

## Overactive Bladder

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Dr. Blount, Dr. Smith, Ms. Gangel, Ms. LaRocque, and Ms. O'Brien have returned disclosure forms indicating that they have no financial interest in or affiliation with any commercial supporter or providers of any commercial services discussed in this educational material.

### Learning Objectives

After reading this *CME Bulletin*, you should be able to:

- Diagnose overactive bladder (OAB) during patient workup using appropriate questions and screening tools.
- Develop an effective individualized plan that takes into consideration the age and behavioral risks (smoking, drinking, poor diet, lack of exercise) of the individual to manage OAB and then incorporate behavioral and pharmacotherapeutic interventions.
- Identify comorbid conditions and factors associated with OAB.

### Introduction

Overactive bladder (OAB) is a common lower urinary tract disorder characterized by urinary urgency, with or without urge incontinence, and is usually accompanied by frequency (>8 micturition events/24 hours) and nocturia (waking 1 or more times per night to urinate).<sup>1,2</sup> While the cause of OAB is unknown, symptoms are usually associated with detrusor muscle overactivity, which may be the result of upregulation of bladder muscarinic receptors or decreased central nervous system control of the bladder.<sup>3,4</sup>

### Prevalence

The overall prevalence of OAB is similar in men (16%) and women (16.9%), although OAB generally develops in men later in life compared with women.<sup>2</sup> Approximately 50% of women and 25% of men with OAB have related episodes of urinary incontinence (UI).<sup>5</sup> In women, the prevalence of OAB with urge incontinence increases with increasing body mass index (BMI), whereas, in men, increased BMI is not associated with OAB.<sup>2</sup> Urgency and UI symptoms resolve spontaneously in approximately 25% of individuals.<sup>6</sup>

Up to 50% of the US long-term care population has OAB or UI.<sup>7</sup> Although the prevalence of OAB increases with age in both men and women (OAB symptoms are reported in 20% of individuals age 70 years or older and in 30% of individuals age 75 years or older), OAB is treatable and should not be considered a normal part of aging.<sup>7</sup>

### Quality of Life

Studies of the effects of OAB show an overall decrease in quality of life.<sup>8</sup> Individuals with OAB report decreased levels of social interaction as

well as activities such as travel, shopping, and work; poor sleep quality and fatigue due to nocturia; decreased intimacy due to fear of odor and leakage during sexual activity; and increased psychological distress.<sup>4,7</sup>

### Risk Factors

Risk factors most commonly associated with OAB and incontinence include age 75 years and older, arthritis, chronic lung disease, depression, diminished cognitive status and delirium, fecal impaction, hysterectomy, immobility, increased BMI in women, diabetes, lumbar disk disease, multiple vaginal deliveries, stroke, urinary tract infection, vaginal or bladder surgery, and white race. Individuals taking alpha-adrenergic blockers, alpha-adrenergic agonists, anticholinergics, antimuscarinics, antidepressants, antipsychotics, beta-adrenergic agonists, calcium channel blockers, diuretics, hormone-replacement therapy, hypnotics, and/or sedatives are also at increased risk of developing OAB symptoms.<sup>5,7,9</sup>

### Comorbidities

Comorbidities associated with OAB include depression, sleep deprivation, urinary tract infections, skin infections, and orthopedic injuries resulting from falls related to OAB.<sup>5</sup>

### Diagnosis

OAB has been called the *hidden condition* because few individuals admit having symptoms; many assume that symptoms are a normal part of aging, and therefore the condition is often undiagnosed.<sup>8</sup> A study of toileting-related attitudes and behaviors of 1,001 adults ages 30 to 70 years in the United States showed that among those reporting bladder control issues, 26% had discussed their symptoms with a physician. Of this 26%, half reported feeling comfortable having such a discussion.<sup>10</sup> The first step toward diagnosis is encouraging at-risk individuals to recognize and discuss symptoms.

