EFFEXOR XR® EXTEND RELEASE REL

Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of EFFEXOR XR or any other antidepressant in a child or adolescent must balance this risk with the clinical need. Patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. EFFEXOR XR is not approved for use in pediatric patients. (See Warnings and Precautions: Pediatric Use.)

Pooled analyses of short-term (4 to 16 weeks) placebo-controlled trials of 9 antidepressant drugs (SSRIs and others) in children and adolescents with Major Depressive Disorder (MDD), obsessive-compulsive disorder (OCD), or other psychiatric disorders (a total of 24 trials involving over 4,400 patients) have revealed a greater risk of adverse events representing suicidal thinking or behavior (suicidality) during the first few months of treatment in those receiving antidepressants. The average risk of such events in patients receiving antidepressants was 4%, twice the placebo risk of 2%. No suicides occurred in these trials.

revealed a greater risk of adverse events representing suicidal thinking or behavior (suicidality) during the first few months of treatment in those receiving antidepressants. The average risk of such events in patients receiving antidepressants was 4%, twice the placebo risk of 2%. No suicides occurred in these trials.

CONTRAINDICATIONS: Hypersensitivity to venlarkaine hydrochloride or to any excipients in the formulation. Concomitant use in patients taking monoamine oxidase inhibitors (MAIOS). WARNINGS: Clinical Worsening and Suicide Risk—Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal tibidation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. There has been a long-standing concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in sort-term studies in children and adolescents with MDD and other psychiatric disorders. It is unknown whether the suicidality risk in pediatric patients extends to longer-term use i. e., beyond several months. It is also unknown whether the suicidality risk extends to adults. All pediatric patients being treated with antidepressants for any indication should be observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. Anxiety, aglitation, panic attacks, insommia, irritability, hostility, aggressiveness impulsivity, adthissia (osychomofor restlessness), hypomania, and mania have been reported in adult and pediatric patients being treated with antidepressants for MDD and other indications, both psychiatric and onpsychiatric. Although a causal link between the emergence of suicidality, on symptoms and either the worsening of depression and/ at least 1 days from the schrönium greatment with an inAUL, at least 1 days should be allowed attention and the substantial increases in bod pressure BP in some patients. Papielar monitoring of BP is recommended. For patients experiencing sustained increase in BP, consider either dose reduction or discontinuation. PRECAUTIONS: General—Discontinuation of Treatment with Effexor XR. Anytot discontinuation or dose reduction of venisfaxine at various doses is associated with new symptoms, the frequency of which increased with increased dose level and longer duration of treatment symptoms include agitation, anorexia, anxiety confusion, coordination impaired, diarrhea, dizziness, dry mouth, dysphoric mood, emotional jability sescication, fability, and the substantial production of the substantial production of the dose rather than abrupt cessation is recommended. If intolerable symptoms cour following a decrease in the dose or upon discontinuation of treatment, consider resuming the previously prescribed dose. Subsequently, conflue decreasing the dose at an armor gradual rate. Insommia and Nervousness Treatmentemengent insommia and nervousness have been reported. In Phase 3 trials, insommia led to drug Andreiby Insorter (XAD) patients. Nervoisness led in drug discontinuation in 0.9% of GAD patients, and in 0% of SAD patients. Changes in Weight: Adult Patients. In short-term MDD trials, 7% of GAD patients, and in 0% of SAD patients. Changes in Weight and 0.3% discontinued for weight loss in 6 effects of XR patients had 5% loss of body weight and 0.3% discontinued for weight loss. In 6 effects of XR patients had 5% loss of body weight and 0.3% discontinued for weight loss in 8 event substances and several patients. Pediatric Patients. Weight loss was seen in patients aque de 1.17 receiving Effexor XR. More Effexor XR patients for weight loss was seen in patients aque de 1.17 receiving Effexor XR. More Effexor XR patients for weight loss was seen in patients with creases in weight less than expected based on data from ag such symptoms on a day-to-day basis, since changes may be abrupt. Such symptoms should be reported to the patient's prescriber or health professional, especially if they are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Symptoms such as these may be associated with an increased risk for suicidal thinking and behavior and indicate a need for very close monitoring and possibly changes in the medication. Caution patients about operating hazardous machinery, including automobiles, until they are reasonably sure that venlafaxine does not adversely affect their abilities. Tell patients to avoid alcohol while taking Effexor XR and to notify their physician 1) if they become pregnant or intend to become prognat during therapy, or if they are nursing; 2) about other prescription or over-the-counter drugs, including herbal preparations, they are taking or plan to take; 3) if they develop a rash, hives, or related allergic phenomena. Laboratory Tests—No specific laboratory tests are recommended. Drug Interactions— Alcohof. A single dose of ethanol had no effect on the pharmacokinetics (PK) of venlafaxine or 0-desmethylvenlafaxine (DV), and venlafaxine did not exaggerate the psychomotor and psychometric effects induced by ethanol. Climetidine: Use caution when administering venlafaxine with cimetidine to patients with pre-existing hypertension or hepatic dysfunction, and the elderly. Diazepam. 4 single dose of diazepam did not appear to affect the PK of either venlafaxine or ODV. Venlafaxine did not have any effect on the PK of diazepam or its active metabolite, desmethyldiazepam, or affect the psychomotric effects induced by diazepam. Lithium: A single dose of lithium did not appear to affect the PK of either venlafaxine does of lithium did not appear to affect the PK of either venlafaxine induced by diazepam. Lithium: A single dose of lithium did not appear to affect the PK of either venlafaxine is not highly bound to plasma proteins; coadministration of Effexor XR with a highly protein-

