Management of male lower urinary tract symptoms (LUTS) in primary care –
An interactive workshop

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• Location of Clinical Practice

**NHS**
– Lister Hospital, Stevenage
– Watford General Hospital
– Hemel Hempstead Hospital

**Private Practice**
– Pinehill Hospital, Hitchin
– Spire Bushey Hospital, North London

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## Today’s agenda

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<th>Session/presentation</th>
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<td>Arrival and Registration</td>
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<td>19.00 – 19.10</td>
<td>Welcome and Introduction</td>
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<td>19.10 – 19.20</td>
<td>Group Discussion – Local LUTS pathway</td>
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<td>19.20 – 20.00</td>
<td>LUTS – Think Prostate and Bladder</td>
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<td>20.00 – 20.20</td>
<td>Practical Session – Diagnostic Test and their interpretation</td>
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<td>20.20 – 20.50</td>
<td>Practical Session – Digital Rectal Examination Test</td>
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<td>20.50 – 21.00</td>
<td>Summary and closing marks</td>
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WELCOME AND INTRODUCTION
Male LUTS are common and often managed sub optimally

- Up to 30% of men over the age of 65 years have bothersome LUTS\(^1\)
- Age is a risk factor for LUTS\(^1\)
  - Incidence is expected to increase with the aging population
- Many patients do not receive optimal treatment\(^2\)
  - Failure to present/delayed presentation to HCP due to a belief that the symptoms are just a normal feature of aging
  - Inadequate assessment of symptoms leading to misdiagnosis and incorrect choice of treatment
  - Lack of medication review or follow up

Patient presents to primary care

Treatment initiated by GP

Follow on management by hospital-based urologist

No follow up or review

Follow on management by hospital-based urologist

Referral to specialist services

High number of unnecessary referrals to urology for relatively straightforward management

There is an opportunity to reduce urology activity and costs in secondary care by managing men with LUTS in a primary care setting with appropriate referrals to urology specialists
Male LUTS can be effectively managed in a primary care setting

With adequate assessment, medical management of male LUTS can be initiated in a primary care setting with review and adjustment of medication if needed, without the need for a specialist opinion.

NICE clinical guidelines 97
Refer for specialist opinion when:
• The patient has a complex presentation
• There is significant diagnostic doubt
• The patients fail to respond to medical management

NICE quality standard 45
The quality standard, in conjunction with the guidance on which it is based, should contribute to improvements outlined in the outcomes framework:
• Domain 2: Enhancing quality of life for people with long-term conditions
• Domain 4: Ensuring that people have a positive experience of care
Today’s objectives

• To increase confidence of GPs in diagnosing male patients with LUTS in the primary care setting
• To provide practical training for GPs on the clinical examinations that are relevant to the management of LUTS, including DREs
• To provide training on the tools available for aiding the diagnosis of LUTS, such as the IPSS and FVC
  – Including how to interpret the results effectively
• To review the available treatment options for managing male patients with LUTS
• To highlight the importance of timely patient review to assess treatment response and adjust medication if required to optimise clinical outcomes
GROUP DISCUSSION – LOCAL LUTS PATHWAY
Group discussion

- Current management of male patients with LUTS in the local primary care setting
Group discussion – suggested questions

• Suggested questions include:
  • How are patients with LUTS assessed and diagnosed?
  • When would patients be referred for specialist assessment?
  • What treatment options are being utilised?
  • How often are patients reviewed to assess treatment response?
  • What are the perceived challenges/areas for improvement to further optimise management of LUTS in primary care?
LUTS – THINK PROSTATE AND BLADDER
Symptoms associated with male LUTS can be categorised into storage, voiding and post-micturition\textsuperscript{1,2}

<table>
<thead>
<tr>
<th>Storage symptoms</th>
<th>Voiding symptoms</th>
<th>Post-micturition symptoms</th>
</tr>
</thead>
</table>
| • Increased daytime frequency  
  • Urgency  
  • Urinary incontinence associated with urgency  
  • Nocturia | • Hesitancy  
  • Intermittency  
  • Straining  
  • Weak or slow stream  
  • Split stream  
  • Terminal dribble | • Sensation of incomplete emptying  
  • Post-micturition dribble |


Most men with LUTS have both storage and voiding symptoms\(^1\)

- Almost 50% of patients have a combination of storage and voiding symptoms\(^2\)

![](chart.png)

**Results from the EpiLUTS survey.**

Of 14,139 men \(\geq 40\) years old surveyed, 10,044 (71%) reported LUTS.

Only 6% of patients currently receive combination therapy with an alpha blocker and an antimuscarinic to address both storage and voiding symptoms\(^3\)

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LUTS are multifactorial in aetiology\textsuperscript{1-3}


Male LUTS significantly impact on quality of life

• Storage symptoms can be particularly bothersome
  – Interfere with day-to-day life\textsuperscript{1-4}
  – Impact upon the patient and their partner
    • e.g. nocturia
  – Impact upon sexual health\textsuperscript{5}

• LUTS can lead to anxiety and depression\textsuperscript{3}

Presentation of male LUTS

- Men may present to their GPs for a variety of reasons, e.g. their partner has told them to go, symptoms have become worse or they fear they have cancer.

