



# Complementary and alternative medicines for bladder control

Complementary and alternative medicines (CAM) are increasingly researched for bladder control and provide an option for conservative management or when other treatments have been unsuccessful. This article explores common bladder control conditions and the latest published research that may assist pharmacists when recommending CAM treatments to improve their patients' bladder health and quality of life.



**Tracey Seipel**,  
naturopath, medical  
herbalist, clinical  
nutritionist and CEO,  
Seipel Group

## Control of micturition

Normal storage and voiding of urine is dependent on a spinal reflex that is modulated by the central nervous system. Sensory nerves within the bladder detrusor muscle (bladder proper) detect bladder stretching as urine volume increases and communicate via the pons to the brain neuronal voiding centre (NVC), located in the cerebral cortex (Figure 1). With a small bladder urine volume, the bladder detrusor muscle relaxes to fill while pelvic floor muscles (PFM) contract to maintain closure of internal and external urinary sphincters. For bladder emptying, the reverse occurs with detrusor muscle contraction and PFM relaxation.<sup>1</sup>

## Poor bladder control

Numerous conditions can cause poor bladder control including prostate enlargement, overactive bladder (OAB), nocturnal

enuresis (bedwetting), urinary incontinence, urinary tract infections, recurring cystitis and neurological disorders. It is important for patients to consult their GP for further medical investigation to determine the best course of action. Conservative management includes dietary modifications such as reducing caffeine, alcohol, spicy foods, carbonated beverages and citrus. Smoking is linked with poor bladder control and should be stopped. Weight loss, if needed, and exercise such as bladder retraining, to teach the bladder to hold urine longer, and pelvic floor exercises can improve continence and physiotherapist advice is recommended. The Continence Foundation of Australia provides further support.<sup>2</sup>

The stigma associated with poor bladder control negatively impacts quality of life.<sup>3,4</sup> Patients with conditions such as incontinence have very poor compliance with prescribed pharmaceuticals (less than 35%, one year post-commencement due to adverse events of increased thirst, dry mouth, impaired cognition with some anticholinergics/antimuscarinics and drug interactions), leaving most to manage their condition with incontinence pads.<sup>5</sup> Incontinence sufferers have interrupted sleep; reduced intimacy; restricted travel to less than one hour from home; reduced exercise; concerns about pad bulkiness, leakage, odour; restricted socialising and become reclusive and isolated.<sup>3,4,6</sup> Incontinence is a leading cause of early admission to aged care homes, alongside cognition and mobility problems.<sup>7</sup>

## Urinary incontinence (UI)

The prevalence of UI in women in Australia has been reported to be as high as 42%.<sup>12</sup> The Continence Foundation states one in three women experiences incontinence and research shows prevalence increases with age affecting approximately half of menopausal women and 77% of those residing in aged care homes.<sup>3,7</sup> Unfortunately, women often view UI as a normal part of being female and most do not seek treatment.<sup>13</sup>

For men, the occurrence of lower urinary tract symptoms (LUTS), OAB, and UI increases with age. Research shows 11% of men older than 40 have experienced an incontinence episode in the past year and daily incontinence is experienced by 11% of men older than 60, increasing to 32% of over the age of 80.<sup>14,15</sup>

### AFTER COMPLETING THIS ACTIVITY, PHARMACISTS SHOULD BE ABLE TO:

- describe the process of micturition;
- identify common symptoms that present in a pharmacy setting for medically diagnosed overactive bladder, urinary incontinence, male lower urinary tract symptoms and bedwetting;
- identify herbal formulations shown in published clinical research to improve symptoms of overactive bladder, urinary incontinence and bladder control that can be recommended in the pharmacy setting;
- outline herbal actions required in the use of complementary medicines for bladder control.

**1.5**  
CPD CREDITS  
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The 2016 Competency Standards addressed by this activity include: 1.4, 2.2, 3.1, 3.2, 3.5, 3.6

