Metabolic Syndrome Raises Risks After Angioplasty

BY BRUCE JANCIN

Denver Bureau

NEW ORLEANS — Metabolic syndrome raises the risk of adverse outcomes following percutaneous intervention, Vidyasagar Kalahasti, M.D., reported at the annual scientific sessions of the American Heart Association.

This new finding is consistent with previous reports saying that patients with metabolic syndrome also have increased

mortality after coronary artery bypass surgery, noted Dr. Kalahasti, a cardiology fellow at the Cleveland Clinic Foundation.

His study was a retrospective chart review including 2,382 patients who underwent percutaneous intervention (PCI) at the Cleveland Clinic. The patients were categorized into five groups based upon how many of four metabolic syndrome components, or risk factors, they had. For the purposes of the study, these four components were dyslipidemia, obesity, any

history of hypertension, and any history of diabetes.

During a median 8-month follow-up after PCI, the study group experienced 209 deaths and a total of 951 major adverse events, defined as MI, repeat revascularization, or death. The risk of a major adverse event showed a strong graded relationship with the number of metabolic syndrome components present.

Among the 781 patients who had just one metabolic syndrome component, the

risk of a major adverse event during follow-up was 35% greater than in the 253 patients with no components of metabolic syndrome. The 715 patients with two metabolic syndrome components had a 42% increased relative risk.

Among the 467 patients with three metabolic syndrome components, the relative risk of a major adverse event was 66% greater than in those with none. And the 166 patients who had all four metabolic syndrome components had a 76% increase in risk.

These findings underscore the importance of aggressively identifying and treating patients with metabolic syndrome, Dr. Kalahasti said.

Metabolic Syndrome Risks Worse in Women

ORLANDO, FLA. — Metabolic syndrome may be a greater risk factor for stroke and vascular events in women than in men, and limited access to social resources appears to contribute to its development, Bernadette Boden-Albala, Ph.D., reported at an international conference on women, heart disease, and stroke.

In the longitudinal Northern Manhattan Study (NOMAS) of 3,297 adult community residents who were stroke-free at study entry and followed for a mean of 5 years, nearly 46% of the 2,077 women and 35% of the men met the criteria for metabolic syndrome at study entry, said Dr. Boden-Albala, assistant professor of neurology and public health at the Neurological Institute, New York.

After adjustment for age, race/ethnicity, education, and risk factors, the estimated effect of metabolic syndrome on vascular events-including ischemic stroke, heart attack, and vascular death was significantly greater in women (hazard ratio 1.8) than in men (1.4). The hazard ratios for stroke risk associated with metabolic syndrome were 2.0 for women and 1.1 for men.

Metabolic syndrome accounted for 27% of vascular events and 30% of stroke events in women in the study, she said during a news conference at the meeting.

Metabolic syndrome was more prevalent in Hispanic women (48%) than in white (36%) or black (34%) women. In a multivariable logistic regression, after adjustment for age, the women with metabolic syndrome were significantly more likely to be Hispanic (hazard ratio 1.6), socially isolated (1.4), Medicaid users (1.3), and physically inactive (1.3)—all factors that Dr. Boden-Albala said represent reduced access to social resources.

The findings are important, given that women and minorities account for the majority of the 47 million Americans with metabolic syndrome, and they suggest that women may be more vulnerable than men to the risks associated with metabolic syndrome, she said.

-Sharon Worcester

Lunesta

BRIFF SUMMARY

INDICATIONS AND USAGE
LUNESTA is indicated for the treatment of insomnia. In controlled outpatient and sleep laboratory studies, LUNESTA administered at bedtime decreased sleep latency and improved sleep maintenance.

WARNINGS

Because sleep disturbances may be the presenting manifestation of a physical and/or spechatric disorder, symptomatic treatment of insomnia should be initiated only after a 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. Worsaning of insomnia or the emergence of new thinking or behavior abnormalities maybe the consequence of an unrecognized psychiatric or physical disorder. Such findings have emerged during the course of treatment with seddiverlympotic drugs, including LUNESTA. Beause some of the important adverse effects of LUNESTA appear to be dose-related, it is important to use the lowest possible effective dose, sepecially in the clearly see DOSAGE AND ADMINIS-TRATION in the Full Prescribing Information.

