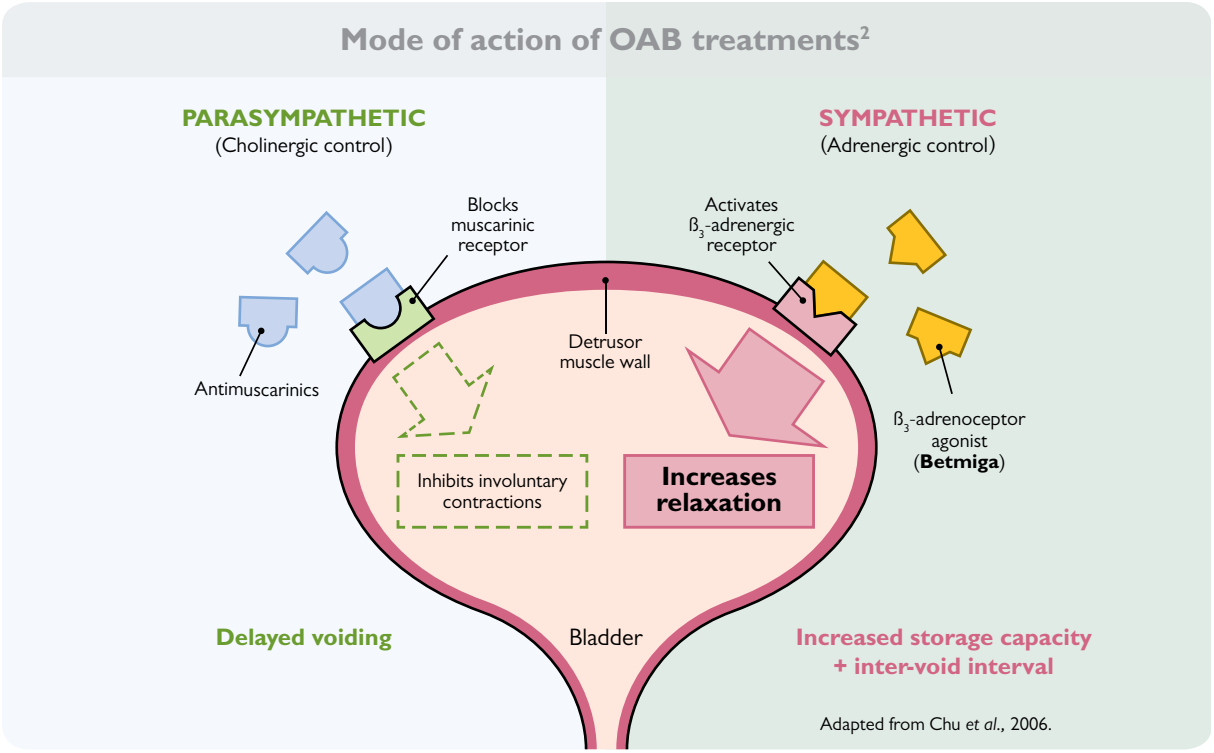
BETMIGA IS AN ENTIRELY NEW APPROACH TO OAB

Betmiga is the first ß$_3$-adrenoceptor agonist licensed to treat OAB.[1]

- A once-daily tablet that works differently to antimuscarinics[1,2]
- Relaxes the bladder during the storage phase via stimulation of ß$_3$-adrenergic receptors in the detrusor muscle[1]
- Improves storage capacity and inter-void interval, without impeding voluntary voiding[1]

