

Most At-Risk Women Ineligible for Tamoxifen

BY SHARON WORCESTER
Tallahassee Bureau

Tamoxifen probably won't prevent many cases of breast cancer in women at risk for the disease because most are ineligible for treatment and those most likely to be eligible are the least likely to develop cancer, according to Carmen L. Lewis, M.D., of the University of North Carolina at Chapel Hill and colleagues.

Of 605 women studied, more than 90% of those found to be at risk for developing breast cancer (based on their responses to a questionnaire about their health and family history) would be ruled out for chemoprevention with tamoxifen due to the risk of adverse events such as blood clots and stroke associated with the drug, the investigators found.

Using the Gail model, they estimated that the percentage of white women in the study with an increased 5-year breast can-

cer risk (defined as a risk of at least 1.66%) was 9% among those in their 40s, 24% among those in their 50s, and 53% of those in their 60s. Among black women, 3% of those in their 40s, 7% of those in their 50s, and 13% of those in their 60s had this level of risk.

In a hypothetical cohort of 10,000 women similar to those in the study (calculations were made only for white women due to the small number of black women in the study) only 7% of those in

their 40s, 6% of those in their 50s, and 10% of those in their 60s met the requirement for discussions about tamoxifen. It is recommended that discussion about chemoprevention take place only with those who have a high potential of benefit and a low potential of harm from using tamoxifen. Those with conditions, such as high blood pressure and diabetes, would be excluded from such discussions because of the increased risk of adverse effects.

With the same hypothetical cohort, and if it is assumed tamoxifen would result in a 49% reduction in the number of invasive breast cancers in high-risk women as demonstrated in the 1998 placebo-controlled National Surgical Adjuvant Breast and Bowel Project (NSABP) Breast Cancer Prevention Trial, a maximum of only 6%-8% of invasive cancers would be prevented (Arch. Intern. Med. 2004;164:1897-1903).

This is likely an inflated figure because it is based on the assumption that 100% of eligible women would use tamoxifen; studies have shown that 24%-40% of such women discontinue treatment, they noted.

The study, which was sponsored by the National Cancer Institute, doesn't question the drug's ability to prevent breast cancer, but does

illustrate the limitations of its use for women in different age groups. For women in their 40s, the overall effect of chemoprevention is likely to be small because the proportion of breast cancers occurring in those with increased risk in this age group is small. For those in their 50s and 60s, the potentially larger number of women with increased risk for breast cancer who could benefit from chemoprevention is reduced by the increased number with a substantial likelihood of adverse effects associated with tamoxifen, the investigators explained.

The findings underscore the need for proper identification of chemoprevention candidates and for studies on how to improve the efficacy—and reduce the side effects—of chemopreventive drugs, Larry Wickerham, M.D., said in an interview.

Dr. Wickerham of the NSABP was an investigator and served as the protocol officer on the Breast Cancer Prevention Trial, which established the efficacy of tamoxifen for preventing invasive breast cancer in high-risk women.

For those who can benefit from chemoprevention with tamoxifen, the benefit is "real and impressive," Dr. Wickerham said, stressing that the findings of the University of North Carolina study don't contradict those of the Breast Cancer Prevention Trial.

"The take-home message isn't to throw out tamoxifen—it's that clinicians should become familiar with how to identify women who can benefit from this drug," he said.

References: 1. Sandrini G, Färkkilä M, Burgess G, Forster E, Haughe S, for the Elettriptan Steering Committee. Elettriptan vs sumatriptan: a double-blind, placebo-controlled, multiple migraine attack study. *Neurology*. 2002;59:1210-1217. 2. Mathew NT, Schoenen J, Winner P, Muirhead N, Sikes CR. Comparative efficacy of elettriptan 40 mg versus sumatriptan 100 mg. *Headache*. 2003;43:214-222.

