

## NHS DORSET CLINICAL COMMISSIONING GROUP

### COMMISSIONING STATEMENT ON THE USE OF MIRABEGRON FOR TREATING THE SYMPTOMS OF OVERACTIVE BLADDER.

The National Institute for Health and Care Excellence (NICE) Technology Appraisal no. 290 states that Mirabegron is recommended as an option for treating the symptoms of overactive bladder only for people in whom antimuscarinic drugs are contraindicated or clinically ineffective, or have unacceptable side effects.

The CCG will commission mirabegron in accordance with NICE TA 290 and the marketing authorization, as a “green” drug, where antimuscarinic drugs are contraindicated or have been used in accordance with the relevant NICE clinical guideline (see below) and have been proved to be clinically ineffective, or have unacceptable side effects.

#### BACKGROUND INFORMATION

##### 1. MARKETING AUTHORISATION AND MODE OF ACTION

- 1.1 Within the summary of product characteristics the therapeutic indication for mirabegron (Betmiga®) is stated as:

*Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome.*

- 1.2 It is a beta-3-adrenoceptor agonist, which activates beta-3-adrenoceptors causing the bladder to relax, which helps it to fill and also to store urine. It is administered orally. Mirabegron will be available as 25 mg and 50 mg tablets, with the recommended dose being 50 mg daily, and 25 mg if there is renal or hepatic impairment.
- 1.3 The summary of product characteristics lists the following adverse reactions for mirabegron: urinary tract infection, tachycardia, vaginal infection, cystitis, palpitation, atrial fibrillation, dyspepsia, gastritis, urticaria, rash, rash macular, rash popular, pruritus, joint swelling, vulvovaginal pruritis, increased blood pressure, increased gamma-glutamyl transpeptidase, increased aspartate aminotransferase, increased alanine aminotransferase, eyelid oedema, lip oedema, leukocytoclastic vasculitis and purpura (rash). For full details of adverse reactions and contraindications, see the summary of product characteristics.
- 1.4 The safety and efficacy of mirabegron in children below 18 years of age have not yet been established.
- 1.5 ▼ This medicinal product has a black triangle and is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions via the MHRA Yellow Card scheme at: <https://yellowcard.mhra.gov.uk/>

## 2. NICE APPRAISALS

### TA 290: MIRABEGRON FOR TREATING SYMPTOMS OF OVERACTIVE BLADDER

Mirabegron is recommended as an option for treating the symptoms of overactive bladder only for people in whom antimuscarinic drugs are contraindicated or clinically ineffective, or have unacceptable side effects.

NICE published an update to their guidance on urinary incontinence in women in September 2013, Clinical Guideline no. 171 provides the following guidance for pharmacological therapies:

#### General principles when using drugs for OAB and UI

When offering antimuscarinic drugs to treat OAB always take account of the woman's coexisting conditions (for example, poor bladder emptying), use of other existing medication affecting the total anticholinergic load and risk of adverse effects.

Before antimuscarinic drug treatment starts, discuss with women:

- the likelihood of success and associated common adverse effects, **and**
- the frequency and route of administration, **and**
- that some adverse effects such as dry mouth and constipation may indicate that treatment is starting to have an effect, **and**
- that they may not see the full benefits until they have been taking the treatment for 4 weeks.

Prescribe the lowest recommended dose when starting a new OAB drug treatment.

If a woman's OAB drug treatment is effective and well tolerated, do not change the dose or drug.

#### Choosing drugs for OAB and UI

Do not use Flavoxate, propantheline and imipramine for the treatment of UI or OAB in women.

Do not offer oxybutynin (immediate release) to frail older women (The Guideline Development Group defined 'frail older women' as those with multiple comorbidities, functional impairments such as walking or dressing difficulties and any degree of cognitive impairment.)

Offer one of the following choices first to women with OAB or mixed UI:

- oxybutynin (immediate release), **or**
- tolterodine (immediate release), **or**
- darifenacin (once daily preparation).

If the first-line treatment for OAB or mixed UI is not well tolerated, offer another drug with the lowest acquisition cost. (see Appendix One)

Offer a transdermal antimuscarinic only to women unable to tolerate oral medication.

## Reviewing drug treatment for OAB and UI

- Offer a face-to-face or telephone review 4 weeks after the start of each new OAB drug treatment. Ask the woman if she is satisfied with the therapy and
  - if improvement is optimal, continue treatment, **or**
  - if there is no or suboptimal improvement or intolerable adverse effects change the dose, or try an alternative OAB drug, and review again 4 weeks later.
- Offer review before 4 weeks if the adverse events of OAB drug treatment are intolerable.
- Offer referral to secondary care if the woman does not want to try another drug, but would like to consider further treatment
- Offer a further face-to-face or telephone review if a woman's condition stops responding optimally to treatment after an initial successful 4-week review
- Offer referral to secondary care if OAB drug treatment is not successful.
- Review women who remain on long-term drug treatment for UI or OAB annually in primary care (or every 6 months for women over 75).

