

Internal Medicine News

Thanks For Making Us #1

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LEXAPRO® (escitalopram oxalate) TABLETS/ORAL SOLUTION

(3% and <1%); Anorgasmia (2% and <1%). Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo B Lexapro: headache, upper respiratory tract infection, back pain, pharyngitis, inflamed injury, anxiety. *Primarily ejaculatory delay. †Denominator used was for males only (N=225 Lexapro; N=188 placebo). ‡Denominator used was for females only (N=490 Lexapro; N=404 placebo). Generalized Anxiety Disorder Table 3 enumerates the incidence, rounded to the nearest percent of treatment-emergent adverse events that occurred among 429 GAD patients who received Lexapro 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients. The most commonly observed adverse events in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were nausea, ejaculation disorder (primarily ejaculatory delay), insomnia, fatigue, decreased libido, and anorgasmia (see TABLE 3). TABLE 3: Treatment-Emergent Adverse Events: Incidence in Placebo-Controlled Clinical Trials for Generalized Anxiety Disorder* Lexapro (N=429) and Placebo (N=427); Autonomic Nervous System Disorders: Dry Mouth (9% and 5%); Sweating Increased (4% and 1%); Central & Peripheral Nervous System Disorders: Headache (24% and 17%); Paresthesia (2% and 1%); Gastrointestinal Disorders: Nausea (18% and 8%); Diarrhea (8% and 6%); Constipation (5% and 4%); Indigestion (3% and 2%); Vomiting (3% and 1%); Abdominal Pain (2% and 1%); Fatulence (2% and 1%); Toothache (2% and 0%); General: Fatigue (8% and 2%); Influenza-like symptoms (5% and 4%); Musculoskeletal: Neck/Shoulder Pain (3% and 1%); Psychiatric Disorders: Somnolence (13% and 7%); Insomnia (12% and 6%); Libido Decreased (7% and 2%); Dreaming Abnormal (3% and 2%); Appetite Decreased (3% and 1%); Lethargy (3% and 1%); Yawning (2% and 1%); Urge/Urge: Ejaculation Disorder (14% and 2%); Anorgasmia (2% and <1%); Menstrual Disorder (2% and 1%). *Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo B Lexapro: inflamed injury, dizziness, back pain, upper respiratory tract infection, rhinitis, pharyngitis. †Primarily ejaculatory delay. ‡Denominator used was for males only (N=182 Lexapro; N=195 placebo). ††Denominator used was for females only (N=247 Lexapro; N=232 placebo). Dose Dependency of Adverse Events The potential dose dependency of common adverse events (defined as an incidence rate of 15% in either the 10 mg or 20 mg Lexapro groups) was examined on the basis of the combined incidence of adverse events in two fixed-dose trials. The overall incidence rates of adverse events in 10 mg Lexapro-treated patients (66%) was similar to that of the placebo-treated patients (61%), while the incidence rate in 20 mg/day Lexapro-treated patients was greater (86%). Table 4 shows common adverse events that occurred in the 20 mg/day Lexapro group with an incidence that was approximately twice that of the 10 mg/day Lexapro group and approximately twice that of the placebo group. TABLE 4: Incidence of Common Adverse Events* in Patients with Major Depressive Disorder Receiving Placebo (N=311), 10 mg/day Lexapro (N=310), 20 mg/day Lexapro (N=125); Insomnia (4%, 7%, 14%); Diarrhea (5%, 6%, 14%); Dry Mouth (3%, 4%, 9%); Somnolence (1%, 4%, 9%); Dizziness (2%, 4%, 7%); Sweating Increased (<1%, 3%, 8%); Constipation (1%, 3%, 6%); Fatigue (2%, 2%, 6%); Indigestion (1%, 2%, 6%). *Adverse events with an incidence rate of at least 5% in either of the Lexapro groups and with an incidence rate in the 20 mg/day Lexapro group that was approximately twice that of the 10 mg/day Lexapro group and the placebo group. Male and Female Sexual Dysfunction with SSRIs Although changes in sexual desire, sexual performance, and sexual satisfaction often occur as manifestations of a psychiatric disorder, they may also be a consequence of pharmacologic treatment. In particular, some evidence suggests that SSRIs can cause such untoward sexual experiences. Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance, and satisfaction are difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experience and performance cited in product labeling are likely to underestimate their actual incidence. Table 5 shows the incidence rates of sexual side effects in patients with major depressive disorder and GAD in placebo-controlled trials. TABLE 5: Incidence of Sexual Side Effects in Placebo-Controlled Clinical Trials (In Males Only; Lexapro (N=407) and Placebo (N=393)); Ejaculation Disorder (primarily ejaculatory delay) (12% and 1%); Libido Decreased (5% and 2%); Impotence (2% and <1%). (In Females Only; Lexapro (N=737) and Placebo (N=639)); Libido Decreased (2% and 1%); Anorgasmia (3% and <1%). There are no adequately designed studies examining sexual dysfunction with escitalopram treatment. Priligam has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects. Vital Sign Changes Lexapro and placebo groups were compared with respect to (1) mean change from baseline in vital signs (pulse, systolic blood pressure, and diastolic blood pressure) and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses did not reveal any clinically important changes in vital signs associated with Lexapro treatment. In addition, a comparison of supine and standing vital sign measures in subjects receiving Lexapro indicated that Lexapro treatment is not associated with orthostatic changes. Weight Changes Patients treated with Lexapro in controlled trials did not differ from placebo-treated patients with regard to clinically important change in body weight. Laboratory Changes Lexapro and placebo groups were compared with respect to (1) mean change from baseline in various serum chemistry, hematology, and urinalysis variables, and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in laboratory test parameters associated with Lexapro treatment. ECG