Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Weight loss	Auwad, 2008[175]	Effects of moderate weight loss in obese women with urodynamic stress UI	64	100	100	Weight reduction program low calorie diet + exercise with a target loss of 5-10%	2 years	Obese women with urodynamic stress UI, 52.5 years old	Weight loss was associated with a significant reduction in pad test loss and significant improvement in quality of life.
Weight loss	Wing, 2010[176]	To examine the relationship between magnitude of weight loss and changes in urinary incontinence frequency.	338	100	100	Patients were randomly assigned to a 6 month weight loss program followed immediately by a 12-month weight maintenance program or to a structured education program. These groups were combined to examine the effects of the magnitude of weight loss on changes in urinary incontinence	18 months	Program to Reduce Incontinence by Diet and Exercise (PRIDE) trial: Women aged 30 years or older, having a body mass index (BMI) of 25–50, and reporting at least 10 urinary incontinent episodes (including both stress and urgency incontinent episodes) on a 7-day voiding diary at baseline.	The adjusted odds of at least 70% reduction in number of incontinent episodes per week in those who had more than 10% weight loss: At 6 months: Total UI: OR=3.8 (95% CI=1.5-9.6); Stress UI: OR=1.6 (95% CI=0.6-3.9); and Urge UI: OR=4.5 (95% CI=1.4-14.1). At 18 months: Total UI: OR=3.3 (95% CI=1.7-6.4); Stress UI:OR=2.3 (95% CI=1.0-5.1); and Urge UI: OR=4.0 (95% CI=2.1-7.9)

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Pelvic floor muscle training	Hines, 2007[177]	To assess factors predictive of high adherence to a behavioral intervention to prevent UI	359, but data used for the treatment arm only (n=164)	100	100	Pelvic floor muscle training and bladder training	1 year	359 community-dwelling, post-menopausal women, aged 55 to 80 years old	Women incorporated PFMT into their lives using either a routine or ad hoc approach (Routine approach = Doing PME at set times of the day or linking with a daily routine that occurs at a set time; ad hoc approach = Doing PME when they think of it or by linking with a sporadic cue or situation). Those using a routine approach at 3 months were 12 times more likely to adhere (odds ratio=12.4, CI=4.0-38.8,p<0.001) at a high level at 3 months and significantly more likely to maintain that level 12 months post-intervention (OR=2.7,CI=1.2-6.0,p<0.014). High adherence to PFMT was operationally defined as an adherence score of 5 to 7 (reporting adherence of >=1 1 set of PFMT each day).

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Pelvic floor muscle training	Sugaya, 2003[178]	Effects of the device to promote adherence to pelvic floor muscle exercise in women with stress UI	46	100	100	Device with a chime to sound three times a day when exercise sessions were scheduled and set a rhythm for the muscle contractions vs. pelvic floor muscle exercise alone	8 weeks	Women with stress UI	Quality of life category was delighted, pleased, or mostly satisfied in 15% patients from the control group and 48% from the device groups
Pelvic floor muscle training	Brubaker, 2008[179]	Effectiveness of nonmedical pelvic floor muscle training class on UI	102	100	99	Pelvic fitness and education class taught by a lay instructor	11 weeks, 1 year of followup	Adult women with urgency or urgency UI 57.9 year, 11% after surgery for UI or prolapse	The training improved quality of life and sexual function improvements in after vs. before UDI-SF scores. Achievement of self selected goal-71% at 11 weeks, 67% at 1 year
Pelvic floor muscle training	Wang, 2000[180]	Efficacy of bladder-sphincter-biofeedback in women with detrusor instability who failed to respond to oxybutynin treatment	31	100	100	Bladder sphincter biofeedback vs. pelvic floor muscle training	5 months	Women with urgency syndrome 44,.3 years who failed previous oxybutynin treatment	Continence 12.5% in biofeedback and 13.33% in exercise group. Improvement 87.5% in biofeedback and 86.67% in exercise group. 140 significant differences were found.
Pelvic floor muscle training	Wang, 2000[180]	Efficacy of bladder-sphincter-biofeedback as a secondary treatment for those women with detrusor instability who failed to respond to oxybutynin chloride	31	100	100	Bladder-sphincter-biofeedback training group or control pelvic floor exercise group	Not reported	Women with detrusor instability who failed to respond to oxybutynin chloride	The cure rate or improvement rate of subjective changes (urgency, and frequency and episodes of urgency incontinence) did not significantly differ between treatments.

