



For Immediate Release

FDA Approves Overactive Bladder Treatment Myrbetriq™ (mirabegron) from Astellas

Myrbetriq is the first and only beta-3 adrenergic agonist indicated for the treatment of overactive bladder

NORTHBROOK, Ill., June 28, 2012 – Astellas Pharma US, Inc. (“Astellas”), a U.S. subsidiary of Tokyo-based Astellas Pharma Inc. (Tokyo: 4503), announced today that the U.S. Food and Drug Administration (FDA) has approved Myrbetriq™ (mirabegron) extended-release tablets for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency and urinary frequency.

“Myrbetriq is the first oral OAB treatment with a distinct mechanism of action since the launch of anticholinergic agents 30 years ago,” said Steven Ryder, MD, president, Astellas Pharma Global Development. “The approval of Myrbetriq represents an important milestone in OAB treatment and in our ongoing commitment to advancing urological health.”

Myrbetriq is a once daily oral beta-3 adrenergic agonist discovered and developed by Astellas. It has been studied extensively in more than 10,000 individuals over 10 years.¹ Myrbetriq offers a new treatment option for patients with OAB. Antimuscarinics are the current OAB treatment standard.

Myrbetriq uses a distinct mechanism of action. Antimuscarinics work by binding to muscarinic receptors in the bladder and inhibiting involuntary bladder contractions.² Myrbetriq relaxes the detrusor smooth muscle during the storage phase of the urinary bladder fill-void cycle by activation of beta-3 adrenergic receptors which increases bladder capacity.³

“OAB impacts each individual differently so it is important to have a variety of treatment options available,” said Victor Nitti, MD, professor of Urology and Ob/Gyn, vice chairman, Department of Urology and director of Female Pelvic Medicine and Reconstructive Surgery NYU Langone Medical Center. “With Myrbetriq, U.S. physicians now have a new therapy option to offer many Americans living with overactive bladder.”

The recommended starting dose for Myrbetriq is 25 mg once daily with or without food. Myrbetriq 25 mg is effective within eight weeks; based on individual efficacy and tolerability, the dose may be increased to 50 mg once daily.⁴

Myrbetriq was studied in patients who were primarily Caucasian (94 percent) and female (72 percent) with a mean age of 59 years (range 18 – 95 years). The population included both naïve patients who had not received prior antimuscarinic pharmacotherapy for OAB (48 percent) and those who had received prior antimuscarinic pharmacotherapy for OAB (52 percent).⁵ The approval of Myrbetriq was based on safety and efficacy data from three placebo-controlled Phase 3 studies, in which treatment with Myrbetriq 25 mg and 50 mg resulted in statistically significant improvement in efficacy parameters of incontinence episodes and number of urinations per 24 hours.⁵

- In treatment with Myrbetriq 25 mg, incontinence episodes were reduced by 1.36 episodes from a baseline of 2.65, a statistically significant reduction of 0.40 vs. placebo in 12 weeks. The number

of urinations was reduced by 1.65 urinations from a baseline of 11.68, a statistically significant reduction of 0.47 vs. placebo in 12 weeks.⁵

- In treatment with Myrbetriq 50 mg, incontinence episodes were reduced by 1.49 episodes from a baseline of 2.71, a statistically significant reduction of 0.40 vs. placebo in 12 weeks. Number of urinations was reduced by 1.75 urinations from a baseline of 11.70, a statistically significant reduction of 0.55 vs. placebo in 12 weeks.⁵
- Myrbetriq was evaluated for safety in more than 2,700 patients in three, 12-week Phase 3 double-blind, placebo-controlled studies and in a one year, randomized fixed dose, active-controlled study in patients with OAB. The most commonly reported adverse reactions (greater than 2 percent of Myrbetriq patients and greater than placebo) were hypertension, nasopharyngitis, urinary tract infection and headache.⁶

Myrbetriq will be supplied in 25 mg and 50 mg tablets and is expected to be available in pharmacies in the fourth quarter of 2012. Mirabegron was approved in Japan in July 2011, and regulatory applications are under review in several other countries.

