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

See NICE NG123 for further information.

Initial assessment by GP
Full history, urine dipstick +/- MSU & treat UTI (NG123), treat vaginal atrophy (page 2), bladder diary for a minimum of 3 days.

Refer Urology or Urogynaecology if any RED FLAGS:
-Presence of haematuria
-Visible prolapse
-Pelvic mass
-Suspected neurological disease
-Recurrent UTI
-Persistent bladder pain
-Symptoms of voiding difficulty
-Suspected fistulae
-Associated faecal incontinence
- Palpable bladder on bimanual or abdominal examination after voiding
-Previous continence surgery
-Previous pelvic cancer surgery
-Previous pelvic radiation therapy.

Conservative Management
Lifestyle and fluid intake interventions (see page 2)
Review medication (e.g. diuretics; antihypertensives, antidepressants)
Bladder training for 6-12 weeks. (NICE NG123 states minimum 6 weeks)
Manage constipation
Smoking cessation
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 medicines for OAB consider:

- **Choice of agent -** anticholinergic Vs beta-3 adrenergic receptor agonists (also see overleaf).
  Consider: age, concurrent conditions, side effects, total anticholinergic burden score (MEDICHEC http://www.medichec.com/).
- **Discuss with the patient:**
  - Likelihood of success and associated common side effects e.g. anticholinergics = dry mouth, constipation, CNS side effects
  - Adverse effects may indicate that treatment is starting to have an effect
  - Substantial benefits may not be seen until they have been taking the treatment for at least 4 weeks and symptoms may continue to improve over time
  - The long-term effects on cognitive function of anticholinergic medicines for overactive bladder are uncertain.

Consider a bladder training programme in combination with a medicine for OAB if frequency is a troublesome symptom.
Prescribe the lowest recommended dose when starting a new medicine for OAB, to reduce the likelihood of side effects.

Choosing medicines for OAB

Anticholinergics: First Line Treatment	**Anticholinergics: Second Line Treatment**
Solifenacin 5mg daily – allow 4 weeks minimum. May be increased to 10 mg daily. **Elderly/Cognitive Impairment** Trospium* IR 20mg twice daily, or MR 60 mg daily **or** switch to Beta-3 adrenergic receptor agonist (see right and below). *(* less propensity to cross the blood brain barrier and cause CNS side effects than other anticholinergics).*	Tolterodine (IR) 2 mg twice daily. Trial reduction to 1 mg twice daily, if necessary, to minimise side effects **or** swap to Tolterodine MR 4 mg daily (**but using MR will increase the cost**). **(*not* in elderly / cognitive impairment: high ACB – see left* and P.3 algorithm).** **If no improvement:** switch to Beta-3 adrenergic receptor agonist (see below). Allow 4 weeks to assess.
Consider **transdermal oxybutynin patch 3.9mg/24 hours** if unable to tolerate oral medication: ONE patch twice weekly.	

Beta-3 adrenergic receptor agonists: if anticholinergics contraindicated/unacceptable side effects/ at least 2 were not effective.

1st line: Vibegron 75 mg daily (see NICE TA999) – tablets also licensed to be crushed and mixed with a tablespoon of soft food. No dose reduction in hepatic or renal impairment, not recommended in severe hepatic or severe renal impairment, (eGFR < 15 mL/min) as no data available. See warning below re: increase in blood pressure (BP) with mirabegron. Be vigilant for similar effects.

2nd line: Mirabegron 50mg daily (NICE TA290) – see www.medicines.org.uk/ for dose reductions in renal impairment / with interacting drugs. Mirabegron may increase BP and is contraindicated in severe uncontrolled hypertension - monitor BP.
If *still* no improvement, may use mirabegron 50mg daily, ***plus*** solifenacin 5mg daily, providing no contra-indications (e.g. elderly / confused) [1, 2, 3, 4, 5, 6]. Note: Use of this combination is outside NICE and off-label.

NICE NG123 recommends starting a drug with the lowest acquisition cost, but as oral oxybutynin has a high discontinuation rate, neither IR or MR formulations are recommended, in this guidance.

Review

- Offer face to face or telephone review 4 weeks after start of new medicine for OAB, or before 4 weeks if adverse effects 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.

When offering anticholinergic medicines to treat OAB:

Do *not* use:

- Flavoxate, propantheline, imipramine.
- *Any* oral oxybutynin (either immediate release (IR) or modified release (MR)) in frail older patients.

Duloxetine should not be routinely used in the treatment of OAB, but may be offered as 2nd line therapy for stress urinary incontinence for women who decline /or are unsuitable for surgery (counsel on adverse effects). Usual dose 20mg BD or 40mg BD. Consult BNF for licensed products.

Other treatment options

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).