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Medical device	Bellin, 1998[181]	Efficacy of CapSure (Re/Stor) continence shield for stress UI in females	100	100	100	CapSure (Re/Stor) continence shield : no control	12 weeks	Women 40-69 years old (mean 54) with pure stress moderate UI and no urgency or urge UI	Continence - 82%, negative pad stress test - 91%; no UI episodes in diary - 48%, Bothersome vaginal or urethral irritation - 12%, positive urine culture - 1.56
Medical device	Crivellaro, 2010[182]	To examine effects of the Adjustable Continence Therapy on female UI	60	100	100	Adjustable Continence Therapy implantation that involves two silicone balloons sited on either side of the proximal urethra under the bladder neck, each attached to a titanium port buried in the labia allowing post operative titration of the balloons.	Once	Adult women with stress urinary incontinence resulting from intrinsic sphincteric deficiency	82% were significantly improved, 8% were moderately improved and 10% remained unchanged. Post-operative complications necessitating device removal included migration seen in 8% of patients and urethral erosion in 3.5% of patients
Medical device	Morris, 2003[183]	Efficacy of contiform incontinence device in women with stress UI and no prolapse	59	100	100	Contiform incontinence device no control	3 weeks	Women, 42-53 years old, with urodynamic mild to severe stress UI and no prolapse	Continence - 20%, withdrawal - 31%, acute bacterial cystitis - 5%, small degree of fracture of the curvature of device - 22%
Medical device	Allen, 2008[184]	Efficacy of contiform intravaginal device for stress UI	73	100		Contiform intravaginal device, no control	4 weeks	Women 41-54 years old with predominant stress UI and no prolapse	Continence - 54%, withdrawal, 29%, residual volume >100 ml - 5.4%

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Medical device	Sander, 2008[185]	The effect of a vaginal device (Continence Guard) on urine leakage and quality of life in women with stress UI	55	100	100	Continence Guard	12 weeks	Women with stress incontinence	Completion -74.5%; subjective cure 20% and improvement in 49%. Score of the Incontinence Impact Questionnaire showed highly significant improvement
Medical device	Hahn, 1996[185]	Effectiveness of vaginal device for the treatment of female stress UI	90			Conveen Continence Guard	4 weeks	90 women with stress incontinence (mean age 47.5 years, range 31-65).	Continence - 46% Improvement - 29% ; objective improvement - 75%; Failure- 25% 72% of the women considered the product to function satisfactorily and 60% expressed a wish to continue with the treatment; local discomfort - 62%
Medical device	Nilsson, 2000[186]	Efficacy of the conveen continence guard (a disposable vaginal device) in the treatment of complicated female stress incontinence	28			Decreases from baseline in RR, QRS and QT intervals for patients receiving duloxetine Conveen continence guard (a disposable vaginal device)	3 weeks	Women, with a urodynamically proven stress UI	Completion rate 68%; continence or improved incontinence 58%; objective improvement 55%
Medical device	Pieper, 1993[187]	The efficacy of external urine-collection device for women with UI	7			External urine-collection device	5 days	Black women with UI, 21-35 years old	1 woman had vulvar irritation and redness; all were satisfied with the device

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Medical device	Versi, 1998[188]	Efficacy of external urethral device in women with genuine stress urinary incontinence	14			FemAssist- non-invasive supple silicone domed cap that fits over the external urethral meatus	3-4 weeks	Women with symptoms of urinary incontinence and a videourodynamic diagnosis of genuine stress incontinence; mean age was 55 years	>50% improvement on their IIQ - 50% ; improvement in UDI - 21.4% UDI.
Medical device	Versi, 1998[189]	Efficacy of external urethral device in women with genuine stress UI	131			FemAssist- non-invasive supple silicone domed cap that fits over the external urethral meatus	4 weeks	Ambulatory women with symptoms of UI	Withdrawal -27%; >50% improvement on the Incontinence Impact Questionnaire 59%; in the Urogenital Distress Inventory- 33%
Medical device	Sirls, 2002[190]	Efficacy of FemSoft urethral insert for female stress urinary incontinence	150			FemSoft urethral insert no control	48-96 weeks	Women with mean age of 53.5 years, stable stress urinary incontinence, mixed UI with predominant stress UI	Continence -93% at 48 months, withdrawal rate - 41%. Adverse effects: urinary tract infection - 31.3%, mild trauma - 6.7%, hematuria - 3.3%. Significant improvement in quality of life.
Medical device	Macaulay, 2007[191]	The effects of Non-Invasive Continence Management System (NICMS) on women with UI	80			Non-Invasive Continence Management System (NICMS)	15 months	Women over 18 years of age with UI	Overall satisfaction 34%; among wheel chair users 21%

