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Study Finds Cymbalta(R) Was As Safe And Well-Tolerated As Routine Drug Treatments For Diabetic Nerve Pain

Cymbalta Patients Functioned As Well As Those Switching Or Adding Therapies

Feb 14, 2006 /PRNewswire-FirstCall via COMTEX News Network/ -- A long-term study of more than 200 patients found that Cymbalta (duloxetine HCl) is as safe and well-tolerated as current routine care that uses one or more medications for the management of pain caused by diabetic nerve damage. Study findings also show that Cymbalta did not adversely affect the progression of diabetes or many of the complications associated with the illness, such as damage to the nerves, kidneys and eyes.

The findings, published in the current issue of the Journal of Palliative Medicine, "suggest that with Cymbalta, clinicians can expect a similar level of quality of life without compromising safety or tolerability," explained Dr. Tim Smith, a study author and clinical instructor of medicine at Washington University School of Medicine.

The 52-week study compared Cymbalta, a non-narcotic prescription medication for the management of diabetic nerve pain, to routine care, defined as therapies that the investigator and the patient believed permitted the optimal benefit to the patient, such as anticonvulsants and antidepressants. The most commonly used prescription pain medications for routine care included Neurontin(R) (gabapentin), Elavil(R) (amitriptyline) and Effexor-XR(R) (venlafaxine extended release). Diabetic management in both the routine care-treated and Cymbalta-treated groups was adjusted at the discretion of the investigator. The data found no significant differences in the overall incidence of either adverse events resulting from treatment or quality of life measures in patients taking Cymbalta compared to those receiving routine care.

While the majority of people with diabetes experience symptoms associated with diabetic neuropathy, such as peripheral neuropathic pain in the toes, feet, legs, hands, arms and fingers, only three million Americans have been diagnosed.(1) Diabetic nerve pain can make simple acts like putting on a shoe or walking nearly impossible. The pain typically worsens at night, also making it difficult to sleep.(2,3) All of these symptoms can leave many patients debilitated, unable to participate in normal daily activities, socialize, or keep a job.

While the study design allowed the routine care group to switch and add therapies to find a more effective or better-tolerated treatment, the Cymbalta group was much less flexible. Despite this disadvantage, 72 percent of patients treated with Cymbalta remained on treatment, compared with 82 percent of the routine care group -- a difference that was not statistically significant.

"Patients with diabetic nerve pain often switch or increase current or add additional medications if their treatments are not offering relief, are causing intolerable side effects, or are worsening their diabetic complications," said Dr. Joel Raskin, the study's lead author and medical fellow at Eli Lilly and Company. "In this study, Cymbalta was shown to be a good treatment option that does not appear to significantly affect management of their disease and may help them resume their normal day-to-day activities."

Additional Study Highlights

* In comparison to the Cymbalta-treated patients:

-- Significantly more routine care-treated patients experienced these treatment emergent adverse events (TEAEs): pain in extremity (15.8 percent vs. 6.2 percent), peripheral edema (15.8 percent vs. 5.0 percent), balance disorder (5.3 percent vs. 0.6 percent), erythema, feeling abnormal and localized infections (3.9 percent vs. 0 percent).

-- A significantly greater percentage of routine care-treated patients experienced one or more serious adverse events (SAE) (28.9 percent vs. 16.8 percent).

-- Significantly less routine care patients discontinued due to adverse events (5.3 percent vs. 10.6 percent).

* In routine care-treated patients, the TEAEs reported by 10 percent or more of patients were peripheral edema and pain in extremity (15.8 percent), somnolence (14.5 percent), and dizziness (13.2 percent).

* In Cymbalta-treated patients, the TEAE reported by 10 percent or more of patients was nausea (10.6 percent).

* No clinically significant therapy-group differences were observed between the Cymbalta- and routine care-treated groups in hemoglobin A1c (0.00 mg/dL plus or minus 0.01 vs. 0.00 mg/dL plus or minus 0.01) and diabetic complications, including progression of retinopathy, neuropathy (0.43 vs. 0.60 points on the Michigan Neuropathy Screening Instrument (MNSI) scale) or nephropathy (microalbumin/creatinine ratio, mean change of 0.05 vs. 0.01).

-- There was also a statistically, but not clinically, significant increase in fasting glucose in the Cymbalta-treated group, compared to the routine care-treated group (0.30 plus or minus 4.34 vs. -0.82 plus or minus 4.45, $p=0.016$).

* Cymbalta-treated patients experienced a slight but statistically significant increase in sitting diastolic blood pressure and pulse (mean changes [SD]: 1.39 [10.71]) and 1.70 [11.82]) compared with routine care- treated patients, who experienced a slight mean decrease in pulse (mean change [SD]: -2.30 [11.29]).

Methods

This study met its primary endpoints, which were to evaluate the safety of Cymbalta over a 52-week open-label extension period, to evaluate the safety of Cymbalta for up to 65 weeks with regard to the progression of diabetic complications, and to assess the impact of Cymbalta treatment and routine care on patient-reported health outcomes.

