



## **Cymbalta Receives European Approval for the Treatment of Generalised Anxiety Disorder**

INDIANAPOLIS, Aug 22, 2008 /PRNewswire-FirstCall via COMTEX News Network/ -- Eli Lilly and Co (NYSE: LLY) and Boehringer Ingelheim have announced that the European Commission has approved the use of Cymbalta(R) (duloxetine) for the treatment of Generalised Anxiety Disorder (GAD). This approval -- the fourth for duloxetine in Europe -- was issued on 28 July following an initial positive opinion issued by the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) on 26 June 2008.

The approval is based upon the results of five clinical studies of GAD -- four double-blind short-term (acute) placebo-controlled studies and a placebo-controlled relapse prevention study -- involving more than 2,000 non-depressed adults with GAD. In each of the four acute placebo-controlled studies safety and efficacy were assessed. Duloxetine significantly improved core anxiety symptoms (as measured by the Hamilton Anxiety Scale) compared with placebo ( $p$  less than or equal to 0.001,  $p=0.02$ ,  $p=0.007$ ,  $p$  less than or equal to 0.001 respectively)(1,2,3,4) and patients demonstrated improvement in role functioning, including ability to perform everyday activities in work, home and in social situations.(5,6) In addition, duloxetine significantly decreased the likelihood of relapse in those patients who initially responded to duloxetine and were maintained on treatment for six months compared with those switched to placebo.(7) The most common side effects in these studies included nausea, fatigue, dry mouth, drowsiness, constipation, insomnia, decreased appetite, hyperhidrosis (excessive perspiration), decreased libido, vomiting, ejaculation delay and erectile dysfunction.

Although global prevalence is not currently known, more than nine million Europeans(8,9) and six million people in Central and South America are estimated to suffer from GAD(10), which is characterised by excessive anxiety and worry about a number of events and activities (such as performance at work or school) over a sustained period of at least six months.(11)

This regulatory approval paves the way for launches in Europe and applies to all 27 countries of the European Union, as well as Norway, Iceland, and Liechtenstein.

Cymbalta(R), a member of a class of drugs commonly referred to as serotonin and noradrenaline reuptake inhibitors,(12) is already approved by the EMA to treat major depressive disorder and diabetic peripheral neuropathic pain. Duloxetine gained marketing authorisation for the treatment of GAD in Mexico in 2006 and in the United States in 2007.

Notes to Editors:

### **About Generalised Anxiety Disorder**

Approximately nine million Europeans(8,9) and six million people in Central and South America are estimated to suffer from GAD.(10) Quality of life is affected, as symptoms of GAD can include exaggerated worry or chronic anxiety, irritability and poor concentration. Ability to work is often compromised with the manifestation of physical symptoms such as muscle tension, fatigue, sleep disturbance and nausea.(11) The illness tends to be chronic with periods of exacerbation and remission. Patients report that episodes of generalised anxiety disorder are often brought on, or worsened, by stressful life events.(13)

### **About Duloxetine**

While duloxetine's mechanism of action in humans is not fully known, it is believed to affect both serotonin- and norepinephrine/noradrenaline-mediated nerve signalling in the brain and the spinal cord. Based on pre-clinical studies, duloxetine is a balanced and potent reuptake inhibitor of serotonin and norepinephrine/noradrenaline. Scientists believe that duloxetine's effects on mood and pain are due to an increase in the activity of serotonin and norepinephrine in the central nervous system.

Duloxetine is approved for the treatment of depression and diabetic peripheral neuropathic pain in many countries and also approved in some countries for the treatment of stress urinary incontinence, fibromyalgia, major depressive disorder and generalised anxiety disorder. Duloxetine is approved only for adults 18 and over. There is a possibility of an increased risk of suicidal thoughts or behaviour in children and young adults treated with antidepressants. Patients should call their doctor right away if they experience worsening depression symptoms, unusual changes in behaviour or thoughts of suicide, especially at the beginning of treatment or after a change in dose.

Patients taking duloxetine may experience dizziness or fainting upon standing. The most common side effects of duloxetine

include:

- For depression: nausea, dry mouth, headache, insomnia, diarrhea
  - For diabetic peripheral neuropathic pain: nausea, somnolence (sleepiness), fatigue, headache, dizziness
  - For stress urinary incontinence: nausea, dry mouth, fatigue
  - For generalised anxiety disorder: nausea, fatigue, dry mouth, drowsiness, constipation, insomnia, decreased appetite, hyperhidrosis, decreased libido, vomiting, ejaculation delay and erectile dysfunction.
- (This is not a complete list of side effects.)

Duloxetine is contraindicated in patients who are allergic to it, who have liver disease resulting in hepatic impairment, who are taking a monoamine oxidase inhibitor (MAOI), fluvoxamine, ciprofloxacin or enoxacin or who have severe kidney disease. The initiation of treatment with duloxetine also is contraindicated in patients with uncontrolled hypertension that could expose them to a potential risk of hypertensive crisis.