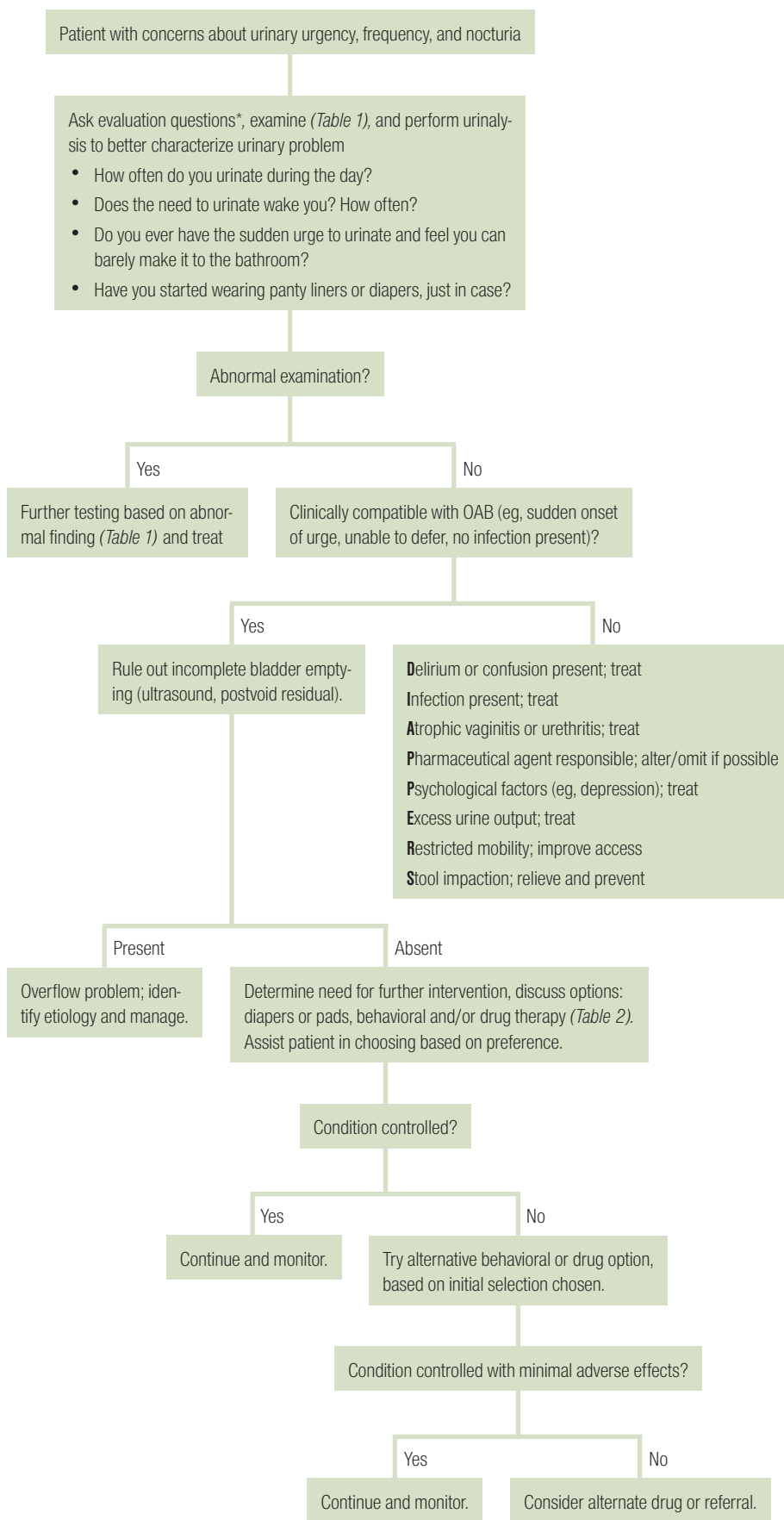
Urgency associated with OAB is different from the normal, progressively strengthening urge to void. The onset of urgency is sudden, and deferring urination is difficult.<sup>7</sup> Urinary frequency and incontinence that are the result of cauda equina syndrome, dementia, surgery, bladder prolapse, pelvic floor dysfunction, and reversible etiologies should be ruled out before considering a diagnosis of OAB. Individuals with symptoms that are caused by neurologic conditions should not be excluded from a diagnosis of OAB.<sup>11</sup> The reversible etiologies of OAB can be remembered with the acronym *DIAPPERS* (see *Figure 1*).



