

OAB in neurological disease is outside the scope of this guideline but is covered in [NICE clinical guideline 148](#)

**INITIAL ASSESSMENT AND CONSERVATIVE MANAGEMENT** e.g. lifestyle interventions (see page 3), bladder training for a minimum of 6 weeks

### BEFORE STARTING OAB DRUGS<sup>1</sup>

When offering antimuscarinic drugs to treat OAB always take account of:

- coexisting conditions (for example, **poor bladder emptying, constipation, glaucoma**)
- use of other existing medication affecting the total antimuscarinic load
- risk of adverse effects.

Discuss with patient:

- 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.

Consider bladder training programme in combination with an OAB drug if frequency is a troublesome symptom.

Prescribe the **lowest** recommended dose when starting a new OAB drug to reduce the likelihood of side-effects. (see individual [summaries of product characteristics](#) for full prescribing information).

### CHOOSING OAB DRUGS

#### FIRST LINE DRUG TREATMENT

- **Oxybutynin (IR)** initially 5 mg two to three times daily. OR
- **Tolterodine (IR)** 2 mg twice daily; reduce to 1 mg twice daily if necessary to minimise side effects. OR (for a once-daily preparation)
- **Darifenacin (MR)** 7.5 mg taken once daily.

Where an initial first line drug is ineffective or not tolerated consider an alternative first line drug.

#### Do NOT use:

- Flavoxate, propantheline or imipramine.
- Oxybutynin (IR) in frail older patients
- Duloxetine should not be routinely used in the treatment of OAB. It may be offered as 2nd line therapy for stress urinary incontinence for women who decline/are not suitable for surgery
- Complementary therapies

Antimuscarinics contraindicated

#### Mirabegron

Prescribing should be in accordance with [NICE TA 290](#), see [Pan Mersey Area Prescribing Committee Policy Statement](#)

### REVIEW

Offer a face-to-face or telephone review 4 weeks after the start of each new OAB drug treatment or before 4 weeks if adverse events of OAB drug are intolerable, and until stable

Review patients on **long-term treatment** annually (or every 6 months if over 75).

If treatment is effective and well-tolerated, do not change the dose or drug

If the patient suffers unacceptable side effects

#### Mirabegron

Prescribing should be in accordance with [NICE TA 290](#), see [Pan Mersey Area Prescribing Committee Policy Statement](#)

OR

Consider **transdermal oxybutynin** if unable to tolerate oral medication

Unsuccessful or long-term treatment

Unsuccessful or long-term treatment

If medication is ineffective

#### SECOND LINE DRUG TREATMENT

Consider another drug with the **lowest acquisition cost**

- **Fesoterodine MR**
- **Mirabegron** (in accordance with [NICE TA 290](#), see [Pan Mersey Area Prescribing Committee Policy Statement](#))
- **Tolterodine MR**
- **Trospium IR**
- **Solifenacin**

### REFERRAL TO SECONDARY CARE e.g.

If conservative measures fail or if a patient does not want to try another drug or if a patient wishes to discuss the options for further management (non-therapeutic interventions and invasive therapy)

## OTHER CONSIDERATIONS

### ASSOCIATED CONDITIONS IN WOMEN:<sup>1</sup>

Offer **intravaginal oestrogens** (but not systemic hormone replacement therapy) for the treatment of OAB symptoms in postmenopausal women with vaginal atrophy. Intravaginal oestrogens can be used in women with an intact uterus without the need for a progestogen to be added<sup>8</sup>.

### INVASIVE THERAPY FOR OAB:<sup>1</sup>

#### First line:

Bladder wall injection with **botulinum toxin A** can be considered after a Multidisciplinary Team (MDT) review for patients with OAB caused by proven detrusor overactivity that has not responded to conservative management (including OAB drug therapy).

- Botox® is the only brand currently licensed for this indication. The drug has **RED** status in Pan Mersey. Therefore prescribing should be initiated by specialists only and ongoing prescribing should be retained within secondary care.
- Botulinum toxin A should only be started if a patient has been trained in clean intermittent catheterisation and has performed the technique successfully, and is able and willing to perform clean intermittent catheterisation on a regular basis for as long as needed.
- NICE recommends a dose of 200 units when offering botulinum toxin A but 100 units of botulinum toxin A could be considered for patients who prefer a dose with a lower chance of catheterisation and accept a reduced chance of success. Some local specialist clinics use a dose of 100 units for idiopathic overactive bladder syndrome and 200 units for neurogenic overactive bladder syndrome.
- If botulinum toxin A treatment is effective, patients should be followed up at 6 months or sooner if symptoms return for repeat treatment without an MDT referral.
- Patients should be provided with information on when to self-refer for prompt specialist review if symptoms return following a botulinum toxin A procedure. Repeat treatment should be given as necessary.
- Botulinum toxin B is NOT recommended for patients with proven detrusor overactivity.