In this trial, 237 patients 18 years and older, with an average age of 60 years, diagnosed with diabetic nerve pain completed a 13-week acute therapy stage. They were randomly assigned in a 2:1 ratio to therapy with 161 patients receiving Cymbalta 60 mg twice daily and 76 patients receiving routine care. Routine care consisted primarily of gabapentin, amitriptyline and venlafaxine. Comparisons with individual therapies were not possible based on the study design. Safety was measured by discontinuation rates, TEAEs, laboratory assessments including lipid profile and glycosylated hemoglobin (HbA1c), weight and electrocardiograms. Health outcome measures were collected by patient-report using the 36-item Short Form Health Survey (SF-36) and the EuroQoL Questionnaire-Version 5-D (EQ-5D).

Progression of neuropathy was measured by the MNSI. Progression of retinopathy was measured using ophthalmology assessments, including visual acuity. Progression of nephropathy was measured by the microalbumin/creatinine ratio.

About Diabetic Peripheral Neuropathy

According to the National Institute of Diabetes & Digestive & Kidney Diseases, approximately half of those with diabetes have some form of nerve damage, or neuropathy, but not all will develop symptoms. While nerve problems can occur at any time, the highest rates are among those who have had diabetes for at least 25 years. People who have had problems controlling their blood sugar levels, have high blood pressure, are overweight, have high levels of blood fat, or are over the age of 40, may also have a greater risk of developing diabetic peripheral neuropathy. Symptoms can include numbness, tingling or pain and weakness in the toes, feet, legs, hands, arms and fingers. These symptoms are often worse at night.(4)

About Cymbalta

"Cymbalta is believed to modulate both serotonin and norepinephrine in the brain and the spinal cord, impacting nerve signaling. Based on pre-clinical studies, Cymbalta is a balanced and potent reuptake inhibitor of serotonin and norepinephrine. While the mechanism of action of duloxetine in humans is not fully known, scientists believe its effect on pain perception is due to increasing the activity of serotonin and norepinephrine in the central nervous system."

Cymbalta is approved in the United States for the treatment of major depressive disorder and the management of diabetic peripheral neuropathic pain, both in adults. Cymbalta is not approved for use in pediatric patients.

Important Safety Information

In clinical studies, antidepressants increased the risk of suicidal thinking and behavior in children and adolescents with depression and other psychiatric disorders. Anyone considering the use of Cymbalta or any other antidepressant in a child or adolescent must balance the risk with the clinical need. Patients who are starting therapy should be observed closely for worsening depression symptoms, suicidal thoughts or behavior, or unusual changes in behavior. Cymbalta is not approved for use in patients under the age of 18.

Patients on antidepressants and their families or caregivers should watch for worsening depression symptoms, unusual changes in behavior and thoughts of suicide, as well as for anxiety, agitation, panic attacks, difficulty sleeping, irritability, hostility, aggressiveness, impulsivity, restlessness, or extreme hyperactivity. Call the doctor if you have thoughts of suicide or if any of these symptoms are severe or occur suddenly. Be especially observant at the beginning of antidepressive treatment or

whenever there is a change in dose.

Prescription Cymbalta is not for everyone. People who are allergic to Cymbalta or the other ingredients in Cymbalta should not take it. If you have recently taken a type of antidepressant called a monoamine oxidase inhibitor (MAOI), are taking Mellaril(R) (thioridazine) or have uncontrolled narrow-angle glaucoma, you should not take Cymbalta. Talk with your doctor before taking Cymbalta if you have liver or kidney problems, glaucoma or consume large quantities of alcohol. Women who are pregnant should talk with their doctor before taking Cymbalta. Nursing while taking Cymbalta is not recommended. Tell your doctor if you are taking other prescription or nonprescription medications.

In clinical studies of Cymbalta for depression, the most common side effects were nausea, dry mouth, constipation, decreased appetite, fatigue, sleepiness, and increased sweating. Nausea was the most common side effect. For most people, the nausea was mild to moderate, and usually subsided within one-to-two weeks. Cymbalta is also approved for the management of neuropathic pain associated with diabetic peripheral neuropathy. In clinical studies of Cymbalta in these patients, the most common side effects were nausea, sleepiness, dizziness, constipation, dry mouth, increased sweating, decreased appetite, and loss of strength or energy. In all clinical trials, most people were not bothered enough by side effects to stop taking Cymbalta. Your doctor may periodically check your blood pressure. Don't stop taking Cymbalta without talking to your doctor.

For full Patient Information, visit www.Cymbalta.com.

For full Prescribing Information, including Boxed Warning, visit <http://www.Cymbalta.com/>.

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About Eli Lilly and Company

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This press release contains forward-looking statements about the potential of Cymbalta for the treatment of DPNP, and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. There is no guarantee that the product will continue to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

1. "American Diabetes Association Survey Finds Most People with Diabetes Don't Know About Highly Prevalent, Serious Complication." Available at <http://www.diabetes.org/for-media/2005-press-releases/diabeticneuropathy.jsp>. Accessed on October 5, 2005.

2. National Institute of Neurological Disorders and Stroke, "Peripheral Neuropathy Fact Sheet." Available at: http://www.ninds.nih.gov/disorders/peripheralneuropathy/detail_peripheralneuropathy.htm. Accessed on October 5, 2005.

3. Foundation for Health in Aging, "Diabetic Neuropathy." Available at: http://www.healthinaging.org/public_education/diabetes/neuropathy.php. Accessed on October 5, 2005.

4. National Diabetes Information Clearinghouse. Diabetic Neuropathies: The Nerve Damage of Diabetes. National Institute of Diabetes and Digestive and Kidney Diseases. <http://www.diabetes.niddk.nih.gov/dm/pubs/neuropathies/>, August 2004.

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