Overactive bladder (OAB) is a symptom syndrome characterized by significant urgency, usually accompanied by voiding frequency, with or without urge urinary incontinence (UI). Multiple treatment options exist for the management of OAB. One of the mainstays of treatment is pharmacotherapy. This article provides an overview of pharmacologic options for the treatment of OAB. Although it is well established that the combination of medical and behavioral therapy is necessary to maximize treatment response, this discussion is limited to the efficacy, safety, and tolerability of medications specifically approved for the treatment of OAB.

When considering the efficacy of an OAB drug, it is necessary to consider precisely what the phrase “successful treatment” means to healthcare providers and to patients and how success is defined in the context of a clinical trial. Although it is tempting to assume that these perceptions are the same in all instances, it is necessary to remember that subjects who participate in clinical trials do not always reflect the patients seen in clinical practices. In addition, even though the principal outcomes measured in clinical trials of antimuscarinic or anticholinergic drugs are similar, the precise protocol for measuring these outcomes differs. Ultimately, comparing the numerous clinical trial results, both risk and benefit, is difficult.

**Pharmacology**

The number of available antimuscarinic agents approved for the management of OAB has grown significantly during the past year. These drugs exert several therapeutic benefits that alleviate lower urinary tract symptoms (LUTS) associated with OAB: (1) inhibit overactive detrusor contractions, (2) increase bladder capacity and time between voiding episodes, (3) diminish daytime and nighttime voiding frequency, and (4) reduce the number of urinary urge incontinence episodes. Figure 1 provides an overview of the desired and undesired effects of these agents.

Although antimuscarinic medications effectively block acetylcholine activity within muscarinic receptors in the bladder wall, muscarinic receptors are not unique to the detrusor muscle. Instead, they are located throughout the body and are, to a greater or lesser extent, affected by the administration of an antimuscarinic drug for treatment of OAB (Figure 2). Five muscarinic subtypes have been identified (M1 thru M5) within the central and peripheral nervous systems. With a wide distribution of muscarinic receptors, it is not surprising that the clinical effectiveness of an antimuscarinic drug represents a balance between its intended effects (alleviation of OAB symptoms) and tolerability (presence of adverse side effects).

All OAB medications have peripheral and central nervous system side effects. The magnitude of central adverse side effects is influenced by the penetration of a drug through the blood-brain barrier (BBB). Peripherally, muscarinic receptors are present in both the bladder and the parotid gland, dry mouth being the most common side effect reported. Other adverse side effects include gastrointestinal reflux, blurred vision, urinary retention, and cognitive changes. Older patients have a lower tolerance for antimuscarinic medications and a higher incidence of medical conditions that complicate pharmacologic treatment of OAB. Specifically, they are more likely to experience drug-drug interactions resulting from polypharmacy and to have certain medical conditions, such as decreased renal function, closed angle glaucoma, or chronic constipation, that may limit tolerability to an antimuscarinic drug, even when given at a lower dose.

**Understanding Clinical Trials**

Much of our knowledge of antimuscarinic agents arises from the results of industry-sponsored randomized clinical trials comparing the investigational agent to a placebo. The primary endpoints (outcomes) used to judge effectiveness are voiding frequency and frequency of urge UI episodes. However, because the majority of clinical trial subjects do not experience urge UI, trials have tended to oversample patients with OAB and urge UI. Other secondary outcomes include changes in voided volume, frequency of urgency episodes, nighttime voiding frequency, psychosocial impact, OAB, and quality of life. Evaluation of these secondary endpoints is important because it may...
Oxybutynin chloride is available in 4 formulations: immediate-release pills, a liquid, an extended-release oral formulation, and a transdermal patch. Immediate-release oxybutynin is available as a 5-mg tablet. The recommended starting dose is 5 mg administered 2 to 3 times daily, although many clinicians choose to begin elderly patients on a reduced dosage of 2.5 mg once or twice daily. A liquid formulation contains 1 mg/mL and is indicated for children who are too young to swallow a pill. A typical dosage for children older than 5 years of age is 5 mL or 5 mg bid to tid. Immediate-release oxybutynin has been used for more than 3 decades to treat OAB symptoms. It inhibits muscarinic action of acetylcholine and exerts a direct antispasmodic effect on smooth muscle. Oxybutynin acts primarily at the M1, M2, and M3 muscarinic receptors subtypes. Although effective in relieving the bothersome OAB symptoms, it is associated with numerous adverse side effects, particularly dry mouth (Table 2), that render adherence to therapy for a period more than 6 months to less than 20%. Conversion of oxybutynin to the metabolite, N-desthyl-oxybutynin (N-DEO) is hypothesized to cause the high incidence of dry mouth (87%) in immediate-release oxybutynin. The immediate-release form is absorbed in the stomach and metabolized in both gut lining and liver; approximately 90% is converted into N-DEO. In contrast, extended-release oxybutynin (Ditropan XL) is absorbed primarily in the colon and only 60% is converted to N-DEO. Clinical trials comparing extended-release oxybutynin to immediate-release oxybutynin found that 87% of those receiving the immediate-release formulation experienced dry mouth, compared to 28% of those randomized to receive
Even though both are administered orally, extended-release oxybutynin is packaged in an osmotic-releasing system containing active drug and a small sponge encased in a capsule with a small hole. As the agent passes through the gastrointestinal tract, water is slowly absorbed into the interior of the system, expanding the sponge and gradually releasing oxybutynin into the body. Because of this formulation, the capsule should not be chewed or crushed and the dose cannot be divided. To offset this potential limitation and to allow clinicians to titrate the dosage to a level that maximizes therapeutic benefit while limiting side effects, Ditropan XL is available in 3 dosages, 5 mg, 10 mg, and 15 mg. Dry mouth is significantly less than that seen with immediate-release oxybutynin, however, dry mouth is dose dependent with Ditropan XL. With all antimuscarinics, the potential for central nervous system side effects remains, especially for frail elderly patients who may experience constipation, somnolence, dizziness, tachycardia, blurred vision, and worsening of gastroesophageal reflux. Theoretically, oxybutynin may also worsen cognitive impairment.

