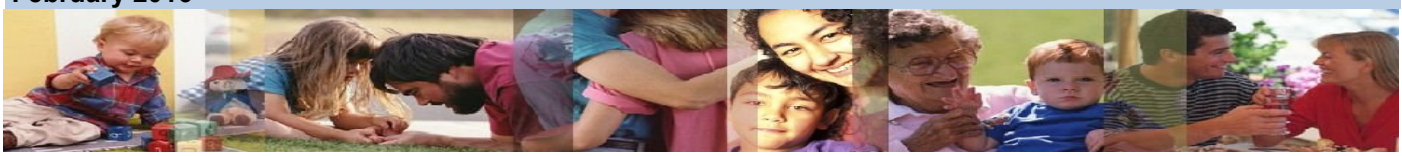
NORTHERN IRELAND MEDICINES MANAGEMENT

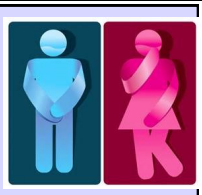
February 2016

Health and Social Care Board



Newsletter supplement: Urinary incontinence

NICE clinical guidelines for urinary incontinence (UI) in women[1] and the management of lower urinary tract symptoms in men[2] define the treatment pathways for UI.
Drug treatment with antimuscarinic therapy should ONLY be considered when the condition has not improved with conservative non-drug therapy management alone.
This supplement aims to highlight the key points in the management of UI for primary care clinicians.



Fast facts on frequent urination

- Frequent urination is not the same as urinary incontinence.
- Frequent urination can be a symptom of an underlying medical condition.
- Frequent urination can result from drinking too many fluids.
- The average person excretes about 1 to 1.8 litres of urine every 24 hours.
- A study has suggested that people who urinate at least twice a night reduce their bladder cancer risk by 40 – 59%.

Initial assessment

Take history of UI, patient should complete a bladder diary (at least 3 days) and this should be used in the assessment.
Check for:

- **Cause —** some conditions may present with increased urine frequency, for example – infection, cystitis, benign prostatic hyperplasia (BPH), bladder cancer bladder stones, diabetes, prostatitis, vaginitis or detrusor over activity.
- **Medicines —** can disrupt the normal process of storing and passing urine, or increase urine output. These include ACE inhibitors, diuretics, donepezil, doxazosin, SGLT-2 inhibitors, some antidepressants, hormone replacement therapy (HRT) and sedatives.
  Stopping these medications if appropriate or counselling patient on their side-effect profile may help resolve incontinence.
- Consider referral to local bladder and bowel service.

