

Overactive Bladder (OAB) Drugs Optimisation and Mirabegron

Background Information

- This guidance has been produced as a local initiative to optimise the management of female patients with urinary incontinence and streamline the use of drugs for the treatment of overactive bladder.
- This guidance includes recommendations for the use of Mirabegron (a 'novel' action OAB drug approved by NICE TA290 in July 2013) to ensure it is used appropriately within the revised treatment pathway.
- Urinary incontinence is a common problem, with a mean annual incidence of 1 to 9 per cent and estimates of remission ranging from 4 to 30 per cent.²
- NICE guidelines² recommend bladder training (for a minimum of 6 weeks) as first-line treatment.
- If this is not effective, antimuscarinics should be offered with regular review.
- Anecdotal evidence suggests medication is often continued long-term without consideration of effectiveness, adverse effects or patients' perceptions of success.
- With this in mind, there is a need to ensure that OAB drug use is optimised. Some patients may only need to take OAB drugs when going out and may not need or want to take them when they are at home.
- Expenditure on OAB drugs in NHS Wiltshire is substantial, from Feb 15 to Jan 16 it was: £1,310,334 .

The following advice is now recommended by our local urology teams:

Patients already receiving treatment with an OAB drug (including those with catheters)

- **1: All patients who have been taking an OAB for at least 6 months OFFER a trial without treatment for 4 weeks** (exclusions include patients with neurological conditions such as multiple sclerosis or difficult social circumstances). A questionnaire at the end of this document will help the patient assess if continuation of drug treatment is required after the 4 weeks. Some patients may prefer to take their OAB 'as required' to suit their daily activities and reduce side effects. Tolterodine is fast acting and so may be a good option for PRN use.
- **2: Remove OABs from 'repeat' item prescriptions for patients who no longer require regular OABs.**

Newly diagnosed patients

- **1: Initial investigations** Comprehensive history of symptoms & frequency and categorisation of incontinence as per NICE Guidance CG171 together with a midstream urine specimen and identification of predisposing and precipitating factors.
- **2: Training methods**
 - **Urge/frequency or mixed urinary incontinence:** Advise about lifestyle changes (fluid intake, weight loss, caffeine reduction) and bladder training methods which may help improve symptoms. Try for a minimum of 6 weeks & if ineffective, consider addition of drug treatment.
 - **Stress or mixed urinary incontinence:** Pelvic floor muscle training (for at least 3 months) under the care of community continence team. If this is not effective refer for specialist assessment.
 - *People with "mixed" urinary incontinence should undertake both bladder & pelvic floor muscle training.*
- **3: Drug treatments**
 - **Offer a trial treatment with an OAB drug for 1 month.** Titrate doses as necessary and reassess **at 4 weekly intervals** until stabilised. **If no benefit after 1 month, stop treatment and try the next drug option (in the table overleaf).**
 - Please note up to 23% of patients will need to try another drug after oxybutynin due to tolerability problems. It is currently a first line option according to NICE CG171. **Offer a trial without treatment every 6 months.**
- **4: Treatment failure** after the above drug interventions consider referral to appropriate specialist.
- See NICE urinary incontinence in women pathway:
- <http://pathways.nice.org.uk/pathways/urinary-incontinence-in-women/urinary-incontinence-in-women-overview>

Treatment Options

	Drug	Traffic light	28 day cost
First Line:	Tolterodine tablets 2mg twice daily	Green	£2.54
First Line:	Oxybutynin tablets 5mg twice daily (<i>not usually tolerated very well</i>) N.B. NOT in frail elderly patients	Green	£2.14
First Line:	Oxybutynin MR tablets 5mg (increasing to 10mg) once daily N.B. NOT in frail elderly patients	Green	£12.85 (5mg) £25.70 (10mg)
Subsequent choices: If the first treatment for OAB or mixed UI is not effective or well-tolerated, offer the drug with the lowest acquisition cost (as per NICE CG171) as follows:			
Second line:	Trospium 20mg BD capsules prescribed as the brand FLOTROS	Green	£14.44
Third Line:	Solifenacin tablets 5mg once a day increasing to 10mg once a day if necessary.	Green	£25.78 (5mg) £33.52 (10mg)
Fourth Line:	Mirabegron tablets 50mg once daily (25mg renal/hepatic impairment). <i>Mirabegron can be used FIRST line ONLY in patients contra-indicated to antimuscarinics – glaucoma, myasthenia gravis, GI obstruction (see SPC for full list) or specific problems with dry mouth e.g. Sjogren's syndrome</i>	Green	£27.07 (both strengths)

NOTE: OAB drugs are not licensed to be used in combination in the UK. There is interest in using mirabegron in combination with other OAB drugs due to its different mode of action.

It is currently being investigated in phase III clinical trials in combination with solifenacin (http://www.ukmi.nhs.uk/applications/ndo/record_view.asp?newDrugID=6067), but has not got a license yet.