<table>
<thead>
<tr>
<th>Common patient profiles</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Middle aged and beyond</td>
<td>Increasing age is a major risk factor for developing LUTS</td>
</tr>
<tr>
<td>Concerns about cancer</td>
<td>May come from either the patient or their partner, friends or family members</td>
</tr>
<tr>
<td>Sleep disruption caused by nocturia</td>
<td>The patient may be constantly tired and their partner's sleep may also be disrupted</td>
</tr>
</tbody>
</table>
| Frequency/urgency impacting on day-to-day life, e.g.:    | Interrupting work meetings
                                                        Unable to play a round of golf
                                                        Having to stop numerous times when driving |
| Comorbidities associated with fluid retention may contribute to storage symptoms, e.g.:  | Hypertension
                                                        Diuretic medication
                                                        Sleep apnoea (may cause nocturnal polyuria) |
PRACTICAL SESSION – DIAGNOSTIC TESTS AND THEIR INTERPRETATION
Optimal management of male lower urinary tract symptoms (LUTS) in primary care
A consensus statement

Astellas Pharma Ltd nominated the consensus group members, organised and funded the consensus group meeting and checked the consensus statement for factual accuracy.

Optimal management pathway of male LUTS in primary care

- Simple patient pathway to aid the management of LUTS in primary care and:
  - Encourage the management of LUTS in primary care with appropriate referral for specialist assessment
  - Provide a generic management pathway that can be moulded to local pathways
  - Compiled by a consensus group:
    - Urologists
    - GPs with special interest
- Aligned with current NICE guidelines

Throughout the pathway it is important to discuss with the patient plans for examinations and investigations and realistic management goals

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Primary care assessment of LUTS

During the initial consultation:

- Break down the nature of the symptoms
- Identify the primary reason for patient presentation
- Differentiate which part of the micturition cycle the most bothersome symptom(s) belong to

Due to time constraints, assessments within primary care may need to be performed over more than one appointment, as is standard practice for any other chronic condition.

*Perform a neurological and/or cardiovascular examination if history suggests comorbidity of these symptoms is a factor.

PSA, prostate specific antigen
Men with bothersome LUTS should be asked to complete a urinary frequency-volume chart (FVC)

• Assesses symptoms of LUTS and engages with the patient
• Interpretation can help uncover and identify:
  – High fluid intake
  – Nocturia
  – Reduced fixed volumes
  – Reduced variable volumes
  – Systemic conditions producing LUTS e.g. diabetes, sleep apnoea and heart failure
    • Only way to diagnose nocturnal polyuria
• Patients complete the chart for a minimum of 3 days
  – Various charts are available, with varying degrees of complexity
  – Most are acceptable to patients if proper instruction is given

The following values may be considered normal on a urinary FVC:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine output</td>
<td>1.5-2.0 L/24 hr</td>
</tr>
<tr>
<td>Number of voids</td>
<td>5-8 voids/24 hr</td>
</tr>
<tr>
<td>Volume of voids</td>
<td>300-500 ml/void</td>
</tr>
</tbody>
</table>
The International Prostate Symptom Score (IPSS) can help determine the severity of symptoms

**IPSS**¹,²

<table>
<thead>
<tr>
<th>Part 1</th>
<th>Seven questions regarding the severity of urinary symptoms</th>
<th>Three storage symptoms (urgency, frequency and nocturia) Four voiding symptoms (weak stream, incomplete emptying, intermittency and straining) Each question scoring 1 to 5, making a maximum total score of 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part 2</td>
<td>One question addressing the impact/bother of these symptoms on the patient’s quality of life</td>
<td></td>
</tr>
<tr>
<td>Score</td>
<td>Score</td>
<td>Symptom severity</td>
</tr>
<tr>
<td>0-7</td>
<td>Mild</td>
<td></td>
</tr>
<tr>
<td>8-19</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>20-35</td>
<td>Severe</td>
<td></td>
</tr>
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</table>

- Symptom score rather than a diagnostic test:²
  - Quantifies the severity of LUTS
  - Quickly identifies the symptoms affecting the patient
  - Measures progression of LUTS or response to treatment

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Prostate Specific Antigen (PSA) should only be performed if clinically indicated

- LUTS are suggestive of bladder outlet obstruction secondary to BPE
- Prostate feels abnormal or DRE
- Concerned about prostate cancer
- Provide adequate counselling
  - Explain the risk of false positives or false negatives
  - Provide written information regarding the PSA test
  - Men should be fully aware that the test may be inconclusive

Refer if red flags are raised

• Refer for assessment by a urologist, GP with special interest or continence advisor, according to the local pathway, if during the course of the primary care assessment red flags are raised.

Red flags:
• Recurrent urinary tract infection
• Nocturnal enuresis
• Haematuria (visible or non-visible)
• Previous or suspected urinary retention
• Renal impairment that is suspected to be secondary to lower urinary tract dysfunction
• Pain with voiding
• Suspected urological cancer

• Red flags suspicious for cancer require a referral within 2 weeks for an urgent urologist opinion.
Referral checklist for specialist assessment

When referring a patient to a urology specialist for LUTS, the following should be included in the referral letter:

**Referral checklist**

- Assessment of symptoms
  - e.g. voiding and/or storage, ideally supplemented by the IPSS
- Medical history
- Drug history
- Social history
- Physical examination, including abdomen, external genitalia, DRE and any signs of neurological or cardiovascular disease, if medical history suggests these are a possibility
- Investigations, including urinalysis (blood, glucose, protein, leucocytes and nitrites), FVC and other tests, such as renal function and PSA, if clinically indicated
- Provisional diagnosis
- Details of any management, conservative or medical
- Specific reason for referral
Tools to support you in optimising management of patients with LUTS