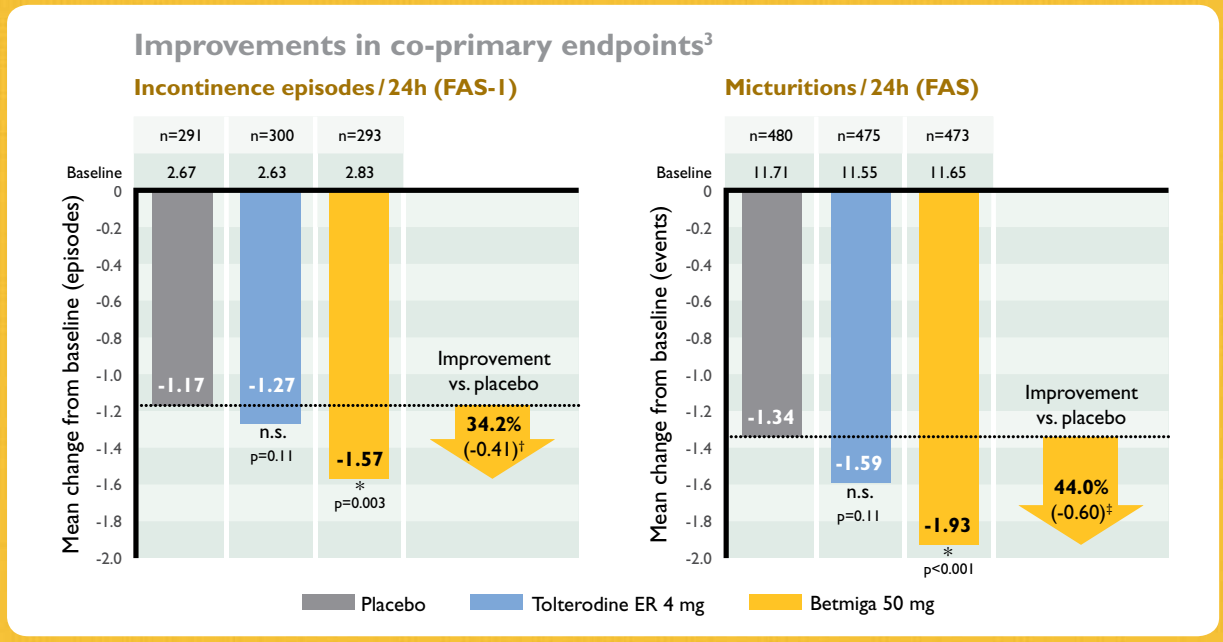


Prescribing information can be found on the second last page.

AN EFFECTIVE OAB TREATMENT[3,4]

In a key European-Australian phase III trial, Betmiga 50 mg:

- Significantly reduced the number of incontinence episodes and micturitions over 24 hours vs. placebo[3]



Adapted from Khullar *et al.*, 2013. Analysis of changes from baseline to final visit in a double-blind, randomised, placebo- and active-controlled phase III trial in 1987 OAB patients (study 046). FAS = full analysis set; FAS-I = all full analysis set patients who had ≥1 incontinence episode at baseline. *Statistically significant improvement vs. placebo. n.s. no statistically significant difference vs. placebo. Tolterodine ER (extended-release) 4 mg was included as an active control in this study. †Adjusted mean difference vs. placebo (95% two-sided CI: -0.72, -0.09). ‡Adjusted mean difference vs. placebo (95% two-sided CI: -0.90, -0.29).

- Demonstrated significant improvements in a range of secondary OAB and health-related quality of life measures vs. placebo[1,3,5]

WITH A MODE OF ACTION THAT'S WELL TOLERATED[3,4]

- Incidences of dry mouth and constipation, the two most bothersome side-effects with antimuscarinics, were similar to placebo with Betmiga 50 mg[3,6]

Incidence of common treatment emergent adverse events (≥2%)[3]

Adverse events, %	**Placebo** (n=494)	**Betmiga 50 mg** (n=493)	**Tolterodine ER 4 mg** (n=495)
Dry mouth	2.6%	2.8%	10.1%
Constipation	1.4%	1.6%	2.0%
Hypertension	7.7%	5.9%	8.1%
Nasopharyngitis	1.6%	2.8%	2.8%
Headache	2.8%	3.7%	3.6%
Influenza	1.6%	2.2%	1.4%
Urinary tract infection	1.4%	1.4%	2.0%

Table adapted from Khullar ***et al.***, 2013.