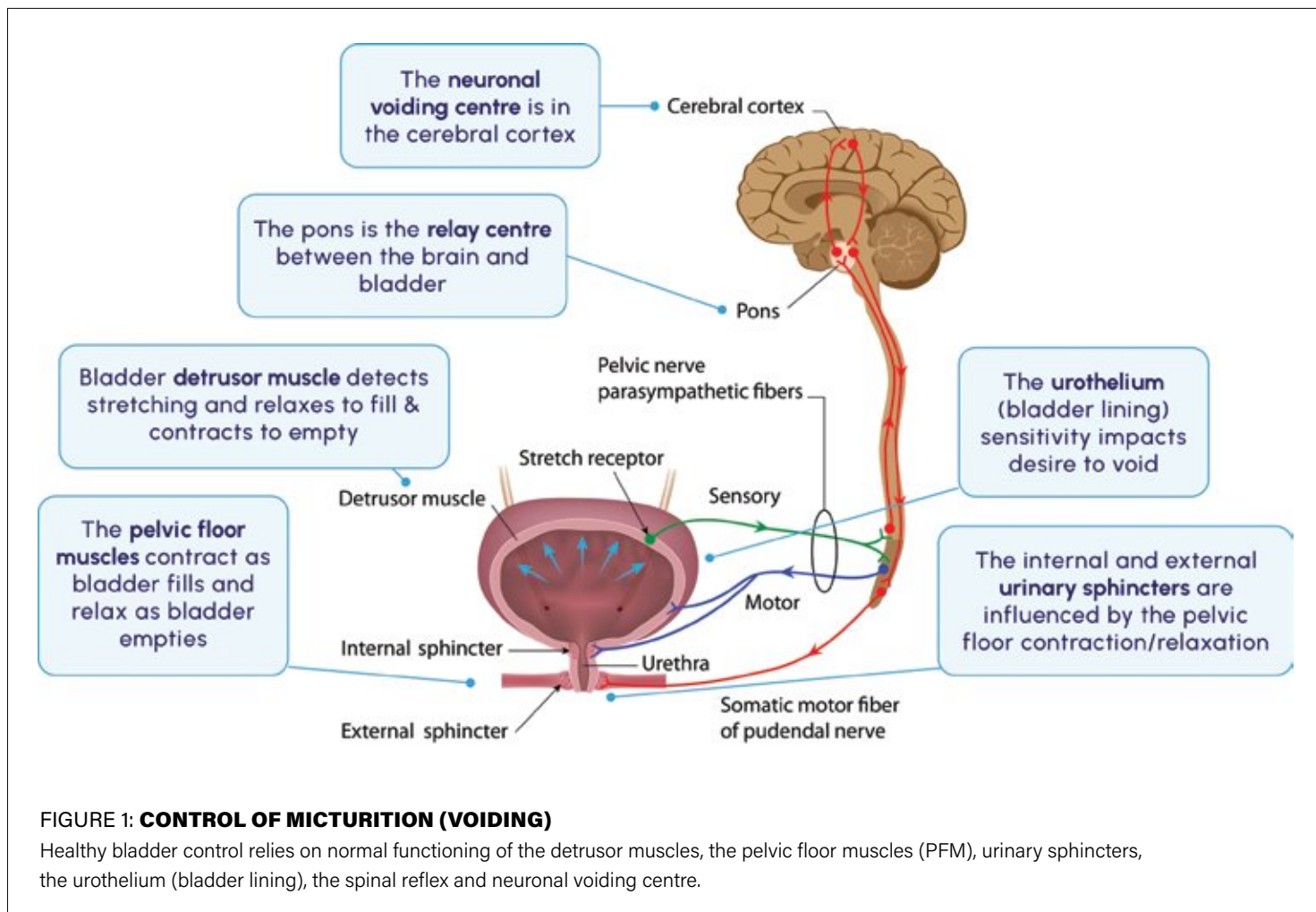


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**FIGURE 1: CONTROL OF MICTURITION (VOIDING)**

Healthy bladder control relies on normal functioning of the detrusor muscles, the pelvic floor muscles (PFM), urinary sphincters, the urothelium (bladder lining), the spinal reflex and neuronal voiding centre.

The most common forms of incontinence are stress UI in younger women and urgency UI or mixed stress and urgency UI in older women.<sup>16</sup> Stress UI can result from stretching of the pelvic floor muscles during pregnancy, childbirth or with chronic constipation or obesity. It occurs without warning when pressure is placed on the pelvic floor due to coughing, laughing, sneezing, etc. Urgency UI can occur with OAB and occurs with warning but the patient can't reach the toilet in time.

Table 1 lists the types of urinary incontinence.

