A Pharmacoeconomic Model Comparing Two Long-Acting Treatments for Overactive Bladder

LES NOE, MPA; RUSSELL BECKER, MA; TODD WILLIAMSON, PhD; and DONNY CHEN, AB

ABSTRACT

OBJECTIVE: To compare the estimated first-line treatment costs of extended-release tolterodine versus controlled-release oxybutynin in patients with overactive bladder (OAB).

METHODS: We developed a decision-analysis model to estimate the patterns of treatment, resource consumption, and cost impact of treating OAB with either controlled-release oxybutynin or extended-release tolterodine as first-line drug therapy. We used data from the published literature to develop the framework for the model and supplemented this information with expert opinion, where necessary. Based on recent clinical studies, we assumed equal efficacy between the comparators and reduced the model to a cost-minimization analysis. The model was constructed from the payer perspective, and all costs are given in 2000 U.S. dollars.

RESULTS: A base-case analysis was generated showing that patients initiating therapy with extended-release tolterodine have probable average 3-month treatment costs of \$1,207 compared to \$1,283 for patients initiating with controlled-release oxybutynin, for a 6.3% difference. First-line OAB direct drug costs account for 19% and 15% of total costs for extended-release tolterodine and controlled-release oxybutynin, respectively. Sensitivity analysis showed these results to be relatively stable.

CONCLUSION: The results from this analysis suggest that for patients with OAB and initiating long-acting pharmacologic therapy in the primary care setting, the treatment with extended-release tolterodine is slightly less costly than treatment with controlled-release oxybutynin. Studies directly comparing these treatment alternatives are needed, however, to determine which approach or combination of approaches is the most cost-effective.

KEYWORDS: Overactive bladder, OAB, Decision-analysis model, Oxybutynin, Tolterodine, Cost minimization

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Authors

LES NOE, MPA, is Vice President of Scientific Affairs, RUSSELL BECKER, MA, is Senior Manager, and DONNY CHEN, AB, is Senior Data Analyst, Ovation Research Group, Highland Park, Illinois; TODD WILLIAMSON, PhD, is Senior Director, Global Health Outcomes, Pharmacia Corporation, Peapack, New Jersey.

AUTHOR CORRESPONDENCE: Russell Becker, Senior Manager, Ovation Research Group, 600 Central Ave., Suite 265, Highland Park, IL 60035. E-mail: rbecker@ovation.org

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The cost of overactive bladder (OAB) is a significant financial burden on patients, families, and the health care system. In 2000, the total economic cost of OAB in the United States was estimated at \$18.2 billion, which is more than either osteoporosis or Parkinson's disease. OAB costs at the community level were approximately \$13.8 billion, while costs at institutions were \$4.4 billion.¹ A study examining insurance claims showed that total annual claims among OAB patients was \$5,018 versus \$1,767 among non-OAB controls (1995 dollars).²

Drug Treatment for OAB

Head-to-head studies comparing 2 immediate-release forms of antimuscarinic drug therapy, oxybutynin, and tolterodine, have shown that they have similar efficacy; however, tolterodine has an improved side-effect profile, most notably less dry mouth, and is associated with fewer treatment withdrawals as a result of drug-related adverse events.³⁻⁷

The side effects from OAB drug therapy have resulted in poor compliance and, subsequently, low persistence with therapy over time.^{4,8,9} Persistence with drug therapy is important for achieving long-term treatment benefits. In a number of retrospective claims studies, patients receiving tolterodine have been shown to remain on therapy longer than those receiving oxybutynin.^{6,9-15} There is also evidence that suggests that OAB patients who are able to continue with medication have greater symptom improvement and use fewer resources.¹⁶

Phase III clinical trials of controlled-release oxybutynin have indicated better patient compliance, reduced side effects, and equivalent efficacy as compared to oxybutynin IR.¹⁷⁻¹⁹ Both extended-release tolterodine and controlled-release oxybutynin have been shown to be more effective and better tolerated than immediate-release tolterodine.^{20,21} These data further suggest that extended-release tolterodine has better tolerability and fewer side effects than controlled-release oxybutynin. Although there are no head-to-head studies to suggest that one of the extended-release drugs is more efficacious than the other, one recent study compared extended-release tolterodine to controlled-release oxybutynin using a 4-way crossover design in a small number of patients.²² Using change in bladder capacity as a surrogate for efficacy, a 6 mg dose of extended-release tolterodine was found to be equivalent to a 20 mg dose of oxybutynin. However, the 6 mg dose of extended-release tolterodine produced a side-effect profile with respect to dry mouth similar to the 10 mg dose of controlled-release oxybutynin. This implies that extended-release tolterodine might be as efficacious as oxybutynin but has an improved tolerability profile.