Changes Electrocardiograms from Lexapro (N=625), racemic citalopram (N=351), and placebo (N=527) groups were compared with respect to (1) mean change from baseline in various ECG parameters and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed (1) a decrease in heart rate of 2.2 bpm for Lexapro and 2.7 bpm for racemic citalopram, compared to an increase of 0.3 bpm for placebo and (2) an increase in QTc interval of 3.9 msec for Lexapro and 3.7 msec for racemic citalopram, compared to 0.5 msec for placebo. Neither Lexapro nor racemic citalopram were associated with the development of clinically significant ECG abnormalities. Other Events Observed during the Premarketing Evaluation of Lexapro Following is a list of WHO terms that reflect treatment-emergent adverse events, as defined in the introduction to the ADVERSE REACTIONS section, reported by the 1428 patients treated with Lexapro for periods of up to one year in double-blind or open-label clinical trials during its premarketing evaluation. All reported events are included except those already listed in Tables 2 & 3, those occurring in only one patient, event terms that are so general as to be uninformative, and those that are unlikely to be drug related. It is important to emphasize that, although the events reported occurred during treatment with Lexapro, they were not necessarily caused by it. Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: Frequent adverse events are those occurring on one or more occasions in at least 1/100 patients; infrequent adverse events are those occurring in less than 1/100 patients but at least 1/1,000 patients; Cardiovascular - Frequent: palpitation, hypertension; Infrequent: bradycardia, tachycardia, ECG abnormal, flushing, varicose vein. Central and Peripheral Nervous System Disorders - Frequent: light-headed feeling, migraine; Infrequent: vertigo, tremor, restless legs, shaking, twitching, disequilibrium, tics, carpal tunnel syndrome, muscle contractions involuntary, sluggishness, coordination abnormal, faintness, hyperreflexia, muscular tone increased. Gastrointestinal Disorders - Frequent: heartburn, abdominal cramp, gastroenteritis; Infrequent: gastroesophageal reflux, bloating, abdominal discomfort, dyspepsia, increased stool frequency, belching, gastritis, hemorrhoids, gagging, polyposis gastric, swallowing difficult. General - Frequent: allergy, pain in limb, fever, hot flushes, chest pain; Infrequent: edema of extremities, chills, tightness of chest, leg pain, asthenia, syncope, malaise, anaphylaxis, fall. Hemic and Lymphatic Disorders - Infrequent: bruise, anemia, nosebleed, hematoma, lymphadenopathy cervical. Metabolic and Nutritional Disorders - Frequent: increased weight, hyperglycemia, thirst, bilirubin increased, hepatic enzymes increased, gout, hypercholesterolemia. Musculoskeletal System Disorders - Frequent: arthralgia, myalgia; Infrequent: jaw stiffness, muscle cramp, muscle stiffness, arthritis, muscle weakness, back discomfort, arthropathy, jaw pain, joint stiffness. Psychiatric Disorders - Frequent: appetite increased, lethargy, irritability, concentration impaired; Infrequent: jitteriness, panic reaction, agitation, apathy, forgetfulness, depression aggravated, nervousness, restlessness aggravated, suicide attempt, amnesia, anxiety attack, bruxism, carbohydrate craving, confusion, depersonalization, disorientation, emotional lability, feeling unreal, tremulousness nervous, crying abnormal, depression, excitability, auditory hallucination, suicidal tendency. Reproductive Disorders/Female - Frequent: menstrual cramps, menstrual disorder; Infrequent: menorrhagia, breast neoplasm, pelvic inflammation, premenstrual syndrome, spotting between menses. *% based on female subjects only; N=905 Respiratory System Disorders - Frequent: bronchitis, sinus congestion, coughing, nasal congestion, sinus headache; Infrequent: asthma, breath shortness, laryngitis, pneumonia, tracheitis. Skin and Appendages Disorders - Frequent: rash; Infrequent: pruritus, acne, alopecia, eczema, dermatitis, dry skin, folliculitis, lipoma, furunculosis, dry lips, skin nodule. Special Senses - Frequent: vision blurred, tinnitus; Infrequent: taste alteration, earache, conjunctivitis, vision abnormal, dry eyes, eye irritation, visual disturbance, eye infection, pupils dilated, metallic taste. Urinary System Disorders - Frequent: urinary frequency, urinary tract infection; Infrequent: urinary urgency, kidney stone, dysuria, blood in urine. Events Reported Subsequent to the Marketing of Escitalopram - Although no causal relationship to escitalopram treatment has been found, the following adverse events have been reported to have occurred in patients and to be temporally associated with escitalopram treatment during post marketing experience and were not observed during the premarketing evaluation of escitalopram: abnormal gait, acute renal failure, aggression, akathisia, allergic reaction, anger, angioedema, atrial fibrillation, choreoathetosis, delirium, delusion, diplopia, dysarthria, dyskinesia, dystonia, ecchymosis, erythema multiforme, extrapyramidal disorders, fulminant hepatitis, hepatic failure, hypoaesthesia, hypoglycemia, hypokalemia, INR increased, gastrointestinal hemorrhage, glaucoma, grand mal seizures (or convulsions), hemolytic anemia, hepatic necrosis, hepatitis, hypertension, leucopenia, myocardial infarction, myoclonus, neuroleptic malignant syndrome, nightmare, nystagmus, orthostatic hypotension, pancreatitis, parosmia, photosensitivity reaction, priapism, prolactinemia, prothrombin decreased, pulmonary embolism, QT prolongation, rhabdomyolysis, seizures, serotonin syndrome, SIADH, spontaneous abortion, Stevens Johnson Syndrome, tardive dyskinesia, thrombocytopenia, thrombosis, torsade de pointes, toxic epidermal necrolysis, ventricular arrhythmia, ventricular tachycardia and visual hallucinations.

