September 7, 2004

FDA Approves Antidepressant Cymbalta for Treatment of Pain Caused by Diabetic Peripheral Neuropathy, Which Affects Up to 5 Million Americans

Agency grants priority approval to first medicine to treat common, painful complication of diabetes

The U.S. Food and Drug Administration (FDA) has approved the antidepressant Cymbalta® (duloxetine HCl; pronounced SIM-BALL-TA), judging it safe and effective for the management of diabetic peripheral neuropathic pain, a symptom of nerve damage that affects up to 5 million Americans, Eli Lilly and Company (NYSE: LLY) announced today.

Cymbalta, a balanced and potent serotonin and norepinephrine reuptake inhibitor, is the first and only FDA-approved treatment for pain caused by diabetic peripheral neuropathy. This approval came after a six-month priority review. More than 18 million Americans have diabetes and are at risk for developing persistent pain - often described as burning, stabbing or shooting pain - as a result of nerve damage believed to be caused by high blood sugar.

"It has been a phenomenal month for Lilly, with four drug approvals since early August," said Sidney Taurel, Lilly's chairman, president and chief executive officer.[1] "Our long-term investment in drug research continues to pay dividends, both to the company and, more importantly, to patients around the world suffering from a variety of illnesses."

This is the second time in a month that the FDA has judged Cymbalta a safe and effective therapy for a major medical disorder. On Aug. 3, the agency approved Cymbalta as a treatment for major depression in adults. It's available immediately by prescription in pharmacies across the United States for the treatment of major depression or pain associated with diabetic peripheral neuropathy.

Lilly proved Cymbalta's safety and efficacy in the treatment of pain caused by diabetic peripheral neuropathy at doses of 60 and 120 mg per day in two randomized, 12-week, double-blind, placebo-controlled, fixed-dose studies in non-depressed adults who had the disorder for at least 6 months. However, doses of 120 mg per day, although safe and effective, were not as well tolerated as 60 mg per day. On average, patients in the studies were 60 years old, suffered from diabetes for 11 years and from related diabetic neuropathy for four years, and at the beginning of the studies, rated their pain as moderate to moderately severe.

In both studies, Cymbalta 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, Cymbalta showed rapid onset of action and sustained effect in reducing pain caused by diabetic neuropathy at both 60 mg per day and 120 mg per day, and was effective in relieving pain at night. Nighttime pain is especially troublesome to many patients with diabetic neuropathy, because it can interfere with sleep.

"Until now, we didn't have a simple and effective therapy for patients living with diabetic neuropathic pain. Instead, we were left with medications that often required multiple dose adjustments, or for patients to take several pills throughout the day. This is difficult for many of these patients, as they already take a host of medications for their diabetes and other conditions, which can put them at increased risk for drug interactions and dose-limiting side effects," said Timothy Smith, M.D., R.Ph., Medical Director, Mercy Health Research, St. Louis, and a Cymbalta investigator. "With Cymbalta, we finally have a therapy proven to provide real relief for many of these patients, without the complicated dosing schedule."

Although Cymbalta does not change the underlying nerve damage caused by diabetic peripheral neuropathy, it does help relieve the stabbing, burning and shooting pain often associated with the disorder. Scientists believe it does this by increasing levels of serotonin and norepinephrine, two neurotransmitters, or chemical messengers, believed to be important in regulating a person's emotions as well as sensitivity to pain. Increasing these levels in a balanced way is thought to improve the body's natural ability to regulate pain.

"We know that Cymbalta, as an antidepressant, is effective at treating both the emotional and painful physical symptoms of depression," said Stephen Stahl, M.D., Ph.D., chairman of the Neuroscience Education Institute and adjunct professor of psychiatry at the University of California at San Diego School of Medicine. "Seeing significant benefit in diabetic neuropathic pain, among patients who did not have depression, helps confirm that this drug has a positive impact on pain that is separate from improvement in mood."

About Cymbalta
Cymbalta comes in a capsule and can be taken once a day. The recommended daily dose for Cymbalta is 60 mg. Cymbalta has not been studied in children, and therefore Lilly discourages its use in those under 18. In addition to depression and pain caused by diabetic peripheral neuropathy, duloxetine hydrochloride, the active ingredient in Cymbalta, also has been approved in Europe for the treatment of moderate to severe stress urinary incontinence, another condition believed to respond to treatment that affects serotonin and norepinephrine levels.

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

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.[2]

Important Safety Information
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 serious 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.

In clinical studies of Cymbalta for pain caused by diabetic neuropathy, the most common side effects were nausea, sleepiness, dizziness, constipation, dry mouth, increased sweating, decreased appetite and fatigue. 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.

Cymbalta is also used to treat depression. Patients being treated with antidepressants should be observed closely for clinical worsening of depressive symptoms and suicidality. Patients and their families should watch for these as well as for anxiety, agitation, panic, difficulty sleeping, irritability, hostility, aggressiveness, impulsivity, restlessness, or overexcitement and hyperactivity. Call the doctor if any of these are severe or occur suddenly. Be especially observant when starting any antidepressant therapy and whenever there is a change in dose.

For full patient information, visit www.Cymbalta.com.

About Lilly
Lilly, a leading innovation-driven corporation, is developing a growing portfolio of first-in-class and 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.

This press release contains forward-looking statements about the potential of Cymbalta 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 development and commercialization. There is no guarantee that the product will prove 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.

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1. The four approvals include:

- On Aug. 3, the FDA approved Cymbalta for the treatment of major depressive disorder in adults.
- On Aug. 12, Yentreve™ received approval across the European Union for the treatment of stress urinary incontinence in women. (Yentreve is a trademark of Eli Lilly and Company. This trademark is pending approval by the FDA as a proprietary drug name for the established name, duloxetine hydrochloride. In November 2002, Eli Lilly and Company and Boehringer Ingelheim signed a global long-term agreement to jointly develop and commercialize duloxetine hydrochloride for the treatment of stress urinary incontinence (SUI), depression and diabetic neuropathic pain. This partnership covers most countries worldwide with few exceptions. In the U.S., the collaboration focuses on SUI.)

- On Aug. 19, the FDA approved Alimta® (pemetrexed) for the second-line treatment of advanced lung cancer
- On Sept. 3, the FDA approved Cymbalta for the treatment of pain caused by diabetic peripheral neuropathy.

2. 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.