A variety of abnormal thinking and behavior changes have been reported to occur in

A variety of abnormal thinking and behivior changes have been reported to occur in association with the use of sedative/hymotics. Some of these changes may be characterized by decreased inhibition (e.g., aggressiveness and extroversion that seem out of charactery, similar to effects produced by alcohol and other CNS depressants. Other reported behavioral changes hav included bizarre behavior, agitation, hallisuriations, and depersonalization, Amness and other neuropsychiatric symptoms and occur unpredictably. In primarily degressed patients, worsening of depression, including suicidad thinking, has been reported in association with the use of sedative/hypnotics.

including suicidal thinking, has been reported in association with the use of sedativerhypnotics.

It can rarely be determined with certainty whether a particular instance of the abnormal behaviors listed above are drug-induced, spontaneous in origin, or a result of an underlying psychiatric or physical disorder. Monetheless, the emergence of any new behavioral sign or symptom of concern requires careful and immediate evaluation. Following rapid dose decrease or abrund discontinuation of the use of sedativerhypnotics, there have been reports of signs and symptoms similar to those associated with withdrawal from other CNS-depressant drugs (see PRUG ABUSE AND DEPENDEDCE). LUNESTA, like other hypnotics, has CNS-depressant effects. Because of the rapid onset of action, LUNESTA should only be ingested immediately prior to going to bed or after the patient has gone to bed and has experienced difficulty falling asleep. Patients receiving LUNESTA should be cautioned against engaging in hazardous occupations requiring complete mental alertness or motro coordination (e.g., operating machinery or driving a motor vehicle) after ingesting the drug, and be cautioned about potential impairment of the perfermance of such activities on the day following ingestion of LUNESTA. LUNESTA, like other hypnotics, may produce additions, anticonvuisants, antilistamines, ethand, and other drugs that themselves produce CNS depression, LUNESTA is administered with other CNS-depressant agents, because of the potentially additive effects.

PRECAUTIONS

A study in healthy volunteers did not reveal respiratory-depressant effects at dose 2.5-fold higher (7 mg) than the recommended dose of eszopicione. Caution is advised, however, if LUNESTA is prescribed to patients with compromised respiratory function. The dose of LUNESTA should be reduced to 1 mg in patients with severe health impairment, because systemic exposure is doubled in such subjects. No dose adjust-ment appears necessary for subjects with mild or moderate health impairment, since less than 10% of eszopicione is excreted unchanged in the urine. The dose of LUNESTA should be reduced to patients who are administered potent inhibitors of OYP3A4, such as ketoconzole, while taking LUNESTA. Downward dose adjustment is also recommended whet LUNESTA is administered with agents hav-ing known CNS-depressant effects.

ing known CNS-depressant effects.

Use In Patients With Depression: Sedative/hypnotic drugs should be administered with caution to patients exhibiting signs and symptoms of depression. Suicidal tendencies may be present in such patients, and protective measures may be required. Intentional overdose is more common in this group of patients: therefore, the east amount of drug that is feasible should be prescribed for the patient at any one time. 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

Ethanol. An additive effect on psychomotor performance was seen with coadministration of eszopiclone and ethanol 0.70 g/kg for up to 4 hours after ethanol administration. tion of eszopiclone and ethanol 0.70 g/kg for up to 4 hours after ethanol administration. Paroxetine: Coadministration of single doses of eszopiclone 3 mg and paroxetine 20 mg daily for 7 days produced no pharmacokinetic or pharmacodynamic interaction. Lorazepam: Coadministration of single doses of eszopiclone 3 mg and forazepam 2 mg did not have clinically relevant effects on the pharmacodynamics or pharmacokinetics of either drug.

Olanzapine: Coadministration of eszopiclone 3 mg and olanzapine 10 mg produced a decrease in DSST scores. The interaction was pharmacodynamic; there was no alteration in the pharmacokinetics of either drug.