**TABLE 1: TYPES OF URINARY INCONTINENCE**

- Stress (associated with pelvic floor weakening and post-partum)
- Urgency (associated with OAB and urgency)
- Mixed (both stress and urge incontinence)
- Functional (physically can't reach the toilet in time)
- Overflow (constant urine dribbling due to incomplete bladder emptying)
- Neurogenic (associated with neurological disorders such as Parkinson's disease and multiple sclerosis)
- Post-micturition (dribbling, often with prostate issues)
- Nocturnal enuresis (bedwetting)

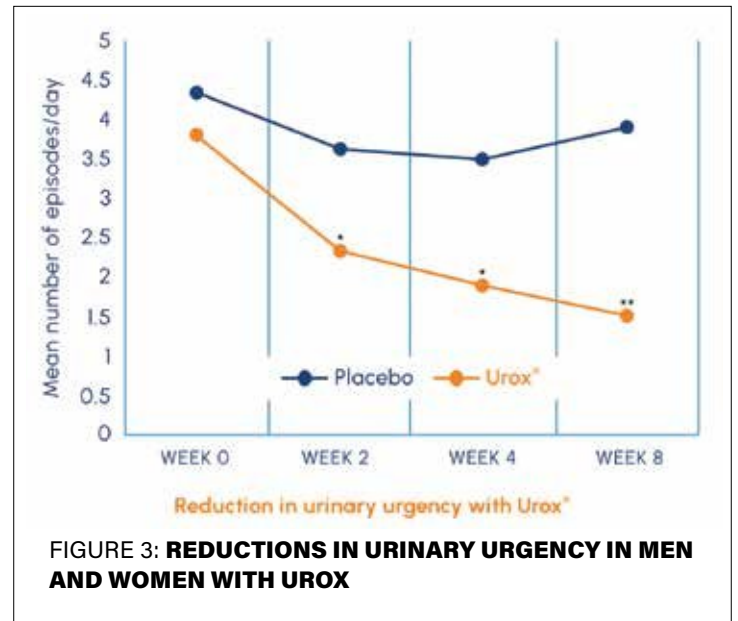
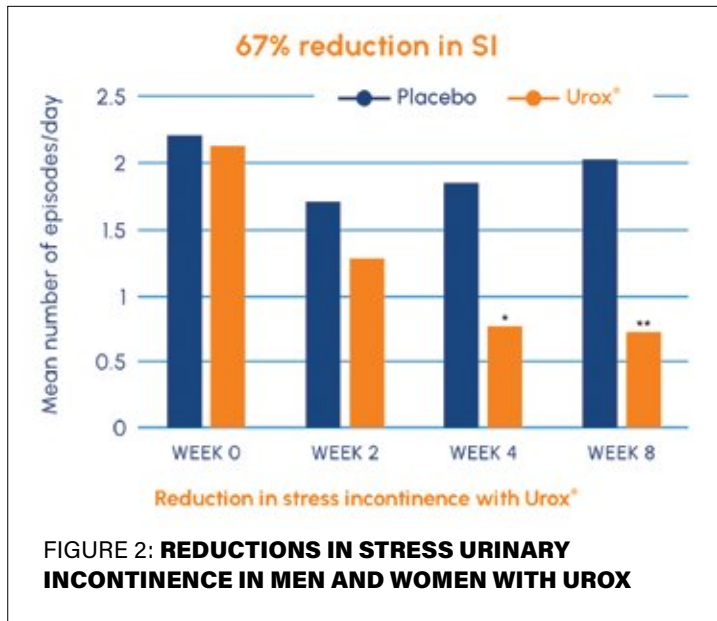
#### Treatment of UI with Urox®

The most researched CAM formula for overactive bladder and urinary incontinence with 14 clinical trials in men, women and children, is the internationally patented Urox formula.<sup>6,8-11</sup> Urox is a three-herbal blend of clinically-researched, specialised extracts containing Cratevox™ (a standardised form of *Crateva magna*), *Equisetum arvense* (Horsetail) and *Lindera aggregata*. Developed in Australia, Urox is marketed in more than 10 countries.

Urox was assessed in an Australian randomised, placebo-controlled trial of 150 men and women.<sup>6</sup> The trial showed statistically significant decreases in stress UI after 4 weeks, and a reduction of 67% by 8 weeks ( $p < 0.001$ ) (Figure 2). It also showed a 56% reduction in urgency UI at 8 weeks ( $p < 0.001$ ). At 8 weeks, 75% of participants had reduced incontinence pad usage and 23% had stopped pad usage or only used them as a precaution. All quality-of-life measures significantly improved. Results showed a Cohen's effect of 0.6, indicating results have a high clinical relevance.<sup>6</sup>

#### Overactive bladder syndrome (OAB)

Overactive bladder syndrome (OAB) affects 11–17% of Australians.<sup>17</sup> Prevalence is similar between men and women although women



experience more urgency UI. Symptoms include urinary urgency (receiving little warning before needing to urinate), frequency (urinating more than 8 times per 24 hours) and nocturia, with urgency UI (i.e. OAB-wet) or without (i.e. OAB-dry).