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TABLE 1 Resources and Cost Inputs

Resource Variable	CPT-4 Code	Cost*
Drug Cost (per day)		
Extended-release tolterodine 2 mg	N/A	\$2.73/day ³⁷
Extended-release tolterodine 4 mg	N/A	\$2.80/day ³⁷
Controlled-release oxybutynin 5 mg	N/A	\$2.44/day ³⁷
Controlled-release oxybutynin 10 mg	N/A	\$2.69/day ³⁷
Controlled-release oxybutynin 15 mg	N/A	\$2.94/day ³⁷
Imipramine 50 mg tid	N/A	\$2.07/day ³⁷
Estrogen 2 gm qod	N/A	\$1.12/day ³⁷
Other Drugs (flavoxate, dicyclomine, hyoscyamine)	N/A	\$2.11/day ³⁷
Physician Costs		
Physician office visit (PCP): outpatient follow-up	99213	\$40.16/visit ³⁶
Physician office visit (PCP): outpatient follow-up	99214	\$63.14/visit ³⁶
Physician office visit (Specialist): outpatient follow-up	99244	\$144.31/visit ³⁶
Incontinence pads	N/A	\$5.17/pad ³⁷
Physical and Behavioral Therapy		
Behavioral therapy	97112	\$24.44 ³⁶
Biofeedback	90911	\$67.04 ³⁶
Electrical stimulation	97014	\$13.33 ³⁶
Other therapy	97139	\$13.51 ³⁶
Procedures/Tests		
Cystoscopy	52000	\$130.32 ³⁶
Cystometrogram/Pressure flow urodynamics	51726	\$75.40 ³⁶
Urine flowmetry	51741	\$44.97 ³⁶
Urethral pressure profile	51772	\$67.59 ³⁶
Cystogram (VCUG)	74430	\$38.78 ³⁶
Urine cytology	88104	\$30.94 ³⁶
Post-void residual	78730	\$50.98 ³⁶
Urinalysis	81005	\$19.81 ³⁶
Dipstick urinalysis	81000	\$19.81 ³⁶
Comorbid Conditions		
Urinary tract infections	N/A	\$53.96 ³¹
Skin infections	N/A	\$21.69 ³¹
Depression	N/A	\$182.87 ^{36,37}
Fractures	N/A	\$2,934.37 ³⁸
Productivity Losses		
Low resource group (per 3 months)	N/A	\$0.00 ³⁴
Medium resource group (per 3 months)	N/A	\$293.66 ³⁴
High resource group (per 3 months)	N/A	\$587.31 ³⁴

* Medication costs are calculated using average wholesale prices (AWP). Urinary tract and skin infection costs are based on claims data from California's Medicaid (Medi-Cal) program. All other costs reflect actual payments based on published DRG and physician fee schedules. All costs were inflation-adjusted, if necessary, to reflect 2000 U.S. dollars using the Bureau of Labor Statistics CPI-U for Medical Care Services.³⁹

Economic considerations of the treatment of OAB have been previously described.²³⁻²⁵ These economic analyses have focused

primarily on comparing the immediate-release forms of tolterodine and oxybutynin or long-acting oxybutynin with immediate-release tolterodine.^{26,27} However, one recent economic analysis compared the 2 long-acting products and suggested that extended-release tolterodine might be less costly overall than controlled-release oxybutynin.²⁸

The objective of our analysis was to develop a decision-analysis model to compare the 3-month economic impact of treating OAB with extended-release tolterodine and controlled-release oxybutynin.

Methods

This model estimates the patterns of treatment, resource consumption, and cost impact of treating OAB with either controlled-release oxybutynin or extended-release tolterodine as first-line drug therapy. We used data from the published literature to develop the framework for the model and supplemented this information with expert opinion, where necessary, due to a lack of published data. Expert opinions were obtained using a modified Delphi method from 4 practicing urologists who have experience in the field of overactive bladder research and treatment. They utilized their own personal knowledge and professional experience in responding to a specific set of questions regarding specific data points. Specifically, we used expert opinion to (1) estimate the percentage of patients who receive various treatments in the model and (2) confirm or modify estimates regarding drug dosing and resource consumption.