The use of desmopressin may be considered specifically to reduce nocturia in women with UI or OAB who find it a troublesome symptom. Use particular caution in people with cystic fibrosis and avoid in those over 65 years of age or with cardiovascular disease or hypertension.

Do not use Duloxetine as a first-line treatment for women with predominant stress UI. Do not routinely offer Duloxetine as a second-line treatment for women with stress UI, although it may be offered as second-line therapy if women prefer pharmacological to surgical treatment or are not suitable for surgical treatment. If duloxetine is prescribed, women should be counselled about its adverse effects.

Do not offer systemic hormone replacement therapy for the treatment of UI.

Offer intravaginal oestrogens for the treatment of OAB symptoms in postmenopausal women with vaginal atrophy.

**NICE CG 97 – lower urinary tract symptoms** states offer an anticholinergic to men to manage the symptoms of OAB.

### **NICE CG 148 – lower urinary tract symptoms:**

Offer antimuscarinic drugs to people with:

- spinal cord disease (for example, spinal cord injury or multiple sclerosis) **and**
- symptoms of an overactive bladder such as increased frequency, urgency and incontinence.

Consider antimuscarinic drug treatment in people with:

- conditions affecting the brain (for example, cerebral palsy, head injury or stroke) **and**
- symptoms of an overactive bladder.

Consider antimuscarinic drug treatment in people with urodynamic investigations showing impaired bladder storage.

Monitor residual urine volume in people who are not using intermittent or indwelling catheterisation after starting antimuscarinic treatment.

When prescribing antimuscarinics, take into account that:

- antimuscarinics known to cross the blood-brain barrier (for example, oxybutynin) have the potential to cause central nervous system-related side effects (such as confusion)
- antimuscarinic treatment can reduce bladder emptying, which may increase the risk of urinary tract infections
- antimuscarinic treatment may precipitate or exacerbate constipation

### 3. POLICY

- 3.1 The CCG will commission mirabegron in accordance with NICE TA 290 and the marketing authorization as a “green” drug where antimuscarinic drugs are contraindicated or have been used in accordance with the NICE clinical guidelines described above and have been proved to be clinically ineffective, or have unacceptable side effects.

### References

1. NICE TA 290  
[www.publications.nice.org.uk/mirabegron-for-treating-symptoms-of-overactive-bladder-ta290](http://www.publications.nice.org.uk/mirabegron-for-treating-symptoms-of-overactive-bladder-ta290).
2. NICE urinary incontinence (update)  
[www.nice.org.uk/nicemedia/live/13019/62660/62660.pdf](http://www.nice.org.uk/nicemedia/live/13019/62660/62660.pdf)
3. NICE CG 97  
[www.publications.nice.org.uk/lower-urinary-tract-symptoms-cg97](http://www.publications.nice.org.uk/lower-urinary-tract-symptoms-cg97)
4. NICE CG 148.  
[www.publications.nice.org.uk/urinary-incontinence-in-neurological-disease-cg148](http://www.publications.nice.org.uk/urinary-incontinence-in-neurological-disease-cg148)

Approved by (committee)	Bournemouth, Dorset and Poole Health Technologies Forum		
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## Appendix One

Comparative costs of mirabegron and antimuscarinic drugs and duloxetine (based on Drug Tariff July 2013 or BNF no.65)

Drug	Dose regimen	Patent expiry (where known)	Annual Cost (£)
Oxybutynin tablets (non-proprietary)	2.5mg twice daily (initial dose in elderly) to 5mg four times daily	Generic	£27 to £87
Tolterodine tablets (non-proprietary)	2mg twice daily	Generic	£58
Trospium (extended release) capsules	60mg daily		£300
Trospium tablets (non-proprietary)	20mg twice daily	Generic	£316
Propiverine m/r capsules	30mg daily		£319
Fesoterodine tablets	4 to 8 mg daily	2022	£336
Tolterodine (extended release)	4mg daily		£336
Mirabegron tablets	50mg daily		£352
Oxybutynin transdermal patch	1 patch twice weekly		£354
Duloxetine capsules	40mg twice daily		£482
Propiverine tablets (non-proprietary)	15mg daily to 60mg daily	Generic	£117 to £469
Oxybutynin (extended release) tablets	5 to 20mg daily		£167 to £670
Darifenacin tablets	7.5mg to 15mg daily	2015	£332
Solifenacin tablets	5 to 10 mg daily	2018	£336 to £437