A series of resources are available to aid you in assessing male patients with LUTS and providing effective management in the primary care setting.
DISCUSSION
PRACTICAL SESSION – PERFORMING A DRE
Importance of performing a DRE

- A digital rectal examination (DRE) should be offered to men with lower urinary tract symptoms at initial assessment\(^1\)
- Performing a digital rectal examination is good practice to identify:\(^1\)
  - Abnormalities of the prostate
  - Associated conditions that might affect bladder function

Performing a DRE in primary care

A step-by-step guide is available for performing a DRE in primary care.
<table>
<thead>
<tr>
<th>Complication</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom progression</td>
<td>17-40%</td>
</tr>
<tr>
<td>Acute urinary retention</td>
<td>1-2%</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>0.1-12%</td>
</tr>
<tr>
<td>Bladder Calculi</td>
<td>0.3-3.4%</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>&lt;2.5%</td>
</tr>
<tr>
<td>Incontinence</td>
<td>&gt;1%</td>
</tr>
<tr>
<td>Haematuria</td>
<td></td>
</tr>
<tr>
<td>Partner’s issues</td>
<td></td>
</tr>
</tbody>
</table>
Flow rate change with time

- Rhodes et al

- 492 men in Olmstead Study

- Flow deteriorated more rapidly
  - Poor initial flow (Flow < 10 ml/sec)
  - Increasing age (Men above 70)
  - Prostate Volume
  - Symp‘
Risk of Acute Urinary Retention in relationship to prostate volume

Risk of Acute Urinary Retention in relationship to prostate volume
Risk of AUR by Baseline Prostate Volume in Untreated Men (Placebo Group)

Approximately 3-fold increase in risk (p<0.010)

Two-year incidence of AUR (%)

<table>
<thead>
<tr>
<th>Prostate volume &lt;40 ml (n=819)</th>
<th>Prostate volume ≥40 ml (n=579)</th>
</tr>
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<tbody>
<tr>
<td>1.6</td>
<td>4.2</td>
</tr>
</tbody>
</table>

Risk of Acute Urinary Retention in relationship to prostate volume / Baseline Serum PSA

![Diagram showing 9-fold increase in risk for acute urinary retention with higher PSA levels.](image-url)
Acute or chronic inflammation in a baseline biopsy on the risk of clinical progression of BPH (MTOPS) J Urol 2005
Patient group are risk of progression

- Prostate Volumes > 30 cc
- PSA > 1.4 ng/ml
- Severe symptoms
- Older men
- Inflammation on prostate biopsies
DRE DEMONSTRATION
TRAINING EXERCISE
Training exercise

- Split into 5 groups of 4
- Use the Bertie Bottoms provided to each practice performing a DRE

DRE, digital rectal examination
TREATMENT OPTIONS FOR MANAGING MALE LUTS
Primary care management of LUTS

- In cases where LUTS are not bothersome, or are mild to moderate, give reassurance and offer conservative management and lifestyle advice
- Medical management should be offered to men with bothersome LUTS
  - Comorbidities and current medications should be considered when offering medical management for LUTS

**GP initiates management**

- **Bothersome voiding LUTS**
  - Conservative management, including lifestyle advice
  - Offer an alpha blocker
  - If prostate enlarged (>30 g or PSA >1.4 ng/ml) consider an alpha blocker + 5-alpha-reductase inhibitor

- **Bothersome storage LUTS + voiding LUTS**
  - Conservative management, including lifestyle advice
  - Offer an alpha blocker
  - If prostate enlarged (>30 g or PSA >1.4 ng/ml) consider an alpha blocker + 5-alpha-reductase inhibitor

- **Bothersome storage LUTS**
  - Conservative management, including lifestyle advice
  - Offer an antimuscarinic
  - Nocturia only
  - Conservative management, including lifestyle advice

†If patients have LUTS that are not bothersome in nature but also have an enlarged prostate and are at high risk of progression offer 5-alpha-reductase inhibitor monotherapy.
Mechanism of action of alpha blockers, 5-alpha-reductase inhibitors and antimuscarinics in the treatment of LUTS


Patients treated with alpha blockers may still experience symptoms

• Patients are most likely prescribed an alpha blocker for initial treatment of moderate to severe LUTS\(^1\)
• Alpha blockers are designed to predominantly treat voiding symptoms\(^2\)
• If patients have mixed LUTS, they may likely still experience storage symptoms\(^2\)
  – Can be treated with antimuscarinics\(^1\)


It is important that treatment is initially reviewed by GPs after 4-6 weeks to assess response to treatment – medication could be adjusted if needed\(^2\)
Combination therapy

- In men with moderate to severe LUTS with voiding AND storage symptoms, alpha blocker monotherapy may not be sufficient.
- **NICE guidelines recommend the addition of an antimuscarinic to alpha blocker therapy to target both voiding and storage symptoms in these patients**\(^2\)

**Alpha blocker + antimuscarinic**

A fixed dose combination tablet of the antimuscarinic, solifenacin succinate, and the alpha blocker tamsulosin hydrochloride, Vesomni\(\text{TM}\) (6 mg solifenacin succinate and 0.4 mg tamsulosin hydrochloride; Astellas Pharma Ltd.), is available for the treatment of moderate to severe storage symptoms and voiding symptoms associated with BPH in men, who are not adequately responding to treatment with monotherapy.\(^3\)

**Alpha blocker + 5-alpha-reductase inhibitor**

Combination therapy with an alpha blocker and 5-alpha-reductase inhibitor is recommended for patients with both moderate to severe LUTS and an enlarged prostate (>30 g or PSA > 1.4 ng/ml).\(^2\)