OAB has a significant negative impact on quality of life as the need to always know bathroom locations and be repeatedly interrupted in the day for the toilet causes constant disruptions. Having to get out of bed at night impairs sleep quality, which contributes to daytime fatigue and reduced exercise.

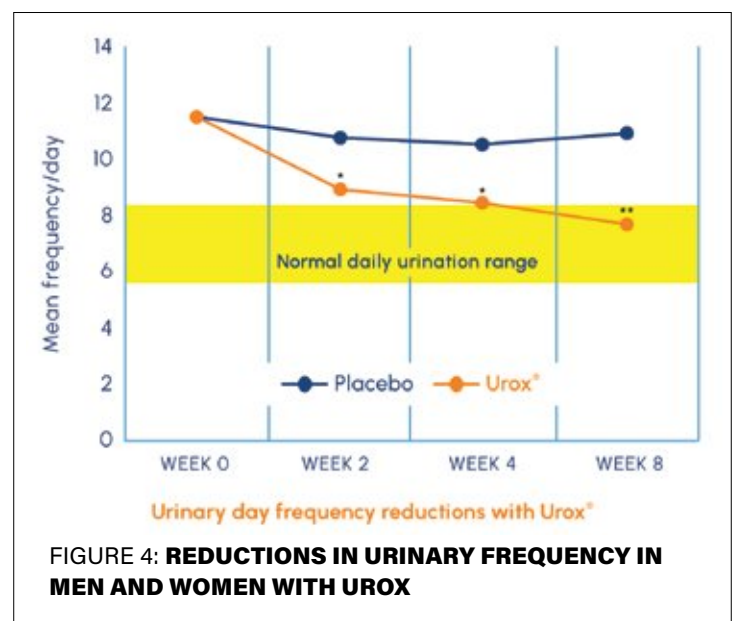
#### Treating OAB with Urox

Urox research showed statistically significant results in improving OAB from 2 weeks and a highly clinically relevant 61% reduction by 8 weeks for urinary urgency ( $p < 0.001$ ) (Figure 3).<sup>6</sup> Urinary frequency also reduced from 2 weeks and by 8 weeks to within the normal range of eight or fewer micturitions per day ( $p < 0.001$ ) (Figure 4).

Mechanism of action (MOA) research shows Urox is effective in improving all of the assessed 14 enzymes and biomarkers for OAB.<sup>10</sup> The enzyme, c-Fos, is a marker of brain neuronal voiding centre (NVC) activity that increases with bladder stimuli and is elevated in OAB. Urox lowers an elevated c-Fos in the NVC.

Direct proof of the effect of Urox on the bladder detrusor muscle stability was the ability of Urox to lower the DOI (detrusor overactivity index). Unstable detrusor contractions in the urine storage period is traditionally used to diagnose OAB. Urox lowers the bladder volume threshold pressure to elicit the NVC response resulting in improved detrusor muscle compliance.<sup>6</sup>

The multiple mechanisms of Urox may be the reason for its effect in improving all symptoms of OAB. Urox safety is supported by the lack of cardiovascular effects for blood pressure or heart rate and no diuretic effect. Urox is well tolerated with no serious adverse effects or known drug interactions.



#### Bedwetting children

Nocturnal enuresis or bedwetting affects approximately 10–20% of children in Australia and has limited treatment options.<sup>16</sup> The exact cause of bedwetting is not fully understood and may be due to nocturnal polyuria (with abnormal nocturnal anti-diuretic hormone release), improper sleep arousal or OAB. Pharmaceutical options include anticholinergic medications and antidiuretic hormone. Many try to manage it by reducing fluid intake in the late afternoon/evening, toileting before bed or using alarms to wake the child while bedwetting.

Bedwetting can be very distressing, especially for the older child, and is associated with low self-esteem, lower reported happiness and poorer school performance. It is important to resolve bedwetting as early as possible to avoid these psychological effects.