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**Figure 1. Approach to the Patient With Suspected Overactive Bladder (OAB)**



Once an individual acknowledges the existence of symptoms, and other etiologies have been excluded, use of a 48- to 72-hour voiding diary can be helpful in estimating bladder capacity and total urinary volume, and determining frequency, number, and type of toileting episodes.<sup>12</sup>

Along with a focused physical examination (see Table 1), identifying incomplete bladder emptying is critical. Palpation of the bladder for fullness after emptying can be performed, but a more accurate assessment can be achieved via ultrasound or postvoid catheterization. A postvoid residual volume >150 mL is considered abnormal and suggests overflow incontinence.<sup>13</sup>

Urodynamic studies may be helpful if the cause of incontinence is not clear or when a neurologic etiology is suspected.<sup>8</sup>

### Management

Numerous options exist for the management of OAB, but not all individuals may wish to undergo treatment; some may prefer frequent toileting and use of pads or diapers without further intervention if symptoms are tolerable. Those who prefer to manage OAB independently should be encouraged to report worsening symptoms and to undergo routine monitoring. Figure 1 is an algorithm for the diagnosis and management of OAB.

### Behavioral Options

Several groups, including the Agency for Health Care Policy and Research, the American College of Obstetricians and Gynecologists, the Consensus Development Conference on Urinary Incontinence in Adults, and the International Consultation on Incontinence recommend non-pharmacologic strategies in the initial treatment of OAB and urge incontinence.<sup>7,12</sup> One study randomized 197 women ages 55 years and older to behavioral therapy, drug therapy (oxybutynin, 2.5 - 5 mg, 3 times/day), or placebo. An average reduction in incontinence episodes of 80.7% was found in the behavioral therapy group compared with 68% in the drug therapy group and 39% in the placebo group.<sup>14</sup> Perceived improvement was also higher among those treated with behavioral therapy.<sup>7</sup> Behavioral strategies include bladder training, pelvic floor muscle exercises, and dietary changes. Other lifestyle modifications include constipation prevention, smoking cessation, and weight loss if appropriate.<sup>14,16</sup> Although behavior-modification techniques require more time and effort, they are safe, inexpensive, and free from the adverse effects that may occur with pharmacologic therapy.<sup>15</sup>

### Bladder Training

The goal of bladder training is to increase bladder capacity and decrease urinary frequency by suppressing involuntary detrusor contractions.<sup>12</sup> Training should include urge-suppression techniques and a scheduled-voiding regimen. Scheduled voiding can help correct frequent-voiding patterns; reduce incontinence

\*Information from Rosenberg MT, Dmochowski RR. Overactive bladder: evaluation and management in primary care. *Cleve Clin J Med.* 2005;72(2):149-156 [Review].

