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New Study Shows Women with Severe Stress Urinary Incontinence May Reconsider Surgery After Experiencing the Benefits of Yentreve

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Multinational study also demonstrates the quick onset of action of Yentreve® and a reduction in continence pad usage

New data published in the September issue of Obstetrics and Gynecology show that for women with severe stress urinary incontinence (SUI), Yentreve® (duloxetine hydrochloride) works quickly to reduce the frequency of their incontinence episodes and improves their quality of life. All women enrolled in the study were awaiting continence surgery however, after eight weeks on Yentreve®, 20 percent of these patients reconsidered their willingness to undergo surgery.¹

"This study has important implications for clinical practice as it shows that Yentreve® may provide an alternative to surgery for some women with stress urinary incontinence. We know that surgery is an effective option but it does not suit all women for a variety of reasons," said Linda Cardozo, the study's principal investigator and Professor of Urogynecology, King's College Hospital, UK. "In addition, the knowledge that a non-surgical intervention exists may encourage more women to seek advice regarding their stress urinary incontinence."

SUI, the most common form of urinary incontinence in women that affects one in seven women, is the accidental leakage of urine during physical activities such as sneezing, coughing, laughing, lifting or exercise.^{2,3} 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.³ 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.³

This new, placebo-controlled, double blind, randomized study evaluated the efficacy of Yentreve® in women with severe SUI, as determined by having an incontinence episode frequency of greater than 14 episodes per week and who were already scheduled to undergo continence surgery.¹ One hundred and nine women aged 33 to 75 years were randomized either to placebo for eight weeks or to Yentreve® 40 mg twice daily for the first four weeks and then increased to 60 mg twice daily for the next four weeks. The study was carried out in 14 clinical centres in Australia, Canada, the Netherlands, and the United Kingdom.¹

Main findings are:

- The median number of incontinence episodes experienced decreased significantly by 60 percent in women treated with Yentreve(r) compared with 27 percent among those women taking placebo ($p < 0.001$).¹ In addition, the quality of life of women treated with Yentreve® improved significantly compared with placebo, with Yentreve®-treated patients averaging a 10.6 point rise in their Incontinence Quality of Life (I-QOL) questionnaire scores compared with a 2.4 point rise in the placebo group ($p = 0.003$).¹
- The study also showed that Yentreve® has a fast onset of action. All the women who responded to Yentreve® did so within the first two weeks of treatment, with the majority responding within one to three days.¹ "Rapid onset of action is highly desirable as it reduces the amount of time that it takes for a patient to decide whether or not she is responding to treatment," Professor Cardozo explained.
- Women in the treatment group also reduced their use of continence pads by more than one-third (34.5 percent), significantly more than those in the placebo group (4.8 percent).¹
- Based on their responses to the Willingness to Consider Surgery rating, 10 of 49 (20.4 percent) women who were unsure about, somewhat interested in, or strongly interested in surgery before taking Yentreve® indicated that they were somewhat or strongly NOT interested in surgery while taking Yentreve®, compared with none of the 45 placebo-treated subjects ($p = .001$)

Yentreve[®] for the Treatment of SUI

Studies show that Yentreve[®] is a balanced dual reuptake inhibitor of the neurotransmitters serotonin and norepinephrine,* neurotransmitters that are believed to play key roles in the closure of the urethral sphincter, the muscle that - if weakened - can cause SUI.^{4,5} 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.

In August 2004, the European Commission granted marketing authorization for Yentreve[®] throughout the European Union for the treatment of moderate to severe stress urinary incontinence in women. Yentreve[®] is now available in Germany, Denmark, Finland, Sweden and the United Kingdom. Eli Lilly and Boehringer Ingelheim will be making Yentreve[®] available in many more European countries in the coming months.

Side effects tended to be mild or moderate, occur early in treatment and did not commonly require discontinuation from the study. The most common side effect was nausea. Other less prevalent side effects included constipation, headache, dry mouth, fatigue, dizziness, insomnia, somnolence and vomiting.¹

Stress Urinary Incontinence (SUI)

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.⁶

Prior to Yentreve[®]'s availability there were no widely approved pharmaceutical options available for the treatment of SUI. Options were limited to treatments such as behavioral therapy, pelvic floor muscle training and 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 10 studies enrolling over 2,000 patients have already been completed prior to launch. 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.

Duloxetine for stress urinary incontinence will be jointly marketed by Lilly and Boehringer Ingelheim in the European Union under the brand name Yentreve[®], except for Spain, Italy and Greece where it will be marketed as Yentreve[®] by Lilly and Ariclim[®] by Boehringer Ingelheim.

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 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.

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

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