Ditropan XL 10 mg was compared to Detrol LA 4 mg in 1 of the few head-to-head trials of long-acting agents. The Overactive Bladder: Performance of Extended Release (OPERA) trial was a 12-week double-blind active-control multicenter trial that evaluated the 2 most commonly prescribed medications for OAB in 2003. The primary endpoint was reduction in urinary urge incontinence episodes in patients with severe OAB (21-60 leaks per week). No statistically significant differences in mean weekly urge incontinence episodes were measured. From a tolerability standpoint, however, fewer patients complained of dry mouth while taking Detrol LA (30% vs 22%) although discontinuation rates during the trial period did not differ significantly.

Results from the OPERA trial indicated that extended-release oxybutynin was more likely to result in “complete” relief from UI episodes than tolterodine. However, reported improvements in disease-related quality-of-life improvements were similar between the two treatment groups, once again emphasizing the need to balance efficacy, tolerability, and patient expectation when choosing a medication to treat OAB.

Transdermal oxybutynin (Oxytrol) received Food and Drug Administration (FDA) approval on February 26, 2003. It is a 7.6-×-5.7 cm 3-layer matrix system patch containing 3.9 mg of oxybutynin that is applied to the skin of the lower abdomen, hips, or buttocks twice weekly. As noted, Oxytrol is associated with comparatively low production of the N-DEO metabolite and a low incidence of dry mouth. Additionally, because transdermal administration avoids metabolism by the liver, it reduces the concomitant risk for potential drug-drug interactions. These advantages, however, must be carefully weighed against the risk for local skin irritation associated with all transdermal administration systems. Fourteen (16.9%) users reported site reactions when using the patch, which constituted the main reason

### TABLE 1.

| Drug            | Formulation | Doses |
|-----------------|-------------|-------|
| Oxybutynin      | IR = generic | 5 mg  |
|                 | ER = Ditropan XL | 5 mg, 10 mg, 15 mg |
|                 | TDS = Oxytrol | 3.9 mg |
| Tolterodine     | IR = Detrol | 2 mg, 4 mg |
|                 | ER = Detrol LA | 2 mg, 4 mg |
| Trosplum chloride | IR = Sanctura | 20 mg |
| Solifenacin succinate | ER = VESIcare | 5 mg, 10 mg |
| Darifenacin hydrobromide | ER = Enaclipse | 7.5 mg, 15 mg |

### TABLE 2.

| Anticholinergic Adverse Events (%) | IR Oral Formulations |
|-----------------------------------|---------------------|
|                                   | OXY-IR\(^{13}\) (n = 52) | TOL-IR\(^{12}\) (n = 514) | TROSP-IR\(^{13}\) (n = 591) |
| M3, M1                            | 87                   | 30                   | 20.1                   |
| M3                                | 31                   | 7.0                  | 9.6                    |
| M1                                | 38                   | 2.0                  | —                      |
| M1                                | 40                   | 3.0                  | —                      |
| M1, M1                            | 17                   | 1.0                  | <1                     |
| Abnormal vision                   |                      |                      |                        |
| Headache                          | —                    | 4.0                  | 4.2                    |
for discontinuation because of adverse side effects. These incidences are derived from pivotal clinical trials where the patch was not rotated to all 6 possible sites, but to only 2. Data from the Multicenter Assessment of Transdermal Therapy in Overactive Bladder with Oxybutynin (MATRIX) Study may provide more insights into the incidence, severity, and bother when a more diverse patient population rotates the patch using all 6 possible sites.

