

DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Primary Care management of Overactive Bladder (OAB)

- 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.
- 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)
- Before commencing OAB drug treatment discuss:
 - o 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.
 - o 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 Central Nervous System & Gastro-intestinal side effects.
- In order people being treated for OAB every effort should be made to employ non-pharmacological treatment first. Use antimuscarinic drugs with caution in elderly patients who are at risk of, or have cognitive dysfunction.
- NICE recommends the most cost-effective agent is used- solifenacin 5mg once daily titrating up to 10mg daily after 4-6 weeks. Review patient for side effects.
 - If the first medicine is not effective or tolerated, offer alternative first line oxybutynin immediate release (IR). Initial dose is up to 5mg twice daily (start elderly at 2.5mg twice daily). Patients should be reviewed for side-effects. Do not offer oxybutynin immediate release to frail older patients who may be at higher risk of a sudden deterioration in their physical or mental health (NICE NG123).
- 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 are usually more expensive. See cost table.
- If patient has unmanageable side-effects or there is lack of efficacy with first/ second line agents, consider alternative 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/urogynaecology 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

<u>Conservative management – non-pharmacological treatments remain the mainstay for patients with OAB</u>

- 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

Post-menopausal women:

Intravaginal oestrogens are recommended for women with vaginal atrophy/OAB symptoms e.g. Ovestin 0.1% cream or Vagirux

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

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

Reviewing medicine

Offer a review in primary care who remain on long-term medicine for overactive bladder or urinary incontinence every 12 months, or every 6 months if they are aged over 75. During the review, re-assess symptoms and quality of life and assess for adverse effects and the need to continue treatment.

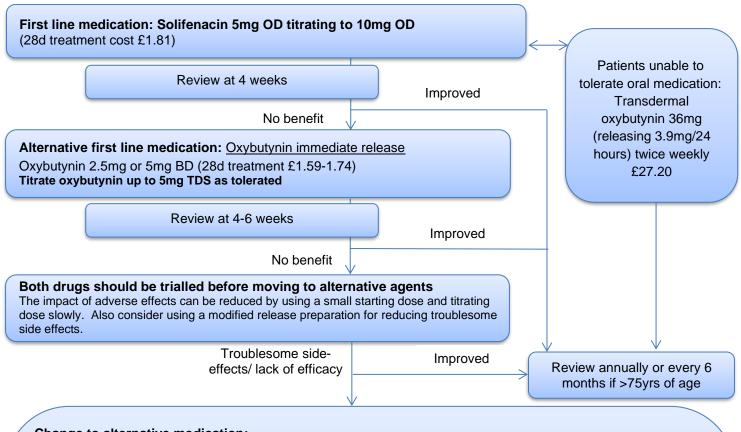
Prescribing in elderly people/ people diagnosed with dementia

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 nonpharmacological 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 oxybutynin and tolterodine are classified **GREY**-only use in those 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



Change to alternative medication:

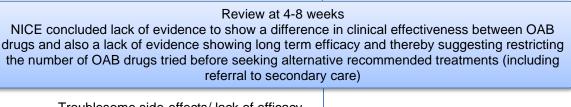
This list is not in order of suggested use and choice of third line agent should take into account possible advantages of specific agents and cost. Clinicians should manage constipation and dry mouth before abandoning effective anti-muscarinic treatment. Management may include bowel management, fluid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

Drug	Notes	28d treatment cost
Tolterodine 2mg BD		£2.80

GREY - to be used after consideration of formulary choices

Drug	Notes	28d treatment cost
Fesoterodine MR 4-8mg OD	Same drug group as tolterodine	£4.46
Tolterodine MR 4mg OD	Preferred brand Blerone (not available in 2mg strength)	£6.90
Trospium 20mg BD	May have fewer CNS side-effect esp. in elderly	£10.67
Oxybutynin MR 5-10mg OD	For those who may be at higher risk of a sudden deterioration in their physical or mental health	£14.86- 29.36
Trospium MR 60mg OD	May have fewer CNS side-effect esp. in elderly	£23.05
Propiverine MR 30mg OD		£24.45
Darifenacin MR 7.5-15mg OD	May have fewer CNS side-effects	£25.48
Mirabegron MR 50mg OD (see Rxing note below)	Beta-3 agonist. Minimises anticholinergic side effects C/I in severe uncontrolled hypertension	£27.07

