Sildenafil Eases Diabetic Neuropathy in Small Study

BY MICHELE G. SULLIVAN Mid-Atlantic Bureau

WASHINGTON — Sildenafil may be useful in treating the pain of diabetic neuropathy, Dr. Thomas Brannagan reported in a poster presented at the annual meeting of the American Association of Neuromuscular and Electrodiagnostic Medicine.

Dr. Brannagan, a neurologist at Cornell University, New York, was inspired to conduct the study after diabetic patients taking sildenafil for erectile dysfunction experienced some relief from their neuropathic pain. The trial included eight patients: six men and two women. All reported pain of above 40 on a 0-100 visual analog pain scale, despite receiving one to seven medications each for neuropathic pain.

The patients received an upwardly titrated dose of sildenafil from 25 mg/day the first week to 50 mg/day after week 1 and up to 100 mg/day thereafter, if necessary and tolerated. They also maintained their existing pain medications. Every week they recorded pain on the following scales: 11-point Likert; a 10-point sleep interference; Rand-36 quality of life; and Toronto Clinical Neuropathy.

Two patients discontinued the drug because of rash, while four patients completed the 8-week trial. The four patients experienced a significant reduction in pain, with the average weekly Likert score decreasing from 5.6 at baseline to 1.5, Dr. Brannagan reported.

When all patients were considered, with the last observation carried forward, the average weekly Likert pain score decreased from 6.3 to 3.7. Four patients had a score reduction of more than two points, and three had at least a 50% reduction in pain. Scores in all other areas improved as well: visual analog pain score, 49 to 31; Rand score, 46 to 65; sleep score, 8 to 4; and Toronto score, 12/19 to 10/19, said Dr. Brannagan, who is a consultant for Eli Lilly & Co.



BRIEF SUMMARY. See package insert for full prescribing information icidality in Children and Adolescents

Suicidaity in Children and Adolescents 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 dinical 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.)

patients. (See Warnings and Precautions: Pediatric Use.) Pooled analyses of short-term (4 to 16 weeks) placebo-controlled trials of 9 anticiperssant drugs (SSRIs and others) in children and adolescents with Major Depressive Disorder (MDD), obsessive-compulsive disorder (0CD), 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%, Write the placebo risk of 2%. No suicides occurred in these trials. Iters, wive use paceed risk of 2%. No suicides occurred in these traits. J ContraIANDCATONS: hypersensitivity to ventications hydrocholinde or to any excipate in the formulation. Concomitant use in patients taking monoamine oxidase inhibitors (MAO). WANNNOS: Clinical Worsening and Suicide Risk—Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and hor the emergence of suicidal indications may have are in inducing worsening of depression and the emergence of suicidally in certain patients. Antidepressants increased the risk of suicidal thinking and betavior (suicidality) in stort-term studies in children and adolescents with MDD and other psychiatric disorders. It is unknown whether the suicidality risk in patients being treated with antidepressants increased the risk of a course of drug therapy, or at times of dose changes, either increases or decreases. Adults with MDD or comorbid depression in the setting of other specifical line patients being treated with antidepressants should be observed similarly for clinical worsening and suicidality, especially during the initial term months of a course of drug therapy, or at times of dose changes, either increases or decreases. Anxiety, aplation, panic attacks, insomina, infraidersmants and maina have been reported in adult and pediatric patients being treated with antidepressants for MDD and other indications, both syschiatic and nonspychiatic. Although a causal link between the emergence of such symptoms and eliter the worsening of depression and/or the emergence of suicidal musikes has not been established, there is concern that such symptoms and eliters worse of regulation of syschiatic, although a causal link between the emergence of such symptoms and eliters worsen on genession is persistently worse, or who are experiencing as is feasible, buenession site metations provide to experience as suicidal to estimation of syschiatic presention of such symptom secences on the estimation of the patient