Oxytrol was compared to Detrol LA 4 mg daily in a head-to-head double blind double-dummy randomized control trial. The overall efficacy of both agents was a 75% reduction in urinary urge incontinence episodes. Interestingly, 13 patients dropped out of the Oxytrol arm, 12 because of site reactions and 2 from the Detrol LA arm, 1 due to dry mouth, 1 for “other” reasons. Despite the lower reported incidence of dry mouth compared to tolterodine LA, transdermal oxybutynin has gained limited acceptance in routine clinical practice.

Tolterodine

Tolterodine tartrate was approved by the USFDA in 1998. It is a muscarinic receptor-antagonist that is now available in a short-acting (Ditropan) or extended-release formulation (Detrol LA). Immediate-release tolterodine is available in 1-mg and 2-mg doses, with the recommended starting dose at 2 mg twice daily. Its onset of action is 30-60 minutes after dosing. Patients with significant renal impairment or hepatic insufficiency should be begun on a dose of 1 mg twice daily. Tolterodine targets muscarinic receptors in the bladder, but it has no pharmacologic specificity for any subtype. Evidence in animal models, however, demonstrated that tolterodine exhibits greater binding affinity for muscarinic receptors in the bladder wall than the parotid gland, raising the argument that the drug provides greater organ specificity for the lower urinary tract, although the mechanism for this specificity remains unknown.

The efficacy and safety of immediate-release have been specifically studied in frail elders residing in long-term care. One hundred and seventy seven patients (mean age 75 years) with OAB were randomized to immediate-release tolterodine 1 mg or 2 mg twice daily or placebo for 4 weeks. Neither dose was associated with serious drug-related adverse events. The most common side effect was mild to moderate dry mouth, which led to treatment discontinuation in 3% of tolterodine treated patients and 2% of placebo treated patients. All OAB symptoms improved significantly. The authors concluded that immediate-release tolterodine, especially 2 mg bid, is safe and shows efficacy for older patients.

Immediate-release tolterodine was compared to extended-release tolterodine in a 12-week randomized placebo-controlled trial, which showed greater efficacy and tolerability for the extended-release formulation. Despite these results, however, immediate-release tolterodine remains an important option for many patients. For example, it may be the ideal agent for patients who wish to use an OAB drug PRN but who experience significant side effects when given even a single does of immediate-release oxybutynin.

Extended-release tolterodine (Detrol LA) is formulated in a 4-mg daily capsule using a beaded technology. Its safety and efficacy were originally established in a 12-week clinical trial comparing extended-release tolterodine to immediate-release tolterodine and placebo. Detrol LA and Ditropan XL were compared in a side-by-side study (not head-to-head in the strict sense) for purposes of determining patients’ perception of improvement in symptoms. This randomized study looked at 1289 patients (mean age 62 years) in an 8-week open-label trial. Patients were randomized to 2 mg or 4 mg of extended-release tolterodine or to 5 mg or 10 mg of extended-release oxybutynin. After 8 weeks, 13% of the oxybutynin treated patients withdrew, whereas 6% prematurely withdrew from the tolterodine arms. Patients treated with 4 mg of extended-release tolterodine perceived the most improvement in their bladder condition. Consistent with the dropout rates, significantly more patients in the oxybutynin group complained of dry mouth. Dry mouth was dose dependent in both drugs, but the oxybutynin 10-mg group reported the greatest degree of dry mouth in all groups. The authors concluded that extended-release tolterodine was superior in tolerability and patient perception on improvement of symptoms when compared to extended-release oxybutynin.

Extended-release tolterodine has also been studied in older (mean age 74) vs younger patients (mean age 51). This double-blind placebo-controlled trial involved 167 centers and 1015 patients. After 12 weeks, withdrawal rates were 5.5% and 5.1% in the younger and older groups, respectively. Despite the average 23-year age difference, the older-aged patients did not report a higher incidence of side effects leading to discontinuation. Additionally, regardless of age, the tolterodine-treated group reported significant improvement in urgency symptoms compared to placebo-treated patients.

