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Lilly and Boehringer Ingelheim Jointly Announce the Recision of U.S. FDA Application for Duloxetine for Treatment of Stress Urinary Incontinence

Companies Confident in SUI Data and Are Evaluating Options

INDIANAPOLIS, Ind. and RIDGEFIELD, Conn., Jan 28, 2005 /PRNewswire-FirstCall via COMTEX/ -- Eli Lilly and Company and Boehringer Ingelheim Pharmaceuticals, Inc. today jointly announced that Lilly has withdrawn from the U.S. FDA's Division of Reproductive and Urologic Drug Products its New Drug Application for duloxetine hydrochloride for the treatment of stress urinary incontinence (SUI). This decision was based on discussions with the FDA suggesting the agency is not prepared at this time to grant approval for duloxetine for the treatment of the SUI patient population based on the data package submitted. The companies will evaluate all options for next steps once they have had time to fully understand the FDA's perspective. Ongoing clinical trials for duloxetine SUI will continue.

This action does not affect the marketing status of duloxetine for the indications of depression and diabetic peripheral neuropathic pain (DPNP) in the United States or the SUI and depression indications outside of the United States.

"Despite this decision, we continue to have confidence in duloxetine, which is currently available for the treatment of stress urinary incontinence in many other countries," said Sidney Taurel, chairman, president and chief executive officer, Eli Lilly and Company.

"We are certainly disappointed with this outcome but are committed to exploring our options for duloxetine, as millions of American women who suffer from SUI do not currently have a pharmaceutical option to help manage their condition," stated Dr. Alessandro Banchi, chairman of the Board of Managing Directors of Boehringer Ingelheim.

Duloxetine for the treatment of SUI, marketed as Yentreve(R) and AriClaim(R) outside of the United States, has been deemed safe and effective by regulatory authorities that have granted its approval in 27 countries throughout the world.

Duloxetine for the treatment of major depressive disorder and DPNP has already been approved by the U.S. FDA as a safe and effective treatment under the brand name Cymbalta(R). The European Commission has approved duloxetine under the trade names of Cymbalta(R) and Xeristar(R) for major depressive episodes. Throughout the world, the drug is approved in 30 countries for major depression.

About SUI

SUI is the accidental leakage of urine during physical activities such as sneezing, coughing, laughing, lifting or exercising. It is an embarrassing and bothersome medical condition that affects nearly 15 million adult women in the United States(1,2) and can have a significant impact on quality of life. With nearly twice the prevalence of urge incontinence, SUI is the most common form of urinary incontinence among women.(3) Although common, it is a medical condition that is not normal at any age; unfortunately, many women do not seek treatment because they are embarrassed, fear surgery, or believe that it is a normal part of aging and that nothing can be done about it. The primary causes of SUI are weakness of the urethral sphincter and/or diminished pelvic support of the bladder and urethra. Risk factors include obesity, childbirth, chronic coughing, and constipation.(4)

About Duloxetine

Based on preclinical studies, duloxetine for SUI is a dual reuptake inhibitor and is believed to affect SUI by blocking the reuptake of serotonin and norepinephrine in the spinal cord.(3) The increase in the neurotransmitters in turn stimulates increased activity of the pudendal nerve that controls the external urethral sphincter. This stimulation is believed to increase contraction of the external urethral sphincter, thereby helping prevent accidental urine leakage with physical activity.

Clinical studies of duloxetine for the treatment of SUI have shown the most commonly reported adverse events (incidence of greater than or equal to 5 percent and significantly more common than placebo) reported by patients receiving duloxetine have been nausea, dry mouth, fatigue, insomnia, constipation, headache, dizziness, somnolence (drowsiness) and diarrhea.(5)

About Cymbalta

Cymbalta (sim-BAWL'-tuh) is indicated in the United States 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(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 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 prescribing information, visit www.Cymbalta.com.

About Lilly and Boehringer Ingelheim

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 peripheral neuropathic pain (DPNP). This partnership covers most countries worldwide with few exceptions. In the U.S., the collaboration focuses on SUI and excludes depression and DPNP.

Eli Lilly and Company

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 on www.lilly.com.

Boehringer Ingelheim Pharmaceuticals, Inc.

Boehringer Ingelheim Pharmaceuticals, Inc., based in Ridgefield, Conn., is the largest U.S. subsidiary of Boehringer Ingelheim Corporation (Ridgefield, Conn.) and a member of the Boehringer Ingelheim group of companies.

The Boehringer Ingelheim group of companies is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, it operates globally with 152 affiliates in 45 countries and more than 34,000 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 2003, Boehringer Ingelheim posted net U.S. sales of $8.37 billion (7.4 billion euro), while spending more than one fifth of net sales in its largest business segment--prescription medicines--on research and development.

For more Prescribing Information, please visit www.boehringer-ingelheim.com.

* Note to Editors:

Duloxetine for major depressive episodes will be marketed by Lilly and Boehringer Ingelheim in all countries included in the partnership under the brand name Cymbalta(R), except for Greece, Italy and Spain. In Greece, Italy and Spain Lilly will market the product as Cymbalta and Boehringer Ingelheim will market the product as Xeristar(R). In the USA the collaboration does not include Cymbalta. In the USA, the collaboration excludes neuroscience indications.

Duloxetine for stress urinary incontinence will be marketed by Lilly and Boehringer Ingelheim in all countries included in the partnership under the brand name Yentreve(R), except for Greece, Italy and Spain. In Greece, Italy and Spain Lilly will market the product as Yentreve and Boehringer Ingelheim will market the product as AriClaim(R).

P-LLY

This press release contains forward-looking statements about the potential of duloxetine for the treatment of stress urinary incontinence 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/or regulatory review. There is no guarantee that the product will receive regulatory approvals and any indication for which it is approved will be determined at the discretion of the Food and Drug Administration. There is also 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.

REFERENCES

1. Diokno A, Burgio K, Fultz N, Kinchen K, Obenchain R, and Bump R. Medical and self-care practices reported by women with urinary incontinence. Am J Managed Care. 2004;10:69-78. The estimate of STRESS URINARY INCONTINENCE prevalence was derived from Diokno et al and based on STRESS URINARY INCONTINENCE prevalence as determined by Hampel et al and by Diokno et al.

2. US Census 2000 Briefs (Age & Gender), US Department of Commerce Web site.

3. Thor K, Katofiasc M. Effects of duloxetine, a combined serotonin and norepinephrine reuptake inhibitor, on central neural control of lower urinary tract function in the chloralose-anesthetized female cat. J Pharmacol Exp Ther. 1995; 274:1014-1024.

4. Fultz NH, Burgio, K, Diokno A, Kinchen K, Obenchain R, and BumpR. Burden of stress urinary incontinence for community-dwelling women. Am J Obstet Gynecol. 2003; 189: 1275-1282.

5. Hurley D, Turner C, Baygani S, Yalcin I, and Viktrup L. Duloxetine for stress urinary incontinence: A meta-analysis of safety. Poster presented at the International Federation of Gynaecology and Obstetrics (FIGO) World Congress, Santiago, Chile. 2-7 November 2003.

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