Betmiga™
mirabegron

PROVEN RELIEF FROM OVERACTIVE BLADDER SYMPTOMS

More choices. *More life.*

astellas

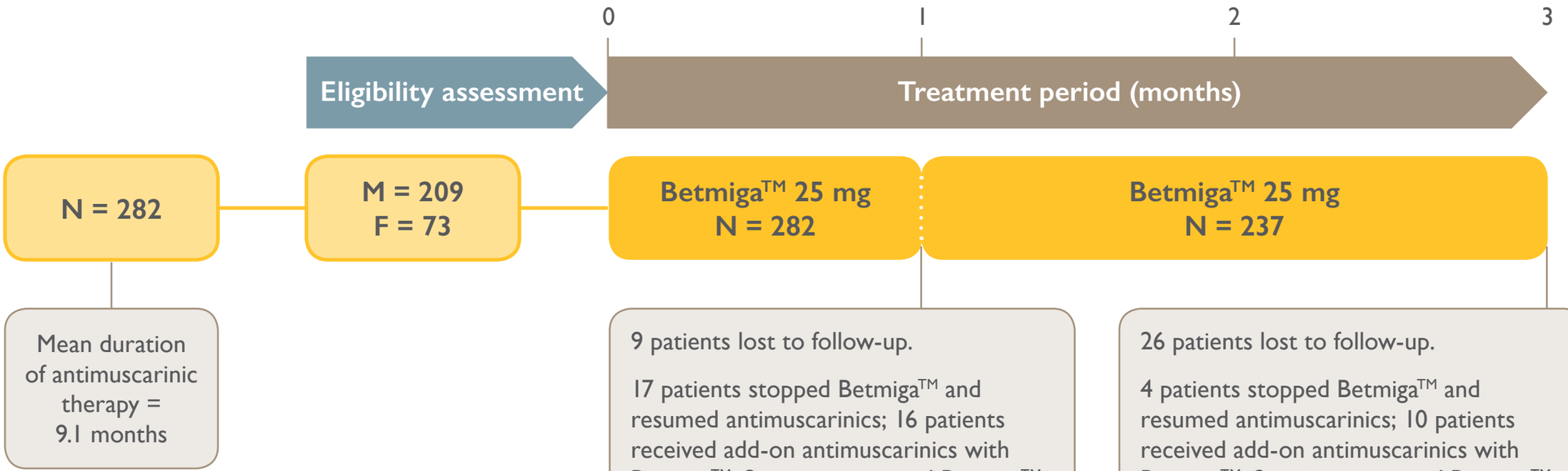
OBSERVATIONAL STUDY

High satisfaction with direct switching from antimuscarinics to Betmiga™ in patients receiving stable antimuscarinic treatment

Study objective[1]

To assess the therapeutic efficacy and safety of directly switching from antimuscarinics to Betmiga™ in patients with OAB receiving stable antimuscarinic treatment.

Study design[1]