Drugs That Intel® CVPSAH (Bacconazule): CVPSAH is a major metabolic pathway for elimination of eszopiclone. The AUC of eszopiclone was increased 2.2-dolf by coad-crististation of eszopiclone. The AUC of eszopiclone was increased 2.2-dolf by coad-crististation of eszopiclone. The AUC of eszopiclone was increased 2.2-dolf by coad-crististation of eszopiclone. The AUC of eszopiclone was increased 2.2-dolf by coad-crististation of estopiclone and ally for 5 days.

ministration of ketoconazole, a potent lightbytor of CYP3A4, 400 mg daily for 5 days. C_{max} and t₁₀ were increased 1.4-fold and 1.3-fold, respectively. Other strong inhibitors of CYP3A4 (e.g. tiraconazole, clarithrouvicin, nefazodone, trolgeandomicin ritionavir

C_{mis} and t_m were increased 1.4-1000 atto 1.5-1001, respectively. Consider some surrough whether of CYPSA4 (e.g. intraconzole, clarithomycin, nelazodone, troleandomycin, ritonavir, nelfinavir) would be expected to behave similarly.

Drugs That Induce CYPSA44 (Rifampicin): Racemic zopicione exposure was decreased 80% by concomitant use of rifampicin, a potent inducer of CYPSA4. A similar effect would be expected with exceptione.

Drugs Highly Bound To Plasma Proteir. Escopicione is not highly bound to plasma proteins (55-59%, bound); therefore, the disposition of escopicione is not expected to be sensitive to alterations in protein binding. Administration of escopicione are to a patient taking another drug that is highly protein-bound would not be expected to cause an alteration in the free consecuration of either drug.

Drugs With A Narrow Therapeutic Index

Drugs with a narrow inelapleutic linear Digoxin: A single dose of eszopiclone 3 mg did not affect the pharmacokinetics of digoxin measured at steady state following dosing of 0.5 mg twice daily for one day and 0.25 mg daily for the next 6 days. Warfam: Eszopiclone 3 mg administend daily for 5 days did not affect the pharma-cokinetics of (R)- or (S)-warfarin, nor were there any changes in the pharmacody-namic profile (profit ormbin time) following a single 25-mg oral dose of warfarin.

namic profile (profilrombin time) following a single 25-mg oral dose of warfarin. Carcinogenesis, Mulagenesis, Impailment of Fertility Carcinogenesis: In a carcinogenicity study in Sprague-Dawley rats in which eszopi-cione was given by oral gavage, no increases in tumors were seen; plasma levels (AUC) of eszopicione at the nighest dose used in this study (16 mg/kg/day) are esti made to be 80 (temsles) and 20 (males) times those in humans receiving the max-inum recommended human dose (MRHD). However, in a carcinogenicity study in

Sprague-Dawley rats in which racemic zopicione was given in the diet, and in which plasma levels of eszopicione were reached that were greater than those reached in the above study of eszopicione, an increase in mammary gland adenocarriomas in males were seen at the highest dose of 100 mg/kg/day. Plasma levels of eszopicione at this dose are estimated to be 150 (females) and 70 (males) times those in humans receiving the MRHD. The mechanism for the increase in mammary adenocarriomas is unknown. The increase in hyproid tumors is thought to be due to increased levels of TSH secondary to increased metabolism of circulating thyroid hormones, a mechanism that is not considered to be relevant to humans.

of TSH secondary to increased metabolism of circulating thyroid hormones, a mechanism that is not considered to be relevant to humans.

In a carcinogenicity study in B662Ff mice in which racemic zopiclone was given in the diet, an increase in pulmonary carcinomas and carcinomas plus aderornes in females and an increase in skin fibromas and sarcomas in males were seen at the highest dose of 100 mg/kg/day. Plasma levels of eszopiclone at this dose are estimated to be 8 (females) and 20 (males) times those in humans receiving the MRHD. The skin tumors were due to skin lesions induced by aggressive behavior, a mechanism that is not relevant to humans. A carcinogenicity study were also performed in which CD-1 mice were given eszopiclone at doses up to 100 mg/kg/day by oral gazage; although this study did not reach a maximum tolerated dose, and was thus inadequate for overalf assessment of carcinogenic potential, no increases in either pulmonary or skin tumors were seen at doses producing plasma levels of eszopiclone estimated to be 90 times those in humans receiving the MRHD—i.e., 12 times the exposure in the racemate study.