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Medical device	Donnelly, 2004[192]	Predictors of successful fit and continuous use of pessaries	239			Pessaries	2 weeks, 48 weeks	Women with stress or mixed UI, 57.4 years old	Successful fit- 89.1%, Discontinuation-45%; Reason for discontinuation %: Persistent UI-58%; Discomfort using pessary-33%; Frequent pessary expulsion-18%; Women with pulmonary disease and those who used diuretics were more likely to use pessaries.
Medical device	Brincat, 2004[193]	Predictors of discontinuation of pessaries use	136			Pessaries: dishes with and without floor, rings with and without floor, pessary rings with floor	96 weeks	Women with UI	Reason for pessary discontinuation and % sexually active women and women with prolapse used pessaries during study period more often
Medical device	Maito, 2006[194]	Predictors of continuous use of pessaries	120			Pessary	24 weeks	Women with UI and/or pelvic floor organ prolapse, 61 years of age	Successful fit - 86% Discontinuation - 11% Predictors of unsuccessful fit - history of prolapse, procedure or hysterectomy. Predictors of discontinuation- severe posterior prolapse; Improved stress UI- 94%
Medical device	Sulak, 1993[195]	Effectiveness of pessaries in women with pelvic relaxation.	107			Pessary Gelhorn	3 years	Women with symptomatic pelvic relaxation, 65.5 years	Discontinuation 46%

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Medical device	Clemons, 2004[196]	Patient satisfaction and UI after pessary use	100			Pessary ring with floor, Gellhorn (Milex)		Women with systematic pelvic organ prolapse. Stage II or greater; 71 years old	Successful fit-73% Improved stress UI-45% Improved urge UI - 21%. De novo urge UI - 6% Dissatisfaction 18% was associated with stress UI (OR 17.1; 95% CI, 1.9, 206)
Medical device	Farrell, 2007[197]	Effectiveness of a new self-positioning women's pessary	32			Pessary Uresta/ EastMed Inc	48 weeks	Women with 41- 50 years old	Satisfaction with pessary - 66% Discontinuation - 34% Continence -47% (among stress UI), 36% (among urge UI) Improved UI- 53% No significant predictions for successful fitting were found
Medical device	Nguyen, 2005[198]	Predictors of successful pessary fitting and continence pessary use	130			Pessary: Milex products, PelX/Des Chutes medical products	4 years	Women with pelvic relaxation 66-69 years old	Successful fit- 74% Reasons for unsuccessful fit % Prolapse repair 29% Cystocele repair 21% Stress UI 69% Discontinuation among successfully fitted 50 %
Medical device	Staskin, 1996[199]	Efficacy of urethral insert for female stress or mixed UI	135			Reliance urinary control insert no control	12 weeks	Women with mean age of 52.6 years of age with pure stress or mixed UI	Continence - 80%, improvement with >80& decrease in urine loss - 95%, adverse events - 13%, bacteriuria - 8%, withdrawal, - 37%

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Medical device	Kocjancic, 2008[200]	Effectiveness of adjustable device for the treatment of recurrent stress UI	49			The Adjustable Continence Therapy (ACT®)	1 year	Women with stress UI who previously failed anti-incontinence surgery	Continence -53%; improvement in UI - 16%; failure- 12%; migrations -12% and urethral or portal erosions -4%
Medical device	Brubaker, 1999[201]	The efficacy and safety of an external urethral barrier for mild/moderate stress UI in adult women.	411			Urethral barrier device	12 weeks	Women with mild to moderate stress UI or mixed UI	Withdrawal – 16% comfortable use - 90% Positive urine culture - 4.1% Trace of blood in urine - 21% Bacterial vaginosis - 16%
Medical device	Moore, 1999[202]	The efficacy and user acceptability of the urethral occlusive device (FemAssist*) for incontinence	97			Urethral occlusive device (FemAssist*)	1 month	Women with UI 65 years of age with UI, 37% with severe UI	Discontinuation rate 41%; Continence 47%; >50% reduction in UI- 33% . Response did not differ by baseline severity of UI or type of UI (stress, urge or mixed incontinence)
Medical device	Sand, 1999[203]	Efficacy of reliance urinary control insert in women with stress UI	63			Uromed Corp, Needham, MA - reliance urinary control insert-no control	48 weeks	Women with mean age of 55 years old, predominant stress UI	Continence - 79%, urinary tract infection - 29%, gross hematuria - 22%, improved physical functioning and quality of life
Medical device	Aboseif, 2009[204]	Efficacy of adjustable continence device in women with recurrent stress UI	162			Uromedica, Plymouth, Minnesota - adjustable continence device. No control	48 weeks	Women 67.4 years old with recurrent stress UI after 6 months of prior conservative or surgical therapy	Continence - 52%, improvement >50% reduction on stress pad test - 80%, complications - 24.4%, most common adverse effect port erosion - 7.5%