discontinuation in 1% of both depressed patients and Panic Disorder (PD) patients and in 3% of both Generalized Anxiety Disorder (GAD) and Social Anxiety Disorder (SAD) patients. Nervousness led to drug discontinuation in 0.9% of depressed patients, in 2% of GAD patients, and in 0% of SAD and PD patients. *Changes in Weight: Adult Patients*. In short-term MDD trials, 7% of Effexor XR patients had 2=5% loss of body weight and 0.1% discontinued for weight loss. In discontinuation in 1% of both depressed patients and Panic Disorder (PD) patients and in 3% of both Generalized Anviety Disorder (GAD) and Social Anviety Disorder (GAD) and Social Anviety Disorder (GAD) and PD patients. Part of Hard Social Anviety Disorder (GAD) and PD patients. Part of Hard Social Construction of a present and DS wiles. The state of the second patients is and the mMD this, 7% of Effector XR patients in and TS. Note: The state of the second patients of the second patients of the second patients in a patients disordiment for weight loss in the verse studies. In 12-week PD traits, 3% of Effector XR patients had 27% loss of body weight and no patients discontinued for weight loss. The state state is the second patients in a patients discontinued for weight loss. The state state is the second patients and 0.1% for the second patients and the second patients and the second patients and the state state state is the second patients and the there are constructed for weight loss alone or in combination with other products. *Pediatric Patients* PADD and GAD studies (1% of Effector XR patients vs. 3.3% of Effector XR patients than placebo patients and effector patients vs. 3.3% of Effector XR patients than placebo patients and the second patients vs. 3.3% of placebo patients PADD and GAD increases in weight loss was not limited to patients vs. 1.2% of placebo patients and 1.2% placebo patients and 1.2% placebo patients are second the second patients and 1.2% placebo patients are second the second patient second patients and 1.2% placebo patients are second patients and 1.2% placebo patients are an average of 1.0 cm. In 1.4%, while placebo patients green anverage of 1.0 cm. In 1.4%, while placebo patients green anverage of 1.0 cm. In 1.4% while placebo patients green anverage of 1.0 cm. In 1.4% while placebo patients green anverage of 1.0 cm. In 1.4% placebo patients green anverage of 1.0 cm. In 1.4% while placebo patients green anverage of 1.0 cm. In 1.4% while placebo patients green anverage of 1.0 cm. I Effexor XR. Clinical Worsening and Suicide Risk: Patients, their families, and their caregivers should be encouraged to be alert to the emergence of symptoms listed in WARNINGS: Clinical Worsening and Suicide Risk, especially those seen early during antidepressant treatment and when the dose is adjusted up or down. Families and caregivers of patients should be advised to observe for the emergence of 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. Surpmotors should be reported to the patient's presenting symptoms, Surpmotors, 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 1) about operating hazardous machinery, including automobiles, until they are to avoid atchol while taking effector XR, and 3) about the risk of serotionin syndrome with the concomitant use of Effexor XR and triptans, tramadol, tryptophan supplements, or other serotonerig cagents. Patients should be advised to notify their physician 1) if they become pregnant or intend to become pregnant or intend to become pregnant or intend to become pregnant prescription or over-the-counter drugs, including hertal preparations and nutritional supplements, they have a history of glaucoma or increased intraocular pressure. Laboratory Tests—No specific laboratory tests are recommended. Drug Interactions— Alconot A single dose of dinano had no effect on the pharmacokinetics (PK) of venifativine or Queschortory tests are recommended. They for the server in the prescription or over-the-counter drugs, including herela prescript on conscriptions on hepatic dystucction, and the elderly. *Diazepam*: A single dose of dinano had no effect on the pharmacokinetics (PK) of venifativine or Quescription on hepatic dystucction, and the elderly. *Diazepam*: A single dose of dinapperiod, increase in ha

Brannagan reported.

pressure and cholesterol increases considered to be clinically relevant were similar to that observed in adult patients. The precatitons for adults apply to pediatric patients. **Geriatric Use**—No overall differences in effectiveness or safety were observed between geriatric and younger patients. Greater sensitivity of some older individuals cannot be ruled out. Hyponatternia and SIADH have been reported, usually in the elioty. **ADVERSE REACTIONS:** Associated with Discontinuation of Treatment—The most commone events leading to discontinuation in MDD, GAD, SAD, and PD trials included nausea, anorexia, aniety, impotence, dry mouth, dizziness, insomnia, somolence, hypertension, diarrhea, paresthesia, tremor, abnormal (mostly blurred) vision, abnormal (mostly delayed) ejacutation, asthema, womiting, nervousness, headcache, vasodilatation, thinking abnormal, decreased libido, and sweating. *Commonly Observed Adverse Events in Controlled Clinical Trials for MDD, GAD, SAD, and PD*— Body as a Whole: asthenia, headache, flu syndrome, accidental injury, abdominal pain. <u>Cardiovascular</u>: vasodilatation, hyperfension, palpitation. <u>Digestive</u>: nausea, constipation, anorexia, vomiting, flatilence, diarrhea, erucitation. <u>Metabolic</u> <u>Nutritional</u>: weight loss. <u>Mervous System</u>: dizziness, somolence, insomnia, dry mouth, nervousness, abnormal dreams, tremor, depression, hyperfonia, paresthesia, libido decreased, agitation, anxiety, twitching. <u>Respiratory System</u>: of colum goragamia) in females. <u>Wita Sign Changes</u>: Effoory RA was associated with a mean increase in pulse rate of about 2 beats/min in depression und GAD trials and a mean increase in pulse rate of about 2 beats/min in doression and GAD trials and a mean increase in pulse rate of about 2 beats/min in doression and GAD trials and a mean increase in pulse rate of about 2 beats/min in doression and GAD trials and a mean increase in pulse rate of about 2 beats/min in doression including anorgasmia) in themates. *With Sign Changes*: Clinically relevant increases in s

edema, esophapitis, gastnis, gastnoenterlis, gastnointestinal ubce; gingvitis, glossits, rectai hermorringe, hermorrhouis, melena, oral monitasis, schnratsky, storattis, predictiones, gastno-respontageal aparam. Cubdretis hermodensis, gastnoscophageal param, cubdretis locatication, here trademess, gastnoscophageal param, cubdretis locatication, bere trademess, gastnoscophageal param, cubdretis locatication, bere trademess, gastnoscophia, bendoritis, produtis, producis, pr

Wyeth[®]

© 2006, Wyeth Pharmaceuticals Inc., Philadelphia, PA 19101 122110-01