### Treating bedwetting with Urox

Australian research assessed Urox in the treatment of nocturnal enuresis in 48 children aged 6–14 years over 8 weeks.<sup>8,9</sup> Results show 62% of children experienced statistically significant reductions in bedwetting ( $p < 0.05$ ) and urinary urgency ( $p < 0.05$ ). Quality of life improved with children experiencing reduced worry, shyness, sadness and feeling different to other children ( $p < 0.05$ ).<sup>8,9</sup>

### Recurring UTI, cystitis and considerations beyond antibiotics

The primary cause of UTI is microbial infection, typically *Escherichia coli* with antibiotics as the first line of treatment.<sup>19</sup>

The significant and often unaddressed problem with UTIs is that they tend to be chronic in nature with recurring UTI or cystitis defined as two or more per six-month period.

Research shows that women with recurrent UTI suffer from bladder oversensitivity.<sup>20</sup> A key theory is the compromised protective urothelium allows the lining to be more sensitive and easily irritated. Even in the absence of an infection, women with recurring UTI have reduced bladder holding capacity and mean voiding volume, and increased urinary frequency.<sup>20</sup> Residual urine volume and incomplete bladder emptying allows bacteria to remain in the bladder and multiply instead of being flushed out with each urination.

Research shows herbal formulations specifically formulated for recurrent UTIs were more effective in reducing infection incidence than the use of herbal formulations targeted for acute UTI.<sup>21</sup>

### Treatment of recurring UTI with Urox

Pilot research with Urox was conducted over a 12-month period in women with recurring UTI and showed 62% experienced reduced frequency, duration and severity of infection and 31% were symptom-free throughout.<sup>11</sup> MOA research shows Urox reduces urothelium sensitivity and increases voiding volume while reducing urinary frequency resulting in more complete bladder emptying and less residual urine.<sup>10</sup>

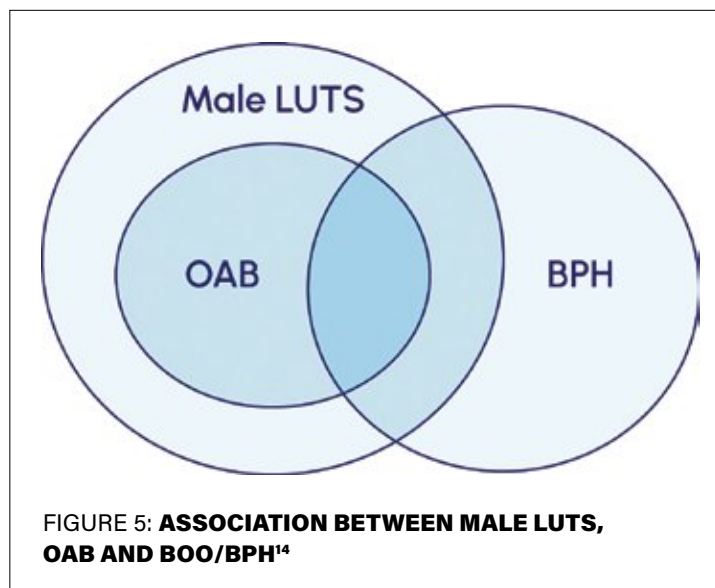
A randomised, placebo-controlled trial with Urox in reducing severity and occurrence of UTIs and cystitis is currently underway.

### Male LUTS—prostate or bladder or both

Men with bladder outlet obstruction (BOO) or benign prostatic hypertrophy (BPH) have an increased detrusor muscle collagen content associated with decreased bladder compliance, detrusor overactivity (DO), detrusor underactivity and urinary retention.<sup>22–24</sup> The chronically increased intravesical pressure with BOO/BPH results in remodelling of the bladder wall causing trabeculation (detrusor hypertrophy/thickening) and fibrosis with accompanying decreased detrusor compliance.<sup>25</sup> The fibrotic bladder loses normal contractility for expelling urine resulting in weak urinary stream, intermittency, increased residual urine sensation, and abdominal straining.<sup>26</sup>

Reducing or removing the obstruction is the traditional basis for the treatment of BOO/BPH, yet for many men who have had surgical treatment of their BPH, the storage symptoms persist post-surgery.<sup>25,26</sup> Bladder detrusor muscle abnormalities occur with BOO/BPH and detrusor muscle treatment is needed to resolve the urinary symptoms.<sup>27</sup>