About Myrbetriq (mirabegron)

Myrbetriq™ (mirabegron) is a beta-3 adrenergic agonist indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency.

Important Safety Information for Myrbetriq (mirabegron)

INDICATIONS AND USAGE

Myrbetriq™ (mirabegron) is a beta-3 adrenergic agonist indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency.

IMPORTANT SAFETY INFORMATION

- Myrbetriq can increase blood pressure. Periodic blood pressure determinations are recommended, especially in hypertensive patients. Myrbetriq is not recommended for use in severe uncontrolled hypertensive patients. (defined as systolic blood pressure \geq 180mm Hg and/or diastolic blood pressure \geq 110 mm Hg)
- Urinary retention in patients with bladder outlet obstruction (BOO) and in patients taking antimuscarinic medications for the treatment of OAB has been reported in postmarketing experience in patients taking mirabegron. A controlled clinical safety study in patients with BOO did not demonstrate increased urinary retention in Myrbetriq patients; however, Myrbetriq should be administered with caution to patients with clinically significant BOO. Myrbetriq should also be administered with caution to patients taking antimuscarinic medications for the treatment of OAB.
- Myrbetriq is a moderate CYP2D6 inhibitor, the systemic exposure to CYP2D6 substrates such as metoprolol and desipramine is increased when co-administered with Myrbetriq. Therefore, appropriate monitoring and dose adjustment may be necessary, especially with narrow therapeutic index drugs metabolized by CYP2D6, such as thioridazine, flecainide, and propafenone .
- When initiating a combination of Myrbetriq and digoxin, prescribe the lowest dose of digoxin; monitor serum digoxin concentration to titrate digoxin dose to the desired clinical effect.
- Most commonly reported adverse reactions ($>$ 2% and $>$ placebo) were hypertension, nasopharyngitis, urinary tract infection and headache.

For full prescribing information for Myrbetriq, please visit www.myrbetriq.com.

About Overactive Bladder

According to the National Association for Continence, one in five adults has overactive bladder.⁷ However, recent studies have found that many more people may be affected, and have not talked to their physicians out of embarrassment or belief that OAB cannot be treated.⁸ For people with OAB, inappropriate signals are sent to the muscles in the bladder causing them to contract before the bladder is full. These bladder contractions may cause strong, sudden urges, and a frequent need to go to the bathroom, sometimes without any advance warning.⁹ Many patients cope with their symptoms by restricting fluids, carrying extra clothing and “mapping” bathroom locations wherever they go.

About Astellas Urology

Astellas Pharma US, Inc., located in Northbrook, Illinois, is a U.S. affiliate of Tokyo-based Astellas Pharma Inc. Astellas is a pharmaceutical company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. The company is committed to being a global category leader in urology and providing solutions for physicians and patients through the discovery of new treatments for OAB and other urologic conditions. Astellas currently markets the number one branded OAB treatment in the U.S. For more information about Astellas Pharma US, Inc., please visit www.astellas.us.

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¹ Mirabegron Advisory Committee Astellas Sponsor Briefing Document, 2012: 27.

² Yamaguchi O. Antimuscarinics and Overactive Bladder: Other Mechanism of Action. *Neurourology and Urodynamics* 2010; 29:112–115

³ Myrbetriq Prescribing Information, Section 12.1, June 2012

⁴ Myrbetriq Prescribing Information, Section 2.1, June 2012

⁵ Myrbetriq Prescribing Information, Section 14, June 2012

⁶ Myrbetriq Prescribing Information, Section 6.1, June 2012

⁷ National Association for Continence. Accessed May 29, 2012. <http://www.nafc.org/media/media-kit/facts-statistics>

⁸ Kin S, et al. Medical Visits Among Adults with Symptoms Commonly Associated with an Overactive Bladder. *BJU International*. 2006;97:551-554.

⁹ Abrams P, Cardozo L, Fall M, et al. Standardisation Sub-committee of the International Continence Society. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourology & Urodynamics*. 2002;21(2):167-78.