Elderly Colorectal Cancer Survivors Return to Their Primary Care Physicians

The proportion seeing only a primary care physician increased from 44% to 62% over the 5-year period.

BY JANE SALODOF MACNEIL
Senior Editor

CHICAGO — Six years after being diagnosed with colorectal cancer, nearly two-thirds of people tracked in a retrospective longitudinal study of 1,541 elderly survivors relied entirely on their primary care physicians for follow-up care.

Over the same time period, the role of oncology specialists was much smaller and declined significantly, as did the amount of cancer screening that they performed.

With the exception of mammography, primary care physicians provided more preventive services than did oncologists. They ordered more flu shots, Pap smears, cholesterol screening, and bone densitometry tests.

Visits to both types of physician resulted in more of all these measures than did visits to either type alone. "Survivors who see both an oncology specialist and a primary care provider are most likely to receive preventive care," lead investigator Claire Snyder, Ph.D., reported at the annual meeting of the American Society of Clinical Oncology.

The study, supported in part by an unrestricted grant from Pfizer Inc., explored the growing issue of who takes responsibility for long-term care of cancer survivors in the United States. "The role of oncology specialists and primary care providers during the posttreatment phase is unclear," said Dr. Snyder, of the division of general internal medicine at Johns Hopkins University, Baltimore.

She and her coauthors linked data from the Surveillance, Epidemiology, and End Results (SEER) registry with Medicare fee-for-services claims to follow patients from 1 year after diagnosis to the end of the sixth year. The study population had an average age of 76 years, included fewer men (42.7%) than women, comprised mostly whites (85.3%), survived stage I or II disease predominantly (82.8%), and had a mean comorbidity index of 1.76.

