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# Cymbalta Provided Sustained Pain Relief for Women with Fibromyalgia

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*Study shows improvement in pain unrelated to effect on mood and presence of major depression*

The antidepressant Cymbalta® (duloxetine HCl; pronounced sim-BAWL'-tuh), a dual-reuptake inhibitor of serotonin and norepinephrine, 60 mg once or twice daily, significantly reduced pain in more than half of women treated for fibromyalgia, with and without major depression, according to 12-week data presented this week at the annual meeting of the American College of Rheumatology.

These data are being presented one month after another study, in which Cymbalta also significantly reduced pain in women with fibromyalgia versus placebo, was published in *Arthritis and Rheumatism*.

"The results in these study patients were very striking in the degree of reduction of pain, which is the primary symptom of fibromyalgia. In addition, Cymbalta significantly improved these patients' quality of life and overall functioning, as measured by quality of life and disability scales," said Lesley M. Arnold, M.D., University of Cincinnati College of Medicine, Cincinnati, Ohio, who presented the study. "For many, the pain of fibromyalgia makes them so sensitive to being touched that even a hug from a loved-one can be intolerable."

In the study, Cymbalta's effect on pain was independent of any effect on mood, and there was no significant difference in response rates between patients in the study with and without major depression.

Fibromyalgia is a chronic disorder that causes widespread pain and tenderness in the muscles and soft tissue of nearly 6 million Americans, predominantly women.[1] According to the National Fibromyalgia Association, patients often experience a deep muscular aching, throbbing, twitching, stabbing and shooting pain that "knows no boundaries, migrating to all parts of the body and varying in intensity." Neurological complaints, such as numbness, tingling and burning, are often present and add to the discomfort of the patient.

While the cause of fibromyalgia remains unknown, it has been linked to abnormalities in the brain's neurotransmitters, serotonin and norepinephrine, the same neurotransmitters believed to play a role in major depressive disorder, diabetic peripheral neuropathic pain and stress urinary incontinence.[1]

There is no approved treatment for fibromyalgia. Cymbalta, a balanced and potent serotonin and norepinephrine reuptake inhibitor, is proven to help treat the emotional and painful physical symptoms of depression. It also is the only approved treatment for management of pain caused by diabetic peripheral neuropathy, a type of nerve damage. Cymbalta is not approved for the treatment of fibromyalgia.

**Study Findings**

- More than half of patients treated with 60 mg of Cymbalta, once or twice daily, responded to treatment after 12 weeks, compared with one-third of those taking a sugar pill.
- Patients treated with 60 mg of Cymbalta, once or twice daily, were significantly more likely to experience a sustained treatment response than those treated with a sugar pill (44 percent, 43 percent and 19 percent, respectively).
- Patients treated with 60 mg of Cymbalta, once or twice daily, had functional improvements on the Sheehan Disability Scale which measures disability at work, in family life and in social life, that were significantly greater than those of patients taking a sugar pill.
- Cymbalta 60 mg once or twice daily directly reduced pain (75.7 and 87.5 percent, respectively) more than the indirect effect attributed to improvement in depressive symptoms (24.4 percent and 12.5 percent, respectively).
- Cymbalta 60 mg twice a day also relieved the pain associated with tender points often associated with fibromyalgia.
- Treatment-emergent adverse events were more common in patients treated with Cymbalta 60 mg once or twice daily, than in those treated with a sugar pill (79.2 percent). Events were typically mild to moderate in severity.
- Patients taking Cymbalta 60 mg once or twice daily were more likely to discontinue because of side effects than those taking placebo (21.2 percent, 23.3 percent and 11.7 percent respectively).

- The most common side effects for patients taking Cymbalta (occurring in at least 5 percent of patients and at twice the rate for those receiving placebo) were nausea, dry mouth, constipation, diarrhea, decreased appetite, nasopharyngitis, increased sweating and anorexia. In addition, for patients taking Cymbalta 60 mg twice daily, sleepiness and feeling jittery were common side effects.

**Methodology**
In a 12-week, double blind study, patients were randomized to receive Cymbalta 60 mg once (n=118) or twice daily (n=116), or placebo (n=120). The primary outcome measure was Brief Pain Inventory (BPI) 24-hour average pain severity score (score range: 0 [no pain] -10 [pain as bad as you can imagine]). Response to treatment was defined as a 30 percent reduction in the BPI 24-hour average pain score. Secondary outcome measures included remaining BPI pain and interference scores, Fibromyalgia Impact Questionnaire (FIQ), the tender point pain threshold and tender point number, Clinical Global Impression of Severity (CGI-Severity), Patient Global Impression of Improvement (PGI-Improvement), and the 17-item Hamilton Rating Scale for Depression.

**About Cymbalta**
Cymbalta is indicated for the treatment of major depression and the management of diabetic peripheral neuropathic pain, both in adults. As Cymbalta has not been studied in children, Lilly discourages its use in those under 18.

Cymbalta should not be confused with Symbyax™ (pronounced SIMM-bee-ax), a medicine for bipolar depression also marketed by Lilly. 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. Cymbalta is available in 20 mg, 30 mg and 60 mg capsules.

**Important Safety Information**
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.

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 the fibromyalgia study of Cymbalta, the most common side effects were nausea, dry mouth, constipation, decreased appetite and anorexia. 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 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 muscle weakness. 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.

**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 fibromyalgia and reflects Lilly's current beliefs. However, as with any pharmaceutical product under development, there are substantial risks and uncertainties in the process of development and regulatory review. There is no guarantee that the company will apply for or receive regulatory approval for this indication. There is also no guarantee that the product with 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. American College of Rheumatology. Fibromyalgia Fact Sheet. Available at: http://www.rheumatology.org/public/factsheets/fibromya.asp. Accessed October 4, 2004.