**Table 1. Strategies for Diagnosing Overactive Bladder**

Strategy	Purpose
Pulmonary and cardiovascular assessment	To assess control of cough or use of drugs such as diuretics <sup>1</sup>
Abdominal examination	To check for scars and rule out diastasis recti, masses, ascites, hernias, and organomegaly. Palpable bladder may imply an obstructive problem. <sup>1,2</sup>
Genitourinary examination	To determine presence/absence of vaginal atrophy <sup>2</sup> To check strength of pelvic-floor muscles and assess for prolapse of pelvic organ, urethral mobility, and stress urinary incontinence <sup>1</sup>
Lumbosacral examination	To assess deep-tendon reflexes, lower extremity strength, sharp/dull sensation, and (in women) the bulbocavernosus reflexes, and to screen for cauda equine syndrome <sup>2</sup>
Neurologic examination	To assess innervation of feet and individual's mental status (dementia, depression) <sup>1</sup>
Rectal examination	To check anal sphincter tone; to determine presence of fecal impaction. In men, also focus on prostate to rule out benign prostatic hyperplasia or prostate cancer. <sup>1</sup>
Urinalysis	To exclude microhematuria, pyuria, urinary tract infection, proteinuria, and glucosuria <sup>1</sup>
Postvoid residual measurement	Not indicated in all patients; helpful in men with both obstructive and OAB symptoms <sup>1</sup>

1. Ellsworth PI. Overactive bladder - etiology, diagnosis, and impact. *eMedicine*. <http://emedicine.medscape.com/article/459502-overview>.

2. Culligan PJ, Heit M. Urinary incontinence in women: evaluation and management. *Am Fam Physician*. 2000;62(11):2433-44,2447,2452 [Review].

episodes; extend voiding intervals; improve bladder control; and increase bladder capacity.<sup>14</sup> Urination patterns recorded in a voiding diary can help determine the initial voiding regimen; for example, if an individual's frequency is greater than once per 60 minutes, then the initial voiding interval is set at 1 hour. The individual should attempt to urinate on schedule and use urge-suppression techniques (taking slow, deep breaths; performing tasks that demand concentration; performing 5 quick, strong pelvic floor muscle contractions; using affirming statements, such as "I can wait") to adhere to the schedule. If the regimen is well tolerated, the voiding interval can be increased by 30 minutes; conversely, if the schedule is not well tolerated, the voiding interval can be decreased by 30 minutes. If no benefit is seen after 6 weeks, a new treatment strategy should be considered.<sup>17</sup>

### Pelvic Floor Strengthening

Kegel exercises build pelvic floor muscle strength and improve control of voluntary muscles.<sup>8</sup> Because it may be difficult for some individuals to identify the target pelvic muscles, showing which muscles to contract is recommended. In the woman, a finger is placed in the posterior vaginal introitus and the woman squeezes that finger. In the man, a finger is placed on the bulbospongiosus, corpus spongiosum, and ischiocavernosus muscles and the man squeezes those muscles; the bulbospongiosus muscle is the most important one to identify in men. In pelvic floor muscle exercises, individuals should contract the muscles, then hold the contraction for 10 seconds, then rest for 10 seconds. Once strength and stamina have been built, individuals should complete 3 to 4 sets of 10 contractions per day.<sup>9</sup> The *knack* or counterbracing method employs an intentional contraction

of the pelvic floor muscle just before increases in intra-abdominal pressure, eg, coughing, to prevent urine leakage in stress urge incontinence.<sup>18</sup>

### Dietary Changes

The effects of dietary changes on OAB symptoms can be significant. Carbonated drinks, artificial sweeteners (particularly aspartame), spicy foods, caffeine, and citrus- and tomato-based products may exacerbate symptoms; individuals should experiment with reducing or eliminating intake of these products.<sup>16</sup> Alcohol consumption in women may worsen OAB symptoms, but a longitudinal study on the relationship between diet and OAB onset in men suggests beer consumption may have a protective effect.<sup>12,19</sup> Although fluid restriction should be discouraged, individuals with nocturia should avoid evening consumption of water-containing fruits and vegetables, avoid or limit fluid intake after 6 pm, and empty the bladder just before bedtime.<sup>12</sup>

Although behavioral therapy has been shown to be effective in reducing OAB symptoms, most individuals find it difficult to continue because symptom improvement occurs gradually over a period of weeks or months.<sup>16</sup> A progress chart or graph that monitors symptom changes can provide the incentive needed to continue long-term behavioral therapy.<sup>16</sup>