One of the more recent trials involving Detrol LA looked specifically at nocturia related to OAB. This trial was undertaken to determine whether taking Detrol LA within 4 hours of bedtime reduced nighttime voiding frequency. The study specifically attempted to differentiate nocturia in patients with OAB from nocturia attributable to other causes. To achieve this goal, a 5-point urgency severity scale was used to rate each void and to link nighttime voiding as a result of uncontrollable urge with fear of leakage (Figure 3). During a 12-week period, patients received Detrol LA 4 mg within 4 hours of bedtime or placebo. Patients who rated their voids as level 1 or 2 (nocturia not associated with bothersome urgency or a fear of UI) showed no improvement. However, the higher the void was rated on the severity scale, the greater percentage of improvement occurred in the patients taking Detrol LA. Voids categorized as 4 or 5 were reduced by as much as 60% by the end of the 12-week trial. Dosing within 4 hours of sleep reduced the likelihood of experiencing adverse side effects. Specifically, 9% of subjects receiving extended-release tolterodine perceived the most improvement in their bladder condition.
release tolterodine experienced dry mouth, compared to 23% in the OPERA trial that used a morning dosing schedule. This effect may occur because evening dosing allows patients to sleep through the “onset of action,” which occurs in 2 to 6 hours. The improved side-effect profile was an unexpected outcome from the nighttime voiding trial, but it has important implications for clinicians seeking to minimize adverse side effects while maximizing therapeutic benefit.

**Trospium**

Trospium chloride (Sanctura) is an anticholinergic agent with predominantly peripheral nonselective antimuscarinic activity. The drug has been available in Europe for 2 decades, and was approved for use by the USFDA in May 2004. There are two main differences between trospium chloride and other agents for OAB symptoms: (1) it is a quaternary amine, whereas all others are tertiary amines, and (2) it is not metabolized via the cytochrome P450 system. The clinical significance of its quaternary amine structure is not clear. Theoretically, quaternary amine compounds are more water soluble, implying that they are less likely to cross the BBB. Additionally, the trospium molecule is positively charged and bulky, which is anticipated to further decrease the ease in which it crosses the BBB. Drugs that are less likely to cross the BBB are believed to cause fewer central nervous system (CNS) side effects occasionally observed when administering antimuscarinic medications. For example, one study compared tolterodine, oxybutynin, trospium, and placebo in a randomized single-blind parallel-group quantitative-topographical EEG (qEEG) trial. Trospium and tolterodine showed no effect, while oxybutynin caused significant power reductions in 5 out of 6 frequencies. The relationship between EEG changes and cognitive changes has not been established. Although water solubility may decrease the risk for adverse CNS side effects, it becomes a concern regarding absorption in the gastrointestinal tract. With the more water-soluble agents, absorption in the gut is decreased. Administration of trospium with a high-fat content meal results in reduced drug absorption. As a result, trospium should be taken 1 hour before meals on an empty stomach.

Even though it is known that trospium is not metabolized by the cytochrome P450 system, the precise metabolic pathway of trospium in humans is not known. Theoretically, the risk for drug-drug interactions associated with administration of trospium may be decreased. However, specific drug-drug interaction studies with trospium have not been conducted, and the potential for reduced interactions is based on pharmacokinetics alone.

Trospium chloride is excreted via active renal tubular secretion. Coadministration of drugs competing for active tubular secretion may not only increase the serum concentration of Sanctura but also increase concentrations of other common drugs, such as digoxin, metformin, and morphine. Studies have also shown that in the elderly population (>75 years of age), increased muscarinic side effects were observed. Therefore, possible dose reduction may be necessary owing to tolerability, potentially decreasing efficacy. Dose modification is necessary in patients who are renally impaired.

The efficacy of trospium chloride is comparable with other OAB agents. In one trial involving 523 patients, Sanctura demonstrated significant improvement in most symptoms associated with OAB, as well as a rapid onset of action. Overall, patients experienced a 71% reduction in incontinence episodes. Interestingly, in a second placebo-controlled trial, trospium was 34%-46% more effective than placebo. Both trials were 12 weeks in length, and the difference in outcomes raises the question of variability of
efficacy. In a head-to-head trial with Ditropan immediate-release 5 mg bid, trospium 20 mg bid showed a more favorable side-effect profile, with similar efficacy.19 Similarly, another trial comparing trospium 20 mg bid to Detrol immediate-release 2 mg bid, found that trospium and toterodine immediate release were equivalent in decreasing urge incontinent episodes.20 The most common adverse events associated with trospium chloride are dry mouth, constipation, and headache.

### Solifenacin

Solifenacin succinate (VESIcare) is a muscarinic receptor antagonist, primarily M3 selective, with antagonistic properties to M2 receptors as well. It was approved in the US by the FDA in November 2004. VESIcare® is available in 5-mg and 10-mg doses and should be swallowed whole with liquids. The recommended starting dose is 5 mg daily; if tolerated, the dose may be increased to 10 mg daily if symptoms persist. The use of VESIcare in the open market will provide much more information regarding its effect on the treatment of patients with OAB. This new agent has been studied in 4 double-blind 12-week trials and similar study designs allowed for pooling of data. Overall, there was a 62% to 66% reduction in urinary urge incontinence and significantly improved urgency, frequency, and volume voided.21 Additionally, a 40-week open-label extension of the two 5-mg double-blind studies evaluated long-term safety. Solifenacin has not been compared to other extended-release agents in double-blind placebo-controlled randomized trials. Studies indicate a slight improvement in efficacy from 5 mg to 10 mg, although there is a significant dose-related increase in reported side effects.22

