyuria, pyelonephritis, renal pain, unitary retention.

nary incontinence. Rarze acute renal failure, dysuria, michaem dysurs, universe acute renal pain, urinary retention. **DBC BAUSE AND DEPENDENCE** Controlled substance. Zolpidem tartrate is classified as a Schedule IV con-trolled substance. Juder the Controlled Substances Act. Examples of other drugs placed in Schedule IV include benzodiazepines (diazepam, alprazolam, etc), and the non-benzodiazepine hynotics (zalepion and eszopicione). **Abuse and dependence:** Studies of abuse potential in former drug abusers found that the effects of single doses of an immediate-release formulation of zolpidem tartrate (Ambien) 40 mg were similar, but not identical, to diazepam 20 mg, while zolpidem tartrate 10 mg was difficult to distinguish from placebox. Sedative/hynotics have produced withdrawal signs and symptoms follow-ing atorupt discontinuation. These reported symptoms range from mild dyspho-tal trial experience from zolpidem totar that may include abdominal and muscle cramps, vomiting, sweating, tremors, and convulsions. The U.S. clini-cal trial experience from zolpidem dose not reveal any clare vidence for within 48 hours following last zolpidem tratement. Tatiyue, nausea, flushing, lightheadedness, uncontrolled crying, emesis, stomach cramps, panic attack, revousness, and abdominal discomfort. These reported adverse events occurred at an incidence of 1% or less. However, available data cannot provide are lable estimate of the incidence, if any of dependence during tratement at recommended doses. Rare post-marketing reports of abuse, dependence and withdrawal bave been received. Because persons with a history of addiction to, or abuse of, dependence and withdrawal bave been received.

ithdrawal have been received. Because persons with a history of addiction to, or abuse of, drugs or alcohol re at increased risk for misuse, abuse and addiction of zolpidem, they should e monitored carefully when receiving zolpidem or any other hypnotic.

Construction of the second second

The recommended dose of Ambien CR for adults is 12.5 mg immediately vfore bedtime.

store beatume. Elderly or debilitated patients may be especially sensitive to the effects of bjoldem. Patients with hepatic insufficiency do not clear the drug as rapidly as ormals. The recommended dose of Ambien CR in these patients is 6.25 mg unediately before bedtime (see *Pracautions*).

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