of ORV Bet Granger aughernamen in regularization concentrations of visualization and decrease concentrations of ORV Bet Granger aughernamen in regularization and engineering confidence of the Visualization of Confidence of CVPCOS and CVPCOS a interval, bundle branch block, QRS prolongation), sinus and ventricular tackycardia, bradycardia, frypotension, altered level of consciousness (ranging from somnolence to coma), seizures, vertigo, and death have been reported. Treatment should consist of those general measures employed in the management of overdosage with any antidepressant. Ensure an adequate airway, oxygenation and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Induction of emesis is not recommended. Gastric lavage with a large bore orogastric tube with appropriate airway protection, if needing hay be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal should be administered. Due to the large volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific artidotes for venlataxine are known. In managing overdosage, consider the possibility of multiple drug involvement. Consider contacting a poison control center for additional information on the treatment of overdose. Telephone numbers for certified poison control centers are listed in the Physicians' Desk Reference" (PDR). DOSAGE AND ADMINISTRATION: Consult full prescribing information for dosing instructions. Switching Patients to or From an MAOI—At least 14 days should elapse between discontinuation of an MAOI and initiation of therapy with Effexor XR At least 7 days should be allowed after stopping Effexor XR Prescribing Information W10404C013, revised January 2005.

Wyeth®

© 2005, Wyeth Pharmaceuticals Inc., Philadelphia, PA 19101

Psychological Distress Lifts Atrial Fib Risk

BY BRUCE JANCIN

Denver Bureau

NEW ORLEANS — Anxiety and other forms of psychological distress constitute a potent independent risk factor for development of new-onset atrial fibrillation in patients with chronic stable coronary artery disease, Charles M. Blatt, M.D., reported at the annual scientific sessions of the American Heart Association.

The relationship is dose dependent. The higher a CAD patient's level of anxiety, depression, somatization, or hostility, the greater the long-term risk of developing atrial fibrillation, explained Dr. Blatt of Harvard Medical School, Boston, and director of research at the Lown Cardiovascular Research Foundation, Brookline,

He reported on 354 men and 95 women with chronic stable CAD who were

The higher a CAD patient's level of anxiety, depression, somatization, or hostility, the greater the longterm risk of developing atrial fibrillation.

prospectively followed for an average of 5 years. Participants in the ongoing observational study are being assessed annually various forms of psychological distress using the 92-item Kellner's Symptom Questionnaire.

The incidence of atrial fibrillation in patients in the lowest Kellner quartile for total psychological distress was 2 cases per 1,000 person-years, compared with 16 cases per 1,000 person-years in those in the fourth quartile. Similarly, the incidence of atrial fibrillation among patients in the lowest quartile for anxiety was 3 cases per 1,000 person-years, versus 16 in those in the highest quartile.

After adjustment for the standard risk factors for atrial fibrillation, including gender and age, patients in the second through fourth quartiles in terms of anxiety level had a 2.1-fold greater risk of developing atrial fibrillation for each quartile

Each quartile of depression level was associated with a 1.7-fold greater risk of developing atrial fibrillation compared with that of patients in the bottom quartile in terms of depression. The risk of atrial fibrillation increased by an additional 50% with each of the second through fourth quartiles of somatization, and by 60% with each quartile of scoring on hostility.

Patients in the second quartile for total psychological distress had an adjusted 2.3fold increased risk of developing atrial fibrillation compared with those in the lowest quartile. Those in the third quartile had an adjusted 4.6-fold increased risk, while patients in the fourth quartile had a 6.9fold greater risk than those in the first quartile, according to Dr. Blatt.

112718-03