Drug Tariff - June 2023 and MIMs online



Troublesome side-effects/ lack of efficacy

Consider referral to urology/ urogynaecology

Produced: September 2013 Reviewed: September 2022 Expiry: August 2025

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Improved

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

Prescribing note- Mirabegron- GREY

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 546868

E-mail: continence.advisoryservice@nhs.net

References

NICE NG123 Urinary incontinence and pelvic organ prolapse in women: management (April 2019) BNF online accessed June 2022

Guidelines on Urinary Incontinence – European Association of Urology (2013, updated 2020)

NICE TA 290 Mirabegron for treating symptoms of overactive bladder (June 2013)

Mirabegron for the treatment of overactive bladder: a review of efficacy, safety and tolerability with a focus on male, elderly and antimuscarinic poor-responder populations, and patients with OAB in Asia. Expert Rev Clin Pharmacol. 2017 Feb;10(2):131-151. doi: 10.1080/17512433.2017.1275570. Epub 2017 Jan 16.

Reviewed by

Clinical Effectiveness Team in consultation with

Mr. Simon Williams 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

Document Updates	Date
Update following formulary review- Solifenacin & oxybutynin both 1st line; tolterodine 2nd line; others as alternatives (grey); Blerone as preferred tolterodine MR brand.	June 2023

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.

Drug	Dose (Max. dose)	28 day costs (Max. dose)	Comments	Side-effects
Solifenacin	5mg od (10mg od)	£1.81 (£1.80)	First line choice Treat patients with severe renal impairment (creatinine clearance ≤ 30 ml/min) and moderate hepatic impairment with a maximum daily dose 5mg od.	Common side effects include dry mouth blurred vision, constipation, nausea, dyspepsia and abdominal pain.
Oxybutynin IR	2.5-5mg bd (5mg qds)	£1.59-1.74 (£3.48)	First line choice Adjust according to response	The most common adverse reactions reported during clinical trials by > 5% of patients were dry mouth, constipation, diarrhoea, headache, somnolence and dizziness
Tolterodine IR	2mg bd	£2.80	Second line choice For people with impaired liver function or severe renal impairment (eGFR ≤30mL/min) or to minimise side effects prescribe 1mg BD	Generally better tolerated than oxybutynin and does not require dose titration
Fesoterodine MR	4 od (8mg od)	£4.46 (£4.67)	Maximum 4mg od with hepatic or renal impairment.	
Tolterodine MR (preferred brand Blerone)	4mg od	£6.90	Reduce dose to 2mg od if impaired liver function or severely impaired renal function (GFR ≤ 30 ml/min) is present (Blerone brand not available in 2mg strength)	The use of MR preparation may offer a lower incidence of dry mouth and may be suitable for patients who require once daily preparations.
Trospium IR	20mg bd	£10.67	Reduce dose to 20mg od or 20mg on alternate days if eGFR is ≤ 10-30mL/min Not recommended in severe hepatic impairment.	May have reduced CNS adverse effects especially in elderly. Hallucination, confusion, agitation occur mostly in the elderly
Oxybutynin MR	5mg od (usually 10mg od)	£14.68 (£29.36)	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	The most common adverse reactions reported during clinical trials by > 5% of patients were dry mouth, constipation, diarrhoea, headache, somnolence and dizziness
Trospium MR	60mg od	£23.05	Not be given to patients with severe hepatic impairment. Not recommended for use in renally impaired patients (10-30mL/min/1.73m²)	
Propiverine MR	30mg od	£24.45	Max. dose 30mg daily in severe renal impairment (CrCl<30ml/min) Contraindicated in moderate/severe hepatic impairment	
Darifenacin MR	7.5mg od (15mg od)	£25.48	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	May have fewer CNS side-effects
Mirabegron MR	50mg od	£27.07	Avoid if eGFR<15ml/min/1.73m ² . Reduce to 25mg od if eGFR 15-29ml/min/1.73m ² . C/I in severe uncontrolled hypertension	Beta-3 agonist. Minimises anticholinergic side effects
Oxybutynin patches 3.9mg/24 hr	Apply 1 patch twice weekly	£27.20	Option in patients unable to tolerate oral oxybutynin Apply to clean, dry unbroken skin on the abdomen, hip or buttock	Adverse effects associated with transdermal oxybutynin are fewer than with oral oxybutynin.

Price based on DT June 2023