Post-menopausal women with vaginal atrophy

Offer **intravaginal oestrogens** (but not systemic hormone replacement therapy) for the treatment of OAB symptoms in post-menopausal women with vaginal atrophy. Intravaginal 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 and this should be considered on an individual basis.

Caffeine reduction: there is some evidence that caffeine reduction leads to less urgency and frequency when used in addition to bladder training.

Smoking cessation: Current and former smokers are more likely to experience OAB than non-smokers, especially younger women. Chemicals ingested when smoking may irritate the bladder lining. Smoking may reduce the urine capacity of the bladder and smoking-induced chronic cough may weaken bladder control.

Weight reduction: There is evidence of an association between obesity and urinary incontinence (UI) or OAB, and in obese women (body mass index is 30 kg/m^2 or greater) weight reduction of at least 5% is associated with relief of UI symptoms.

Anticholinergics

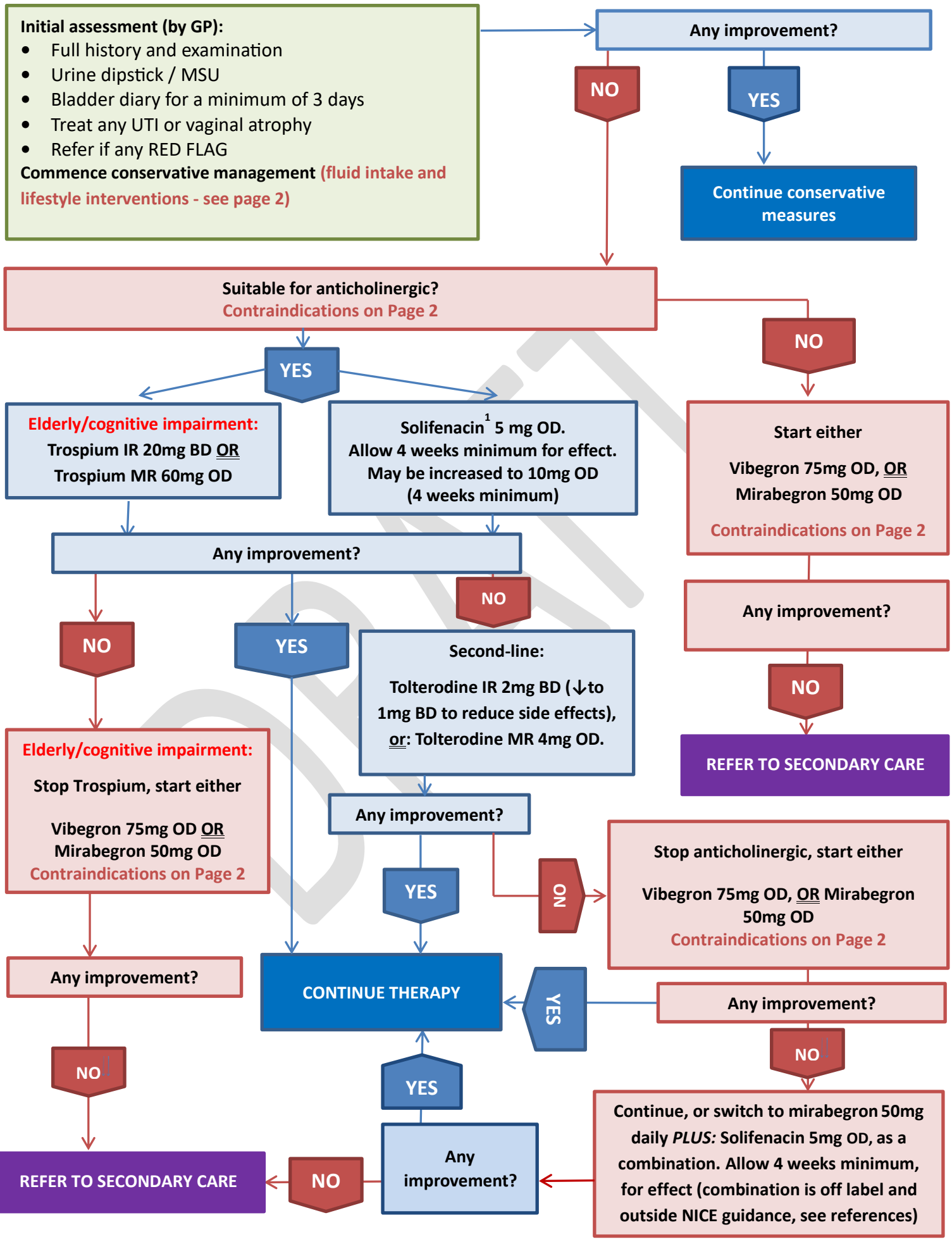
CONTRAINDICATIONS - Myasthenia Gravis, narrow angle glaucoma, Sjogren syndrome, significant bladder outflow obstruction or urinary retention, severe ulcerative colitis, toxic megacolon and gastro-intestinal obstruction.
CAUTIONS - elderly especially frail and those with dementia / cognitive impairment. Other concurrent medication e.g. where additive anticholinergic-burden score >3 **(see MEDICHEC http://www.medichec.com/).**

Beta-3 adrenergic receptor agonists (only if antimuscarinic contraindicated/unacceptable side effects/ at least 2 not effective).