### NOCTURNAL SYMPTOMS:<sup>1,2</sup>

- Consider oral **desmopressin** to reduce nocturia in patients who find it a troublesome symptom if other medical causes have been excluded and they have not benefited from other treatments.
- Use particular caution in patients with cystic fibrosis and avoid in those over 65 years with cardiovascular disease or hypertension.
- Symptomatic hyponatraemia is more likely to occur soon after treatment initiation. Pre-treatment and early post-treatment (3 days after the first dose) serum sodium monitoring is recommended. If serum sodium is reduced to below the normal range, stop desmopressin treatment.
- Advise restriction of night-time intake of fluid to reduce the risk of fluid retention and water intoxication.<sup>3</sup>

### URINARY RETENTION DUE TO BENIGN PROSTATIC HYPERPLASIA (BPH) IN MEN:<sup>2</sup>

Treatment of Lower Urinary Tract Symptoms (LUTS) should be in accordance to NICE CG 97

- NICE recommends an alpha blocker (tamsulosin, alfuzosin, doxazosin or terazosin) in men with moderate to severe LUTS. The alpha blockers recommended by the Pan Mersey Area Prescribing Committee (APC) are [tamsulosin](#), [alfuzosin](#), [doxazosin \(immediate release\)](#) or [terazosin](#).
- An antimuscarinic drug should be considered as well as an alpha blocker in men who still have storage symptoms after treatment with an alpha blocker alone.  
**NICE guidance<sup>2</sup> on the management of LUTS in men does not give recommendations on choice of antimuscarinic drugs and therefore the choice of OAB drugs has been extrapolated from the NICE CG 171 Urinary incontinence: the management of urinary incontinence in women.**<sup>1</sup> Refer to the flowchart on the front page for recommended OAB drug choices.

#### Important Prescribing Recommendation

**Vesomni® - the Pan Mersey APC does NOT recommend the routine use of this drug in primary care.**

- Vesomni is a fixed-dose combination product containing solifenacin 6mg and tamsulosin MR 400 micrograms.
- Most of the evidence for its use comes from the NEPTUNE trial<sup>4</sup>. This was a short-term (12 weeks) phase 3 study that compared the combination product to tamsulosin alone or placebo in males with moderate to severe storage symptoms; from this, combination therapy emerged as effective in improving symptom control in males with moderate to severe storage symptoms and was generally well tolerated.
- In patients for whom concomitant use of solifenacin succinate and tamsulosin hydrochloride is appropriate, Vesomni® allows administration of a single tablet at a lower cost compared to the individual components administered separately. The saving is mainly the price of generic tamsulosin MR 400 mcg capsules (£3.93 for 30 capsules<sup>5</sup>) which is currently falling gradually. Vesomni® and the separate agent solifenacin 5mg (Vesicare®) are priced the same at £27.62<sup>5</sup> for 30 tablets.
- **Darifenacin** is a selective antimuscarinic drug similar to solifenacin and a recommended **first line treatment**<sup>1</sup>. Darifenacin is now off patent so the price of darifenacin is expected to fall as generic alternatives become available. Darifenacin is therefore the preferred selective antimuscarinic drug.
- The Pan Mersey APC has concluded that endorsing Vesomni® will continue to inappropriately promote solifenacin first line.