Eszopiclone did not increase tumors in a p53 transgenic mouse bioassay at oral doses up to 300 mg/kg/day.

Mutagenesis: Eszopiclone was positive in the mouse lymphoma chromosomal aberration assay and produced an equivocal response in the Chinese hamster ovary cell chromosomal aberration assay, it was not mutagenic or clastogenic in the bacterial Ames gene mutation assay, in an unscheduled DNA synthesis assay, or in an in vive mouse bone marrow micronucleus assay.

(S)-N-desmethyl zopiclone, a metabolite of eszopiclone, was positive in the Chinese hamster ovary cell and human lymphocyte chromosomal aberration assays. It was negative in the bacterial Ames mutation assay, in an *in vitro* 3:p-postlabeling DNA adduct assay, and in an *in vivo* mouse bone marrow chromosomal aberration and micronucleus assay.

micronucleus assay.

Impairment Of Fertifity: Eszopicione was given by oral gavage to male rats at dose up to 45 mg/kg/day from 4 weeks premating through mating and to female rats at doses up to 180 mg/kg/day from 2 weeks premating through day 7 of pregnancy. An additional study was performed in which only females were treated, up to 180 mg/kg/day. Eszopicione decreased fertifity, probably because of effects in both males and females, with no females becoming pregnant when both males and females were treated with the flighest dose; the no-effect dose in both sexes was 5 mg/kg (16 times the MRHD on a mg/m² basis). Other effects included increased preimplantation loss (no-effect dose 25 mg/kg), and decreases in sperm number and motility and increases in morphologically abnormal sperm (no-effect dose 5 mg/kg).

Pregnancy Category C: Eszopicione administered by oral gavage to pregnant rats and rabbits during the period of organogenesis showed no evidence of teratogenicity up to the highest doses tested (250 and 16 mg/kg/day in rats and rabbits, respectively; these doses are 900 and 100 times, respectively, the maximum rocommended human dose (MRHD) on a mg/m² basis). In the rat, slight reductions in fetal weight and evidence of developmental delay were seen at maternally toxic doses of 125 and 150 mg/kg/day, but not at 62.5 mg/kg/day (200 times the MRHD on a mg/m² basis). Eszopicione was also administered by oral gavage to pregnant rats throughout the pregnancy and lactation periods at doses of up to 180 mg/kg/day. Increased post-implantation loss, decreased postnatal pup weights and survival, and increased pus startle response were seen at all doses; the lowest dose tested, 60 mg/kg/day, is consistent with the control of the mg/kg/day, is 200 times the MRHD on a mg/m² basis. These doses did not produce significant maternal toxicity. Eszopicione had no effects on other behavioral measures or reproductive function in the offspring.

Labor And Delivery: LUNESTA has no established use in labor and delivery

Laws new veryery. LUNES IA has no established use in labor and delivery.

Nursing Mothers: It is not known whether LUNESTA is excreted in human milk.

Because many drugs are excreted in human milk, caution should be exercised when

LUNESTA is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of eszopiclone in children below the age of 18

have not been established.

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Geriatric Use: A total of 287 subjects in double-blind, parallel-group, placebo-controlled clinical trials who received eszopicione were 65 to 86 years of age. The overall pattern of adverse events for elderly subjects (median age 27 typars) in 2-week studies with nighttime dosing of 2 mg eszopicione was not different from that seen in younger adults. LUNESTA ing exhibited significant reduction in sleep latency and improvement in sleep maintenance in the elderly population.

APVERSE REACTONS

The premarketing development program for LUNESTA included eszopicione exposures in patients and/or normal subjects in clinical pharmacology/pharmacokinetic studies, and approximately 400 normal subjects in clinical pharmacology/pharmacokinetic studies, and approximately 455 patients in placebo-controlled clinical effectiveness studies, corresponding to approximately 263 patient-exposure years. The conditions and duration of treatment with LUNESTA varied greatly and included (in overlapping actagories) open-label and doubtle-blind phases of studies, inpatients and outpatients, and short-torm and longer-term exposure. Adverse reactions were assessed by collecting adverse events, results of physical examinations, vital signs, weights, laboratory analyses, and ECGs.