Lifestyle advice

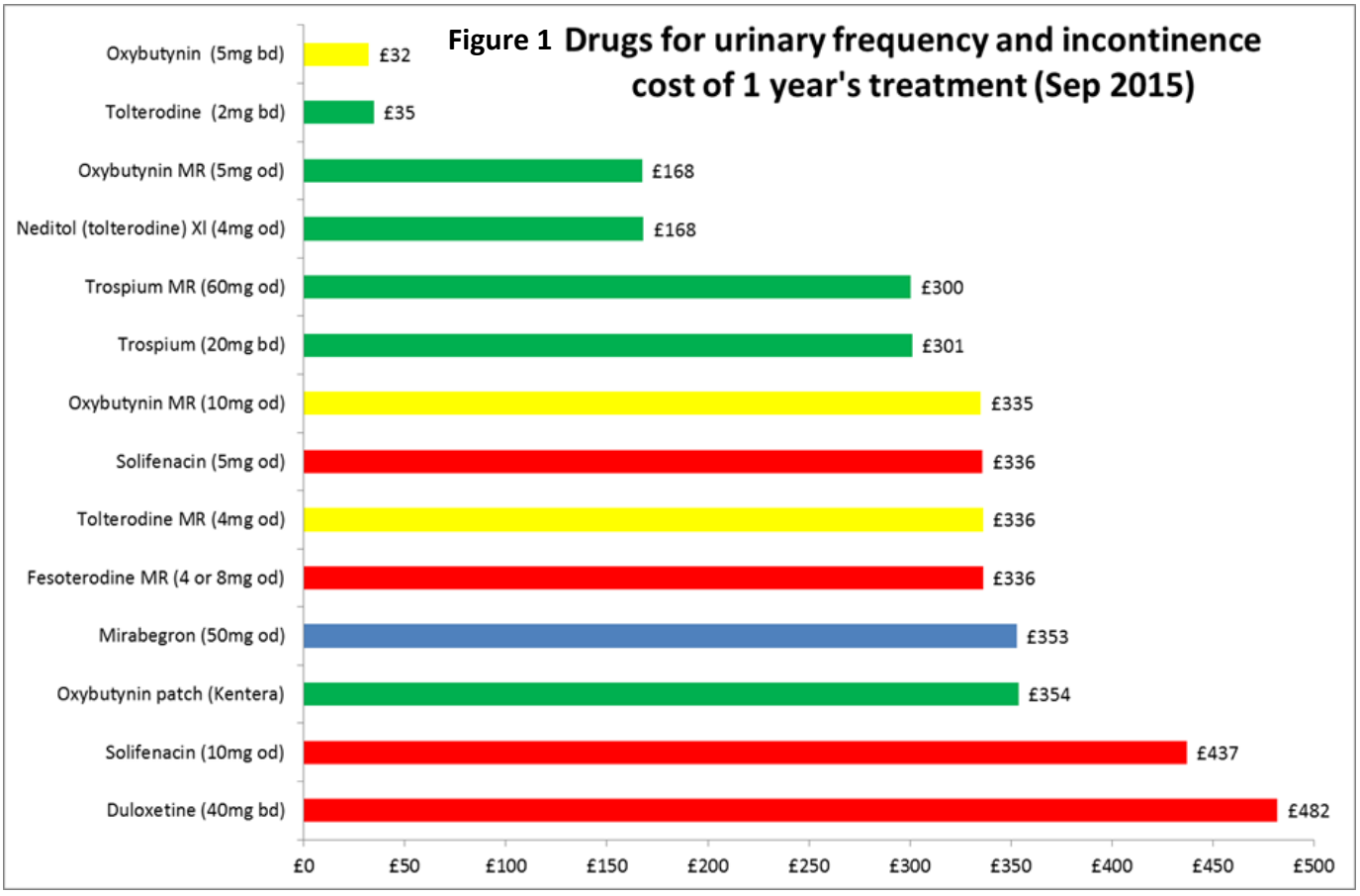
- Treat contributory factors such as constipation /chronic cough
- Advise regarding modification of high or low fluid intake, especially if in excess of 1.5 litres/day
- Reduce caffeine intake – increase water based fluids
- Decrease weight if BMI > 30
- Patient education on self-management of condition – www.bladderandbowelfoundation.org

Non-pharmacological interventions

- A trial of supervised pelvic floor muscle training of at least 3 months' duration should be offered as first-line treatment in stress and mixed UI, for more information see http://patient.info/health/pelvic-floor-exercises
- Bladder training lasting for a minimum of 6 weeks should be offered as first-line treatment in urge and mixed UI.

Drug treatment
Do NOT prescribe unless the patient has been assessed and first line non-drug conservative management has been tried for an adequate duration and has failed:

- Drugs **only** provide **modest benefit**. Placebo-controlled trials estimate that, as a class, antimuscarinics have very limited effect, with approximately one fewer incontinent episode and one fewer voiding episode per 48 hours.
- Remind patients that antimuscarinic drug treatments are for **short term use ONLY** and will be stopped to determine effectiveness of treatment.
- There is no clinical difference between the different agents, no evidence that one treatment is better than another. The lowest cost drug should be used, see figure 1.
    - 1ST LINE – Oxybutynin Immediate Release (IR) 5mg BD – TDS or Tolerodine Immediate Release (IR) 2mg BD. Avoid oxybutynin in frail elderly patients.
    - 2nd LINE – Neditol XL® (Tolterodine Modified Release) MR 4mg OD.
- Educate the patient to manage their expectations of drug treatment outcome.
- Discuss likelihood of success (only modest benefit) and counsel patient about adverse effects. These are more common in the elderly and include: dry mouth (up to 30%), constipation, blurred vision, nausea, dyspepsia, flatulence, palpitations, arrhythmias, dizziness, insomnia and skin reactions.
- Long term prescribing of antimuscarinics is associated with an increased risk of cognitive impairment, dementia and mortality.
- Carry out a medication review four weeks after starting or changing medication.
- Review regularly. Only continue treatment if benefit is maintained.
- Review long term patients annually or every 6 months if > 75 years.
    - Trial a drug holiday for appropriate patients receiving long term treatment—see review tool[3].
    - If treatment needs to be restarted after 4 week drug holiday consider first line choices.
- A recent study in GP practices in Northern Ireland showed that 77% of patients did not restart drug treatment for urinary incontinence following a 4 week drug holiday, for more information on this see http://niformulary.hscni.net/PrescribingNewsletters/PDF/NIMM_2015/NIMM_NewsletterVol6Issue5May15.pdf



Safety Update

MHRA Mirabegron (Betmiga®▼): Risk of severe hypertension and associated cerebrovascular and cardiac events

Hypertension is a known side effect of mirabegron. However, cases of severe hypertension have now been reported, including hypertensive crisis associated with cardiac and cerebrovascular events (mainly transient ischaemic attack or stroke).
The following advice has now been published by the MHRA:

- Mirabegron is contraindicated in patients with severe uncontrolled hypertension (systolic blood pressure ≥180 mm Hg or diastolic blood pressure ≥110 mmHg, or both).
- Blood pressure should be measured before starting treatment and monitored regularly during treatment, especially in patients with hypertension.
- Suspected side effects of mirabegron should be reported via the Yellow Card reporting system.

Mirabegron (Betmiga®▼) for treating symptoms of overactive bladder

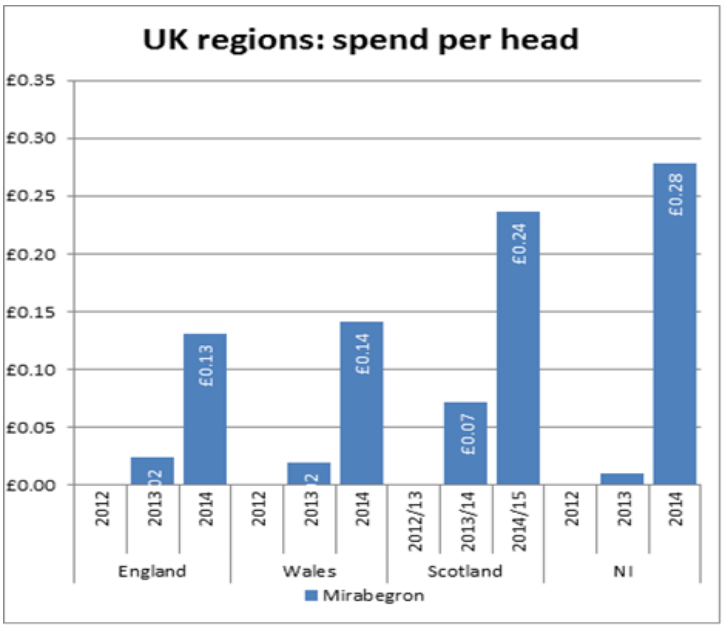
NICE technology appraisal guidance [TA290] published date: June 2013 has been endorsed for use in NI in primary and secondary care and a Service Notification has been issued accordingly
http://www.hscboard.hscni.net/NICE/TA2013/TA290Mirabegron.pdf

Guidance

1.1 Mirabegron is recommended as an option for treating the symptoms of overactive bladder only for people in whom antimuscarinic drugs are contraindicated or clinically ineffective, or have unacceptable side effects.
1.2 People currently receiving mirabegron that is not recommended for them in 1.1 should be able to continue treatment until they and their clinician consider it appropriate to stop.