Advice on fluid intake and lifestyle <sup>1,3</sup>			Important Points from NICE CG171 <sup>1</sup>	
<p><b>Fluid intake</b> Consider advising modification of high or low fluid intake. Both excessive and inadequate fluid intake may lead to lower urinary tract symptoms; this should be considered on an individual basis.</p> <p><b>Lifestyle</b> advice may include:</p> <ul style="list-style-type: none"> <li>⇒ A trial of caffeine reduction - there is some evidence that caffeine reduction leads to less urgency and frequency when used in addition to bladder training</li> <li>⇒ Smoking cessation</li> <li>⇒ Weight reduction if body mass index is 30 kg/m<sup>2</sup> or greater. There is evidence of an association between obesity and urinary incontinence (UI) or OAB, and in obese women weight reduction of at least 5% is associated with relief of UI symptoms</li> </ul>			<ul style="list-style-type: none"> <li>• NICE carried out a health economic analysis which showed that despite its higher discontinuation rate compared with other OAB drugs, oxybutynin IR was the most cost-effective option for first-line treatment due to its lower price and higher rates of effectiveness than all other drugs except tolterodine IR.</li> <li>• Trospium (extended release or MR), oxybutynin (MR), fesoterodine, oxybutynin topical gel, tolterodine (MR) and solifenacin had a zero per cent chance of being cost effective as first-line drugs. Since NICE CG171 was published trospium has reduced in cost.</li> <li>• Given the lack of difference in effectiveness between OAB drugs, the relative cost effectiveness was determined mostly by the difference in cost between the drugs. NICE guidance states that the more expensive drugs do not confer sufficient additional benefit (in terms of either continuation or continence) to justify their current higher cost. The Guideline Development Group considered that the arguments for recommending the most expensive OAB drugs as second-line treatment on the basis of improved side-effects profile were inadequate since these drugs had not been widely compared with other OAB drugs in head-to-head trials.</li> <li>• The review from original NICE guidelines in 2006 provided evidence that flavoxate, imipramine, other tricyclic antidepressants and propantheline offered little or no improvement and they were not recommended.</li> <li>• Patients should be told about the known side-effects of each antimuscarinic drug. Many of the side-effects are dose-related. Dry mouth is one of the most common adverse effects of all antimuscarinics. Reduced salivary secretions could result in dental caries, parodontosis or oral candidiasis.<sup>7</sup> Patients should maintain good oral hygiene and may require regular dental check-ups.</li> </ul>	
Cost Comparison			Common Serious Interactions with Antimuscarinics <sup>6</sup> <small>(these are interactions that are highlighted in the BNF)</small>	
Drug	Typical doses <sup>6</sup>	Cost per 28 days <sup>5,6</sup>	Itraconazole	<i>plasma concentration of solifenacin possibly increased by itraconazole</i>
Darifenacin MR tablets	7.5mg or 15mg daily	£25.48	Ritonavir	<i>plasma concentration of solifenacin possibly increased by ritonavir</i>
Fesoterodine MR tablets	4mg or 8mg daily	£25.78	Amiodarone	<i>increased risk of ventricular arrhythmias when tolterodine given with amiodarone</i>
Mirabegron tablets	50mg daily	£27.07	Disopyramide	<i>increased risk of ventricular arrhythmias when tolterodine given with disopyramide</i>
Oxybutynin IR tablets	5mg BD to TDS	£1.49-£2.24	Flecainide	<i>increased risk of ventricular arrhythmias when tolterodine given with flecainide</i>
Oxybutynin MR tablets	5mg or 10mg daily	£13.77-27.54	Sotalol	<i>increased risk of ventricular arrhythmias when tolterodine given with sotalol</i>
Oxybutynin 36mg patches	One patch twice weekly	£27.20		
Solifenacin tablets	5mg or 10mg daily	£25.78—£33.52		
Solifenacin 6mg + tamsulosin 400mcg MR tablets (Vesomni)	One daily	£25.78		
Tolterodine IR tablets	2mg BD	£1.81		
Tolterodine MR capsules	4mg daily	£25.78		
Trospium IR tablets	20mg BD	£12.14		
<p>This table does not imply therapeutic equivalence of drugs or doses. IR = immediate release MR = modified release All prices shown are correct at the time of writing.</p>				

## REFERENCES

1. NICE CG 171. Urinary incontinence in women: Management, September 2013
2. NICE CG 97. Lower urinary tract symptoms in men : management . May 2010
3. NICE Clinical Knowledge Summaries. Incontinence - urinary, in women. Last revised in June 2015
4. Philip van Kerrebroeck et al. Combination Therapy with Solifenacin and Tamsulosin Oral Controlled Absorption System in a Single Tablet for Lower Urinary Tract Symptoms in Men: Efficacy and Safety Results from the Randomised Controlled NEPTUNE Trial. *European Urology*, 2013; 64(6): 1003-1012
5. NHS Business Service Authority. Drug Tariff, Accessed 28 December 2016
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