Eli Lilly and Company and Boehringer Ingelheim

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 neuroscience indications in most countries outside of the United States and Japan, with few exceptions.

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.co.uk](http://www.lilly.co.uk).

About Boehringer Ingelheim

The Boehringer Ingelheim group is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, it operates globally with 135 affiliates in 47 countries and almost 38,900 employees. Since it was founded in 1885, the family-owned company has been committed to researching, developing, manufacturing and marketing novel products of high therapeutic value for human and veterinary medicine. In 2007, Boehringer Ingelheim posted net sales of 10.9 billion euro while spending one fifth of net sales in its largest business segment Prescription Medicines on research and development. For more information please visit [www.boehringer-ingelheim.com](http://www.boehringer-ingelheim.com)

Duloxetine for major depressive episodes is marketed by Lilly and Boehringer Ingelheim in all countries included in the partnership under the brand name Cymbalta, except for Greece, Italy and Spain. In Greece, Italy and Spain Lilly markets the product as Cymbalta and Boehringer Ingelheim markets the product as Xeristar(R). In the United States, Cymbalta is marketed by Lilly and Quintiles. In Japan, duloxetine will be co-developed and co-marketed by Lilly and Shionogi & Co., Ltd.

Duloxetine for stress urinary incontinence is marketed by Lilly under the brand name Yentreve.(R)

P-LLY

1 Koponen, H., et al. Efficacy of Duloxetine for the Treatment of Generalized Anxiety Disorder: Implications for Primary Care Physicians. *Prim Care Companion J Clin Psychiatry* 2007; 9(2):100-107

2 Rynn M., et al. Efficacy and Safety of Duloxetine in the Treatment of Generalized Anxiety Disorder: A Flexible-Dose, Progressive-Titration, Placebo-Controlled Trial. *Depression and Anxiety* 2007; 25(3): 182-189.

3 Hartford, J., et al. Duloxetine as an SNRI Treatment for Generalized Anxiety Disorder: Results from a Placebo- and Active-Controlled Trial. *Int Clin Psychopharmacol* 2007; 22(3):167-74.

- 4 Nicolini H, et al. Improvement of psychic and somatic symptoms in adult patients with generalized anxiety disorder: Examination from a duloxetine, venlafaxine extended-release, and placebo-controlled study. In Press at Psychological Medicine.
- 5 Endicott, J., et al. Duloxetine Treatment for Role Functioning Improvement in Generalized Anxiety Disorder: Three Independent Studies. The Journal of Clinical Psychiatry 2007: 68(4):518-24
- 6 Allgulander, C., et al. Pharmacotherapy of Generalized Anxiety Disorder: Results of Duloxetine Treatment from a Pooled Analysis of 3 Clinical Trials. Current Medical Research and Opinion 2007: 23(6): 1245-1252
- 7 Davidson JRT, et al. Duloxetine treatment for relapse prevention in adults with generalized anxiety disorder: A 26-week randomized placebo- controlled study. Poster presented at the American College of Neuropsychopharmacology annual conference 2007. Boca Raton, Florida
- 8 Lieb, R, et al. The epidemiology of generalised anxiety disorder in Europe. European Neuropsychopharmacology 2005 Aug;15(4):445-52.
- 9 National Institute of Economic and Social Research. Summarized from the National Institute Economic Review,194, 28 October 2005.
- 10 Calculated extrapolations of prevalence rates against the populations of a particular country or region, based upon prevalence of generalized anxiety disorder in the US, UK, Canada or Australia. Available at: [http://www.cureresearch.com/g/generalized\\_anxiety\\_disorder/stats-country.htm](http://www.cureresearch.com/g/generalized_anxiety_disorder/stats-country.htm) . Accessed on 2.4.08
- 11 National Institute of Mental Health (NIMH). Anxiety Disorders. Available at: <http://www.nimh.nih.gov/health/publications/anxiety-disorders/generalized-anxiety-disorder-gad.shtml> . Accessed on 2.5.08
- 12 Bymaster, FP et al. The Dual Transporter Inhibitor Duloxetine: A Review of its Preclinical Pharmacology, Pharmacokinetic Profile, and Clinical Results in Depression. Current Pharmaceutical Design. 2005; 11: 1475-1493.
- 13 [Patient.co.uk](http://www.patient.co.uk). Generalized anxiety disorder. Available at <http://www.patient.co.uk/showdoc/27000122/> . Accessed on 2.5.08

(Logo: <http://www.newscom.com/cgi-bin/prnh/20031219/LLYLOGO> )

(Logo: <http://www.newscom.com/cgi-bin/prnh/20070319/NYM004LOGO> )

SOURCE Eli Lilly and Company

Copyright (C) 2008 PR Newswire. All rights reserved

News Provided by COMTEX