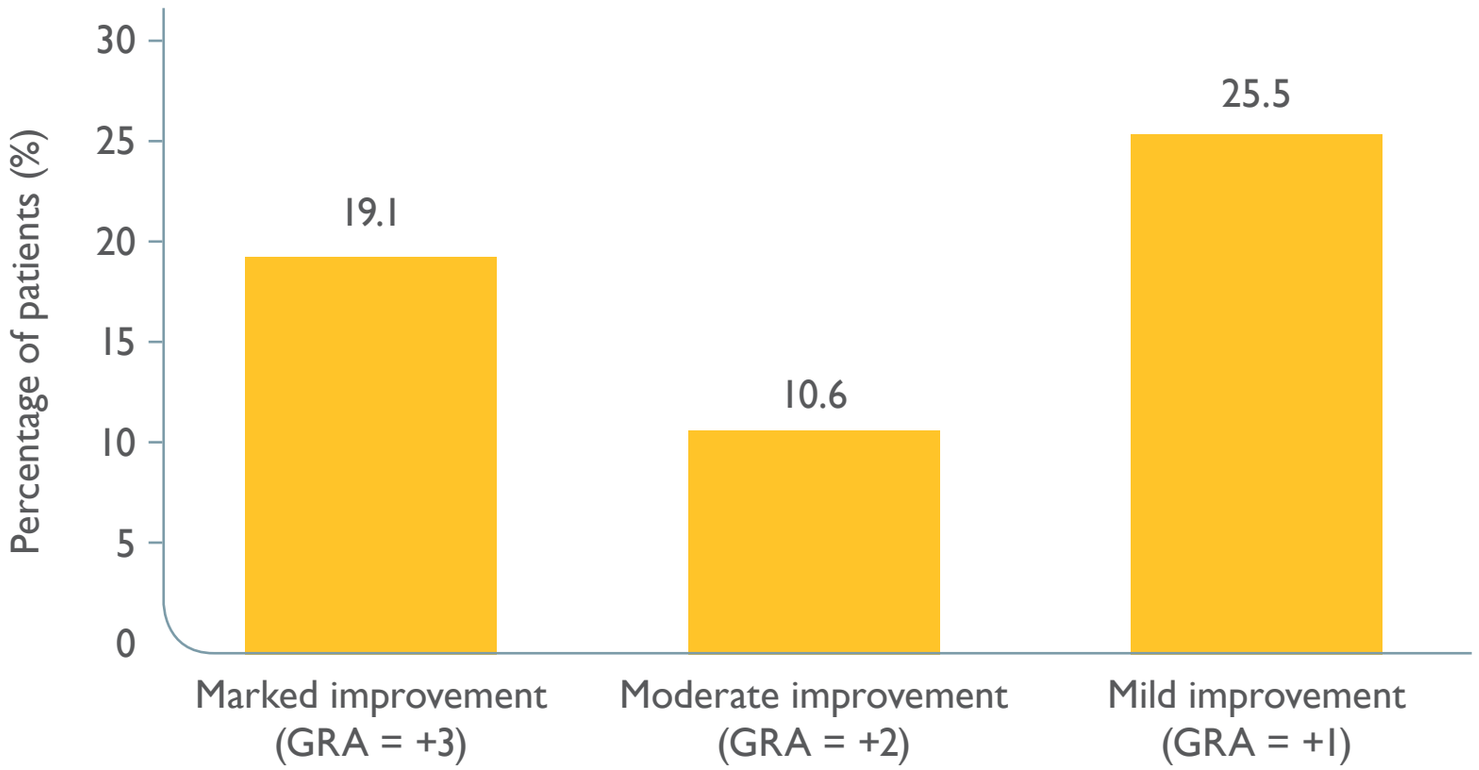
Adapted from Liao CH, Kuo HC. Medicine 2016.

OAB: overactive bladder.

Reference
1. Liao CH, Kuo HC. High satisfaction with direct switching from antimuscarinics to mirabegron in patients receiving stable antimuscarinic treatment. *Medicine* 2016;95:45.

1 in 2 patients who switched from antimuscarinics to Betmiga™ experienced better outcomes[1]

One month after switching to Betmiga™, 55.3% of patients reported improved outcomes (GRA ≥ 1)



Patients rated their symptoms after medication switching as compared to that at baseline by using a validated GRA scale, which comprises of 7 points, from markedly worse (-3) to markedly improved (+3).
Adapted from Liao CH, Kuo HC. Medicine 2016.

GRA: global response assessment.

Patients with GRA ≥ 1 had significantly improved storage and voiding symptoms.[1]