A fixed dose combination tablet of the 5-alpha-reductase inhibitor, dutasteride, and the alpha blocker, tamsulosin is available, Combodart\(\text{®}\) (0.5 mg dutasteride and 0.4 mg tamsulosin hydrochloride; GlaxoSmithKline).\(^4\)
Combination therapy – alpha blocker + 5 DHT inhibitor

**Cumulative incidence of AUR**

- Placebo (n=737)
- Finasteride (n=768)
- Doxazosin (n=756)
- Combination (n=786)

Combination vs. Placebo 81% risk reduction

- Finasteride alone reduced the risk of AUR by 68% vs. placebo
- Doxazosin alone did not significantly reduce the risk of AUR vs. placebo

**Cumulative incidence of BPH-related surgery**

- Placebo (n=737)
- Finasteride (n=768)
- Doxazosin (n=756)
- Combination (n=786)

Combination vs. Placebo 67% risk reduction

- Finasteride and doxazosin significantly reduced the incidence of BPH-related surgery vs. placebo
- Finasteride alone significantly reduced the incidence of BPH-related surgery 64% vs. placebo
- Doxazosin alone did not significantly reduce the incidence of BPH-related surgery

Combination therapy

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Rationale for Vesomni

Solifenacin (Vesicare®)¹

- Antimuscarinics inhibit detrusor smooth muscle contractions in the bladder
- Predominantly storage symptom relief, including urgency and frequency

Tamsulosin OCAS (Flomaxtra XL®)²

- α-blockers relax smooth muscle in the prostate and bladder neck
- Predominantly voiding symptom relief, including hesitancy, weak stream and terminal dribble

Once-daily, fixed-dose combination tablet of solifenacin 6mg and tamsulosin OCAS 0.4mg (Vesomni™)³

OCAS, oral controlled absorption system

¹ Astellas Pharma Ltd. Vesicare Summary of Product Characteristics. 2013
² Astellas Pharma Ltd. Flomaxtra XL Summary of Product Characteristics. 2014
³ Astellas Pharma Ltd. Vesomni Summary of Product Characteristics. 2014
Vesomni: Improves prostate symptoms

- Total International Prostate Symptom Score (IPSS) was a co-primary endpoint of the Phase 3 NEPTUNE trial
- Vesomni was non-inferior to tamsulosin OCAS for total IPSS, and both significantly improved IPSS vs. placebo
- 30% relative reduction in total IPSS with Vesomni vs. placebo (-7.0 vs. -5.4)

Adapted from van Kerrebroeck P et al 2013. Non-inferiority (margin 0.5) demonstrated for Vesomni vs. tamsulosin OCAS 0.4mg in a randomised, 12-week study (p=0.001)
Vesomni: Improves bladder symptoms

- Total Urgency and Frequency Score (TUFS) was a co-primary endpoint of the Phase 3 NEPTUNE trial
- Vesomni significantly reduced urgency and frequency vs. placebo, as measured by TUFS
- 84% relative reduction in urgency and frequency with Vesomni vs. placebo (-8.1 vs. -4.4)

Adapted from van Kerrebroeck P et al 2013. TUFS: Total Urgency and Frequency Score: a validated measure capturing the two important parameters, urgency and frequency, in a single measure.
Vesomni: significant improvement in sleep & QoL\(^1\)∗

- Vesomni was associated with a 43% higher sleep score improvement from baseline than placebo (11.9 vs. 8.3)\(^1\)
- In a long-term study, the quality of life of Vesomni-treated patients improved from baseline within 1 month and was maintained over 12 months\(^2\)

Adapted from van Kerrebroeck P et al 2013.
∗As measured by mean change from baseline in the internationally validated and recognised OAB-q health-related quality of life (HRQoL) sleep score in a randomised, 12-week study.

QoL, quality of life

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2. Data on file, VSO13042UK. Astellas Pharma Ltd.
Vesomni: generally well tolerated\(^1\)

| Incidence of drug treatment-emergent adverse events (TEAEs) % (n)\(^1\) |
|-----------------------------|-----------------------------|-----------------------------|
|                              | Placebo (n=341)             | Tamsulosin OCAS 0.4mg (n=326) | Vesomni (n=337) |
| Retrograde ejaculation       | 0                           | 0                           | 0.3% (1)       |
| Nausea                      | 0.3% (1)                    | 1.2% (4)                    | 0.3% (1)       |
| Urinary retention           | 0                           | 0.3% (1)                    | 0.6% (2)       |
| Fatigue                     | 0.6% (2)                    | 0.6% (1)                    | 1.2% (4)       |
| Headache                    | 0.6% (2)                    | 0.6% (1)                    | 1.2% (4)       |
| Dyspepsia                   | 0.3% (1)                    | 0.3% (1)                    | 1.8% (6)       |
| Constipation                | 0.3% (1)                    | 0.3% (1)                    | 2.7% (9)       |
| Dry mouth                   | 1.2% (4)                    | 0.3% (1)                    | 8.0% (27)      |

Adapted from van Kerrebroeck P et al. 2013\(^1\)

- Incidences of TEAEs with Vesomni were generally lower than reported separately for the individual drugs, as per their SmPCs\(^1-4\)
Vesomni: low incidence of AUR\textsuperscript{1}

