Guidelines for Pharmacological Management of Overactive Bladder Syndrome (OAB) /Mixed UI in Adult Women in Primary Care

NHS
York and Scarborough Medicines Commissioning Committee

Initial Assessment
Full history, urine dipstick-treat UTI, treat vaginal atrophy (page 2), bladder diary for a minimum 3 days

Refer Urology or Uro-gynaecology if
-Presence of haematuria
-Visible prolapse,
-Pelvic Mass
-Suspected neurological disease
-Recurrent UTI
-Persistent bladder pain
-Symptoms of voiding difficulty
-Suspected fistulae
-Associated faecal incontinence

Conservative Management
Lifestyle Interventions-e.g reduce weight if BMI>30, reduce caffeine intake, modify fluid intake (page 2)
Review Medication (e.g. diuretics/anti-hypertensives, anti-depressants)
Bladder Training for a minimum of 6 weeks, Manage Constipation
Supervised pelvic floor muscle training for at least 3 months
Consider medical/medication causes if nocturia present in elderly women, as less likely to be caused by OAB.

Pharmacological Treatment
Before starting OAB Drugs discuss with the patient:
- Likelihood of success and associated common side effects such as dry mouth and constipation
- Adverse effects may indicate that treatment is starting to have effect
- Frequency and route of administration
- Full benefits may not be seen 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

Choosing OAB Drugs

First Line Treatment	Second Line Treatment
Tolterodine (IR) 2 mg twice daily, reduce to 1 mg twice daily if necessary to minimise the side effects	Tolterodine MR 4 mg daily **or** Solifenacin 5-10 mg daily **Elderly/Cognitive Impairment** Trospium MR 60 mg daily **or** Mirabegron 50 mg daily (if 2nd line treatment not tolerated see below)
If anti-muscarinic not suitable or contra-indicated eg. Patient with dementia, elderly, anticholinergic burden score >3 **Mirabegron** 50 mg daily, reduce to 25 mg daily if hepatic or renal impairment, prescribing should be in accordance with NICE TA 290	
Consider **transdermal oxybutynin patch** if unable to tolerate oral medication 1 patch twice weekly	
Desmopressin (Noqdirna) may be considered specifically to reduce nocturia secondary to nocturnal polyuria (assessed by bladder diary if more than ⅓ of the total daily urine output occurs at night). Use with caution in women with cystic fibrosis and avoid in those over 65 years with cardiovascular disease or hypertension. (Amber specialist recommendation)	

NB. Nice 171 initially recommends one the following oxybutynin IR, tolterodine IR, darifenacin. Oxybutynin is the most cost-effective drug but with higher discontinuation rates and has been omitted from this guidance.

When Offering anti-muscarinic 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 anti-muscarinic load (page 3)
- Risk of adverse effects

Do not use:
- Flavoxate, propantheline, imipramine
- Immediate release (IR) oxybutynin in older frail patients
- **Duloxetine** should not be routinely used in the treatment of OAB, but maybe offered as 2nd line therapy for stress urinary incontinence for women who decline /or are unsuitable for surgery

Review
- Offer face to face or telephone review 4 weeks after start of 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 years if treatment is effective and well tolerated, do not change the dose or the drug

Referral to Secondary care for Urodynamics and/or Botulinum Toxin
If second line drug therapy fails/ patient does not want to try another drug/ patient wishes to discuss the options for further management (non- therapeutic intervention and invasive therapy)

Post-menopausal women with vaginal atrophy
Offer **intra-vaginal oestrogens** (but not systemic hormone replacement therapy) for the treatment of OAB symptoms in post-menopausal women with vaginal atrophy. Intra-vaginal oestrogens can be used in women with an intact uterus without the need for a progestogen to be added.

Advice on fluid Intake and Lifestyle

Fluid Intake
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

Lifestyle advice may include:
Caffeine reduction-there is some evidence that caffeine reduction leads to less urgency and frequency when used in addition to bladder training

Smoking cessation

Weight reduction
If body mass index is 30 kg/m^2 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.