RELAPX[®] (elettriptan hydrobromide) Tablets

BRIEF SUMMARY OF PRESCRIBING INFORMATION

CONTRAINDICATIONS: RELAPX Tablets should not be given to patients with ischemic heart disease (e.g., angina pectoris, history of myocardial infarction, or documented silent ischemia) or to patients who have symptoms, or findings consistent with ischemic heart disease, coronary artery vasospasm, including Prinzmetal's variant angina, or other significant underlying cardiovascular disease (see WARNINGS). RELAPX Tablets should not be given to patients with cerebrovascular syndromes including (but not limited to) strokes of any type as well as transient ischemic attacks (see WARNINGS). RELAPX Tablets should not be given to patients with peripheral vascular disease including (but not limited to) ischemic bowel disease (see WARNINGS). Because RELAPX Tablets may increase blood pressure, it should not be given to patients with uncontrolled hypertension (see WARNINGS). RELAPX Tablets should not be administered to patients with hemiplegic or basilar migraine. RELAPX Tablets should not be used within 24 hours of treatment with another 5-HT_{1B/1D} agonist, an ergotamine-containing or ergot-like medication such as dihydroergotamine (DHE) or methysergide. RELAPX Tablets should not be used in patients with known hypersensitivity to elettriptan or any of its inactive ingredients. RELAPX Tablets should not be given to patients with severe hepatic impairment.

WARNINGS: RELAPX Tablets should only be used where a clear diagnosis of migraine has been established. CYP3A4 Inhibitors: Elettriptan should not be used within at least 72 hours of treatment with the following potent CYP3A4 inhibitors: ketoconazole, itraconazole, nefazodone, toleandomycin, clarithromycin, rifonaxin, and neflavinir. Elettriptan should not be used within 72 hours with drugs that have demonstrated potent CYP3A4 inhibition and have this potential effect described in the CONTRAINDICATIONS, WARNINGS, or PRECAUTIONS sections of their labeling. In a coronary angiographic study of rapidly infused intravenous elettriptan to concentrations exceeding those achieved with 80 mg oral elettriptan in the presence of potent CYP3A4 inhibitors, a small dose-related decrease in coronary artery diameter similar to that seen with a 6 mg subcutaneous dose of sumatriptan was observed. Risk of Myocardial Ischemia and/or Infarction and Other Cardiac Events: Because of the potential of 5-HT_{1B/1D} agonists to cause coronary vasospasm, elettriptan should not be given to patients with documented ischemic or vasospastic coronary artery disease (CAD) (see CONTRAINDICATIONS). It is strongly recommended that elettriptan not be given to patients in whom unrecognized CAD is predicted by the presence of risk factors (e.g., hypertension, hypercholesterolemia, smoker, obesity, diabetes, strong family history of CAD, female with surgical or physiological menopause, or male over 40 years of age) unless a cardiovascular evaluation provides satisfactory clinical evidence that the patient is reasonably free of coronary artery and ischemic myocardial disease or other significant underlying cardiovascular disease. The sensitivity of cardiac diagnostic procedures to detect cardiovascular disease or predisposition to coronary artery vasospasm is modest, at best. It, during the cardiovascular evaluation, the patient's medical history, electrocardiographic, or other investigations reveal findings indicative of, or consistent with coronary artery vasospasm or myocardial ischemia, elettriptan should not be administered (see CONTRAINDICATIONS). For patients with risk factors predictive of CAD, who are determined to have a satisfactory cardiovascular evaluation, it is strongly recommended that administration of the first dose of elettriptan take place in the setting of a physician's office or similar medically staffed and equipped facility unless the patient has previously received elettriptan. Because cardiac