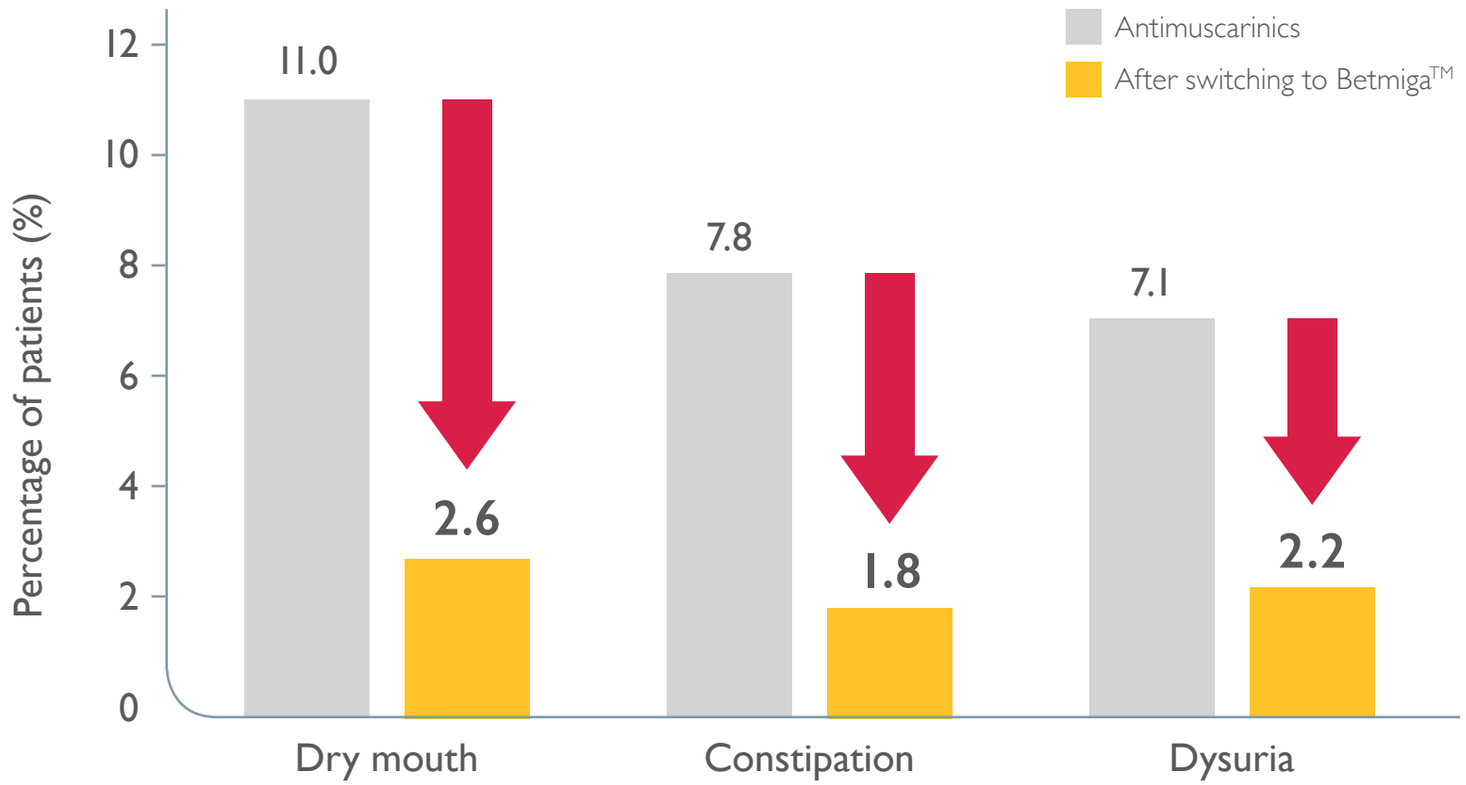
Overall, patients receiving Betmiga™ had:[1]

- Decreased postvoid residual urine.
- Significantly improved voiding symptoms and quality of life index.

Reference
1. Liao CH, Kuo HC. High satisfaction with direct switching from antimuscarinics to mirabegron in patients receiving stable antimuscarinic treatment. *Medicine* 2016;95:45.

Rate of AEs dropped significantly with Betmiga™ 1

Rate of common AEs due to antimuscarinic treatment were decreased significantly after switching to Betmiga™ 1



Adapted from Liao CH, Kuo HC. Medicine 2016.

AE: adverse event.

The overall AE rate **decreased from 24.1% to 12.8%** after switching to Betmiga™.[1]

All AEs experienced were mild and tolerable.[1]

Nearly **7 in 10** patients remained on Betmiga™ for longer than 3 months without adding or switching back to antimuscarinics.[1]

Reference

1. Liao CH, Kuo HC. High satisfaction with direct switching from antimuscarinics to mirabegron in patients receiving stable antimuscarinic treatment. *Medicine* 2016;95:45.

Patients with higher baseline OAB symptom score may have better outcomes when switched to Betmiga™[1]

Patients who achieved GRA ≥ 1 after switching to Betmiga™ had higher baseline IPSS-S, OAB-SS, and PPBC values.[1]

Baseline parameters in patients achieving GRA ≥ 1 after change to Betmiga™[1]

IPSS-S
5.3 ± 2.9

OAB-SS
5.5 ± 3.6

PPBC
2.8 ± 1.8

Hypothetical patients.
Adapted from Liao CH, Kuo HC. Medicine 2016.

Logistic regression analysis indicated that higher baseline IPSS-S (odds ratio, OR 1.114; p = 0.018) and OAB-SS (OR 1.103; p = 0.010) could serve as predictors of satisfactory outcome (GRA ≥ 1) with Betmiga™.[1]

OAB: overactive bladder; GRA: global response assessment; IPSS-S: international prostate symptom score storage subscore; OAB-SS: overactive bladder symptom score; PPBC: patient perception of bladder condition.

