



September 13, 2004

Yentreve

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Women in European countries now have hope to overcome this debilitating medical condition

Yentreve[®] (duloxetine hydrochloride) is now available in certain European countries, giving women suffering from moderate to severe stress urinary incontinence (SUI) a pharmaceutical treatment option for the first time.¹ Previous treatment options for SUI have been limited to conservative therapies* and surgery.^{2, 3} With the introduction of Yentreve[®], physicians in Germany, Denmark, Finland, Sweden and the United Kingdom now have a pharmaceutical treatment available that has been proven effective in significantly reducing the frequency of incontinence episodes and improving the quality of life of women with moderate to severe SUI.^{4, 5} It is anticipated that Yentreve[®] will launch in further European countries in the near future.

SUI, the most common form of urinary incontinence in women, affects one in seven women and is the accidental leakage of urine during physical activities such as sneezing, coughing, laughing, lifting or exercise.^{6, 7} This distressing condition, affecting the social and emotional well-being of sufferers, leaves many women unable to enjoy daily activities such as exercising, laughing with friends or even lifting a child for fear of leakage.⁷ The majority of women with SUI do not seek professional help for their condition and are often too embarrassed to talk about it even with their closest friends.⁷

"Yentreve[®] is a perfect example of delivering on our commitment to provide first-in-class products. With Yentreve[®] now available, women have even more reason to break their silence, talk to their physicians about this medical condition and ask for help," said Rich Pilnik, President of European Operations at Eli Lilly and Company.

Dr. Alessandro Banchi, Chairman of the Board of Managing Directors at Boehringer Ingelheim, added: "It is a milestone achievement to have Yentreve[®] available in the markets for the first time. The relatively short time between approval and availability of Yentreve[®] is testimony to the success of the partnership Boehringer Ingelheim has with Lilly and Boehringer Ingelheim's long standing expertise in urology. We look forward to making Yentreve[®] available in many more countries in Europe in the coming months."

The European Commission granted marketing authorization for Yentreve[®] throughout the European Union for the treatment of moderate to severe stress urinary incontinence in women on August 12, 2004. The approval was based on ten studies across five continents involving more than 2,000 women with SUI. The studies demonstrated that Yentreve[®] reduces the number of leakages by 50 to 100% in more than half of women with SUI, improves their quality of life and is generally well tolerated with mild and manageable side effects, the most common of which is transient nausea.^{5, 8}

"Many women are reluctant to seek help from their doctors as they believe that little can be done to help them or that the only option is surgery. Hopefully Yentreve[®] will bridge the gap that exists between pelvic floor exercises, which not all women can do or find helpful, and surgery, which is not appropriate or desirable for all women with stress urinary incontinence," said Linda Cardozo, Professor of Urogynecology, King's College Hospital, United Kingdom.

Simone, 47, an SUI sufferer from the United Kingdom, commented that "The condition was preventing me from exercising and leading my life to the full. It put me under great pressure to reconsider my career as a fitness instructor. Both physically and emotionally, life was becoming impossible. I had fantastic support from my husband, but not all women are as fortunate. A medicine gives the many women who aren't interested in surgery for SUI light at the end of the tunnel." Simone is the owner of two health clubs and a registered personal trainer and Pilates teacher.

Yentreve[®] for the Treatment of SUI

Studies show that Yentreve[®] is a balanced dual reuptake inhibitor of the neurotransmitters serotonin and norepinephrine,⁹ neurotransmitters that are believed to play key roles in the normal closure of the urethral sphincter, the muscle that - if weakened - can cause SUI.^{9, 10} By increasing neurotransmitter concentration, Yentreve[®] is believed to increase the tone and

contraction of the urethral sphincter, which helps prevent accidental urine leakage during physical activities such as sneezing, coughing, laughing, lifting or exercising.

The side effect profile of Yentreve is consistent with that seen with other drugs that have an impact on serotonin and norepinephrine. The most commonly reported adverse event was nausea, although it was usually mild to moderate and resolved within one week to one month in most patients. Other less prevalent adverse events included headache, insomnia, constipation, dry mouth, dizziness, and fatigue,¹¹ which tended to be non-progressive and mild to moderate in almost all patients.

Stress Urinary Incontinence

With nearly twice the prevalence as urge incontinence, SUI is the most common form of urinary incontinence in women. Although common, SUI is a medical condition that should not be considered a normal part of aging. SUI causes embarrassment and even social isolation, which may have a profound negative impact on the quality of life of the affected individuals. Even though many women are bothered by their symptoms of SUI, they often do not seek appropriate medical attention because they are embarrassed or they believe it is a normal part of aging. Several risk factors or contributing variables to the development of SUI have been suggested over the last decade and include childbirth, obesity, pelvic organ prolapse or chronic coughing.¹² Presently available treatment options range from behavioral therapy and pelvic floor muscle training to surgery.

About the Yentreve® Clinical Research Program

The Yentreve® clinical research program is striving to improve the lives of millions of women worldwide who suffer from SUI. It is a long-term, extensive and evolving global initiative, sponsored by Eli Lilly and Company and Boehringer Ingelheim, and is designed to investigate SUI, its impact on women's quality of life, and the efficacy and safety of Yentreve® in a wide range of patients and clinical settings.

More than ten studies enrolling over 2,000 patients have already been completed. Other studies are planned and new studies will be initiated as the clinical research program evolves and the development of Yentreve® continues.

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. In addition to the treatment of stress urinary incontinence in women, duloxetine is also currently being developed for the treatment of depression and diabetic neuropathic pain. This partnership covers most countries worldwide with few exceptions. In the USA, the collaboration excludes neuroscience indications.

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.

Boehringer Ingelheim

The Boehringer Ingelheim group 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 sales of 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 information please visit www.boehringer-ingelheim.com

This press release contains forward-looking statements about the potential of duloxetine for the treatment of stress urinary incontinence and reflects Lilly's and Boehringer Ingelheim's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties and no guarantees that the product will prove to be commercially successful. Lilly and Boehringer Ingelheim undertake no duty to update forward-looking statements.

Note: The terms norepinephrine and noradrenaline are synonymous and therefore can be used interchangeably.

1. Calculated estimate: (Female UI prevalence: 35%)i; (UI subtype prevalence: 49% SUI; 29% SUI + UUI: 22% UUI) ii; (Severe or bothersome rates: 17%-24% SUI; 38%-47% SUI + UUI; 28%-36% UUI)iii; (1998 Population Estimates: US Bureau of the Census, Report WP/98 = 307 million female SUI sufferers worldwide) iv: i/ii Hampel C, et al. Prevalence and natural history of female incontinence. *Eur Urol.* 1997;32 Suppl 2:3-12; iii Haanestad et al 2000; iv 1998 Population Estimates: US Bureau of the Census, Report WP/98

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