ischemia can occur in the absence of clinical symptoms, consideration should be given to obtaining on the first occasion of use an electrocardiogram (ECG) during the interval immediately following administration of RELAPX Tablets, in these patients with risk factors. It is recommended that patients who are intermittent long-term users of 5-HT_{1B/1D} agonists including RELAPX Tablets, and who have or acquire risk factors predictive of CAD, as described above, undergo periodic cardiovascular evaluation as they continue to use RELAPX Tablets. The systematic approach described above is intended to reduce the likelihood that patients with unrecognized cardiovascular disease will be inadvertently exposed to elettriptan. Cardiac Events and Fatalities Associated With 5-HT_{1B/1D} Agonists: Serious adverse cardiac events, including acute myocardial infarction, stroke, and other cerebrovascular events have been reported in patients treated with 5-HT_{1B/1D} agonists. Considering the extent of use of 5-HT_{1B/1D} agonists in patients with migraine, the incidence of these events is extremely low. Premarketing experience with elettriptan among the 7,143 unique individuals who received elettriptan during pre-marketing clinical trials: In a clinical pharmacology study, in subjects undergoing diagnostic coronary angiography, a subject with a history of angina, hypertension and hypercholesterolemia, receiving intravenous elettriptan (C₅₀ of 127 ng/mL equivalent to 60 mg oral elettriptan), reported chest tightness and experienced angiographically documented coronary vasospasm with no ECG changes of ischemia. There was also one report of myocardial infarction and death in a patient with cardiovascular risk factors (hypertension, hyperlipidemia, strong family history of CAD) in association with inappropriate concomitant use of elettriptan and sumatriptan. The uncontrolled nature of postmarketing surveillance, however, makes it impossible to determine definitively if the case was actually caused by elettriptan or to reliably assess causation in individual cases. Cerebrovascular Events and Fatalities Associated With 5-HT_{1B/1D} Agonists: Cerebral hemorrhage, subarachnoid hemorrhage, stroke, and other cerebrovascular events have been reported in patients treated with 5-HT_{1B/1D} agonists. In a number of cases, it appears possible that the cerebrovascular events were primary, the agonist having been administered in the incorrect belief that the symptoms experienced were a consequence of migraine, when they were not. It should be noted that patients with migraine may be at increased risk of certain cerebrovascular events (e.g., stroke, hemorrhage, and transient ischemic attack). Other Vasospasm-Related Events: 5-HT_{1B/1D} agonists may cause vasospastic reactions other than coronary artery vasospasm. Both peripheral vascular ischemia and colonic ischemia with abdominal pain and bloody diarrhea have been reported with 5-HT_{1B/1D} agonists. Increase in Blood Pressure: Significant elevation in blood pressure, including hypertensive crisis, has been reported on rare occasion in patients receiving 5-HT_{1B/1D} agonists with and without a history of hypertension. In clinical pharmacology studies, oral elettriptan (at doses of 60 mg or more) was shown to cause small, transient dose-related increases in blood pressure, predominantly diastolic, consistent with its mechanism of action and with other 5-HT_{1B/1D} agonists. The effect was more pronounced in renally impaired and elderly subjects. A single patient with hepatic cirrhosis received elettriptan 80 mg and experienced a blood pressure of 220/96 mm Hg five hours after dosing. The treatment-related increase in blood pressure was observed in patients with uncontrolled hypertension (see CONTRAINDICATIONS). An 18% increase in mean pulmonary artery pressure was seen following dosing with another 5-HT_{1B/1D} agonist in a study evaluating subjects undergoing cardiac catheterization.