Adverse side effects specifically related to M3 blockade include dry mouth, constipation, and abnormal vision. Only 10.9% of patients on 5 mg daily of VESIcare reported dry mouth, which is comparable to Oxytrol (4.1%) or Detrol LA when administered in the evening (8.9%). The lower the percentage of the side effect specific to a muscarinic receptor, the more selective a drug is for the bladder over the salivary gland. Abnormal vision was reported almost 4 times as often with 5 mg of solifenacin and 5 times as often with 10 mg of solifenacin compared to 4 mg of Detrol LA. Visual disturbances may not be well tolerated, especially for the elderly who may have impaired vision resulting from cataracts or other reasons.

Solifenacin was compared to Detrol immediate release as an active comparator in a small 12-week placebo-controlled trial study.22 Both agents achieved statistically significant reductions in micturition frequency and urge UI episodes when compared to placebo. Solifenacin has a 53-hour half-life. If a patient has an adverse event related to VESIcare, then the prolonged washout period may lead to slow resolution of the side effect. On the other hand, a long half-life may result in more constant therapeutic levels of therapy. If continuation on a medication after the completion of a study indicates patient satisfaction, 91% of patients who completed 2 of the 12-week trails continued with VESIcare. Of the total 1811 patients enrolled in VESIcare studies, the overall rate of serious adverse events (AEs) was 2%. Unfortunately, these AEs included 1 fecal impaction, 1 colonic obstruction, and 1 intestinal obstruction; all of these patients were treated with the 10-mg dose of VESIcare.23

### Darifenacin

Darifenacin hydrobromide (Enablex) is a highly selective M3 receptor antagonist, available in 7.5-mg and 15-mg doses. Figure 4 demonstrates the high degree of selectivity for the muscarinic receptor subtype 3. In theory, M3 receptors are primarily responsible for bladder contractility. The
more nonselective agents should stimulate broader side effects. By sparing central M1 receptors, the associated CNS effects of somnolence and cognitive impairment should be avoided. In a 12-week trial, 129 subjects, mean age 71, received either 7.5 mg of Enablex or 15 mg. The mean change from baseline showed no statistically difference from placebo. Darifenacin reduces the number of weekly incontinence episodes by up to 77%, The main side effects noted were constipation and dry mouth, which resulted in low discontinuation rates. Results from a pooled analysis of 3 multicenter double-blind placebo-controlled studies on darifenacin (1059 patients), revealed decreased frequency, increased bladder capacity, and decreased feelings of urgency. Long-term safety was studied for up to 1 year; CNS and cardiovascular safety were comparable to placebo.26

Although the affinity to M3 receptors may spare blockade of other muscarinic receptors (ie, avoiding certain adverse events), the high affinity for other peripheral M3 receptors may result in worsening M3-related AEs. At 15 mg, 35.3% of patients reported dry mouth and 21.3% reported constipation, compared to 20.2% and 14.8%, respectively, at the 7.5-mg dose. These AEs are significantly higher than the other extended-release agents. In a related study of human bladder and parotid gland tissue, the inhibitory effects of tolterodine in the bladder were greater than in the parotid gland, whereas the effects of oxybutynin and darifenacin where greater in the parotid gland.27 The highly selective affinity for the M3 receptor Enablex is unique. Nevertheless, greater clinical use is critical to understanding the clinical effectiveness of this novel agent for the management of OAB.

To better provide the adverse events of the extended-release formulations, Table 3 shows the reported percentages from various clinical trials.

### Contraindications and Precautions

Certain contraindications and precautions apply to all antimuscarinic medications. They are contraindicated in patients with uncontrolled narrow angle glaucoma, gastric reflux, or urinary retention. Caution should be used in patients with hepatic or renal impairment, gastrointestinal obstructive disorders, bladder outflow obstruction, ulcerative colitis, intestinal atony, myasthenia gravis, and gastroesophageal reflux.

#### Prescribing and Evaluating an OAB Drug

Conservative measures, such as education, fluid, and dietary alterations, habit retraining, and pelvic floor muscle rehabilitation are effective for the treatment of OAB and are often recommended as first-line therapy. However, pharmacologic agents are an important adjunct and may be a first-line treatment for many patients. When should the clinician begin a patient with OAB on an antimuscarinic drug and when should alternative treatments be explored? An OAB medication may be prescribed as first-line treatment based on symptom severity and patient preference and in combination with behavioral interventions. Arguments in favor of first-line use of an OAB medication include a relatively rapid onset of action, a robust evidence base supporting its efficacy, and research demonstrating that combination therapy (pharmacologic and behavioral treatment) is the most effective way to alleviate or relieve OAB.