### Pharmacotherapy

#### Antimuscarinics

Drugs from many classes have been used in the management of OAB, but most studies have focused on the antimuscarinics. This article focuses primarily on the antimuscarinics because these drugs are considered first-line choices for pharmacologic management of OAB.<sup>17</sup> Antimuscarinics may not be the optimal choice for individuals with OAB symptoms that are the result of conditions such as bladder-outflow obstruction or benign prostatic enlargement; in men with OAB and prostatic obstruction, surgically treating obstruction relieves detrusor overactivity and may, therefore, resolve OAB symptoms.<sup>20</sup>

Antimuscarinic drugs are thought to act mainly during the urine-storage phase by blocking the parasympathetic acetylcholine pathway to muscarinic receptors, which in turn reduces detrusor muscle contraction, thereby decreasing urgency and increasing bladder capacity.<sup>21</sup> Six antimuscarinic drugs (see *Table 1*) are currently approved by the Food and Drug Administration for the management of OAB; all are considered equally effective.<sup>17</sup> Authors of the National Institute for Health and Clinical Excellence (NICE) guideline on the treatment of women with urinary incontinence state that there is "no evidence of clinically important difference in efficacy between antimuscarinic drugs. However, immediate release non-proprietary oxybutynin is the most cost effective of the available options."<sup>17</sup>

Extended-release (ER) forms have been shown to be as effective as immediate-release (IR) forms, but ER forms generally are associated with fewer adverse effects such as dry mouth (68% for oxybutynin ER vs. 87% for oxybutynin IR; and 23% for tolterodine ER vs 30% for tolterodine IR).<sup>12,22</sup> Antimuscarinic discontinuation rates are high (70% to 90%), in part due to adverse effects, but also because of perceptions of lack of benefit or because the severity of symptoms requiring management is not sufficiently reduced.<sup>22</sup> A combination of behavioral and drug therapy has been shown to be more effective than either treatment alone.<sup>23</sup>

Because none of the antimuscarinics acts exclusively on the bladder's muscarinic receptors, other organ systems are affected as well.<sup>24</sup> Dry mouth (4.1% to 29.0%) and constipation (3.3% to 14.8%) are the most commonly reported adverse effects.<sup>21</sup> M<sub>2</sub> receptors play a prominent role in cardiac function; cardiac effects including increased

resting heart rate, QT prolongation (resulting from the inhibition of the hERG potassium channel in the heart), arrhythmia, peripheral edema, and induction of polymorphic ventricular tachycardia have been reported with therapeutic dosages of antimuscarinics.<sup>11,22,25</sup> Although there has been concern that antimuscarinic use in men will result in urinary retention, particularly in individuals with bladder outlet obstruction, studies have shown that antimuscarinics are safe and effective in men with OAB.<sup>26</sup>

### Other Pharmacologic Options

NICE provides several A-level guidelines on other pharmacologic management options for OAB symptoms:<sup>17</sup>

- Propiverine should be considered as an option to manage urinary frequency in women with OAB but is not recommended for the management of UI.
- Flavoxate, propantheline, and imipramine should not be used for the management of UI or OAB in women.
- Desmopressin may be considered specifically to reduce nocturia in women with UI or OAB.
- Duloxetine is not recommended as a first-line management option for women with predominant stress UI, nor should it be routinely be used as a second-line option for women with stress UI; it may

be used as second-line therapy if women prefer pharmacologic therapy to surgery or are not candidates for surgery.

- Systemic hormone replacement therapy is not recommended for the management of UI.
- Intravaginal estrogens are recommended for the management of OAB symptoms in postmenopausal women with vaginal atrophy.

### Other Management Options

Other treatments with proven benefit for OAB that might be recommended include botulinum neurotoxin injections and sacral neuromodulation.<sup>27,28</sup> These treatments, however, are associated with a number of adverse effects including inability to void voluntarily for the former, and pain, infection, and lead migration for the latter.