PRECAUTIONS: General: As with other 5-HT_{1B/1D} agonists, sensations of tightness, pain, pressure and heaviness have been reported after treatment with elettriptan in the precordium, throat, and jaw. Events that are localized to the chest, throat, neck and jaw have not been associated with arrhythmias or ischemic ECG changes in clinical trials; in a clinical pharmacology study of subjects undergoing diagnostic coronary angiography, one subject with a history of angina, hypertension and hypercholesterolemia experienced chest tightness and experienced angiographically documented coronary vasospasm with no ECG changes of ischemia. Because 5-HT_{1B/1D} agonists may cause coronary artery vasospasm, patients who experience signs or symptoms suggestive of angina following dosing should be evaluated for the presence of CAD or a predisposition to Prinzmetal's variant angina before receiving additional doses of medication, and should be monitored electrocardiographically if dosing is resumed and similar symptoms recur. Similarly, patients who experience other symptoms or signs suggestive of decreased arterial flow, such as ischemic bowel syndrome or Raynaud's syndrome following the use of any 5-HT_{1B/1D} agonist are candidates for further evaluation (see CONTRAINDICATIONS and WARNINGS). **Hepatically Impaired Patients:** The effects of severe hepatic impairment on elettriptan metabolism was not evaluated. Subjects with mild or moderate hepatic impairment demonstrated an increase in both AUC (34%) and half-life. The C₅₀ was increased by 18%. Elettriptan should not be used in patients with severe hepatic impairment. No dose adjustment is necessary in mild to moderate impairment. **Binding to Melanin-Containing Tissues:** In rats treated with a single intravenous (3 mg/kg) dose of radiolabeled elettriptan, elimination of radioactivity from the retina was prolonged, suggesting that elettriptan and/or its metabolites may bind to the melanin of the eye. Because there could be accumulation in melanin-rich tissues over time, this raises the possibility that elettriptan could cause toxicity in these tissues after extended use. Although no systematic monitoring of ophthalmologic function was undertaken in clinical trials, and no specific recommendations for ophthalmologic monitoring are offered, prescribers should be aware of the possibility of long-term ophthalmologic effects. **Corneal Opacities:** Transient corneal opacities were seen in dogs receiving oral elettriptan at 5 mg/kg and above. They were observed during the first week of treatment, but were not present thereafter despite continued treatment. Exposure at the no-effect dose level of 2.5 mg/kg was approximately equal to that achieved in humans at the maximum recommended daily dose. **Laboratory Tests:** No specific laboratory tests are recommended. **Drug Interactions: Ergot-containing drugs:** Ergot-containing drugs have been reported to cause prolonged vasospastic reactions. Because these effects may be additive, use of ergotamine-containing or ergot-like medications (like dihydroergotamine [DHE] or methysergide) and elettriptan within 24 hours of each other is not recommended (see CONTRAINDICATIONS). **CYP3A4 Inhibitors:** Elettriptan is metabolized primarily by CYP3A4 (see WARNINGS regarding use with potent CYP3A4 inhibitors). **Monoamine Oxidase Inhibitors:** Elettriptan is not a substrate for monoamine oxidase (MAO) enzymes; therefore there is no expectation of an interaction between elettriptan and MAO inhibitors. **Propranolol:** The C₅₀ and AUC of elettriptan were increased by 10 and 33% respectively in the presence of propranolol. No interactive increases in blood pressure were observed. No dosage adjustment appears to be needed for patients taking propranolol. **Selective serotonin reuptake inhibitors (SSRIs):** SSRIs (e.g., fluoxetine, fluvoxamine, paroxetine, sertraline) have been reported, rarely, to cause weakness, hyperreflexia, and incoordination when coadministered with 5-HT_{1B/1D} agonists. If concomitant treatment with elettriptan and an SSRI is clinically warranted, appropriate observation of the patient is advised. **Other 5-HT_{1B/1D} agonists:** Concomitant use of other 5-HT_{1B/1D} agonists within 24 hours of RELAPX treatment is not recommended (see CONTRAINDICATIONS). **Drug/Laboratory Test Interactions:** RELAPX Tablets are not known to interfere with commonly employed clinical laboratory tests. **Carcinogenesis:** Lifetime carcinogenicity studies, 104 weeks in duration, were carried out in mice and rats by administering elettriptan in the diet. In rats, the incidence of testicular interstitial cell adenomas was increased at the high dose of 75 mg/kg/day. The estimated exposure (AUC) to parent drug at that dose was approximately 6 times that achieved in humans receiving the maximum recommended daily dose (MRDD) of 80 mg, and at the no-effect dose of 15 mg/kg/day it was approximately 2 times the human exposure at the MRDD. In mice, the incidence of hepatocellular adenomas was increased at the high dose of 400 mg/kg/day. The exposure to parent drug (AUC) at that dose was approximately 18 times that achieved in humans receiving the MRDD, and the AUC at the no-effect dose of 90 mg/kg/day was approximately 7 times the human exposure at the MRDD. **Mutagenesis:** Elettriptan was not mutagenic in bacterial or mammalian cell assays *in vitro*, testing negative in the Ames reverse mutation test and the hypoxanthine-guanine phosphoribosyl transferase (HGPRT) mutation test in Chinese hamster ovary cells. It was not clastogenic in two *in vivo* mouse micronucleus assays. Results were equivalent in *in vitro* human lymphocyte chromosome tests, in which the incidence of polyploidy was not increased in the absence of metabolic activation. **Impairment of Fertility:** In a rat fertility and early embryonic development study, doses tested were 50, 100 and 200 mg/kg/day, resulting in systemic exposures to parent drug in rats, based on AUC, that were 4, 8 and 16 times MRDD, respectively, in males and 7, 14 and 28 times MRDD, respectively, in females. There was a prolongation of the estrous cycle at the 200 mg/kg/day dose due to an increase in duration of estrus, based on vaginal smears. There were also dose-related, statistically significant decreases in mean numbers of corpora lutea per dam at