The long-term safety and tolerability of Betmiga 50 mg in OAB patients over a 12-month period is supported by a European-North American phase III trial.[4]

BETMIGA OFFERS A FRESH START IN OAB

Betmiga 50 mg is an effective treatment for OAB patients.[1,3,4]

- Including treatment-naïve and those who discontinued antimuscarinic therapy due to lack of efficacy[1]

Betmiga 50 mg is well tolerated and helps relieve the burden of OAB.[1,3,4]

- Dry mouth rate was comparable to placebo[3]
- Significantly improved patient quality of life compared with placebo[1,3]

Prescribing Information.
Presentation: Betmiga™ prolonged-release tablets containing 25 mg or 50 mg mirabegron. **Indication:** Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome. **Dosage:** *Adults (including the elderly):* Recommended dose: 50 mg once daily with or without food. *Children and adolescents:* Should not be used. **Contraindications:** Hypersensitivity to active substance or any of the excipients. **Warnings and Precautions:** Has not been studied in patients with end-stage renal disease, severe hepatic impairment or severe uncontrolled hypertension and therefore should not be used. Dose adjustment to 25 mg is recommended in patients with severe renal and moderate hepatic impairment. Not recommended in patients with severe renal impairment or moderate hepatic impairment concomitantly receiving strong CYP3A inhibitors. Dose adjustment to 25 mg is recommended in patients with moderate renal or mild hepatic impairment receiving strong CYP3A inhibitors concomitantly. Caution in patients with a known history of QT prolongation or in patients taking medicines known to prolong the QT interval. Not recommended during pregnancy and in women of childbearing potential not using contraception. Not recommended during breastfeeding. **Interactions:** Clinically relevant drug interactions between Betmiga™ and medicinal products that inhibit, induce or are a substrate for one of the CYP isozymes or transporters are not expected, except for inhibitory effect on the metabolism of CYP2D6 substrates. Betmiga™ is a moderate and time-dependant inhibitor of CYP2D6 and weak inhibitor of CYP3A. No dose adjustment needed when administered with CYP2D6 inhibitors or CYP2D6 poor metabolisers. Caution if co-administered with medicines with a narrow therapeutic index and significantly metabolised by CYP2D6. Caution is also advised if mirabegron is co-administered with CYP2D6 substrates that are individually dose titrated. When initiating in combination with digoxin the lowest dose for digoxin should be prescribed and serum digoxin should be monitored. **Adverse Effects:** Urinary tract infection, tachycardia, palpitations, atrial fibrillation, blood pressure increase, leukocytoclastic vasculitis. *Prescribers should consult the Summary of Product Characteristics in relation to other side effects.* **Pack and Prices:** Country specific. **Legal Category:** POM. **Product Licence Number:** Betmiga™ 25 mg EU/1/12/809/001-007; Betmiga™ 50 mg EU/1/12/809/008-14. **Date of Preparation:** January 2013. **Further information available from:** Astellas Pharma Europe Ltd, 2000 Hillswood Drive, Chertsey, Surrey, KT16 0RS, UK. Betmiga™ is a Registered Trademark. For full prescribing information please refer to the Summary of Product Characteristics.

Adverse events should be reported. Report adverse events to Astellas Pharma Europe by email to safety-eu@astellas.com, by facsimile to +31 (0)71-545 5208, or contact your local Astellas office (www.astellas.eu/contact/locations/)

References: 1. Betmiga Summary of Product Characteristics, February 2013. **2.** Chu F, Dmouchwski R. *Am J Med* 2006; **119**: 3S–8S. **3.** Khullar V *et al. Eur Urol* 2013; **63**: 283–95. **4.** Chapple CR *et al. Eur Urol* 2013; **63**: 296–305. **5.** Astellas data on file, MIR/12/0001/EU. **6.** Athanasopoulos A, Giannitsas K. *Adv Urol* 2011; 820816. Epub 2011 Jan 7.

Date of preparation: August 2013

Approval code: BET/13/0104/EU

IT'S TIME TO THINK OF SOMETHING ELSE.

The first ß$_3$-adrenoceptor agonist to treat overactive bladder

Betmiga™
mirabegron

A fresh start in OAB