Adverse events during exposure were obtained primarily by general inquiry and recorded by clinical investigators using terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals swere investigators using terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of the viction of the proportion of the propo

The stated frequencies of adverse events represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed. An event was considered treatment-emergent if in Cocurred for the first time or worsened while the patient was receiving therapy following baseline evaluation.

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Adverse Findings Observed in Placebo-Controlled Trials

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Adverse Events Resulting in Discontinuation of Treatment: In placebo-controlled, parallel-group clinical trials in the elderly, 3.8% of 208 patients who received placebo, 2.3% of 215 patients who received 2 mg LUNESTA, and 1.4% of 72 patients who received 1 mg LUNESTA discontinued treatment due to an adverse event. In the 6-week parallel-group study in adults, no patients in the 3 mg arm discontinued because of an adverse event. In the 16-week parallel-group study in adults, no patients in the 3 mg arm discontinuad because of an adverse event. In the 16-week parallel-group study in adults, no patients in the 3 mg arm discontinuad to received 3 mg LUNESTA discontinued due to an adverse event. No event that resulted in discontinuation occurred at a rate of greater than 2%.

Adverse Events Observed at an Incidence of 2:2% in Controlled Trials. The following lists the incidence (% palecebo, 2 mg, 3 mg, respectively) of treatment-emergent adverse events from a Phase 3 placebo-controlled study of LUNESTA at doses of 2 or 3 mg in non-elderly adults. Treatment duration in this trial was 44 days. Data are limited to adverse events that occurred in 2% or more of patients treated with LUNESTA was greater than the incidence in palecidence in patients treated with LUNESTA was greater than the incidence in placebo-created patients (n=99). Bodru as a whole; headache (13%, 5%, 7%), dynspepsia (4%, 4%, 5%), anssea (4%, 5%), contiling (1%, 5%, 7%), dynspepsia (4%, 4%, 5%), anssea (4%, 5%), somolence (5%, 10%, 6%). Resonation (5%, 0%, 0%), son, 5%), errousasses (3%, 5%, 0%), bronusses (3%, 5%, 0%), bronusses (3%, 5%, 0%), bronusles (3%, 5%, 0%), bronusles (3%, 5%, 5%, 0%), bronusles

'Events for which the LUNESTA incidence was equal to or less than placebo are not listed, but included the following: abnormal dreams, accidental injury, back pain, diarrhea, flu syndrome, mysliga, pain, pharyngtis, and trinitis.

Adverse events that suggest a dose-response relationship in adults include viral infection, dry mouth, dizzness, hallucinations, infection, rash, and unpleasant taste, with this relationship clearest for unpleasant taste.

with this relationship clearest for unpleasant taste. The following lists the incidence (% placebo, 2 mg, 3 mg, respectively) of treatmer emergent adverse events from combined Phase 3 placebo-controlled studies LUNESTA at losses of 1 or 2 mg in elderly adults (ages 65-69). Treatment during these trials was 14 days. Data are limited to events that occurred in 2% or more patients treated with LUNESTA in mg (n=2) or 2 mg (n=215) in which the incidence in patients.

Somnolence.

Adverse events that suggest a dose-response relationship in elderly adults include pain, dry mouth, and unpleasant taste, with this relationship again clearest for unpleasant taste. These figures cannot be used to predict the incidence of adverse events in the course of usual medical practice because patient characteristics and other factors may differ from those that prevailed in the clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators.

tigations involving different treatments, uses, and investigators.

The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contributions of drug and non-drug factors to the adverse event incidence rate in the population studied.

Other Events Observed During The Premarketing Evaluation Of LUNESTA. Following is a list of modified COSTART terms that reflect treatment-emergent adverse events as defined in the introduction to the ADVERSE REACTIONS scion and reported by approximately 1550 subjects treated with LUNESTA at doses in the range of 1 to 3.5 mg/day during Phase 2 and 3 clinital traits throughout the United States and Canada. All reported events are included except those already listed here or listed elsewhere in labeling, minor events common in the general population, and events unlikely to be drug-related. Although the events reported occurred during treatment with LUNESTA, they were not necessarily caused by it.

events unlikely to be drug-related. Although the events reported occurred during treatment with LUNESTA, they were not necessarily caused by it. Blowing definitions: frequent adverse events are those that occurred on nor or more occasions at least 17.00 patients, intraquent adverse events are those that occurred in fewer than 17.00 patients, better adverse events are those that occurred in fewer than 17.00 patients, better adverse events are categorized based on their incidence for the appropriate gender. Frequent, chest pain, impraine, peripheral edema.