Reference
1. Liao CH, Kuo HC. High satisfaction with direct switching from antimuscarinics to mirabegron in patients receiving stable antimuscarinic treatment. *Medicine* 2016;95:45.

Betmiga™
mirabegron

Efficient and well-tolerated action against OAB symptoms

Increases bladder storage[1,2]

Lower incidence of antimuscarinic side effects[3,4]

Resolves OAB symptoms[1-3]

Enhances quality of life[2,3]

Giving patients more choices. *More life.*

References

1. Andersson KE. On the site and mechanism of action of 3-adrenoceptor agonists in the bladder. *Int Neurourol J.* 2017;21:6-11. **2.** Betmiga (mirabegron) full prescribing information. **3.** Khullar V, Amarenco G, Angulo JC, *et al.* Efficacy and tolerability of mirabegron, a (3)-adrenoceptor agonist, in patients with overactive bladder: results from a randomised European-Australian phase 3 trial. *Eur Urol.* 2013;63:283-95. **4.** Kelleher C, Hakimi Z, Zur R, *et al.* Efficacy and tolerability of mirabegron compared with antimuscarinic monotherapy or combination therapies for overactive bladder: a systematic review and network meta-analysis. *Eur Urol.* 2018;74:324-33.

BETMIGA™ ABBREVIATED PRESCRIBING INFORMATION

Presentation: 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 18 years and above (including elderly patients): The recommended starting dose is 25 mg once daily with or without food. Betmiga 25mg is effective within 8 weeks. Based on individual patient efficacy and tolerability the dose may be increased to 50 mg once daily. Renal and hepatic impairment patients: No dose adjustment is necessary in patients with mild to moderate renal impairment. In patients with severe renal impairment, the recommended dose is 25 mg dose once daily. No dose adjustment is necessary in patients with mild hepatic impairment (Child-Pugh Class A). In patients with moderate hepatic impairment (Child-Pugh Class B) the recommended dose is 25 mg once daily. Renal impairment patient with strong CYP3A inhibitors: Mild to moderate renal impairment 25 mg once daily. Severe renal impairment not recommended. Hepatic impairment patient with strong CYP3A inhibitors: Mild hepatic impairment (Child-Pugh Class A) 25 mg once daily. Moderate hepatic impairment (Child-Pugh Class B) not recommended. Method of Administration: Betmiga is to be taken once daily, with liquids, swallowed whole and is not to be chewed, divided, or crushed. **Contraindication:** Hypersensitivity to the active substance or to any of the excipients listed in section list of excipients. Severe uncontrolled hypertension defined as systolic blood pressure ≥180 mm Hg and/or diastolic blood pressure ≥110 mm Hg. **Special Precautions:** Renal impairment: Betmiga has not been studied in patients with end stage renal disease (GFR < 15 mL/min/1.73 m2 or patients requiring haemodialysis) and, therefore, it is not recommended for use in this patient population. Data are limited in patients with severe renal impairment (GFR 15 to 29 mL/min/1.73m2); based on a pharmacokinetic study (see full prescribing information) a dose reduction to 25 mg is recommended in this population. Betmiga is not recommended for use in patients with severe renal impairment (GFR 15 to 29 mL/min/1.73m2) concomitantly receiving strong CYP3A inhibitors (see full prescribing information). Hepatic impairment: Betmiga has not been studied in patients with severe hepatic impairment (Child-Pugh Class C) and, therefore, it is not recommended for use in this patient population. Betmiga is not recommended for use in patients with moderate hepatic impairment (Child-Pugh B) concomitantly receiving strong CYP3A inhibitors (see full prescribing information). Increases in Blood Pressure: Mirabegron can increase blood pressure. Blood pressure should be measured at baseline and periodically during treatment with Betmiga, especially hypertensive patients. Data are limited in patients with stage 2 hypertension (systolic blood pressure ≥ _160 mm Hg or diastolic blood pressure ≥ _100 mm Hg). In two, randomized, placebo-controlled, healthy volunteer studies, Betmiga was associated with dose-related increases in supine blood pressure. In these studies, at the maximum recommended dose of 50 mg, the mean maximum increase in systolic/diastolic blood pressure was approximately 3.5/1.5 mmHg greater than placebo. In contrast, in OAB patients in clinical trials, the mean increase in systolic and diastolic blood pressure at the maximum recommended dose of 50 mg was approximately 0.5 - 1 mmHg greater than placebo. Worsening of preexisting hypertension was reported infrequently in Betmiga patients. Patients with congenital or acquired QT prolongation: Betmiga, at therapeutic doses, has not demonstrated clinically relevant QT prolongation