### When to Refer

Patients who do not respond to initial behavioral and/or drug treatment should be referred to a physician who specializes in OAB and UI. Patients with hematuria, recurrent urinary tract infection (ie, 3-4 episodes annually), pelvic pain or painful urination, overflow incontinence, and large postvoid residual volume and/or significant anatomic defects such as bladder, uterus, or rectum prolapse should also be considered for referral.<sup>4</sup>

**Table 2. Drugs for the Management of Overactive Bladder**

Drug	Dosages	Benefits	Common Adverse Effects
Darifenacin	<ul style="list-style-type: none"> <li>• Oral: 7.5 mg, 15 mg, 1 time/day</li> <li>• Daily dose should not exceed 7.5 mg in those taking potent CYP3A4 inhibitors.*</li> </ul>	<ul style="list-style-type: none"> <li>• Decreases frequency, severity of urgency and UUI episodes, nocturia</li> <li>• Increases warning time</li> </ul>	<ul style="list-style-type: none"> <li>• Dry mouth</li> <li>• Constipation</li> </ul>
Fesoterodine	<ul style="list-style-type: none"> <li>• Oral: 4 mg, 8 mg, 1 time/day</li> <li>• Daily dose should not exceed 4 mg in those taking potent CYP3A4 inhibitors. No dosage adjustments recommended by manufacturer with concurrent use of fesoterodine and CYP3A4 inducers.</li> </ul>	<ul style="list-style-type: none"> <li>• Decreases frequency, detrusor pressure</li> <li>• Inhibits bladder contraction</li> <li>• Increases volume at first detrusor contraction, bladder capacity</li> </ul>	<ul style="list-style-type: none"> <li>• Dry mouth</li> </ul>
Oxybutynin oral	<ul style="list-style-type: none"> <li>• Oral IR: 2.5 mg up to 30 mg/day</li> <li>• Oral ER: 5 mg initially, 1 time/day. Dosage may be adjusted weekly in 5 mg increments based on effectiveness and tolerability; maximum 30 mg/day.</li> </ul>	<ul style="list-style-type: none"> <li>• Decreases frequency</li> </ul>	<ul style="list-style-type: none"> <li>• Dry mouth</li> <li>• Constipation</li> <li>• Somnolence</li> </ul>
Oxybutynin transdermal patch	<ul style="list-style-type: none"> <li>• 3.9 mg patch, 2 times/week</li> </ul>	<ul style="list-style-type: none"> <li>• Decreases frequency</li> </ul>	<ul style="list-style-type: none"> <li>• Dry mouth</li> <li>• Skin irritation</li> <li>• Urinary tract infection</li> </ul>
Solifenacin	<ul style="list-style-type: none"> <li>• Oral 5 mg, 10 mg, 1 time/day</li> </ul>	<ul style="list-style-type: none"> <li>• Decreases nocturia, severity of urgency and UUI episodes, mean number of voids/24 hours</li> <li>• Increases mean voided volume</li> </ul>	<ul style="list-style-type: none"> <li>• Dry mouth</li> <li>• Constipation</li> <li>• Blurred vision</li> </ul>
Tolterodine	<ul style="list-style-type: none"> <li>• Oral IR: 2 mg, 2 times/day</li> <li>If significant renal or hepatic disease is present or if concurrently taking CYP3A4-inhibiting drugs, reduce to 1 mg 2 times/day.</li> <li>• Oral ER: 4 mg, 1 time/day</li> <li>If significant renal or hepatic disease is present or if concurrently taking CYP3A4-inhibiting drugs, reduce to 2 mg 1 time/day.</li> </ul>	<ul style="list-style-type: none"> <li>• Decreases frequency, urgency, urge-related incontinence</li> </ul>	<ul style="list-style-type: none"> <li>• Dry mouth</li> </ul>
Trospium	<ul style="list-style-type: none"> <li>• Oral IR: 20 mg, 2 times/day</li> <li>• Oral ER: 60 mg, 1 time/morning</li> <li>If CrCl &lt; 30 mL/min, reduce to 20 mg 1 time/day at bedtime. ER forms are not recommended.</li> </ul>	<ul style="list-style-type: none"> <li>• Decreases frequency, UI episodes, severity of urgency</li> <li>• Increases cystometric capacity, mean voided volume</li> </ul>	<ul style="list-style-type: none"> <li>• Dry mouth</li> <li>• Constipation</li> <li>• Minimal cognitive effects</li> </ul>