<table>
<thead>
<tr>
<th>Incidence of AUR: % (n)\textsuperscript{1}</th>
<th>Placebo (n=341)</th>
<th>Tamsulosin OCAS 0.4mg (n=326)</th>
<th>Vesomni (n=337)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary retention</td>
<td>0</td>
<td>0.3% (1)</td>
<td>0.6% (2)</td>
</tr>
<tr>
<td>AUR requiring catheterisation</td>
<td>0</td>
<td>0.3% (1)</td>
<td>0.3% (1)</td>
</tr>
</tbody>
</table>

- Vesomni had a similar incidence of acute urinary retention (AUR) to that seen with tamsulosin OCAS\textsuperscript{1,2}
  - The incidence of the most serious adverse event, AUR requiring catheterisation, was uncommon at 0.3%\textsuperscript{1}

Vesomni: after 12 months

• In a 12-month extension study:
  – Only 3.9% discontinued Vesomni due to adverse events (n=42/1066; 3.9% at 12 weeks, n=13/337)\(^1,2\)
  – 81% were satisfied with the efficacy and safety of Vesomni after one year (n=572/702)\(^3\)

Vesomni: an option for male LUTS patients who do not respond to monotherapy

Vesomni, compared with tamsulosin OCAS:

- Significantly reduced urgency and frequency symptoms, as measured by TUFS
- Significantly improved patients’ sleep and quality of life
- Generally well tolerated, with a low incidence of AUR

THE IMPORTANCE OF TREATMENT REVIEW
Symptom review at 4-6 weeks in patients receiving an alpha blocker or antimuscarinic*

(Bothersome storage LUTS + voiding LUTS)
If storage symptoms persist despite treatment with an alpha blocker alone consider combination therapy of an alpha blocker + antimuscarinic

(Bothersome storage LUTS)
If still symptomatic consider 2nd line antimuscarinic or a beta 3-adrenoceptor agonist

(Nocturia only)
If still symptomatic refer for specialist assessment‡

Symptom review at 4-6 weeks in patients receiving an alpha blocker and/or antimuscarinic

If still symptomatic refer for specialist assessment‡

If stable review at 6-12 months

*As it can take up to 6 months before a response is observed, it is recommended that patients receiving 5-alpha-reductase inhibitors are reviewed at 3-6 months.

‡A specialist assessment may be performed by a urologist, GP with special interest or continence advisor, according to the local pathway. Red flags suspicious for cancer require a referral within 2 weeks for an urgent urologist opinion.

Encourage patients to book their next appointment before they leave the surgery and only prescribe up to 6 weeks of medication.
Symptom questionnaire

Can also be used as part of a patient’s treatment review to assess response during their follow-up appointment.
A patient support service is now available

• Will remind patients to book a follow up appointment with their GP if still experiencing voiding (prostate) and/or storage (bladder) symptoms¹
• Can be offered to patients as a reminder at 4 and 6 weeks¹
• Offers a choice of receiving either voice or text messages¹
• Details outlined in an information leaflet for GPs to provide to patients¹
• Pharmacists will also remind patients of the importance of a follow up appointment when they pick up their alpha blocker prescription²

DISCUSSION
Prostate size

- Walnut: 20cc
- Ping-pong ball: 33cc
- Golf ball: 40cc
- Clementine: 65cc
- Tennis ball: 130cc
SUMMARY AND CLOSING REMARKS
Summary (1)

• LUTS are common and have a significant impact on quality of life\(^1\)
  – Nearly 50% of men with LUTS have a combination of storage AND voiding symptoms\(^2\)

• Following adequate assessment, LUTS can be effectively managed in primary care in the majority of cases\(^1\)
  – There is a need to reduce the number of unnecessary referrals for specialist assessment

• A consensus statement has been produced to provide clear guidance on the optimal management of LUTS\(^3\)
  – Developed by a group of urologists and GPs with special interest
  – In line with NICE guidelines for the management of LUTS in men

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Summary (2)

- Management options vary according to type and severity of symptoms
  - For patients with bothersome voiding LUTS, with or without storage LUTS, offer an alpha blocker; if the prostate is enlarged (>30 g or PSA >1.4 ng/ml) consider an alpha blocker + 5-alpha-reductase inhibitor
  - For patients with bothersome storage LUTS only offer an antimuscarinic
  - If patients have LUTS that are not bothersome in nature but also have an enlarged prostate and are at high risk of progression offer 5-alpha-reductase inhibitor monotherapy

- Patients should initially be reviewed to assess response to treatment, adjust medication or refer for specialist assessment if needed
  - For men with mixed symptoms, monotherapy with an alpha blocker may not resolve storage symptoms, and combination therapy with an antimuscarinic can be considered
  - Once stable, patients should be monitored every 6-12 months

## NICE guideline CG97

<table>
<thead>
<tr>
<th>Indication</th>
<th>Treatment guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate to severe LUTS</td>
<td>Offer an α-blocker (alfuzosin, doxazosin, tamsulosin or terazosin)</td>
</tr>
<tr>
<td>OAB</td>
<td>Offer an anticholinergic</td>
</tr>
<tr>
<td>LUTS and a prostate estimated to be larger than 30g or PSA &gt;1.4ng/ml, and high risk of progression</td>
<td>Offer a 5α-reductase inhibitor</td>
</tr>
<tr>
<td>Bothersome moderate to severe LUTS, and a prostate estimated to be larger than 30g or PSA &gt;1.4ng/ml</td>
<td>Consider an α-blocker plus a 5α-reductase inhibitor</td>
</tr>
<tr>
<td>Storage symptoms despite treatment with an α-blocker</td>
<td>Consider an anticholinergic as well as an α-blocker</td>
</tr>
</tbody>
</table>