Initially, 37% of survivors went to both a primary care physician and an oncology specialist, but this fell to 21% by the end

of the study. Meanwhile, the proportion seeing only a primary care physician increased from 44% to 62% over the 5-year period, while those seeing only an oncology specialist fell from 8% to 4%.

In any given year, slightly more than 10% of survivors saw neither type of physician, but some visited other specialists, often cardiologists, according to Dr. Snyder.

Additionally, the average number of visits to a primary care physician increased from 4.2 in the first year to 4.7 during the fifth year. Visits to an oncology specialist fell from 1.3 in the first year to 0.5 in the fifth year. Both changes were statistically significant ($P = .0001$).

"Most primary care provider visits were to internal medicine or family physicians, and most of the oncology specialist visits were to medical oncologists, hematologist/oncologists, or general surgeons," Dr. Snyder said.

The primary care physician category also included general, ob.gyn., geriatric, and multispecialty practices. The oncology specialist category included colorectal surgery, surgical oncology, and radiation oncology practices.

Who provides care is important, Dr. Snyder said, because survivors have special medical needs. She cited surveillance for recurrence; monitoring for long-term and late treatment effects; general primary and preventive care; and care for comorbid conditions, which can be chronic in these patients.

To assess how the physician mix affected preventive services, her group looked at influenza vaccination and cholesterol screening for the entire population, along with mammography, cervical cancer screening, and bone densitometry in women, with the mammography standard being applied only to women younger than 76 years of age.

The investigators found that the mammography rate fell from 54% in the first

year to 43% in the fifth year, and cervical cancer screening from 19% to 11%. "There were no clear trends in flu shots, cholesterol screening, or bone densitometry," she said.

Cumulative 5-year data on these measures showed statistically significant differences (P less than or equal to .0001) for all based on the medical provider. For example, flu shots were documented for 61.7% of people seen by a primary care physician and an oncologist, for 52.4% of those who visited only a primary care physician, and for 49.2% of those who visited only an oncologist. The rate dropped to 31.4% when survivors saw neither.

Dr. Snyder cautioned that the investigators had no way to ask why some services were not provided. "Did the physician not offer the service? Did the patient refuse it?" she asked, noting that "some question the usefulness of certain screening procedures in the very old."

The study's main implication, she concluded, is that there is a need for survivorship care plans that clearly delineate the roles and responsibilities of oncologists and primary care physicians in providing future care to cancer survivors.

Discussant Julia H. Rowland, Ph.D., director of the National Cancer Institute's office of cancer survivorship, seconded the call for such plans along with treatment summaries.

Today, the U.S. population includes more than 10.8 million cancer survivors, according to Dr. Rowland. Not only are more people surviving cancer, but survivors are living longer. Some 72% are aged 60 years and older, and 14% were diagnosed 20 or more years ago.

Dr. Patricia A. Ganz of the University of California, Los Angeles, also addressed the need for better communication between oncologists and primary care physicians in a press briefing at the meeting. The average cancer patient sees three specialists, according to Dr. Ganz, director of cancer prevention and control research at the university's Jonsson Comprehensive Cancer Center.

Because most referrals to medical oncologists come from surgeons, Dr. Ganz pointed out that the medical oncologist might not even know who the patient's primary care physician is. Oncologists need to provide a survivorship care plan directly to the patient, she said, so that survivors and their physicians can keep track of "what has been done and what needs to be done in the future." ■



Oncologists need to provide a survivorship care plan directly to the patient.

DR. GANZ

Higher Rate of Preventive Care in Patients Who Visit Both a Primary Care Physician and an Oncologist

	Both PCP* and Oncologist	PCP Only	Oncologist Only	Neither PCP nor Oncologist
Influenza vaccination	61.7%	52.4%	49.2%	31.4%
Mammography**	54.3%	32.1%	42.3%	19.9%
Cholesterol screening	35.7%	33.5%	24.3%	15.4%
Cervical cancer screening**	20.6%	14.3%	11.9%	5.1%
Bone densitometry**	12.0%	10.7%	5.5%	5.4%

*Primary care physician. **Percentages are for women only.

Note: Based on a 5-year longitudinal study of 1,541 elderly colorectal cancer survivors.

Source: Dr. Snyder