After the first round of estimates were obtained, each panel member was provided, in a blinded manner, with the estimates obtained from the other experts and given the opportunity to make adjustments, if they felt it was necessary. The results from the second round were averaged to obtain the final estimates used in the model. The ranges were used in sensitivity analyses.

This analysis was conducted from a payer perspective. All costs were obtained from published literature and standardized databases (Table 1) and are given in 2000 U.S. dollars.

Treatment Comparators

We limited our comparison to the long-acting forms of oxybutynin and tolterodine. Given that the limited number of studies including one or both of these drugs did not suggest that one treatment is more effective than the other, we assumed they were equally effective.

Model Design

Figure 1 shows a schematic of the decision-analysis model used. The model includes outpatients with a diagnosis of OAB seeking treatment from primary care physicians (PCPs). Patients entering the model are diagnosed as having OAB with an age range of 20 to 89 years (mean 60 years), matching that of key, published clinical studies.^{20,21} Patients are assumed to be already using behavioral therapy techniques in addition to drug

treatment. Patients with surgically curable causes of incontinence are not included. Patients are prescribed either extended-release tolterodine or controlled-release oxybutynin and are treated for a 12-week (3-month) period. At the end of the 3-month period, patients may be referred to a specialist for further evaluation and treatment, based on their treatment course. The cost associated with the referral, as well as typical diagnostic procedures that are performed by a specialist, is included. Infrequently used second-line treatments (<5% use) are not included. Treatment rates obtained from expert opinion are shown in Table 2.

Resource Consumption

The following resources are included in the model: medications, physician visits, incontinence pads, physical/behavioral therapy, procedures/tests, treatment of comorbid conditions, and productivity losses (Table 1). Medication costs are calculated using average wholesale prices (AWP). Urinary tract and skin infection costs are based on claims data from California's Medicaid (Medi-Cal) program. All other costs reflect actual payments based on published diagnosis-related group and physician fee schedules. All costs were inflation-adjusted, if necessary, to reflect 2000 U.S. dollars using the U.S. Bureau of Labor Statistics CPI-U for Medical Care Services.

We assume that the use of incontinence pads, the incidence of comorbid conditions, and the degree of productivity loss will vary based on the extent to which patients required modifications to their initial treatment. For these resources, we assume 3 levels of possible consumption: low, medium, and high. The low and high consumption levels are based on information in the published literature and from expert opinion, while the medium consumption level is calculated as an average of the low and high estimates. The levels are applied to all patients within a specific patient group, as outlined below:

- Continue Monotherapy (no dosing changes)—low consumers
- Add or Switch Therapy (and monotherapy dosing changes)—medium consumers
- Discontinue All OAB Therapy—high consumers

Variable resource rates used in the model are shown in Table 3. Our rationale for assigning these varying levels of resources was

FIGURE 1 Model Schematic

based on a retrospective study,²⁹ where patients switching OAB medication during the follow-up period had approximately 12% higher median per-member-per-month (PMPM) total costs from baseline. In comparison, the group that was maintained on the same OAB therapy had approximately 45% lower median PMPM total costs from baseline. This suggests that patients who switched OAB medication in the follow-up period due to treatment failure incurred PMPM total costs 56.6% higher than subjects who remained on the same OAB medication.

The model does not include patients with OAB who do not seek professional treatment and, hence, presumably consume few medical resources. Resource consumption characteristics and patient quality of life have not been adequately studied in patients who do not seek treatment for OAB.

Resource utilization associated with key adverse events, such as dry mouth, are reflected in the treatment rates as well as subsequent dose reductions, therapy changes, and discontinuations. Other adverse events are considered to be similar in terms of rates and/or resource utilization between comparators.³⁻⁷