- Combination therapy needs to be considered for men who inadequately respond to monotherapy\(^1\)
- NICE guidelines recommend anticholinergic and α-blocker combination therapy for storage symptoms that persist despite treatment with an α-blocker alone\(^1\)
- Review men taking α-blockers at 4–6 weeks and every 6–12 months\(^1\)

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\(^1\) NICE clinical guidelines 2010. The management of lower urinary tract symptoms in men, CG97

Date of preparation: December 2013. VSO13071UK.
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Prescribing information

Vesomni™ (solifenacin 6mg/tamsulosin 0.4mg) Prescribing Information

Presentation: Vesomni™ 6mg/0.4mg modified release tablets containing a layer of 6mg solifenacin succinate and a layer of 0.4mg tamsulosin hydrochloride.

Indication: Treatment of moderate to severe storage symptoms (urgency, increased micturition frequency) and voiding symptoms associated with benign prostatic hyperplasia (BPH) in men who are not adequately responding to treatment with monotherapy. Dosage: Adult males (including older people): Recommended dose: One tablet (6mg/0.4mg) once daily taken orally with or without food. Children and adolescents: No relevant indication for use in children and adolescents. Contraindications: Patients hypersensitive to the active substance or any of the excipients, or undergoing haemodialysis, or with severe hepatic impairment, or with severe renal or moderate hepatic impairment and also treated with a strong CYP3A4 inhibitor. Severe gastrointestinal conditions (including toxic megacolon), myasthenia gravis or narrow-angle glaucoma and patients at risk for these conditions. Patients with a history of orthostatic hypotension. Warnings and Precautions: Use with caution in patients with: severe renal impairment, risk of urinary retention, gastrointestinal obstructive disorders, risk of decreased gastrointestinal motility, hiatus hernia/gastroesophageal reflux and/or who are concurrently taking medicinal products (such as bisphosphonates) that can cause or exacerbate oesophagitis, autonomic neuropathy. Other conditions which can cause symptoms similar to BPH should be investigated and excluded. Other causes of frequent urination (heart failure or renal disease) should be assessed. Treat urinary tract infections with appropriate antibacterial therapy if present. QT prolongation and Torsade de Points have been observed in patients with risk factors such as pre-existing long QT syndrome and hypokalaemia, treated with solifenacin succinate. Angioedema with airway obstruction have been reported in some patients on solifenacin succinate and tamsulosin. Anaphylactic reaction has been reported in some patients treated with solifenacin succinate. Vesomni™ should be discontinued if angioedema occurs, or in patients who develop anaphylactic reactions and appropriate therapy and/or measures should be taken. A reduction in blood pressure can occur during treatment with tamsulosin, as a result of which, rarely, syncope can occur. Patients starting treatment with Vesomni™ should be cautioned to sit or lie down at the first signs of orthostatic hypotension (dizziness, weakness) until the symptoms have disappeared. Initiation of Vesomni™ is not recommended in patients for whom cataract or glaucoma surgery is scheduled. Intraoperative Pupillary Block Syndrome (IFS) has been observed during cataract and glaucoma surgery and may increase the risk of eye complications during and after the operation in some patients on or previously treated with tamsulosin. During the pre-operative assessment, cataract surgeons and ophthalmic teams should consider whether patients scheduled for cataract or glaucoma surgery are being or have been treated with tamsulosin in order to ensure appropriate measures are in place to manage the IFS during surgery. Use with caution in combination with moderate and strong CYP3A4 inhibitors and it should not be used with strong CYP3A4 inhibitors in patients who are of the CYP2D6 poor metaboliser phenotype or who are using strong CYP2D6 inhibitors. Interactions: Concomitant medication with any medicinal products with anticholinergic properties may result in more pronounced therapeutic effects and undesirable effects. Allow one week after stopping Vesomni™ before commencing any anticholinergic therapy. Concomitant administration of Vesomni™ with moderate and strong inhibitors of CYP3A4 may lead to increased exposure to both tamsulosin and solifenacin. Solifenacin can reduce the effect of stimulators of gastrointestinal tract motility. Co-administration with other alpha1-adrenoceptor antagonists could lead to hypotensive effects. Diclofenac and warfarin may increase the elimination rate of tamsulosin. Adverse Effects: Dry mouth, constipation, dyspepsia, dizziness, blurred vision, fatigue, ejaculation disorders, pruritus and urinary retention for Vesomni™. Nausea and abdominal pain were also commonly reported events for solifenacin. In post-marketing surveillance for solifenacin, Torsade de Points, electrocardiogram QT prolonged, atrial fibrillation, tachycardia have been observed. During post-marketing surveillance of tamsulosin, IFS has occurred in some patients during cataract surgery. Atrial fibrillation, arrhythmia, tachycardia and dyspnoea have also been reported in association with tamsulosin use from post-marketing experience. Prescribers should consult the Summary of Product Characteristics in relation to other side effects. Pack and prices: Vesomni™ 6mg/0.4mg pack of 30 tablets £27.62 Legal Category: POM. Product Licence Number: Vesomni™ 6mg/0.4mg PL 00160/0404. Date of Preparation: December 2013. Further information available from: Astellas Pharma Ltd, 2000 Hillwood Drive, Chertsey, Surrey, KT16 0RS, UK. Vesomni™ is a Registered Trademark. For full prescribing information please refer to the Summary of Product Characteristics. For Medical Information phone 0800 783 5018.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Astellas Pharma Ltd. Please contact 0800 783 5018.
Prescribing Information