There are now 5 FDA-approved compounds in 8 different formulations and 14 doses. Variables that influence the decision to prescribe 1 medication vs another are individualized but include preexisting medical conditions, such as age, previous treatments for OAB, complicating condition, and current medications. Other considerations include the cost of the medication, formulary access, and availability for the new agents. Barring hypersensitivity to a specific agent, no persuasive data exist that clearly establish one medication as superior to all others. Tolterodine and oxybutynin have the most comprehensive clinical data elucidating their safety, efficacy, and tolerability. Trospium has been available in Europe for approximately 20 years, although it has only recently been approved for use in the United States. Solifenacin and darifenacin are both new to the market and have yet to withstand the test of time. Because efficacy, for all practical purposes, does not separate the medications, experienced clinicians usually choose based on their past ex-

#### TABLE 3.

**Anticholinergic Adverse Events (%): ER Oral Formulations**

|            | OXY-ER11 (n = 185) | TOL-ER12 (n = 507) | SOL-ER23 5 mg (n = 1811) | SOL-ER23 10 mg (n = 1811) | DAR-ER23 7.5 mg (n = 337) | DAR-ER23 15 mg (n = 334) |
|------------|-------------------|--------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| M3, M1     | Dry mouth         | 28                 | 23                       | 10.9                     | 27.6                     | 20.2                     | 35.3                     |
| M3         | Constipation      | 7.0                | 6.0                      | 5.4                      | 13.4                     | 14.8                     | 21.3                     |
| M1         | Dizziness         | 4.9                | 2.0                      | 1.9                      | 1.8                      | 0.9                      | 2.1                      |
| M1         | Somnolence        | 4.3                | 3.0                      | —                        | —                        | —                        | —                        |
| M3, M1     | Abnormal Vision   | 2.2                | 1.0                      | 3.8                      | 4.8                      | —                        | —                        |
| —          | Headache          | 8.1                | 6.0                      | —                        | —                        | —                        | —                        |

*Total of 1,811 patients evaluated in clinical trial.*
perience. Given the significant increase in drug options, WOC nurses should use every opportunity to gain knowledge regarding the efficacy and tolerability of the antimuscarinic medications for treatment of OAB.

Follow-up after initiating a drug is critical to long-term success. Most patients should be evaluated 4-6 weeks after beginning a medication, and the degree of symptom relief (preferably supported by a 3-day voiding diary) should be evaluated. The dosage of the medication should be adjusted if necessary, and adherence to both medication and behavioral interventions carefully evaluated. If adverse side effects or lack of efficacy occurs, it is advisable to begin a new medication, which may provide superior results to the initial drug choice. The reason for individual response to a particular medication is not known, but it may be attributable to differences in the underlying causes of OAB in a particular patient, the drug’s ability to control the most bothersome symptom associated with OAB, or pharmacogenetic factors that we do not yet understand. Fortunately, clinical experience has clearly shown that having multiple choices increase the chances that healthcare providers will find the best treatment option for an individual patient.