Drug Dosing

We assume a starting dose of 4 mg daily for extended-release

TABLE 2 Treatment Rates–Base-Case Analysis

	Extended-release Tolterodine	Controlled-release Oxybutynin
Node A		
Continue	70%	61%
Change therapy	30%	39%
Node B		
Continue	83%	83%
Add therapy	17%	17%
Node C		
Switch therapy	80%	80%
Discontinue OAB therapy	20%	20%
Node D		
Increase dose	14%	32%
Decrease dose	5%	6%
Same dose	81%	62%
Node E		
Pharmacologic therapy	80%	83%
Nonpharmacologic therapy	20%	17%
Node F		
Pharmacologic therapy	90%	90%
Nonpharmacologic therapy	10%	10%
Node G		
Referred to specialist	75%	75%
Lost-to-followup	25%	25%
Node H		
Imipramine	38%	38%
Estrogen	33%	33%
Other drug therapy	29%	29%
Node I		
Biofeedback	72%	72%
Electrical stimulation	23%	23%
Other nonpharmacologic therapy	5%	5%
Node J		
Imipramine	18%	17%
Estrogen	8%	7%
Controlled-release oxybutynin or extended-release tolterodine	71%	74%
Other drug therapy	3%	2%
Node K		
Biofeedback	58%	58%
Electrical stimulation	37%	37%
Other nonpharmacologic therapy	5%	5%

tolterodine and 5 mg daily for controlled-release oxybutynin with an increase to 10 mg after one week (package insert).³⁰ We assume that patients requiring a dosage increase at 6 weeks will be prescribed extended-release tolterodine 6 mg daily or controlled-release oxybutynin 15 mg daily. Patients requiring a dosage decrease will be prescribed extended-release tolterodine 2 mg daily or controlled-release oxybutynin 5 mg daily. Patients receiving imipramine received 50 mg 3 times daily, and patients

receiving estrogen received estrogen cream 2 gm every other day. For patients receiving “Other Drug Therapy,” we developed a representative cost based on commonly prescribed doses of flavoxate, dicyclomine, and hyoscyamine.

Office Visits

Our model assumes an initial consultation with a PCP when beginning drug treatment. Follow-up visits occur at 6 weeks and 3 months following initiation of drug treatment. We assume that all patients in the “Discontinue OAB Treatment” group have one PCP physician visit at 6 weeks, and that by 3 months, these patients are either referred to a specialist or discontinue treatment altogether. We assume that all patients seeking treatment are established patients rather than new patients, and they are assigned CPT-4 codes of 99213 or 99214 for the office visits, depending upon whether a change in treatment was required. For urologist-referral visits, a CPT-4 code of 99244 was assigned.

Physical/Behavioral Therapy

We assume that all patients enter the model already receiving behavioral therapy and that drug therapy can be used in combination. Additional nonpharmacologic therapies include biofeedback and electrical stimulation.

Procedures/Tests

We assume all patients have had a urinalysis before entering the model and beginning drug treatment. We assume that patients who are referred to urologists will have another urinalysis. We assume that some patients who add or switch therapy will receive another urinalysis during their next office visit and that patients who continue to be managed by their PCP will have no further monitoring or tests. Patients referred to urologists will have additional procedures, as shown in Table 4.

Incontinence Pad Usage

For the proportion of OAB patients with urge incontinence (37%),⁵ we assume they use an average of 4 pads per day at baseline. After treatment, low resource consumers require an average of 2 pads per day, the medium group will use 3 pads per day, and high resource consumers continue to use 4 pads per day.

Comorbid Conditions

We included the cost of treating urinary tract infections (UTIs), skin infections, fractures, and depression as OAB patients are at greater risk for all of these comorbid conditions.^{31,32} The rates of these events were determined from published literature.^{26,31,33} The frequency of treatment for these events vary based on treatment characteristics, such that low resource consumers experience fewer events and require the fewest treatment services, while high resource consumers experience more frequent events and require more treatment services.

Productivity and Work Loss

Employer costs of OAB include sick leave, short-term disability, worker's compensation, pharmacy costs, medical insurance costs, and lost productivity. A study of employer costs showed an annual cost of \$4,020 for OAB patients compared to \$2,633 in the non-OAB population.³⁴ We used the incremental difference in employer costs between the OAB and non-OAB populations to estimate 3-month productivity losses for each resource group. We conservatively assumed that patients in the low resource group experienced no productivity losses over 3 months.

Referral Rates

We estimated, using expert opinion, the referral rates to a specialist and the percentage of patients who would be lost to follow-up at 3 months. The cost of a referral includes an office visit to a specialist as well as the cost of procedures (weighted by the percentage of patients expected to receive each procedure) that are likely to be performed at the first visit. Referral rates are shown in Table 5.