Betmiga™ (mirabegron) Prescribing Information

**Presentation:** Betmiga™ prolonged-release film-coated tablets containing 25mg or 50mg mirabegron. **Indication:** Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome. **Dosage:** Adults (including the elderly): Recommended dose: 50mg once daily. **Children and adolescents:** Should not be used. **Contraindications:** Hypersensitivity to active substance or any of the excipients. **Warnings and Precautions:** Should not be used in patients with end stage renal disease (or patients requiring haemodialysis), severe hepatic impairment and severe uncontrolled hypertension. Not recommended in patients with severe renal impairment and/or moderate hepatic impairment concomitantly receiving strong CYP3A inhibitors. Dose adjustment to 25mg is recommended in patients with mild/moderate renal and/or mild hepatic impairment receiving strong CYP3A inhibitor concomitantly and in patients with severe renal and/or moderate hepatic impairment. Caution in patients with a known history of QT prolongation or in patients taking medicines known to prolong the QT interval. Use with caution in patients with significant bladder outlet obstruction (BOU) and in patients taking antimuscarinics for OAB. Not recommended during pregnancy and in women of childbearing potential not using contraception. Not recommended during breastfeeding. **Interactions:** Clinically relevant drug interactions between Betmiga™ and medicinal products that inhibit, induce or are a substrate for one of the CYP isoenzymes or transporters are not expected, except for inhibitory effect on the metabolism of CYP2D6 substrates. Betmiga™ is a moderate and time-dependent inhibitor of CYP2D6 and weak inhibitor of CYP3A. No dose adjustment needed when administered with CYP2D6 inhibitors or CYP2D6 poor metabolisers. Caution if co-administered with medicines with a narrow therapeutic index and significantly metabolised by CYP2D6. When initiating in combination with digoxin, the lowest dose for digoxin should be prescribed and serum digoxin should be monitored and used for titration of digoxin dose. Substances that are inducers of CYP3A or P-gp decrease the plasma concentrations of Betmiga™. No dose adjustment is needed for Betmiga™ when administered with therapeutic doses for rifampicin or other CYP3A or P-gp inducers. The potential for inhibition of P-gp by Betmiga™ should be considered when combined with sensitive P-gp substrates. Increases in mirabegron exposure due to drug-drug interactions may be associated with increases in pulse rate. **Adverse Effects:** Urinary tract infection, tachycardia, vaginal infection, cystitis, palpitation, atrial fibrillation, dyspepsia, gastritis, urticaria, rash, rash macular, rash papular, pruritus, joint swelling, vulvovaginal pruritus, blood pressure increase, liver enzymes increase, eyelid oedema, lip oedema, leukocytoclastic vasculitis, purpura and angioedema. **Prescribers should consult the Summary of Product Characteristics in relation to other side effects.** **Pack and prices:** Betmiga™ 25mg and Betmiga™ 50mg pack of 30 tablets £29.00. **Legal Category:** POM. **Product Licence Number:** Betmiga™ 25mg EU/1/12/809/001 - 007; Betmiga™ 50mg EU/1/12/809/008 - 014. **Date of Preparation:** November 2014. **Further information available from:** Astellas Pharma Ltd, 2000 Hillswood Drive, Chertsey, Surrey, KT16 0RS, UK. Betmiga™ is a Registered Trademark. For full prescribing information please refer to the Summary of Product Characteristics. **For Medical Information phone 0800 783 5018.**

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard
Adverse events should also be reported to Astellas Pharma Ltd. Please contact 0800 783 5018
### Vescicare® Prescribing Information

**Presentation:** Vescicare® film-coated tablets containing 5 mg or 10 mg solifenacin succinate.  
**Indication:** Symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in patients with overactive bladder syndrome.  
**Dosage:** Adults: Recommended dose: 5 mg once daily. If needed, the dose may be increased to 10 mg once daily.  
**Children and adolescents:** Should not be used.  
**Contraindications:** Urinary retention, severe gastrointestinal condition (including toxic megacolon), myasthenia gravis or narrow-angle glaucoma and in patients at risk for these conditions. Patients hypersensitive to the active substance or to any of the excipients, or undergoing hemodialysis, or with severe hepatic impairment, or with severe renal or moderate hepatic impairment and on treatment with a potent CYP3A4 inhibitor.  
**Warnings and Precautions:** No clinical data are available from women who became pregnant while taking solifenacin. Caution should be exercised when prescribing to pregnant women. The use of Vescicare® should be avoided during breastfeeding. Assess other causes of frequent urination before prescribing. Use with caution in patients with clinically significant bladder outflow obstruction at risk of urinary retention, gastrointestinal obstructive disorders, risk of decreased gastrointestinal motility, severe renal or moderate hepatic impairment (doses not to exceed 5 mg), concomitant use of a potent CYP3A4 inhibitor, hiatus hernia/gastroesophageal reflux and/or patients currently taking medicines that can cause or exacerbate oesophagitis, autonomic neuropathy. QT prolongation and Torsades de Pointes have been observed in patients with risk factors, such as pre-existing long QT syndrome and hypokalaemia. Safety and efficacy have not yet been established in patients with a neurogenic cause for detrusor overactivity. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.  
**Angioedema with airway obstruction and anaphylactic reaction have been reported with some patients on Vescicare®.**  
**Interactions:** Concomitant medication with other medicinal products with anticholinergic properties may result in more pronounced therapeutic effects and undesirable effects. Allow one week after stopping Vescicare® before commencing other anticholinergic therapy. Therapeutic effect may be reduced by concomitant administration of cholinergic receptor agonists. Can reduce effects of stimulants of gastrointestinal tract motility. If used concomitantly with ketoconazole or other CYP3A4 potent inhibitor, maximum dose should be 5 mg due to 2-3 fold increase in AUC of Vescicare®.  
**Pharmacokinetic interactions are possible with other CYP3A4 substrates with higher affinity and CYP3A4 inducers.**  
**Adverse Effects:** Dry mouth, blurred vision, constipation, nausea, dyspepsia, abdominal pain, urinary tract infection, peripheral oedema, colonic obstruction, rash, urinary retention, hallucinations, confusional state, angioedema, anaphylactic reaction, delirium, Torsades de Pointes, electrocardiogram QT prolonged, atrial fibrillation, tachycardia. **Prescribers should consult the Summary of Product Characteristics in relation to other side effects.**  
**Basic NHS Cost:** Vescicare® 5 mg blister packs of 30 tablets £27.62; Vescicare® 10 mg blister packs of 30 tablets £35.91.  
**Legal Category:** POM.  
**Product Licence Number:** Vescicare® 5 mg PL 00165/0197; Vescicare® 10 mg PL 00165/0198.  
**Date of Revision:** August 2013.  
**Further information available from:** Astellas Pharma Ltd, 2000 Hillswood Drive, Chersey, KT16 8PS. Vescicare® is a Registered Trademark. For full prescribing information please refer to the Summary of Product Characteristics.  
For medical information phone 0800 783 5018.