in clinical studies (see full prescribing information). However, since patients with a known history of QT prolongation or patients who are taking medicinal products known to prolong the QT interval were not included in these studies, the effects of mirabegron in these patients is unknown. Caution should be exercised when administering mirabegron in these patients. Patients with bladder outlet obstruction and patients taking antimuscarinics medications for OAB: 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 patients treated with Betmiga; however, Betmiga should be administered with caution to patients with clinically significant BOO. Betmiga should also be administered with caution to patients taking antimuscarinic medications for the treatment of OAB. **Interactions:** Inhibitory effect on the metabolism of CYP2D6 substrates. Betmiga is a moderate and time-dependent inhibitor of CYP2D6 and weak inhibitor of CYP3A. Increased AUC in the presence of the strong inhibitor of CYP3A/P-gp ketoconazole. Caution if co-administered with medicines with a narrow therapeutic index and significantly metabolised by CYP2D6. When initiating in combination with digoxin the lowest dose for digoxin should be prescribed and serum digoxin should be monitored. **Undesirable Effects:** Summary of the safety profile: The safety of Betmiga was evaluated in 8433 patients with OAB, of which 5648 received at least one dose of mirabegron in the phase 2/3 clinical program, and 622 patients received Betmiga for at least 1 year (365 days). In the three 12-week phase 3 double blind, placebo controlled studies, 88% of the patients completed treatment with Betmiga, and 4% of the patients discontinued due to adverse events. Most adverse reactions were mild to moderate in severity. The most common adverse reactions reported for patients treated with Betmiga 50 mg during the three 12- week phase 3 double blind, placebo controlled studies are tachycardia and urinary tract infections. The frequency of tachycardia was 1.2% in patients receiving Betmiga 50 mg. Tachycardia led to discontinuation in 0.1% patients receiving Betmiga 50 mg. The frequency of urinary tract infections was 2.9% in patients receiving Betmiga 50 mg. Urinary tract infections led to discontinuation in none of the patients receiving Betmiga 50 mg. Serious adverse reactions included atrial fibrillation (0.2%). Adverse reactions observed during the 1-year (long term) active controlled (muscarinic antagonist) study were similar in type and severity to those observed in the three 12-week phase 3 double blind, placebo controlled studies. Tabulated list of adverse reactions: The table below reflects the adverse reactions observed with mirabegron in the three 12-week phase 3 double blind, placebo controlled studies. The frequency of adverse reactions is defined as follows: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. Infections and infestations: *Common:* Urinary tract infection; *Uncommon:* Vaginal infection Cystitis. Psychiatric disorders: *Not known:* Insomnia (observed during post-marketing experience). Eye disorders: *Rare:* Eyelid oedema. Cardiac disorders: *Common:* Tachycardia; *Uncommon:* Palpitation, Atrial fibrillation. Vascular disorders: *Very rare:* Hypertensive crisis (observed during post-marketing experience). Gastrointestinal disorders: *common:* Nausea (observed during post-marketing experience), Constipation (observed during post-marketing experience), Diarrhoea (observed during post-marketing experience); *Uncommon:* Dyspepsia, Gastritis; *Rare:* Lip oedema. Skin and subcutaneous tissue disorders: *Uncommon:* Urticaria, Rash. Rash macular, Rash popular, Pruritus; *Rare:* Leukocytoclastic, vasculitis, Purpura Angioedema (observed during post-marketing experience). Musculoskeletal and connective tissue disorders: *Uncommon:* Joint swelling. Reproductive system and breast disorders: *Uncommon:* Vulvovaginal, pruritus. Investigations: *Uncommon:* Blood pressure increased, GGT increased, AST increased, ALT increased. Renal and urinary disorders: *Rare:* Urinary retention (observed during post-marketing experience). Nervous system disorders: *Common:* Headache (observed during post-marketing experience), Dizziness (observed during post-marketing experience). **Packs:** 30 prolonged-release tablets of 25 mg, 50 mg. **API date:** 29th Jan 2018

Full prescribing information available upon request.

For healthcare professionals only.

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Astellas Pharma Malaysia Sdn Bhd, Suite 18.05, Level 18, Centrepoint North Tower,
Mid Valley City, Lingkaran Syed Putra, 59200 Kuala Lumpur
Tel: +603-2202 6999 **Fax:** +603-2202 6988

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