Primary Care management of Overactive Bladder (OAB)

- All medicines for OAB have similar dose-related efficacy. More than one agent (up to three in succession) may need to be tried, due to different side effect profiles – trial of at least 28 days is suggested (NICE CG171, 2013/ NICE NG123, 2019).

- NICE recommends the most cost-effective agent is used—either tolterodine immediate release (IR) or oxybutynin IR.

- When similar dosage forms of OAB drugs are compared (IR to IR; SR to SR), the side effect profiles are similar. The IR formulations are generally associated with more anti-cholinergic side effects than the SR formulations which can affect compliance but significantly more expensive.

- Before commencing OAB drug treatment discuss:
  - 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 the patient may not see the full benefit until they have been taking the treatment for 4 weeks.
  - The long-term effects of anticholinergic medicines on cognitive function are uncertain.

- Take into consideration the ‘Anticholinergic burden’ patient may have due to other medications. This is to reduce CNS & Gastro-intestinal side effects.

- Oxybutynin immediate release (IR) is one of the recommended first line treatment choices. Initial dose is up to 5mg bd (start elderly at 2.5mg bd) as long as the patient is reviewed by the prescriber for side-effects. (NICE NG123 advises not to offer oxybutynin immediate release to those older women who may be at higher risk of a sudden deterioration in their physical or mental health).

- If patient has unmanageable side-effects or there is lack of efficacy with first/second line agents, consider a third line medication taking into account possible advantages of specific agents and cost. e.g trospium in elderly patients for its reduced CNS side effects.

- Currently there is very limited evidence for the use of mirabegron in combination with an antimuscarinic. More evidence would be required to assess whether combination is appropriate. However, this may be an option after specialist recommendation.

- Patients not responding to medical treatment (refractory OAB) should be referred to Urology department for further investigations and management.
Primary Care Management of Overactive Bladder

At the initial clinical assessment, categorise the urinary incontinence as stress urinary incontinence (SUI), urgency urinary incontinence (UUI)/overactive bladder (OAB), or mixed UI. Start initial treatment on this basis.

- OAB is urgency with or without urge incontinence, usually with frequency and nocturia
- UUI is involuntary leakage of urine associated with urgency
- Mixed urinary incontinence is involuntary leakage of urine associated with both urgency and physical stress (exertion, sneezing or coughing).

**Initial assessment**
- Full history
- Frequency/volume chart
- Consider measurement of post-void residue
- Urinalysis (to exclude infection in patients under 65 years old, haematuria and glycosuria)
- If suspected UTI in over 65- Obtain MSU and send to microbiology
- Physical examination
- Pad test if quantification of leakage is desired

**Conservative management – non-pharmacological treatments remain the mainstay for patients with OAB**

- All patients should have conservative treatment prior to commencement of medication or referral to secondary care.
- Patients can be referred to Continence Advisory Service for assessment and conservative treatment (see p5 for contact details)
- Should include patient education, lifestyle advice, bladder training and pelvic floor exercises (for women).

**Post-menopausal women:**
Intravaginal oestrogens are recommended for women with vaginal atrophy/OAB symptoms e.g. ovestin 0.1% cream or vagifem

**Offer men**
- Temporary containment products
- Supervised bladder training

**Pelvic floor exercise (for women)**
Taught using vaginal or rectal examination (at least 3 months)

**Bladder retraining**
Minimum of 6 weeks (NICE 2006)

**Lifestyle advice**
- Modify high or low fluid intake
- Advise on drugs, co-morbidity
- Avoid caffeine
- Smoking cessation, weight loss, exercise
- Constipation advice, healthy eating
- Consider intervention related to cognitive impairment (scheduled voiding)
- Offer timed or prompted voiding in elderly/care dependant people
- Offer pads or other containment device if needed

**Review at 3 months**
- Improved
- Continue
Before starting OAB drugs

When offering antimuscarinic drugs to treat OAB always take account of
- Coexisting conditions (e.g. poor bladder emptying, cognitive impairment or dementia, BPH, constipation, glaucoma)
- Anticholinergic burden- use of other existing medications affecting the total antimuscarinic load (see relevant resources on anticholinergic drugs/burden)
- Risk of adverse effects, including cognitive impairment

Discuss with the 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.
- The long-term effects of anticholinergic medicines on cognitive function are uncertain

Prescribe the lowest recommended dose when starting a new OAB drug to reduce the likelihood of side-effects

Prescribing in elderly people/ people diagnosed with dementia

Antimuscarinic drugs may affect cognitive function in elderly people and those with dementia, hence when prescribing this group of drugs in elderly patients the following should be taken into account:

- In older people being treated for urinary incontinence, every effort should be made to employ non-pharmacological treatments first.
- Use antimuscarinic drugs with caution in elderly patients who are at risk of, or have, cognitive dysfunction.
- In older people who are being prescribed antimuscarinic drugs for control of urinary incontinence, consider the anticholinergic burden including other existing medications. Modifications to medications to help reduce CNS or GI adverse effects may be considered.
- Check mental function in patients on antimuscarinic medication if they are at risk of cognitive dysfunction.