Base-Case Analysis and Sensitivity Analysis

A base-case analysis was run to determine the probable average 3-month treatment cost per patient initiating therapy with either extended-release tolterodine or controlled-release oxybutynin. We performed sensitivity analyses on key parameters of cost, resource utilization, and treatment rate, using a $\pm 10\%$ and 25% range around key variables. The variables included first-line drug costs, non-first-line drug costs, all costs, resource utilization, all treatment rates, and treatment rates at specific nodes. Wider cost ranges using retail pharmacy prices were applied to the highly variable cost of incontinence pads. Tornado diagrams (Figures 2 and 3) were used to show the impact of several key variables. A tornado diagram visually displays the results of single-factor sensitivity analyses. The uncertainty in the parameter associated with the widest bar has the maximum impact on the result, with each successive lower bar having a lesser impact.

Results

Base-Case Analysis

The base-case analysis showed that an average patient initiating therapy with extended-release tolterodine has 3-month treatment costs of \$1,207 compared to \$1,283 for controlled-release oxybutynin, a 6.3% difference. First-line OAB drug costs account for 19% and 15% of total costs for extended-release tolterodine and controlled-release oxybutynin, respectively. Results for the base-case analysis are shown in Table 6.

The rate at which an average patient will continue monotherapy with extended-release tolterodine is higher compared to controlled-release oxybutynin, 58.1% versus 50.6%, respectively. At the same time, the average probable costs for a patient continuing monotherapy was 6.4% lower with extend-

TABLE 3 Model Rates for Variable Resources

Resource	Low	Medium	High
Incontinence pads (per day) ³⁹	2 pads	3 pads	4 pads
Comorbid Conditions			
UTIs (22.5% of population) ³¹	1.9 services	2.6 services	3.3 services
Skin infections (8% of population) ³¹	0.65 services	1.15 services	1.65 services
Depression ³²	0.17	0.385	0.60
Fractures ^{13,33}	0.00208	0.00235	0.00263

TABLE 4 Procedures Performed by a Specialist

Procedure	% of Patients Receiving Procedure
Cystoscopy	69%
Complex cystometrogram/Pressure flow urodynamics	75%
Urine flowmetry	30%
Urethral pressure profile	8%
Cystogram (VCUG)	8%
Urine cytology	53%
Post-void residual	78%
Urinalysis	100%

TABLE 5 Referral Rates

Node	% of Patients Referred
Node D Pathways	26%
Node G Pathways	75%
Node H Pathways	64%
Node I Pathways	61%
Node J Pathways	51%
Node K Pathways	51%

ed-release tolterodine (\$963 to \$1,041). Conversely, a controlled-release oxybutynin patient was 7.2% more likely to switch therapy, although costs were only slightly higher compared with extended-release tolterodine (\$1,491 to \$1,482). The other post-first-line drug therapy options (add therapy, and discontinue OAB therapy) all showed less than a 2% difference in probable cost per patient between the comparators.

Compared to extended-release tolterodine, the controlled-release oxybutynin results show that a larger percentage of the total costs come from not continuing first-line therapy. On average, more than 36% of costs for a patient will come from switch-

TABLE 6 Model Analysis Results

	Extended-release Tolterodine	Controlled-release Oxybutynin	Difference* (%)
Total Probable Cost per Patient	\$1,206.86	\$1,283.20	\$76.34 (6.3%)
Components of Total Probable Cost per Patient—% of costs			
Continue monotherapy	46.4%	41.0%	-5.4%
Add therapy	16.4%	13.3%	-3.1%
Switch therapy	29.5%	36.3%	6.8%
Discontinue OAB therapy	7.7%	9.4%	1.7%
TOTAL	100.0%	100.0%	0.0%
Total Probable Cost per Patient with Each Treatment Option (% = average rate of treatment)			
Continue monotherapy	\$963.37 (58.1%)	\$1,040.51 (50.6%)	\$77.14 (-7.5%)
Add therapy	\$1,667.73 (11.9%)	\$1,649.34 (10.4%)	-\$18.39 (-1.5%)
Switch therapy	\$1,481.94 (24.0%)	\$1,491.49 (31.2%)	\$9.55 (7.2%)
Discontinue OAB therapy	\$1,545.37 (6.0%)	\$1,538.61 (7.8%)	-\$6.76 (1.8%)

* Controlled-release oxybutynin minus extended-release tolterodine.

ing therapy, and more than 9% of costs come from discontinuing OAB therapy. In contrast, less than 30% of extended-release tolterodine costs come from switching therapy, and less than 8% of costs come from discontinuing OAB therapy.

