

Cymbalta[®] (duloxetine HCl) Fact Sheet

INDICATION: Cymbalta, a selective serotonin and norepinephrine reuptake inhibitor (SNRI), has been approved in adults age 18 and older by the FDA for the following indications:

- Acute treatment of major depressive disorder (MDD) in August 2004
- Management of diabetic peripheral neuropathic pain (DPNP) in September 2004
- Acute treatment of generalized anxiety disorder (GAD) in February 2007
- Maintenance treatment of MDD in November 2007
- Management of fibromyalgia in June 2008

MECHANISM OF ACTION: Although the exact way that Cymbalta works in people is unknown, it is believed to be related to an increase in the activity of serotonin and norepinephrine, which are two naturally occurring substances in the brain and spinal cord. Cymbalta is in a class of medications called selective SNRIs.

DOSAGE: Cymbalta is available in 20, 30 and 60 mg capsules. The recommended daily dose for Cymbalta is as follows: MDD acute: 40-60 mg; MDD maintenance: 60 mg; GAD: 60 mg; DPNP: 60 mg; and fibromyalgia: 60 mg. Refer to the full Prescribing Information for complete details about dosage and administration.

SAFETY AND EFFICACY IN MDD AND GAD: The efficacy of Cymbalta as an acute treatment for MDD was established in four randomized, double-blind, placebo-controlled, fixed-dose studies in adults age 18 and older. In all four studies, Cymbalta demonstrated superiority over placebo as measured by improvement in the 17-item Hamilton Depression Rating Scale Total Score.¹ In studies of 60 mg per day, Cymbalta-treated patients experienced significantly greater improvement in the core emotional symptoms associated with depression as early as week one, compared to those treated with placebo, as measured by the HAMD₁₇ Maier subscale.² Although patients may notice improvement in one to four weeks, they should continue therapy as directed.¹ Full antidepressant response may take four to six weeks. Results may vary from person to person.

The efficacy of Cymbalta for maintenance treatment for MDD was established in one trial in which patients received Cymbalta 60 mg per day during an initial 12-week open-label treatment phase, and responders were then randomly assigned in a double-blind manner to continue Cymbalta at the same dose or to placebo for six months. Patients on Cymbalta experienced a statistically significantly longer time to relapse of depression than did patients on placebo.³

The efficacy of Cymbalta as an acute treatment for GAD was established in three randomized, double-blind, placebo-controlled studies in non-depressed adults.¹ In all three studies, Cymbalta improved core anxiety symptoms as measured by the Hamilton Anxiety Scale, compared with placebo. Cymbalta patients also reported greater improvement in the global functional impairment as measured by the Sheehan Disability Scale (SDS).⁴ The SDS is a widely used and well-validated scale that measures the extent emotional symptoms disrupt patient functioning in three life domains: work/school, social life/leisure activities, and family life/home responsibilities. Results may vary from person to person.

The most commonly observed adverse events in pooled MDD and GAD placebo-controlled trials in patients treated with Cymbalta (N=2,995) (≥ 5 percent and at least twice placebo) were nausea (25 percent), dry mouth (15 percent), constipation (10 percent), sleepiness (10 percent), decreased appetite (7 percent) and increased sweating (6 percent). In the placebo-controlled acute clinical trials for MDD, the overall discontinuation rates due to adverse events for Cymbalta vs. placebo were 9 percent and 5 percent, respectively. In the placebo-controlled acute clinical trials for GAD, the overall discontinuation rates due to adverse events for Cymbalta vs. placebo were 15 percent and 4 percent, respectively.¹

SAFETY AND EFFICACY IN DPNP: The efficacy of Cymbalta in the management of DPNP was established in two randomized, 12-week, double-blind, placebo-controlled, fixed-dose studies in non-depressed adults age 18 and older having DPNP for at least six months.¹ In both studies, Cymbalta significantly reduced mean 24-hour average pain scores, compared with placebo. Some patients experienced a reduction in pain as early as week one, which persisted throughout the studies.¹ Results may vary from person to person.