Modified release preparations are significantly more expensive than immediate release but may be beneficial in the frail elderly who may be at higher risk of a sudden deterioration in their physical or mental health (those with multiple comorbidities, functional impairments such as walking or dressing difficulties and any degree of cognitive impairment)
Pharmacological treatment of overactive bladder

First line medication: tolterodine OR oxybutynin
28 days treatment
Tolterodine 2mg bd £2.14
(If modified release preparation of tolterodine is indicated, the preferred brand across Derbyshire is Neditol XL® 4mg = £12.89 x 28 days)
Oxybutynin 2.5mg bd £2.18
Oxybutynin 5mg bd £3.19
Titrate oxybutynin to 5mg tds as tolerated
Modified release preparations are significantly more expensive than immediate release but may be beneficial in the frail elderly (those with multiple comorbidities, functional impairments e.g. walking or dressing difficulties and any degree of cognitive impairment)
Oxybutynin MR 5mg x 28 = £12.85
Oxybutynin MR 10mg x 28 = £25.70

Review at 4 weeks

Second line medication: oxybutynin OR tolterodine, whichever not already tried

Review at 4-6 weeks

Both drugs should be trialled before moving to third line.
The impact of adverse effects can be reduced by using a small starting dose and titrating dose slowly. Also consider using a modified release preparation for reducing troublesome side effects.

Troublesome side-effects/ lack of efficacy

Improved

No benefit

Improved

Review annually or every 6 months if >75yrs of age

Change to third line medication:
This list is not in order of suggested use and choice of third line agent should take into account possible advantages of specific agents and cost. Clinicians should manage constipation and dry mouth before abandoning effective anti-muscarinic treatment. Management may include bowel management, fluid management, dose modification or alternative anti-muscarinic.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes</th>
<th>Cost for 28 days treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trospium 20mg BD</td>
<td>May have fewer CNS side-effect esp. in elderly</td>
<td>£5.71</td>
</tr>
<tr>
<td>Solifenacin 5-10mg OD</td>
<td>There is a once daily preparation £24.45 (28days)</td>
<td>£8.67-£11.64</td>
</tr>
<tr>
<td>Propiverine 15mg OD-TDS</td>
<td>Same drug group as tolterodine</td>
<td>£9.00 - £27.00</td>
</tr>
<tr>
<td>Darifenacin MR 7.5-15mg OD</td>
<td>May have fewer CNS side-effects</td>
<td>£25.48</td>
</tr>
<tr>
<td>Fesoterodine MR 4-8mg OD</td>
<td></td>
<td>£25.78</td>
</tr>
</tbody>
</table>
| Mirabegron MR 50mg OD (see Rxing note below) | Beta-3 agonist. Minimises anticholinergic side effects | £27.07

Review at 4-8 weeks

NICE concluded lack of evidence to show a difference in clinical effectiveness between OAB drugs and also a lack of evidence showing long term efficacy and thereby suggesting restricting the number of OAB drugs tried before seeking alternative recommended treatments (including referral to secondary care)

Troublesome side-effects/ lack of efficacy

Consider referral to urology/urogynaecology

Improved

Review annually or every 6 months if >75yrs of age

Produced: September 2013 Reviewed: October 2019
Expiry: September 2022
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Prescribing note- Mirabegron

NICE TA290 (June 2013) - mirabegron is an option only for patients in whom antimuscarinic drugs are ineffective, contra-indicated, or not tolerated. Follow treatment flowchart below.

MHRA, Oct 2015 has issued a safety warning stating 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.

Contact details

Continence Advisory Service, 
Alfreton Primary Care Centre, 
Church Street, Alfreton, 
Derbyshire, 
DE55-7AH. 
Tel: 01773 854868 
Fax: 01773 546976 
E-mail: continence.advisoryservice@nhs.net

References

NICE NG123 Urinary incontinence and pelvic organ prolapse in women: management (April 2019) 
BNF online accessed August 2019 
Management of Urinary Incontinence in Primary Care – SIGN 79 (2004) 

Produced by

Clinical Effectiveness Team in consultation with 
Mr. Peracha, consultant urologist University hospital of Derby and Burton NHS Foundation Trust 
Mr. David Shipstone, consultant urologist Chesterfield Royal Hospital NHS Foundation Trust 
Helen Greaves, Lead Clinical Nurse Specialist- Continence, Derbyshire Community Health Services NHS Foundation Trust