Sensitivity Analyses

Results from sensitivity analyses are shown in Table 7. These results are graphically depicted as tornado diagrams in Figures 2 and 3.

Costs

Sensitivity analyses on costs were relatively stable. No cost parameter change resulted in an overall cost advantage for controlled-release oxybutynin. The magnitude of extended-release tolterodine's cost advantage was most affected by changes in all other costs, i.e., costs other than first-line drug costs (where a 25% increase/decrease in costs resulted in a 34% increase/decrease in the cost advantage). Changes in either drug costs or all costs had less impact on the magnitude of extended-release tolterodine's cost advantage.

Break-even costs for the OAB first-line drugs were also calculated. The cost of extended-release tolterodine can be increased up to 34% above the base case before equaling controlled-release oxybutynin. Conversely, the cost of controlled-release oxybutynin would have to be reduced by 39% before achieving cost parity.

Resource Utilization

A sensitivity analysis was also performed on the key assumption that variations in resource utilization depend on the effective-

ness of the drug therapy. If no difference in resource utilization is assumed, and patients are assigned low, medium, or high resource utilization, then any cost differential between the 2 therapies disappears, with controlled-release oxybutynin having a slight (less than 1%) cost advantage over extended-release tolterodine. Overall cost differences between the 2 treatments are, therefore, highly dependent on the assumption that resource consumption is related to the patterns of treatment.

Treatment Rates

Sensitivity analysis on treatment rates shows they are key parameters driving the results of the model. Several scenarios were examined, including (1) reversing the treatment rates for extended-release tolterodine and controlled-release oxybutynin, (2) assigning both treatment groups the extended-release tolterodine treatment rates, (3) assigning both groups the controlled-release oxybutynin treatment rates, and (4) varying the rates at key nodes. The first scenario, which reversed the treatment rates for the 2 products, showed that costs for patients receiving controlled-release oxybutynin would be 10% less than for patients receiving extended-release tolterodine, as one would expect. The second scenario, where treatment rates are equal, resulted in similar costs between the 2 products, with controlled-release oxybutynin being approximately 1% less costly.

Varying the probabilities at nodes A and D also demonstrated some sensitivity. At node A, if the rate of continuing extended-release tolterodine was decreased by about 20 percentage points, or if the rate of continuing controlled-release oxybutynin was increased 20 percentage points, the overall costs would be equal. It was also found that if the rates of dose increases were equal

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TABLE 7 Sensitivity Analysis Results (Bold Indicates Base-Case Costs)

Parameter	Change	Extended-release Tolterodine	Controlled-release Oxybutynin
Base-Case Analysis	0.00	\$1,206.86	\$1,283.20
First-line Drug Costs			
	-25%	\$1,150.08	\$1,233.89
	-10%	\$1,184.15	\$1,263.24
	+10%	\$1,229.56	\$1,302.93
	+25%	\$1,263.63	\$1,332.51
All Costs Except First-line Drug Costs			
	-25%	\$961.91	\$1,012.00
	-10%	\$1,108.88	\$1,174.72
	+10%	\$1,304.83	\$1,391.69
	+25%	\$1,451.80	\$1,554.41
All Costs			
	-25%	\$905.14	\$962.69
	-10%	\$1,086.17	\$1,155.00
	+10%	\$1,327.54	\$1,411.41
	+25%	\$1,508.57	\$1,603.72
Resource Utilization			
	All high utilization	\$1,960.27	\$1,953.19
	All medium utilization	\$1,442.67	\$1,435.58
	All low utilization	\$925.09	\$918.00
Treatment Rates			
	Reverse treatment rates	\$1,306.65	\$1,190.81
	Use all extended-release tolterodine rates	\$1,206.86	\$1,190.81
	Use all controlled-release oxybutynin rates	\$1,306.65	\$1,283.20
Node A Treatment Rates			
	0.5	\$1,289.07	\$1,322.46
	0.6	\$1,247.96	\$1,286.77
	0.61	\$1,243.85	\$1,283.20
	0.7	\$1,206.86	\$1,251.08
	0.8	\$1,165.75	\$1,215.39
	0.9	\$1,124.64	\$1,179.70
Node D Treatment Rates*			
(Increase Dose/Same Dose)	0.05/0.90	\$1,172.08	\$1,205.07
	0.14/0.81	\$1,206.86	\$1,230.22
	0.15/0.80	\$1,210.72	\$1,233.02
	0.25/0.70	\$1,249.36	\$1,260.96
	0.32/0.63	\$1,279.53	\$1,283.20
	0.35/0.60	\$1,288.00	\$1,288.91
	0.45/0.50	\$1,326.64	\$1,316.85

* Changes made only to increase dose/same dose arms, holding decrease dose arm constant.