Mirabegron—key facts

- There have been no direct head to head comparison trials between mirabegron and current therapies
- Mirabegron appears to offer **similar** efficacy to current antimuscarinic therapies
- Scottish Medicines Consortium (SMC) analysis of results suggests 'that mirabegron 50mg was not significantly different than comparators in efficacy outcomes, with the exception of being **less effective** than solifenacin 10mg in micturition frequency and urge incontinence'
- Mirabegron and placebo had a lower incidence of dry mouth compared to the active tolterodine **BUT** the number of patients discontinuing treatment was about the same in all treatment groups. Hence, it is unclear if the lower incidence of dry mouth in the mirabegron group would actually translate to less discontinuation or treatment switching in clinical practice
- NI Service Notification estimated 'that **only about a third** of people trying mirabegron will have sufficient effect for them to continue long-term with the drug'.
- Northern Ireland spends more on mirabegron than the rest of the UK.
- In 2014/15 NI spend on mirabegron was approximately £1 million, with prescribing trend continuing to increase.



Action for GPs

Mirabegron safety update

- Review patients currently treated with mirabegron in light of MHRA recommendations to ensure treatment is in line with guidelines and blood pressure is monitored regularly.
- Other factors to consider during review:
  contra-indications - severe hypertension
  Cautions - history of QT-interval prolongation and concomitant use with drugs that prolong the QT interval
  hepatic and renal impairment
  side-effects including tachycardia, urinary tract infection, atrial fibrillation, hypertension, palpitation

All patients prescribed urinary incontinence medication including mirabegron

- Review all patients on long-term treatment and trial '4 week drug holiday' as per HSCB review tool.
- Review patients overall anticholinergic burden with aim to reduce their anticholinergic load, for more information on anticholinergic medication review see http://niformulary.hscni.net/PrescribingNewsletters/MedicinesManagement/vol7/Pages/default.aspx
- Consider switch to first or second line choice agents in suitable patients.
- Recommendations to prescribe should follow NI formulary choices http://niformulary.hscni.net/Formulary/Adult/7.0/7.4/7.4.2/Pages/default.aspx and mirabegron NICE TA290, GPs may challenge any recommendations that do not follow prescribing guidance and forward examples to their MMA.

Action for community pharmacists

- Advise patients about the side-effect profile of medicines known to disrupt the normal process of storing and passing urine (see page 1 for details)
- Advise patients prescribed these medicines for the first-time that their treatment is likely to be short-term. Their treatment will be reviewed to determine its effectiveness
- Where appropriate, promote / support patients taking a 'drug holiday' from their urinary incontinence drug treatment
- Ensure patients receiving treatment with mirabegron have their blood pressure monitored frequently during treatment
- Report any side-effects associated with the use of mirabegron to MHRA via the yellow card reporting system

References

1. National Institute for Health and Care Excellence (NICE). Clinical Guideline 171. The management of urinary incontinence in women. September 2013. http://guidance.nice.org.uk/CG171
2. National Institute for Health and Care Excellence (NICE). Clinical Guideline 97. The management of lower urinary tract symptoms in men. June 2009. http://guidance.nice.org.uk/CG97
3. HSCB. Review of medication for urinary incontinence in primary care. 2015 http://primarycare.hscni.net/pdf/UrinaryIncontinenceMediciationReviewWebVersion.docx
4. MHRA. Mirabegron (Betmiga®▼): Risk of severe hypertension and associated cerebrovascular and cardiac events. MHRA Drug Safety Update, 2015. https://www.gov.uk/drug-safety-update/mirabegron-betmiga-risk-of-severe-hypertension-and-associated-cerebrovascular-and-cardiac-events

This newsletter has been produced for GP practice staff and Pharmacists by the Regional Pharmacy and Medicines Management Team. If you have any queries or require further information on the contents of this newsletter, please contact one of the Medicines Management pharmacists in your local HSCB office.

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