



February 18, 2005

EU Scientific Committee Recommends Approval of Cymbalta(R) For the Treatment of Diabetic Peripheral Neuropathic Pain

Committee Makes Recommendation After Reviewing Data Package Supporting the Product's Safety and Efficacy Profile

INDIANAPOLIS, Indiana, February 18, 2005 /PRNewswire-FirstCall via COMTEX/ -- The medical advisory board of the European Medicines Agency (EMA), which regulates pharmaceuticals in Europe, has recommended the approval of duloxetine hydrochloride (sold in the United States as Cymbalta) as safe and effective for the management of diabetic peripheral neuropathic pain (DPNP) in adults, Eli Lilly and Company announced today.

If, as expected, the European Commission accepts the recommendation of its Committee for Medicinal Products for Human Use (CHMP), it would be the second major approval of Cymbalta for the management of DPNP, following the September 2004 approval by the U.S. Food and Drug Administration. Also, the drug was twice approved as safe and effective for other major medical conditions in Europe - once under the name Yentreve(R), for the treatment of moderate-to-severe stress urinary incontinence, and once as Cymbalta, for the treatment of major depressive episodes[1]. Duloxetine is not approved in the United States for the treatment of stress urinary incontinence.

"This regulatory opinion could soon pave the way for a new safe and effective treatment in Europe for a very debilitating condition," said Dan Ziegler, M.D., German Diabetes Clinic of the German Diabetes Research Center, M.D. "Many people with diabetic peripheral neuropathic pain are elderly, have multiple health problems and are on multiple medications."

Although it does not change the underlying nerve damage caused by diabetic peripheral neuropathy, Cymbalta does help relieve the burning, stabbing and shooting pain that is the hallmark of this condition. In addition to its once-a-day dosing schedule, Cymbalta is not a controlled substance, unlike some other medications used to manage DPNP.

The CHMP, which comprises regulators from the 25 European Union countries, based its positive opinion on its review of the comprehensive data package that included, in part, data from two randomized, 12-week, double-blind, placebo-controlled, fixed-dose studies of 60 and 120 mg per day, in 791 non-depressed adults who had the disorder for at least six months.

In both studies, duloxetine significantly reduced 24-hour average pain, compared with placebo. Improvements were noted as early as the first week of treatment and continued for the duration of the studies. In addition, duloxetine showed rapid onset of action and effect in reducing pain caused by diabetic neuropathy at both 60mg per day and 120mg per day, and was effective in relieving pain at night[2]. Nighttime pain is especially troublesome to many patients with diabetic neuropathy because it can interfere with sleep.

On average, patients in the studies were 60 years old, suffered from diabetes for 11 years and related diabetic neuropathy for four years, and rated their pain as moderate to moderately severe at the start of the trials.

Following the CHMP's positive opinion for duloxetine for diabetic peripheral neuropathic pain, the European Commission is expected to grant marketing authorization within the next few months.

About Cymbalta

Serotonin and norepinephrine are two neurotransmitters, or chemical messengers, believed to help regulate a person's emotions and sensitivity to pain. Research suggests that increasing levels of serotonin and norepinephrine in the brain and spinal cord can reduce the body's sensation of pain from the nerve damage caused by diabetes.

Based on preclinical data, Cymbalta (pronounced sim-BAWL'-tuh) is a balanced and potent reuptake inhibitor of serotonin and norepinephrine[3]. It is indicated in the United States for the treatment of major depression and the management of diabetic peripheral neuropathic pain. The European Commission has also approved duloxetine for the treatment of major depression and moderate-to-severe stress urinary incontinence in adults. As duloxetine has not been studied in children, Lilly discourages its use in those under 18.

Cymbalta should not be confused with Symbyax(TM) (pronounced SIMM-bee-ax), a medicine for bipolar depression also marketed by Lilly. Symbyax is a combination of olanzapine, the active ingredient in Zyprexa(R), and fluoxetine, the active ingredient in Prozac(R). Symbyax is available in capsules of 6 mg/25 mg (olanzapine/fluoxetine), 12 mg/25 mg, 6 mg/50 mg and 12 mg/50 mg. Cymbalta is available in 20 mg, 30 mg and 60 mg capsules.

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. Families and caregivers should discuss with the doctor any observations of worsening depression symptoms, suicidal thinking and 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 are severe or occur suddenly. Be especially observant at the beginning of treatment or whenever there is a change in dose.

Prescription Cymbalta is not for everyone. People who are allergic to duloxetine hydrochloride 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 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. Breast feeding while taking Cymbalta is not recommended.

In clinical studies of Cymbalta for depression, the most common side effects were nausea, dry mouth, constipation, decreased appetite, fatigue, sleepiness, and increased sweating. Cymbalta also is 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 prescribing information, including Boxed Warning, visit www.Cymbalta.com.

About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of best-in-class pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers-through medicines and information-for some of the world's most urgent medical needs. Additional information about Lilly is available at www.lilly.com.

P-LLY

This press release contains forward-looking statements about the potential of duloxetine for the treatment of diabetic neuropathic pain and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of commercialization. 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.

References

[1] In November 2002, Eli Lilly and Company and Boehringer Ingelheim signed a long-term agreement to jointly develop and commercialize duloxetine hydrochloride. This partnership covers most countries worldwide with few exceptions. In the United States, the collaboration excludes neuroscience indications. In the United States, Cymbalta for depression and diabetic peripheral neuropathic pain are marketed by Lilly and Quintiles.

[2] Wernicke JF, Lu Y, D'Souza DN, Waninger A, Tran PV. Duloxetine at doses of 60 mg QD ad 60 mg BID is effective treatment of diabetic neuropathic pain. Paper presented at: American Academy of Neurology; April 24-May 1, 2004; San Francisco, CA.

[3] Bymaster F, Dreshfield-Ahmad L, Threlkeld P, Shaw J, Thompson B, Nelson D, et al. Comparative affinity of duloxetine and venlafaxine for serotonin and norepinephrine transporters in vitro and in vivo, human serotonin receptor subtypes, and other neuronal receptors. *Neuropsychopharmacology*. 2001;25(6):871-880.

SOURCE Eli Lilly and Company and Boehringer Ingelheim GmbH

Refer to: David Shaffer (U.S.) +1-(317)-651-3710 voice, +1-(877)-656-9084 pager,
djshaffer@lilly.com Jennifer Yoder (Outside U.S.), +1-(317)-433-3445 voice,
+1-(317)-652-0912 mobile jenyoder@lilly.com

<http://www.prnewswire.com>

Copyright (C) 2005 PR Newswire. All rights reserved.

News Provided by COMTEX