(node D), the 2 drugs would be nearly cost-equivalent.

Discussion

The model results suggest that extended-release tolterodine yields a small cost advantage over controlled-release oxybutynin when used as a first-line therapy in the PCP setting. Extended-release tolterodine patients would be expected to incur fewer costs related to resources such as physician visits and referrals, comorbidities, and productivity loss. Although most patients

continued monotherapy, more patients taking extended-release tolterodine continued without dosage changes, and more patients on controlled-release oxybutynin incurred dose increases. Thus, in this model, fewer resources were consumed by extended-release tolterodine patients.

While sensitivity analysis showed that the results are stable for a range of costs, both drug and nondrug, the model did show some degree of sensitivity to assumptions related to resource utilization and treatment rates. We assumed that

FIGURE 2 Tornado Diagram for Extended-release Tolterodine

resource consumption varied depending on treatment effectiveness. If we assume resource utilization is unrelated, overall treatment costs are virtually identical between the 2 treatments. Key treatment rates were those showing that extended-release tolterodine patients would continue on first-line monotherapy without dosage changes at a higher rate than controlled-release oxybutynin patients. If these rates are made equal or reversed, the cost advantage for extended-release tolterodine disappears. However, discussions with clinical experts, along with existing retrospective studies,^{10,35} suggest higher continuation rates, and greater persistence can be expected for extended-release tolterodine as compared to controlled-release oxybutynin.

The model does not address a few important issues. Information regarding resources consumed by patients who do not seek treatment for OAB is lacking; therefore, these patients were excluded. We did not include other possible treatments for OAB or the effectiveness of nonpharmacologic treatments, whether alone or in combination with drug therapy, as these are not well-documented. The quality-of-life (QOL) impact of OAB has been studied, but insufficient information is available regarding patient utilities to incorporate quality of life into the model. The long-term impact of drug treatment is unknown, and was not considered in the model.

Drug compliance is an important issue for OAB treatment; however, in our model, compliance was not addressed directly. Since the model was conducted from a payer perspective, different compliance rates do not impact the cost calculations in the model as the amount of drug purchased would be the same regardless of compliance. Noncompliance leading to changes in therapy or discontinuation of treatment was considered in developing treatment rate estimates. The possible effect of differing compliance rates on efficacy among the comparators is not known.

While clinical trials of drugs for OAB have most often focused on reducing the number of incontinence episodes as the primary efficacy endpoint, other variables are also relevant, such as reduced micturitions, smaller urine volume, reduced urgency, minimal side effects, ability to tolerate and remain on medication, and nighttime incontinence and urgency, to name a few. Quality of life, social issues, coping skills, nonpharmacologic interventions, and the patient's motivation to comply with those interventions all play a role in an OAB patient's treatment. This complexity makes it difficult to comprehensively model the disease and its treatment while taking these aspects into consideration.

Many variables contribute to whether or not a particular treatment is effective. The symptoms of OAB—which include not only urge incontinence but also urgency and/or frequency—have a significant, negative impact on patient QOL, and the goal of treatment is to reduce symptoms and improve QOL. Also, a patient must remain on therapy for it to have the chance to be effective. Therefore, products that are better tolerated are more likely to produce a positive outcome. A therapy that reduces symptoms, improves QOL, and is well-tolerated should reduce the need for other medical resources that are used to treat the disease.

Conclusion

The results from this analysis suggest that for patients with OAB who are initiating long-acting pharmacologic therapy in the primary care setting, treatment with extended-release tolterodine is slightly less costly than treatment with controlled-release oxybutynin. With recent studies showing better persistency and tolerability for extended-release tolterodine compared to controlled-release oxybutynin, further clinical and economic studies need to incorporate the complex interaction of effectiveness,

FIGURE 3 Tornado Diagram for Controlled-release Oxybutynin

tolerability, persistence, and QOL changes and the resulting cost offsets. These efforts will add to the base knowledge gained from our analysis and help decision makers further distinguish between the 2 drugs.

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