all 3 doses, resulting in decreases in mean numbers of implants and viable fetuses per dam. This suggests a partial inhibition of ovulation by elettriptan. There was no effect on fertility of males and no effect on fertility of females.

Reproductive Toxicity Category 2: In reproductive toxicity studies in rats and rabbits, oral administration of elettriptan was associated with developmental toxicity (decreased fetal and pup weights and an increased incidence of fetal structural abnormalities). Effects on fetal and pup weights were observed at doses that were, on a mg/m² basis, 6 to 12 times greater than the clinical maximum recommended daily dose (MRDD) of 80 mg. The increase in structural alterations occurred in the rat and rabbit at doses that, on a mg/m² basis, were 12 times greater than (rat) and approximately equal to (rabbit) the MRDD. When pregnant rats were administered elettriptan during the period of organogenesis at doses of 10, 30 or 100 mg/kg/day, fetal weights were decreased and the incidences of ventral and sternal variations were increased at 100 mg/kg/day (approximately 12 times the MRDD on a mg/m² basis). The 100 mg/kg/day dose was also maternally toxic, as evidenced by decreased maternal body weight gain during gestation. The no-effect dose for developmental toxicity in rats exposed during organogenesis was 30 mg/kg, which is approximately 4 times the MRDD on a mg/m² basis. When doses of 5, 10 or 50 mg/kg/day were given to New Zealand White rabbits throughout organogenesis, fetal weights were decreased at 50 mg/kg, which is approximately 12 times the MRDD on a mg/m² basis. The incidences of fused sternebrae and vena cava deviations were increased in all treated groups. Maternal toxicity was not produced at any dose. A no-effect dose for developmental toxicity in rabbits exposed during organogenesis was not established, and the 5 mg/kg/day dose is approximately equal to the MRDD on a mg/m² basis. There are no adequate and well-controlled studies in pregnant women; therefore, elettriptan should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Nursing Mothers:** Elettriptan is excreted in human breast milk. In one study of 8 women given a single dose of 80 mg, the mean total amount of elettriptan in breast milk over 24 hours in this group was approximately 0.02% of the administered dose. The ratio of elettriptan mean concentration in breast milk to plasma was 1:4, but there was great variability. The resulting elettriptan concentration-time profile was similar to that seen in the plasma over 24 hours, with very low concentrations of drug (mean 1.7 ng/mL) still present in the milk 18-24 hours post dose. The N-desmethyl active metabolite was not measured in the breast milk. Caution should be exercised when RELAPX is administered to nursing women. **Pediatric Use:** Safety and effectiveness of RELAPX Tablets in pediatric patients have not been established; therefore, RELAPX is not recommended for use in patients under 18 years of age. The efficacy of RELAPX Tablets (40 mg) in patients 11-17 was not established in a randomized, placebo-controlled trial of 274 adolescent migraineurs. Adverse events observed were similar in nature to those reported in clinical trials in adults. Postmarketing experience with other triptans includes a limited number of reports that describe pediatric patients who have experienced clinically serious adverse events that are similar in nature to those reported rarely in adults. Long-term safety of elettriptan was studied in 76 adolescent patients who received treatment for up to one year. A similar profile of adverse events to that of adults was observed. The long-term safety of elettriptan in pediatric patients has not been established. **Geriatric Use:** Elettriptan has been given to only 50 patients over the age of 65. Blood pressure was increased to a greater extent in elderly subjects than in young subjects. The pharmacokinetic disposition of elettriptan in the elderly is similar to that seen in younger adults. In clinical trials, there were no apparent differences in efficacy or the incidence of adverse events between patients under 65 years of age and those 65 and above (n=50). There is a statistically significant increased half-life (from about 4.4 hours to 5.7 hours) between elderly (65 to 93 years of age) and younger adult subjects (18 to 45 years of age).