Research shows less than 50% of cases of male bladder dysfunction



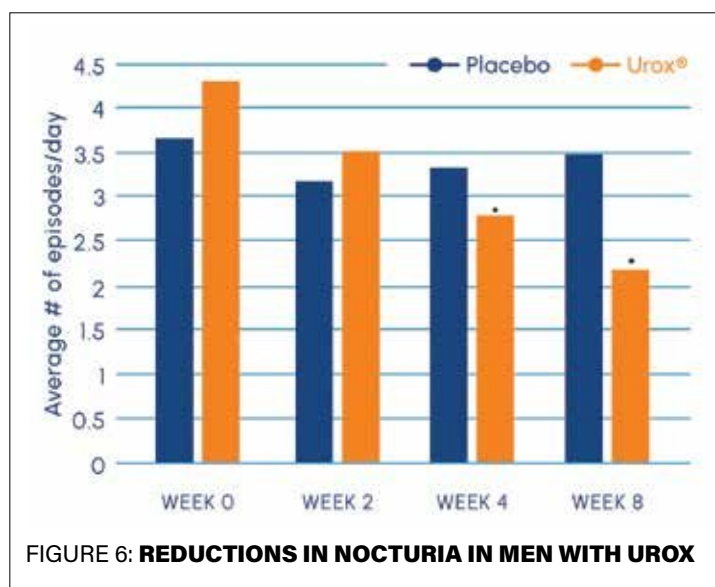
have urodynamically proven BOO that may be attributed to BPH or other obstructive causes (Figure 5).<sup>14</sup> An approach that targets prostate size reduction alone is limited as it does not address the need to support and correct the detrusor muscle functioning.

### Urox reduces nocturia

Urox research with men showed a clinically relevant, halving of nocturia at 8 weeks ( $p < 0.01$ ) (Figure 6) with day frequency improving to normal range.<sup>6</sup>

MOA research shows Urox improves bladder detrusor muscle contractility and bladder compliance and thus improves the ability of the bladder to fill and empty. Urox normalises all of the bladder storage and voiding stages.<sup>10</sup>

Male LUTS may be caused by a primary prostate disorder (BOO/BPH) with secondary bladder involvement or a primary bladder disorder





(such as OAB) without prostate involvement. In either scenario, treatment targeted for the bladder needs inclusion. When treating the prostate and bladder together, the bladder improvements will typically occur within weeks and before prostate improvements.

### The role of the pharmacist

Up to 70% of sufferers don't tell their doctor or spouse about their incontinence due to embarrassment and hold the view that they just have to live with the problem.<sup>3,4</sup> So they are likely not receiving the best possible care or management of their bladder control. Pharmacists have a unique role to play. As sufferers self-manage their condition and rely heavily on incontinence pads, often purchased from pharmacies, pharmacists can more readily reach out to patients, speak to them about their bladder control and how they are managing it and, if appropriate, suggest they discuss with their doctor. The pharmacist can also discuss and assess if other options, such as complementary medicines, can improve management and their quality of life.

### Pharmacy formulations containing Urox

#### Urox® Bladder Control

Seipel Group Urox is formulated for men and women and contains the dosage and standardisations that match published clinical research trials on Urox. Improvements are observed from 2 weeks with best effects from 8 weeks. Urox is formulated for long-term use.

#### Seipel Group Prorox®

Seipel Group Prorox is formulated for men for complete bladder and prostate support. Prorox contains the full Urox dosage to match clinical research, combined with clinically researched saw palmetto, zinc, selenium and vitamin D3 for additional prostate support.

#### Seipel Group Urox® Junior

Urox Junior is a Urox formula for children to improve bedwetting and daytime bladder control. ■

1.5

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**ADVANCING YOUR PRACTICE**

**Complementary and alternative medicines for bladder control**

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**1. Healthy micturition does NOT involve normal functioning of the:**

- A** detrusor and pelvic floor muscles.
- B** core abdominal muscles.
- C** urothelium.
- D** the spinal reflex and neuronal voiding centre.

**2. Chronically increased intravesical bladder pressure with B00/BPH causes:**

- A** detrusor muscle thinning.
- B** fibrosis of the detrusor muscle.
- C** enlargement of the prostate.
- D** urinary tract infection.

**3. The Urox herbal formulation has been shown in published clinical research to be effective in reducing symptoms of:**

- A** stress urinary incontinence and day frequency.
- B** urinary urgency and urgency urinary incontinence.
- C** nocturia.
- D** bedwetting.
- E** All of the above

**4. Symptoms of overactive bladder include:**

- A** urgency, frequency, infection.
- B** nocturia, bedwetting, cystitis.

**C** urgency, frequency, nocturia.

**D** bedwetting, cystitis, poor stream.

**5. Urox may assist recurrent UTI and cystitis by:**

- A** reducing bladder sensitivity and need for incontinence pads.
- B** increasing voiding volume.
- C** decreasing urine output.
- D** A and B
- E** None of the above

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