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<thead>
<tr>
<th>Document Updates</th>
<th>Date</th>
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Produced: September 2013 Reviewed: October 2019 
Expiry: September 2022
Licensed doses of antimuscarinic drugs

Antimuscarinic adverse effects can limit treatment success. Adverse effects can be reduced by starting at a low dose and gradually increasing until a satisfactory clinical response is achieved.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (Max. dose)</th>
<th>28 day costs (Max. dose)</th>
<th>Comments</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolterodine IR</td>
<td>2mg bd</td>
<td>£2.14</td>
<td>First/second line choice For people with impaired liver function or severe renal impairment (eGFR ≤30mL/min) or to minimise side effects prescribe 1mg BD</td>
<td>Generally better tolerated than oxybutynin and does not require dose titration</td>
</tr>
<tr>
<td>Tolterodine MR</td>
<td>4mg od</td>
<td>£12.89</td>
<td>Reduce dose to 2mg od if impaired liver function or severely impaired renal function (GFR ≤ 30 ml/min) is present</td>
<td>The use of MR preparation may offer a lower incidence of dry mouth and may be suitable for patients who require once daily preparations.</td>
</tr>
<tr>
<td>(preferred brand</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Neditol XL)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Oxybutynin IR</td>
<td>2.5-5mg bd</td>
<td>£2.18 £3.19</td>
<td>First/second line choice Adjust according to response</td>
<td>The most common adverse reactions reported during clinical trials by &gt; 5% of patients were dry mouth, constipation, diarrhoea, headache, somnolence and dizziness</td>
</tr>
<tr>
<td>(usually 10mg od)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxybutynin MR</td>
<td>5mg od</td>
<td>£12.85 (£25.70)</td>
<td>MR are significantly more expensive than IR but may be beneficial in the frail elderly. There should be an interval of at least 7 days between any dose changes</td>
<td></td>
</tr>
<tr>
<td>(usually 10mg od)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxybutynin patches</td>
<td>Apply 1 patch</td>
<td>£27.20</td>
<td>Option in patients unable to tolerate oral oxybutynin Apply to clean, dry unbroken skin on the abdomen, hip or buttock</td>
<td>Adverse effects associated with transdermal oxybutynin are fewer than with oral oxybutynin.</td>
</tr>
<tr>
<td>3.9mg/24 hr</td>
<td>twice weekly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trospium IR</td>
<td>20mg bd</td>
<td>£5.71</td>
<td>Reduce dose to 20mg od or 20mg on alternate days if eGFR is ≤ 10-30mL/min Not recommended in severe hepatic impairment.</td>
<td>May have reduced CNS adverse effects especially in elderly. Hallucination, confusion, agitation occur mostly in the elderly</td>
</tr>
<tr>
<td>Trospium MR</td>
<td>60mg od</td>
<td>£23.05</td>
<td>Not be given to patients with severe hepatic impairment. Not recommended for use in renally impaired patients (10-30mL/min/1.73m²)</td>
<td></td>
</tr>
<tr>
<td>Propiverine</td>
<td>15mg od-tds (15mg qds)</td>
<td>£9.00-£27.00 (£36.00)</td>
<td>MR once daily preparation also available. Max. dose 30mg daily in severe renal impairment (CrCl&lt;30ml/min) Contraindicated in moderate/severe hepatic impairment</td>
<td></td>
</tr>
<tr>
<td>Darifenacin MR</td>
<td>7.5mg od</td>
<td>£25.48</td>
<td>Contraindicated in patients with severe hepatic impairment No dose adjustment is required in patients with impaired renal function. However, caution should be exercised when treating this population</td>
<td>May have fewer CNS side-effects</td>
</tr>
<tr>
<td>(15mg od)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fesoterodine MR</td>
<td>4 od (8mg od)</td>
<td>£25.48</td>
<td>Maximum 4mg od with hepatic or renal impairment.</td>
<td></td>
</tr>
<tr>
<td>Solifenacin</td>
<td>5mg od (10mg od)</td>
<td>£8.67 (£11.64)</td>
<td>Treat patients with severe renal impairment (creatinine clearance ≤ 30 ml/min) and moderate hepatic impairment with a maximum daily dose 5mg od.</td>
<td></td>
</tr>
<tr>
<td>Mirabegron MR</td>
<td>50mg od</td>
<td>£27.07</td>
<td>Avoid if eGFR&lt;15mL/min/1.73m² Reduce to 25mg od if eGFR 15-29mL/min/1.73m² Beta-3 agonist. Minimises anticholinergic side effects</td>
<td></td>
</tr>
</tbody>
</table>

Price based on DT October 2019