References

1. Burgio KL, Locher JL, Goode PS. Combined behavioral and drug therapy for urge incontinence in older women. J Am Geriatr Soc. 2000;48:370-374.
2. Garely AD, Burrows L. Benefit-risk assessment of tolterodine in the treatment of overactive bladder in adults. Drug Safety. 2004;27:1043-1057.
3. Chapple CR. Muscarinic receptor antagonists in the treatment of overactive bladder. Urology. 2000;55(Suppl):33-46.
4. Skidmore-Roth L. Mosby’s 2005 Drug Reference. St. Louis: Mosby; 2005:779.
5. Versie E, Appell R, Mobjly D, et al. Dry mouth with conventional and controlled release oxybutynin in urinary incontinence. The Ditropan XL Study Group. Obstet Gynecol. 2000;95:718-721.
6. Watson Pharmaceuticals, Corona CA. Oxytrol® United States prescribing information. Date of issuance: February 2003.
7. Waldeck K, Larsson B, Andersson KE. Comparison of oxybutynin and its active metabolite, n-desethyl-oxybutynin, in the human detrusor and parotid gland. J Urol. 1997;157:1093-1097.
8. Diokno AC, Appell RA, Sand PK, et al. A prospective, randomized, double-blind study of the efficacy and tolerability of the extended-release formulations of oxybutynin and tolterodine: results of the OPERA trial. Mayo Clinic Proc. 2003;78:687-695.
9. Dmochowski RR, Sand PK, Zinner NR, et al. Comparative efficacy and safety of transdermal oxybutynin and oral tolterodine versus placebo in previously treated patients with urge and mixed incontinence. Urology. 2003;62:237-242.
10. Hornbass TH, Wickersham RM, Novak KK, et al. Tolterodine tartrate. In: Facts & Comparisons. St Louis: Wolters Kluwer; 2002:600-623.
11. Malone-Lee JG, Walsh JB, Maugoand MF. Tolterodine—a safe and effective treatment for older patients with overactive bladder. J Am Geriatr Soc. 2001;49:700-705.
12. Van Kerrebroeck P, Kreder J, Jonas U, et al, and the Tolterodine Study Group. Tolterodine once-daily: superior efficacy and tolerability in the treatment of the overactive bladder. Urology. 2001;57:414-421.
13. Sussman D, Garely A. Treatment of overactive bladder with once daily extended release tolterodine or oxybutynin: the antimuscarinic clinical effectiveness trial (ACET). Curr Med Res Opin. 2002;18:177-184.
14. Zinner NR, Mattiason A, Stanton S. Efficacy, safety and tolerability of extended-release once-daily tolterodine treatment for overactive bladder in older versus younger patients. J Am Geriatr Soc. 2002;50:799-807.
15. Taylor P, Zhonghong G, Wang J. Nighttime dosing with tolterodine reduces overactive bladder-related nocturnal frequency in patients with overactive bladder and nocturia: a 12-week, double-blind, placebo-controlled, randomized study in 850 adults with nocturia (abstract from study 037). Presented at the American Academy of Physician Assistants, Orlando, May 2005.
16. Todorova A, Vanderheiden-Guth B, Dimpfel W. Effects of tolterodine, trospium chloride and oxybutynin on the central nervous system. J Clin Pharmacol. 2001;41:636-644.
17. Zinner N, Gittleman M, Harris R, et al, and the Trospium Study Group. Trospium chloride improves overactive bladder symptoms: a multicenter phase III trial. J Urol. 2004;171:2311-2315.
18. Odyssey Pharmaceuticals, Inc., East Hanover, NJ, and Indevus Pharmaceuticals, Inc., Lexington, MA, Sanctura™ United States prescribing information. Date of issuance: July 2004.
19. Halaska M, Ralph G, Wiedmann A, et al. Controlled, double-blind, multi-center clinical trial to investigate long-term tolerability and efficacy of trospium chloride in patients with detrusor instability. World J Urol. 2003;20:392-399.
20. Junemann KP, Al-Shukri. Efficacy and tolerability of trospium chloride and tolterodine in 234 patients with urge syndrome: a double blind, placebo-controlled, multicenter clinical trial. Presented at International Continence Society annual meeting, Tampere, August 28, 2000.
21. Cardozo L, Lesec M, Millard R, et al. Randomized, double-blind placebo controlled trial of the once daily antimuscarinic agent solifenacin succinate in patients with overactive bladder. J Urol. 2004;172:1919-1924.
22. Chapple CR, Recherber T, Al-Shukri S, et al. Randomized, double-blind placebo and tolterodine-controlled trial of the once-daily antimuscarinic agent solifenacin in patients with symptomatic overactive bladder. Br J Urol Int. 2004;93:303-310.
23. Yamanouchi Pharma America, Paramus, NJ, and GlaxoSmithKline, Research Triangle Park, NC. VESIcare United State prescribing information. Date of issuance: November 2004.
24. Lipton R, Kolodner K, et al. Darifenacin, an M3 selective receptor antagonist for the treatment of overactive bladder, does not affect cognitive function in elderly volunteers. Abstract S13. Department of Epidemiology and Population Health, Albert Einstein College of Medicine, NY.
25. Chapple C. Darifenacin is effective in improving the major symptoms of overactive bladder: a pooled analysis of phase III studies. Poster presented at XIXth European Assoc of Urology Congress, Vienna.
26. Chapple C, Kelleher C, Perrault L, et al. Darifenacin, an M3 selective receptor antagonist, improves quality of life on patients with overactive bladder. Poster presented at World Health Organization’s 3rd International Consultation on Incontinence, Monte Carlo.
27. Oki T, Mikami Y, Takeda M, et al. Muscarinic receptor binding characteristics of anticholinergic agents used to treat OAB, in human bladder and parotid glands. Biol Pharm Bull. 2001;24:391-395.
28. Wyman JF. Treatment of urinary incontinence in men and older women: the evidence shows the efficacy of a variety of techniques. Am J Nurs. 2003;March(suppl):26-35.
29. Napier C, Gupta P. Proct ICS. 2002:445. (Abstract). Heading CE. Curr Opin CPNS Inves Drugs.2000;3:321-325.
Supplement: Taylor

30. Heading CE. Conus peptides and neuroprotection. Curr Opin Inves Drugs. 2002;6:915-920.
31. Appell RA, Sand P, Dmochowski R, et al. Prospective randomized controlled trial of extended-release oxybutynin chloride and tolterodine tartrate in the treatment of overactive bladder: results of the OBJECT Study. Mayo Clin Proc. 2001;76:358-363.
32. Novartis Pharmaceuticals Corporation, East Hanover, NJ. Enablex United States prescribing information. Date of issuance: November 2004.
33. Anderson RU, Mobley D, Blank B, et al. Once daily controlled versus immediate release oxybutynin chloride for urge urinary incontinence. J Urol. 1999;161:1809-1812.