\*A list of CYP3A4 inhibitors is available at [http://medicine.iupui.edu/clinpharm/ddis/p450\\_Table\\_Oct\\_11\\_2009.pdf](http://medicine.iupui.edu/clinpharm/ddis/p450_Table_Oct_11_2009.pdf).

CrCl=creatinine clearance; ER=extended release; IR=immediate release; UI=urinary incontinence; UUI=urge urinary incontinence.

Darifenacin. Fesoterodine. Oxybutynin. Solifenacin. Tolterodine. Trospium. Available by subscription at <http://www.clinicalpharmacology.com>.

### Table 3. A-Level Recommendations\* for Management of Overactive Bladder

- Behavioral therapy, including bladder training and timed voiding, improves symptoms of urge and mixed incontinence and can be recommended as a noninvasive treatment in many women.<sup>1</sup>
- Pelvic floor training appears to be an effective treatment for adult women with stress and mixed incontinence and can be recommended as a noninvasive treatment for many women.<sup>1</sup>
- In women with UI who also have cognitive impairment, prompted and timed voiding programs are recommended as strategies for reducing leakage episodes.<sup>2</sup>
- Bladder training lasting a minimum of 6 weeks should be offered as first-line treatment for women with urge or mixed incontinence.<sup>2</sup>
- Non-proprietary IR oxybutynin should be offered to women with OAB or mixed urinary incontinence as first-line antimuscarinic drug treatment if bladder training has been ineffective. If IR oxybutynin is not well tolerated, darifenacin, solifenacin, tolterodine, trospium, or an extended-release or a transdermal oxybutynin form should be considered as alternatives.<sup>2</sup>

IR=immediate release, OAB=overactive bladder, UI=urinary incontinence.

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\*Recommendations are based on good and consistent scientific evidence; at least one meta-analysis, systematic review or randomised controlled trial (RCT) rated as 1+++, and is directly applicable to the target population; or a systematic review of RCTs or a body of evidence that consists principally of studies rated as 1+, is directly applicable to the target population and demonstrates overall consistency of results; or evidence drawn from a National Institute for Health and Clinical Excellence (NICE) technology appraisal.

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## Self-Assessment Quiz

- Which of the following symptoms need not be present to make a diagnosis of overactive bladder?
  - Urgency
  - Frequency
  - Urge incontinence
  - Nocturia
- Which of the following statements about the prevalence of overactive bladder (OAB) is true?
  - The overall prevalence of OAB in men and women is approximately equal.
  - OAB with related urinary incontinence is more prevalent in men than in women.
  - The prevalence of OAB with urge incontinence increases with increasing body mass index.
  - Symptoms associated with OAB are reported in 30% of individuals 65 years and older.
- Which of the following behavioral options is recommended for correcting frequent-voiding patterns?
  - Keeping a voiding diary
  - Adhering to a voiding schedule
  - Performing Kegel exercises
  - Making dietary changes
- Which of the following drug classes is the only one with proven effectiveness in the management of overactive bladder?
  - Beta blockers
  - Alpha blockers
  - Antimuscarinics
  - Antidepressants
- Which of the following behavior-modification techniques carries an A-level recommendation (based on good and consistent scientific evidence) for the management of urinary incontinence?
  - Pelvic floor muscle rehabilitation
  - Smoking cessation
  - Constipation prevention
  - Caffeine intake reduction

Answers: 1. C, 2. A, 3. B, 4. C, 5. A

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