Price

Drug Name	Dose	Cost per 28 days
Oxybutynin Hydrochloride	2.5 mg twice daily to 5 mg four times daily	£1.11-£2.64
Tolterodine Tartrate (IR)	1-2 mg twice daily	£1.55-£2.17
Solifenacin	5-10mg once daily	£27.62 - £35.91
Trospium Chloride (MR)	60 mg once daily	£23.05
Mirabegron (MR)	50 mg once daily	£29.00
Tolterodine Tartrate (MR)	4 mg once daily	£25.78
Oxybutynin HCl 3.9 mg/24hrs transdermal patch	1 patch twice weekly	£27.20

Prices are taken from the Drug Tariff January 2018

ANTICHOLINERGICS

CONTRA-INDICATIONS
Myasthenia Gravis, narrow angle glaucoma, Sjogren syndrome, significant bladder outflow obstruction or urinary retention, severe ulcerative colitis, toxic megacolon and gastro-intestinal obstruction
CAUTIONS
Many prescription and non-prescription drugs have anticholinergic activity. The cumulative effect of this anticholinergic burden can increase the frequency and severity of adverse events. Anticholinergics should be used with caution in the elderly (especially if frail), in those with autonomic neuropathy, and in those susceptible to angle-closure glaucoma
See BNF for individual drug profiles

MIRABEGRON

CONTRA-INDICATIONS
Contra-indicated in severe uncontrolled hypertension (systolic ≥180 mmHg or diastolic ≥ 110 mmHg)
CAUTIONS
Caution in patients with stage 2 hypertension (systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥ 100 mm Hg), History of QT-interval prolongation.
Blood Pressure to be measured before starting and regularly monitored (MHRA October 2015)
See BNF for full drug profile.

Anti-cholinergic scale

It has been shown that an increase in the number of anticholinergic drugs taken by the patients directly increases their anticholinergic burden (ACB). Increasing a patient's ACB by one point has shown to increase the risk of mortality by 26%. Furthermore, patients with an ACB score greater than 3 have a 'high risk' of mortality. To calculate the ACB, find the drug's ACB score from the relevant tables and add the scores up. If the patient's ACB is 3 or more- re view the anticholinergic medicines by asking the following questions and monitoring patient symptoms. These may reduce the risk of falls by reducing the patient's ACB.

1. It the medication essential?
2. Is there an alternative medication with a lower ACB score.
3. Patient monitoring (side effects they may suffer from).

Common drugs on the anticholinergic scale

ACB Score 1 (Mild)	ACB Score 2 (Moderate)	ACB Score 3 (Severe)
Alprazolam	Amantidine	Amytryptaline and most TCSs
Alverine	Belladona alkaloids	Amoxapine
Aripiprazole	Carbamazipine	Atropine
Asenaoine	Cyclobenzaprine	Benztropine
Beta-blockers (atenolol, metoprolol)	Cyproheptadine	Brompheramine
Bupropion hydrochloride	Loxapine	Carinoxamine
Captopril	Mepridine	Chlorpromazine
Cetrizine (and Levicetrizine)	Methotrimeprazine	Clamastine
Chlorthalidone	Molidone	Clomipramine
Cemitidine & H2RAs	Nefopam	Clozapine
Codeine and other opiates	Oxcarbazepine	Darifenacin
Colchicine	Pimozide	Desipramine
Desloratidine		Dicyclomine
Diazepam		Dimenhydramine
Digoxin		Doxepin
Dipyridamole		Doxylamine
Fentanyl		Fesoterodine
Frusemide and other diuretics		Flavoxate
Fluvoxamine		Hydroyzine
Haloperidol		Imipramine
Hydralazine		Meclizine
Hydrocortisone		Methocarbamol
Isosorbide preparations		Nortriptyline
Loperamide		Olanzapine
Loratidine		Orphenadrine
Morphine		Oxybutynin
Nifedipine		Paroxetine
Paliperodone		Perphenadine
Prednisolone		Promethazine
Quinidine		Propantheline
Ranitidine		Proverine
Risperidone		Quetiapine
Theophyline		Scopolamine
Trazodone		Solifenacin
Triamterene		Thiordiazine
Venlafaxine		Tolteradine
Warfarin		Trifluperazine
		Trospium

This list is not exhaustive

The anticholinergic cognitive burden scale can help to assess risk and is available to download at www.gpnotebook.co.uk

References:

1. Nice Clinical guidelines 171. The management of urinary incontinence in women; September 2013
2. Nice TA 290. Mirabegron for treating symptoms of overactive bladder; June 2009
3. BNF Formulary
4. Fox C, Richardson K. Maidment ID, et al. Anticholinergic use and cognitive impairment in the older population; the Medical Research Council Cognitive Function and Aging Study. Journal of the American Geriatrics Society 2011; 59: 1477-83