CONTRAINDICATIONS - Pregnancy and breastfeeding; *severe* hepatic impairment (Child-Pugh C); end-stage renal impairment (eGFR<15mL/minute).
CAUTIONS - Urinary retention has been reported. The risk may be increased in patients with bladder outlet obstruction and concomitant anticholinergic drugs. Monitor urinary retention signs and symptoms, before and during treatment.
Mirabegron may increase blood pressure and is contraindicated in severe uncontrolled hypertension - monitor BP (see MHRA Safety Update Oct 2015[11]). Although this is not listed as a caution for vibegron, be vigilant for effects on blood pressure.

Referral to secondary care for urodynamics and/or intradetrusor Botulinum Toxin

If second line drug therapy fails, or the patient does not want to try another drug and bladder, or pelvic floor training have failed.


Initial assessment (by GP):
• Full history and examination
• Urine dipstick / MSU
• Bladder diary for a minimum of 3 days
• Treat any UTI or vaginal atrophy
• Refer if any RED FLAG
Commence conservative management (fluid intake and lifestyle interventions - see page 2)
Any improvement?
NO
YES
Continue conservative measures
Suitable for anticholinergic?
Contraindications on Page 2
YES
NO
Elderly/cognitive impairment:
Trospium IR 20mg BD OR
Trospium MR 60mg OD
Solifenacin[1] 5 mg OD.
Allow 4 weeks minimum for effect.
May be increased to 10mg OD
(4 weeks minimum)
Start either
Vibegron 75mg OD, OR
Mirabegron 50mg OD
Contraindications on Page 2
Any improvement?
NO
YES
NO
Any improvement?
NO
REFER TO SECONDARY CARE
Second-line:
Tolterodine IR 2mg BD (↓to 1mg BD to reduce side effects), or: Tolterodine MR 4mg OD.
Elderly/cognitive impairment:
Stop Trospium, start either
Vibegron 75mg OD OR
Mirabegron 50mg OD
Contraindications on Page 2
Any improvement?
YES
NO
Stop anticholinergic, start either
Vibegron 75mg OD, OR Mirabegron 50mg OD
Contraindications on Page 2
Any improvement?
NO
CONTINUE THERAPY
YES
Any improvement?
NO
YES
REFER TO SECONDARY CARE
NO
Any improvement?
Continue, or switch to mirabegron 50mg daily PLUS: Solifenacin 5mg OD, as a combination. Allow 4 weeks minimum, for effect (combination is off label and outside NICE guidance, see references)

Appendix 1

Frequency Volume Chart patterns

Voided volume	Frequency	Interpretation
Normal (1,500-2,000mL / 24 hours; 300-500mL / void).	Normal (5-8 voids in 24 hours; 1-2 voids at night).	Normal.
Normal (1,500-2,000mL / 24 hours; 300-500mL / void).	Increased.	Suspect polydipsia; occasionally, diabetes Insipidus/ diabetes mellitus.
Reduced and consistently fixed in both day and night.	Increased.	Suspect reduced bladder capacity.
Reduced and variable voided volume day and night with urgency and urge incontinence.	Increased	Overactive bladder.
Early morning: Normal voided volume; Daytime voided volume: Variable with no night time waking.	Normal.	Suspect psychosomatic.
Normal.	Normal in the day time; Night-time frequency increased with total voided volume at night at 33% of 24 hour total.	Consider Nocturnal Polyuria.

Appendix 2

Bladder Training

Instead of rushing to the toilet as soon as you get the urge it is important to learn how to hold on and get over the urge to void. This will enable your bladder to hold on to a greater amount of urine rather than your bladder getting used to being sensitive to a smaller amount of urine. It should be carried out in small stages. If you get the urge to go to toilet say, every half an hour, then try to extend it by 10 minutes for a week and then 15 minutes for a week and then 30 minutes etc. Ideally, you should aim to hold on for 3 to 4 hours between toilet visits.

Learn to suppress the urgency

There are different techniques for this. Here are some suggestions:

1) Sit straight on a hard seat.

2) Take your mind off the urge to void, by distracting yourself with other activities, e.g. reading a newspaper, counting from 100 backwards or solving a crossword puzzle. You need to plan in advance how you will distract yourself.

3) Contract your pelvic floor muscles, which will help to reduce urgency and incontinence.

You may find it helpful to keep a diary of when you go to the toilet, before you start bladder training and then again, a few months later. You may see more improvement than you expected.

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