This policy statement is approved by Halton, Knowsley, Liverpool, South Sefton, Southport and Formby, St Helens, Warrington, and Wirral CCGs

Ha Kn Li SS SF SH Wa Wi

PAN MERSEY APC

PAN MERSEY AREA PRESCRIBING COMMITTEE
PRESCRIBING POLICY STATEMENT
REF: PS82 FINAL
APC BOARD DATE: 30-JUL-2014

NHS
Pan Mersey
Area Prescribing Committee

MIRABEGRON prolonged-release tablets (Betmiga®▼)

GREEN

The Pan Mersey Area Prescribing Committee recommends the prescribing of MIRABEGRON prolonged-release tablets (Betmiga®▼) for overactive bladder syndrome (OAB) in accordance with NICE TA290.

NICE TA 290 recommends mirabegron (Betmiga®▼) as an option only for people in whom anti-muscarinic drugs are contra-indicated, clinically ineffective, or have unacceptable side effects. It is licensed for the symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with OAB.[1,3]

Current treatment includes non-pharmacological approaches e.g. life style advice, pelvic floor exercises and bladder training, or pharmacological treatment.

First line treatment in women includes oxybutynin (immediate release), or tolterodine (immediate release), or darifenacin (once daily). If the first treatment for OAB or mixed urinary incontinence is not effective or well tolerated, offer another drug with the lowest acquisition cost[4] i.e. try another different antimuscarinic.

These treatment options are outlined in:

- Urinary incontinence in women: The management of urinary incontinence in women. NICE Clinical Guideline 171, 2013.
- Lower urinary tract symptoms: The management of lower urinary tract symptoms in men. NICE Clinical Guideline 97, 2010.

Note: Patients who are not eligible for treatment under this policy may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. If appropriate an exceptional funding request will be required following the usual locally defined process.

MIRABEGRON prolonged-release tablets (Betmiga® ▼)

EFFECTIVENESS[2]

Mirabegron is a first in class potent and selective beta-3-adrenoceptor agonist which is dominant in detrusor muscle, and together with beta-3- adrenoceptor stimulation in the bladder trigone causes flattening and lengthening of the bladder base, facilitating urine storage.

The efficacy of mirabegron has been assessed in patients with symptomatic OAB in two phase three randomised, double-blind, parallel group, placebo-controlled 12 week multi centre studies and an active-controlled (tolterodine) 12-month study. Participants were required to be aged ≥18 years with symptoms of OAB for ≥3 months. The primary endpoints assessed were change from baseline to final visit in the mean number of incontinence episodes/24 hours and micturitions/24 hours based on a 3-day micturition diary. Key secondary endpoints included changes in the mean volume voided per micturition, and changes in the mean number of incontinence episodes/micturitions/24 hours at week 4, based on a 3-day micturition diary. Additional secondary endpoints were the effect of treatment on urgency symptoms and quality of life (QoL) measures. In all studies the mean age of participants was about 60 years and approximately 70% were female.

Mirabegron was more effective than placebo in reducing the mean number of incontinence and micturition episodes in 24 hours. Improvements in QoL scores were significant for tolterodine and mirabegron compared with placebo.

SAFETY[3]

The safety of mirabegron 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 mirabegron for at least 1 year. In the three 12-week phase 3 double blind, placebo controlled studies, 88% of the patients completed treatment with mirabegron, 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 are tachycardia and urinary tract infections (UTI). The frequency of tachycardia was 1.2% and led to discontinuation in 0.1%. The frequency of UTI was 2.9% and led to no discontinuation.

Serious adverse reactions included atrial fibrillation (0.2%). Adverse reactions observed during the 1-year (long term) active controlled muscarinic antagonist (tolterodine) study were similar in type and severity to those observed in the three 12-week phase 3 double blind, placebo controlled studies.

Refer to summary of product characteristics (SPC) for further details: www.medicines.org.uk

COST

Per 28 days (or 30 days for*) BNF May 2014

Mirabegron 25mg, 50mg	£29*
Oxybutynin IR 2.5mg, 5mg	£5 - £21.99
Oxybutynin MR 5mg,10mg	£13.77 - £27.54*
Solifenacin 5mg, 10mg	£27.62 - £35.91*
Tolterodine IR 1mg, 2mg	£4.35 - £30.56
Tolterodine MR 4mg	£20.62 – £25.78

NICE estimates that with 20% future use, it will cost £40,800 per 100,000 population.[1]

The costing template includes a number of assumptions and variables e.g. discontinuation rate. It also assumes that 50% of patients will have mirabegron started by a consultant. It does not include savings e.g. reduction of incontinence pad use, or reduced number of people requiring Botox.[1]

PATIENT FACTORS[3]

Mirabegron has not been studied in patients with end stage renal disease (GFR < 15 mL/min/1.73 m^2 or patients requiring haemodialysis) or severe hepatic impairment (Child-Pugh Class C) and it is therefore not recommended for use in these patient populations. A dose reduction table is provided in the SPC for mirabegron for patients with renal or hepatic impairment, with or without concomitant strong CYP3A inhibitors (e.g. itraconazole, ketoconazole, ritonavir, clarithromycin).

Care is also required in hypertensive patients (> 160/100mmHg) and patients with congenital or acquired QT prolongation.

It is not recommended below 18 years, during pregnancy, breastfeeding, or in women of childbearing potential not using contraception.

PRESCRIBING INFORMATION & IMPLEMENTATION NOTES

Mirabegron 25mg or 50mg is to be taken orally once daily with or without food and is not to be chewed, divided or crushed. As above, dose reduction is required in renal or hepatic impairment.

REFERENCES

1. National Institute for Health and Clinical Excellence. TA 290. Mirabegron for treating symptoms of overactive bladder. June 2013 http://publications.nice.org.uk/mirabegron-for-treating-symptoms-of-overactive-bladder-ta290. Accessed 03/06/14
2. Regional Drugs & Therapeutic Centre. New Drug Evaluation No. 123: Mirabegron (February 2013)
3. Astellas Pharma Ltd. Summary of Product Characteristics: Betmiga 25mg & 50mg prolonged-release tablets. http://www.medicines.org.uk/emc Accessed 03/06/14
4. National Institute for Health and Clinical Excellence. CG 171. Urinary incontinence in women: The management of urinary incontinence in women. September 2013. http://publications.nice.org.uk/urinary-incontinence-cg171. Accessed 03/06/14