Intrequent: acne, agitation, allergic reaction, alopecia, amenorriea, anemia, anorexia, apathy, arthrifts, asthma, atasi, breast enporgement, breast enlargement, breast enlargement breast eneplesm, breast pain, bronchitis, burstis, cellutitis, cholelithiasis, conjunctivitis, contact dermatitis, cystitis, dry eyes, dry skin, dysprea, dysuria, eczema, ear pain, upsethesia, incoordination, increased appetite, insomma, joint disorder (mainly swelling, stiffness, and pain), kidney calculus, kidney pain, laryngitis, leg cramps, the store, of this media, persethesia, photosensitivity, reflexes decreased, skin discoloration, sweating, thinking abnormal (mainly difficulty concentrating), t

usoruer, weight gain, weight loss.

Rare: abnormal gait, arthrosis, colitis, dehydration, dysphagia, erythema multiforme, euphoria, frunculousis, gastriitis, gout, hepatitis, hepatomegaly, herpes zoster, hirsutism, hyperacusis, hyperashesia, hyperlipemia, hypokalemia, hypokinesia, iritis, liver damage, maculopanular rash, mydraiss, myonathy, neuritis, neuropathy oliguria, photophobia, ptosis, pyelonephritis, rectal hemorrhage, stomach ulcer, stomatitis, stupor, thrombophiebitis, tongue edema, tremor, urethritis, vesiculobullous rash.

stomatitis, stupor, thrombophiebitis, longue edema, tremor, urethritis, vesticulobullous rash.

PRUG ABUSE AND DEPENDENCE
Controlled Substance Class: LUNESTA is a Schedule IV controlled substance under the Controlled Substance Class: LUNESTA is a Schedule IV controlled substance under the Controlled Substances Act Other substances under the same classification are benzoliazepines and the nonbenzodiazepine sphontois zalepion and zolpidem. While eszopidone is a hypnotic agent with a chemical structure unrelated to benzodiazepines, it shares some of the pharmacologic properties of the benzodiazepines, and spendence, and Tolerance

Abusa Dependence, and Tolerance

Abusa and Dependence, in a study of abuse liability conducted in individuals with known histories of benzodiazepine abuse, eszopicilone at closes of 6 and 12 mg produced euphoric effects similar to those of diazepam 20 mg. In this study, at closes in reports of amnesia and hallucinations was observed for both LUNESTA and diazepam. The clinical trial experience with LUNESTA revealed no evidence of a serious withdrawal syndrome. Nevertheless, the following adverse events control in SM-IV criteria for uncomplicated sedative/hypnotic withdrawal were reported during clinical irisks following placebo substitution occurring within 48 hours following the last LUNESTA treatment: anxiety, abnormal dreams, nausea, and upset stomach. These reported adverse events occurred at an incidence of 2% or less. Use of benzodiazepines and similar agents may lead to physical and psychological dependence. The risk of abuse and dependence increases with the dose and duration of treatment and concomitant use of other psychoactive drugs. The risk is also greater or patients who have a history of abcolo to drug abuse or history of psychiatric disorders. These patients should be under careful surveillance when receiving LUNESTA or any other hypnotic.

Tolerance: Some loss of efficacy to the hypnotic effect of benzodiazepines and baruseton.

Indicates, some loss or entacts of the hypothol enter to be adoption and decided and the decid

often associated with overdose with other CNS-depressant agents. 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. As in all cases of drug overdose, respiration, pulse, blood pressure, and other appropriate signs should be monitored and general supportive measures employed. Hypotension and CNS depression should be monitored and treated by appropriate medical intervention. The value of dialysis in the treatment of overdosage has not been determined.

Poison Control Center: As with the management of all overdosage, the possibility of multiple drug ingestion should be considered. The physician may wish to consider contacting a poison control center for up-to-date information on the management of hypnotic drug product overdosage.

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