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**Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.**  
Adverse events should also be reported to Astellas Pharma Ltd. Please contact 0800 783 5018.
Prescribing information

Flomaxtra® XL Prescribing Information

**Presentation:** Flomaxtra®XL tablets containing 400 micrograms of tamsulosin hydrochloride in a film-coated prolonged release formulation. Flomaxtra®XL is formulated as an Oral Controlled Absorption System (OCAS). **Indication:** Treatment of functional symptoms of benign prostatic hyperplasia (BPH).

**Dosage:** One tablet daily to be taken with or without food. The tablets should be swallowed whole and should not be crushed or chewed as this will interfere with the prolonged release of the active ingredient. **Contraindications:** Hypersensitivity to tamsulosin hydrochloride or any other component of the product; a history of orthostatic hypotension; severe hepatic insufficiency. **Warnings and Precautions:** Orthostatic hypotension can occur; if dizziness is experienced the patient should sit or lie down, and not drive or operate machines. Rarely, syncope may occur during treatment. Digital rectal examination (DRE) and, when necessary, determination of Prostate Specific Antigen (PSA) are recommended before and regularly during treatment. Patients with severe renal impairment should be treated with caution. Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract and glaucoma surgery and may increase the risk of eye complications during and after the operation in some patients on or previously treated with tamsulosin. The initiation of tamsulosin is not recommended in patients for whom cataract or glaucoma surgery is scheduled. During the pre-operative assessment, cataract surgeons and ophthalmic teams should consider whether patients scheduled for cataract or glaucoma surgery are being or have been treated with tamsulosin in order to ensure appropriate measures are in place to manage the IFIS during surgery. Tamsulosin should not be given in combination with strong inhibitors of CYP3A4. In patients with poor metaboliser CYP2D6 phenotype, Tamsulosin should be used with caution in combination with strong and moderate inhibitors of CYP3A4. **Interactions:** No interactions have been seen when tamsulosin was given concomitantly with atenolol, enalapril or theophylline. Concomitant cimetidine brings about a rise and furosemide a fall in plasma concentrations of tamsulosin, but as levels remain within the normal range posology need not be changed. Diofenac and warfarin may increase the elimination rate of tamsulosin. There is a theoretical risk of enhanced hypotensive effect when given concurrently with drugs which may reduce blood pressure, including anaesthetic agents and other alpha-adrenergic receptor antagonists. **Fertility:** Ejaculation disorders have been observed in short and long term clinical studies with tamsulosin. Events of ejaculation disorder, retrograde ejaculation and ejaculation failure have been reported in the post authorization phase. **Adverse Effects:** The following adverse reactions have been reported during the use of tamsulosin; Common: dizziness and ejaculation disorders. Uncommon: headache, palpitations, orthostatic hypotension, rhinitis, nausea, vomiting, diarrhoea, constipation, rash, pruritus, urticaria and anaesthesia. As with other alpha-blockers, drowsiness, blurred vision, dry mouth or oedema can occur. During post-marketing surveillance, IFIS has occurred in some patients during cataract surgery. Atrial fibrillation, arrhythmia, tachycardia and dyspnoea have been reported in association with tamsulosin use from post-marketing experience. Prescribers should consult the Summary of Product Characteristics in relation to other side effects. **Basic NHS Cost:** Flomaxtra®XL 400 microgram blister packs of 30 tablets £10.47. **Legal Category:** POM. **Product Licence Number:** Flomaxtra®XL PL 0166/0199. **Date of revision:** August 2014. **Further Information available from:** Astellas Pharma Ltd, 2000 Hillswood Drive, Chertsey, KT16 9FS. Flomaxtra® is a Registered Trademark. Summary of Product Characteristics with full prescribing information available upon request. **For medical information phone** 0800 783 5018.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard

Adverse events should also be reported to Astelles Pharma Ltd. Please contact 0800 783 5018.