CE Test

Gaining Control: Making Sense of OAB
This activity is supported by an unrestricted educational grant from Pfizer Inc.

Instructions:
- Read the articles beginning on page S1.
- Take the test, recording your answers in the test answer section (Section B) of the CE enrollment form. Each question has only one correct answer.
- Complete registration information (Section A) and course evaluation (Section C).
- Mail completed test with registration fee to: Lippincott Williams & Wilkins, CE Group, 333 7th Avenue, 19th Floor, New York, NY 10001.
- Within 4-6 weeks after your CE enrollment form is received, you will be notified of your test results.
- If you pass, you will receive a certificate of earned contact hours and answer key. If you fail, you have the option of taking the test again at no additional cost.
- Need CE STAT? Visit www.nursingcenter.com for immediate results, other CE activities and your personalized CE planner tool.
- No Internet access? Call 800-903-6525 ext. 6617 or 6621 for other rush service options.
- Questions? Contact Lippincott Williams & Wilkins: (646) 674-6617 or (646) 674-6621

Registration Deadline: June 30, 2007

Provider Accreditation:
This Continuing Nursing Education (CNE) activity for 7 contact hours (Pharmacology credit: 1.5) and is provided by Lippincott Williams & Wilkins, which is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center’s Commission on Accreditation and by the American Association of Critical-Care Nurses (AACN 00012278, CERP Category A). This activity is also provider approved by the California Board of Registered Nursing, Provider Number CEP 11749 for 7 contact hours (Pharmacology credit: 1.5). LWW is also an approved provider of CNE in Alabama, Florida, and Iowa and holds the following provider numbers: AL #ABNP0114, FL #FBN2454, IA #75.

Your certificate is valid in all states. This means that your certificate of earned contact hours is valid no matter where you live.

Payment and Discounts:
- The registration fee for this test is waived courtesy of Pfizer Inc.
- Take this test free at www.nursingcenter.com compliments of Pfizer Inc. If you choose to mail your enrollment form, the handling fee is $6.95.

CE TEST QUESTIONS

GENERAL PURPOSE: To provide registered professional nurses with a comprehensive overview of overactive bladder syndrome.

LEARNING OBJECTIVES: After reading this article and taking this test, you will be able to:
1. Define overactive bladder (OAB) dysfunction and discuss its impact, epidemiology, and pathophysiology.
2. Describe assessment strategies for identifying patients with OAB and distinguishing high-tone and low-tone pelvic floor dysfunction.
3. Outline behavioral interventions and pharmacologic agents used in the management of OAB.

1. The characteristic symptom of overactive bladder (OAB) is
   a. bothersome urgency.
   b. daytime voiding frequency.
   c. nocturia.
   d. hematuria.

2. The current emphasis on a symptoms-based approach to diagnosis of OAB has
   a. removed the stigma previously associated with this syndrome.
   b. eliminated the need for complex urodynamic testing within specialty practices.
   c. facilitated management of the syndrome within primary care settings.
   d. led to a greater reliance on urodynamic testing in all care settings.

3. Urine loss caused by physical exertion, coughing, or sneezing
   a. is known as urge urinary incontinence (UI).
   b. is known as stress UI.
   c. is associated with voiding frequency.
   d. may be categorized as either urge UI or stress UI.

4. Findings from two major prevalence studies reveal
   a. a significantly higher incidence of OAB in women than in men.
   b. a similar presentation of OAB in both men and women.
   c. that the majority of patients with OAB also experience urge UI.
   d. that men and women are equally affected by OAB with women more likely to experience urge incontinence.

5. The greatest negative impact of OAB may be related to
   a. quality of life.
   b. multiple aspects of physical health.
   c. an increased incidence of urinary tract infections.
   d. an increased potential for falls and fractures.

6. An individual with OAB is most likely to
   a. seek out medical care related to the condition.
   b. manage troublesome symptoms with minimal impact on social situations.
   c. experience some fatigue associated with the condition.
   d. conceal the conditions from healthcare providers.

7. OAB dysfunction is strongly associated with
   a. poor innervation of the detrusor muscle.
   b. pelvic trauma.
   c. detrusor overactivity alone.
   d. both detrusor overactivity and increased bladder sensations.

8. Urodynamic findings
   a. elucidate the underlying cause of detrusor overactivity.
   b. clarify the pathophysiologic mechanisms underpinning OAB dysfunction.
   c. suggest a single mechanism underpinning OAB dysfunction.
   d. have led to novel interventions in the management of OAB dysfunction.