ADVERSE REACTIONS: Serious cardiac events, including some that have been fatal, have occurred following the use of 5-HT_{1B/1D} agonists. These events are extremely rare and most have been reported in patients with risk factors predictive of CAD. Events reported have included coronary artery vasospasm, transient myocardial ischemia, myocardial infarction, ventricular tachycardia, and ventricular fibrillation (see CONTRAINDICATIONS, WARNINGS and PRECAUTIONS). Incidence of reported adverse cardiac events are presented. Because the reports include events observed in open studies, the role of RELAPX Tablets in their causation cannot be reliably determined. Furthermore, variability associated with adverse event reporting, the terminology used to describe adverse events, etc., limit the value of the quantitative frequency estimates provided. Event frequencies are calculated as the number of patients reporting an event divided by the total number of patients (N=4,719) exposed to RELAPX. All reported events are included except those already listed in Table 1, those too general to be informative, and those not reasonably associated with the use of the drug. Events are further classified within body system categories and enumerated in order of decreasing frequency using the following definitions: frequent adverse events are those occurring in at least 1/100 patients, infrequent adverse events are those occurring in 1/100 to 1/1000 patients and rare adverse events are those occurring in fewer than 1/1000 patients. **General: Frequent were back pain, chills and pain. Infrequent were face edema and malaise. Rare were abdomen enlarged, abscess, accidental injury, allergic reaction, fever, flu syndrome, halitosis, hernia, hypothermia, lab test abnormal, moniliasis, rheumatoid arthritis and shock. **Cardiovascular:** Frequent was palpitation. Infrequent were hypertension, migraine, peripheral vascular disorder and tachycardia. Rare were angina pectoris, arrhythmia, atrial fibrillation, AV block, bradycardia, hypotension, syncope, thrombophlebitis, cerebrovascular disorder, vasospasm and ventricular arrhythmia. **Digestive:** Infrequent were anorexia, constipation, diarrhea, eructation, esophagitis, flatulence, gastritis, gastrointestinal disorder, glossitis, increased salivation and liver function tests abnormal. Rare were gingivitis, hematemesis, increased appetite, rectal disorder, stomatitis, tongue disorder, tongue edema and tooth disorder. **Endocrine:** Rare were goiter, thyroid adenoma and thyroiditis. **Hemic and Lymphatic:** Rare were anemia, cyanosis, leukopenia, lymphadenopathy, myelofibrosis and purpura. **Metabolic:** Infrequent were creatine phosphokinase increased, edema, peripheral edema and thirst. Rare were alkaline phosphatase increased, bilirubinemia, hyperlophemia, weight gain and weight loss. **Musculoskeletal:** Infrequent were arthralgia, arthritis, arthrosis, bone pain, myalgia and myasthenia. Rare were bone neoplasm, joint disorder, myopathy and tenosynovitis. **Neurological:** Frequent were hypertonía, hypesthesia and vertigo. Infrequent were abnormal dreams, agitation, anxiety, apathy, ataxia, confusion, depersonalization, depression, emotional lability, euphoria, hyperesthesia, hyperkinesia, incoordination, insomnia, nervousness, speech disorder, stupor, thinking abnormal and tremor. Rare were abnormal gait, amnesia, aphasia, catatonic reaction, dementia, diplopia, dystonia, hallucinations, hemiplegia, hyperalgesia, hypokinesia, hysteria, manic reaction, neuropathy, neurosis, oculogyric crisis, paralysis, psychotic depression, sleep disorder and twitching. **Respiratory:** Frequent was pharyngitis. Infrequent were asthma, dyspnea, respiratory disorder, respiratory tract infection, rhinitis, voice alteration and yawn. Rare were bronchitis, choking sensation, cough increased, epistaxis, hiccup, hyperventilation, laryngitis, sinusitis and sputum increased. **Skin and Appendages:** Frequent was sweating. Infrequent were pruritus, rash and skin disorder. Rare were alopecia, dry skin, eczema, exfoliative dermatitis, maculopapular rash, psoriasis, skin discoloration, skin hypertrophy and urticaria. **Special Senses:** Infrequent was abnormal vision, conjunctivitis, ear pain, eye pain, lacrimation disorder, photophobia, taste perversion and tinnitus. Rare were abnormality of accommodation, dry eyes, ear disorder, eye hemorrhage, otitis media, parosmia and ptosis. **Urogenital:** Infrequent were impotence, polyuria, urinary frequency and urinary tract disorder. Rare were breast pain, kidney pain, leukorrhea, menorrhagia, menstrual disorder and vaginitis.**

DRUG ABUSE AND DEPENDENCE: Although the abuse potential of RELAPX has not been assessed, no abuse, of tolerance to, withdrawal from, or drug-seeking behavior was observed in patients who received RELAPX in clinical trials or their extensions. The 5-HT_{1B/1D} agonists, as a class, have not been associated with drug abuse.

OVERDOSES: No significant overdoses in premarketing clinical trials have been reported. Volunteers (N=21) have received single doses of 120 mg without significant adverse effects. Daily doses of 160 mg were commonly employed in Phase III trials. Based on the pharmacology of the 5-HT_{1B/1D} agonists, hypertension or other more serious cardiovascular symptoms could occur on overdose. The elimination half-life of elettriptan is about 4 hours and therefore monitoring of patients after overdose with elettriptan should continue for at least 20 hours, or longer should symptoms or signs persist. There is no specific antidote to elettriptan. In cases of severe intoxication, intensive care procedures are recommended, including establishing and maintaining a patent airway, ensuring adequate oxygenation and ventilation, and monitoring and support of the cardiovascular system. It is unknown what effect hemodialysis or peritoneal dialysis has on the serum concentration of elettriptan.

Rev 2, September 2003