Mirabegron - key facts

- Mirabegron is contraindicated in patients with severe uncontrolled hypertension (systolic blood pressure ≥ 180 mm Hg or diastolic blood pressure ≥ 110 mm Hg, or both)
- Blood pressure should be measured before starting treatment and monitored regularly during treatment, especially in patients with hypertension. For further information see Drug Safety Update reference below.
- Please report suspected side effects to mirabegron on a Yellow Card (see BNF)
- Is a first-in-class beta-3 adrenoceptor (β_3 -AR) agonist licensed for the symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence.
- There have been no trials directly comparing mirabegron and current therapies.
- Appears to offer a treatment option of **similar** efficacy to current antimuscarinic therapies
- Appears to have a **different** side effect profile to antimuscarinics.
- Is recommended by **NICE TA290**¹ as an option for symptoms of overactive bladder **ONLY** for people in whom antimuscarinics are contraindicated or clinically ineffective, or have unacceptable side effects.
- Contra indicated in end stage renal disease $\text{GFR} < 15 \text{ml/min/1.73m}^2$, severe uncontrolled hypertension, severe hepatic impairment, pregnancy.
- Interactions: drugs that prolong QT interval, digoxin, dabigatran, Side Effects – UTI, tachycardia. See SPC for full list.

References:

- 1.) Drug Safety Update. Mirabegron (Betmiga ▼): risk of severe hypertension and associated cerebrovascular and cardiac events October 2015. <https://www.gov.uk/drug-safety-update/mirabegron-betmiga-risk-of-severe-hypertension-and-associated-cerebrovascular-and-cardiac-events>
- 2.) NICE TA290 Mirabegron for treating symptoms of overactive bladder June 2013 <https://www.nice.org.uk/guidance/ta290>
- 3.) NICE CG171 Urinary incontinence in women October 2013 <http://guidance.nice.org.uk/CG171>

Further information:

BNF: <http://www.medicinescomplete.com/mc/bnf/current/PHP5068-urinary-incontinence.htm>

Resources for patients: Useful resources for patients can be found here: <http://www.patient.co.uk/health/Overactive-Bladder-Syndrome.htm>
<https://www.bladderandbowelfoundation.org/bladder/for-women/>

Annex 1 – Questionnaire to patients

Stage 1: Prior to trial of stopping antimuscarinic

<p>Choose the statement which best describes how bothered the patient is by each symptom during the last 4 weeks</p> <p><i>Not at all A little bit Quite a bit A great deal A very great deal</i></p>
<p>During the past 4 weeks, how bothered were you by a sudden or uncomfortable urge to urinate</p> <p><i>Not at all A little bit Quite a bit A great deal A very great deal</i></p>
<p>During the past 4 weeks, how bothered were you by accidental loss of small amounts of urine</p> <p><i>Not at all A little bit Quite a bit A great deal A very great deal</i></p>
<p>During the past 4 weeks, how bothered were you by waking up at night because you had to go to the toilet</p> <p><i>Not at all A little bit Quite a bit A great deal A very great deal</i></p>
<p>During the past 4 weeks, how bothered were you by urine loss associated with a strong desire to urinate</p> <p><i>Not at all A little bit Quite a bit A great deal A very great deal</i></p>
<p>Which of the following statements describes your bladder condition best at the moment?</p> <p><i>Does not cause me any problems at all Causes me some minor problems Causes me (some) moderate problems</i> <i>Causes me severe problems Causes me many severe problems</i></p>
<p>How often do you take your medicine?</p> <p><i>Daily Most days Infrequently Only when going out Not taking</i></p>
<p>Have you had any advice on bladder training or how you can change your lifestyle to improve symptoms?</p> <p><i>Yes No Not Sure</i></p>

Stage 2: Follow up after trial of stopping antimuscarinic

<p>After stopping medication, how bothered were you by a sudden or uncomfortable urge to urinate</p> <p><i>Not at all A little bit Quite a bit A great deal A very great deal</i></p>
<p>After stopping medication, how bothered were you by accidental loss of small amounts of urine</p> <p><i>Not at all A little bit Quite a bit A great deal A very great deal</i></p>
<p>After stopping medication, how bothered were you by waking up at night because you had to go to the toilet</p> <p><i>Not at all A little bit Quite a bit A great deal A very great deal</i></p>
<p>After stopping medication, how bothered were you by urine loss associated with a strong desire to urinate</p> <p><i>Not at all A little bit Quite a bit A great deal A very great deal</i></p>
<p>Which of the following statements describes your bladder condition best at the moment?</p> <p><i>Does not cause me any problems at all Causes me some minor problems Causes me (some) moderate problems</i> <i>Causes me severe problems Causes me many severe problems</i></p>
<p>Did you need to restart your medicine?</p> <p><i>Yes No</i></p>