The most commonly observed adverse events in DPNP patients treated with Cymbalta (N=568) (≥ 5 percent and at least twice placebo) were nausea (24 percent), sleepiness (16 percent), dizziness (13 percent), constipation (11 percent), dry mouth (9 percent), increased sweating (7 percent), decreased appetite (6 percent) and asthenia (5 percent).^{1,5} The overall discontinuation rates due to adverse events in the two pooled DPNP studies for Cymbalta vs. placebo were 14 percent and 7 percent, respectively.¹

SAFETY AND EFFICACY IN FIBROMYALGIA: The efficacy at three months for Cymbalta for the management of fibromyalgia was established in two randomized, double-blind, placebo controlled, fixed-dose studies in adults age 18 and older meeting the American College of Rheumatology criteria for fibromyalgia (a history of widespread pain for three months, and pain present at 11 or more of the 18 specific tender point sites). Treatment with Cymbalta significantly improved the endpoint mean pain scores from baseline and increased the proportion of patients with at least a 50 percent reduction in pain score from baseline.¹ Some patients experienced a decrease in pain as early as week one.¹

Patients taking Cymbalta 60 mg daily reported feeling better at endpoint as measured by the Patient Global Impression of Change (PGI). The PGI is a patient-rated scale that evaluates how much improvement has occurred since beginning treatment. Cymbalta was superior to placebo on the Fibromyalgia Impact Questionnaire (FIQ) Total Score. The FIQ is a scale that is used to assess and evaluate the impact of fibromyalgia on aspects of functioning believed to be most affected by the disorder.

The most commonly observed adverse events in fibromyalgia patients treated with Cymbalta (N=876) (≥ 5 percent and at least twice placebo) were nausea (29 percent), dry mouth (18 percent), constipation (15 percent), decreased appetite (11 percent), sleepiness (11 percent), increased sweating (7 percent) and agitation (6 percent). In the placebo-controlled clinical trials, the overall discontinuation rates due to adverse events for Cymbalta vs. placebo were 20 percent and 12 percent, respectively.¹



Important Safety Information

Cymbalta is approved to treat major depressive disorder and generalized anxiety disorder, and to manage diabetic peripheral neuropathic pain and fibromyalgia. **Antidepressants can increase suicidal thoughts and behaviors in children, adolescents, and young adults. Patients should call their doctor right away if they experience new or worsening depression symptoms, unusual changes in behavior, or thoughts of suicide. Be especially observant within the first few months of treatment or after a change in dose. Cymbalta is approved only for adults 18 and over.**

Cymbalta is not for everyone. Patients should not take Cymbalta if they have recently taken a type of antidepressant called a monoamine oxidase inhibitor (MAOI), are taking Mellaril® (thioridazine), or have uncontrolled glaucoma. Patients should speak with their doctor about any medical conditions they may have including kidney problems, glaucoma, or diabetes. Patients should talk to their doctor if they have itching, right upper belly pain, dark urine, yellow skin or eyes, or unexplained flu-like symptoms, which may be signs of liver problems. Severe liver problems, sometimes fatal, have been reported. They should also talk to their doctor about alcohol consumption. Patients should tell their doctor about all their medicines, including those for migraine, to avoid a potentially life-threatening condition. Symptoms may include high fever, confusion, and stiff muscles. Taking Cymbalta with NSAID pain relievers, aspirin, or blood thinners may increase bleeding risk. Patients should consult with their doctor before stopping Cymbalta or changing the dose and if they are pregnant or nursing.

Patients taking Cymbalta may experience dizziness or fainting upon standing. The most common side effects of Cymbalta include nausea, dry mouth, sleepiness, and constipation. This is not a complete list of side effects.

If patients have any questions, they should talk to their doctor before taking Cymbalta.

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

For full Prescribing Information, including Boxed Warning and Medication Guide, visit <http://www.cymbalta.com>.

1. Cymbalta full Prescribing Information (2009) Eli Lilly and Company.
2. Data on file, Lilly Research Laboratories: CYM20090505A.
3. Perahia DG et al. "Duloxetine in the prevention of relapse of major depressive disorder. Double-blind placebo-controlled study." *Br J Psychiatry*. 2006; 188:346-353.
4. Endicott J et al. "Duloxetine Treatment for Role Functioning in Generalized Anxiety Disorder: Three Independent Studies." *J Clin Psychiatry*. 2007; 68:518-524.
5. Data on file, Lilly Research Laboratories: CYM20050318AB.