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Stimulation	Indrekvam, 2001[205]	Effectiveness of home managed electrical stimulation in women with stress or mixed UI	3,198			Home managed 2 main types of vaginal/anal electro stimulators, Vitacon Norway AS and Conmax Sports Enterprises	2 years	Women with urge stress, or mixed UI	Discontinuation of treatment - 12% Continence, doctor assessment - 7%, continence patient self report - 4%. Compliers, doctor assessment - 14%, patient self report - 8%. Continence or much better, doctor assessment - 43%, patient self report - 31%. OR of treatment effect assessed by women : Increasing frequency of leakage - 0.82 (0.69;0.96), increasing amount of leakage - 0.77 (0.62;0.95), increasing discomfort with treatment - 0.77 (0.7;0.84)
Stimulation	Galloway, 2000[206]	Effects of extracorporeal magnetic innervation for stress 111 in women	111			Extracorporeal magnetic innervation (ExMI) therapy using Neocontrol chair, 20 minutes, 2 times/ week; 5-50h2	6 weeks, 6 month of followup	Women with stress UI, 55 years old	Countenance - 28% No pad or <1 pad per day- 53% Reduced pad use- 70% In women with recurrent after therapy stress UI or hysterectomy countenance rate was 18% and + improvement - 40%

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Stimulation	Bergstrom, 2000[207]	Efficacy of manual acupuncture could influence urge- or mixed-type incontinence among elderly women who failed previous treatments	15			Manual acupuncture	12 times, 3 months of followup	Elderly women with stress or mixed UI who failed previous treatments	Improvement rate 80%
Stimulation	Nuhoglu, 2006[208]	Efficacy of Stoller afferent nerve stimulation (SANS) in women with overactive bladder who failed anticholinergic treatment	35			Stoller afferent nerve stimulation (SANS)	10 weeks	With overactive bladder who failed therapy with oxybutynin	54% (n=19) women were continent at the end of the treatment but only 23% at followup
Stimulation	van Kerrebroeck, 2004[209]	Efficacy of copolymer system on female UI	42			Nonanimal stabilized hyaluronic acid/dextranomer copolymer injected transurethrally into the urethra via the Implacer TM device	1 year	Women not previously treated by invasive therapy and with urodynamically verified SUI	Satisfaction rate at 3 months -71%, at 9 months- 60%; failure 43%
Stimulation	van Kerrebroeck, 2004[210]	Effects of the novel system (NASHA/Dx copolymer insertion using the Implacer) on female UI	42			Nonanimal stabilized hyaluronic acid/dextranomer (NASHA/Dx) copolymer for transurethral injection	12 months	Therapy-naive female patients with stress UI	Improvement - 76%; improvement by at least one category on the 6-point patient perception scale - 69%; Treatment-related AEs-36%.

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Stimulation	Chapple, 2005[211]	Efficacy of non-endoscopic injection of nonanimal stabilized hyaluronic acid/dexranomer (NASHA/Dx) gel and Implacer device on female stress UI	142			Zuidex TM system for injection of bulking agent NASHA/Dx gel and Implacer TM device	8 weeks, 12 months	Women with stress UI for >12 months 55.7 years old, who failed prior nonsurgical treatments and were not treated with invasive methods.	Reduction in provocation test leakage 750% vs. baseline - 77% at 1 year Continuance- 62% at 1 year Improvement of quality of life - 67% Adverse effects: Urinary retention - 29/142 Urinary tract infection - 17/142 Micturition urgency - 17/142 Injection sit reaction- 11/142 Vaginal discomfort- 10/142 Injection in injection site- 3 serious/142

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Evidence-based self-management tool	Tannenbaum, 2010[212]	To develop and evaluate an evidence -based self-management urinary incontinence risk factor modification tool designed specifically for older women.	103	100	100	Self-management tool developed using evidence from a systematic review on risk factor modification for incontinence and input from focus groups of health care experts and incontinent women. Six risk factors were incorporated into a self-management tool with associated strategies for change and self-monitoring: 1) weak pelvic floor muscles, high caffeine intake (>400mg/day), high body mass index, vision and hearing impairment, smoking and constipation	3 months without intervention and 3 months with intervention	English and French speaking incontinent women 50 years of age and older who reported experiencing urinary incontinence at least twice a week for a period lasting at least 3 months during the prior 2 years were recruited via community-advertising. MMSE scores >24/30	Self-Efficacy Index (max score 150): Coefficient (mean change)=8.7 with 95% highest posterior density interval (CI)=3.6-13.7. UDI-6 (max score 100): Coefficient (mean change)=-7.3 with 95% highest posterior density interval (CI) =-12.3- -2.1. IIQ-7 (max score 100):Coefficient (mean change) =-0.5 with 95% highest posterior density interval (CI) =-5.4-4.9
Adjustable continence therapy	Crivellaro, 2010[182]	The Adjustable Continence Therapy is a minimally invasive treatment for females with Stress Urinary incontinence resulting from Intrinsic Sphincteric Deficiency (ISD). This study represents the term results of the first series of patients	60	100	100	Adjustable Continence Therapy implantation that involves two silicone balloons sited on either side of the proximal urethra under the bladder neck, each attached to a titanium port buried in the labia allowing post operative titration of the balloons	Once	Women with stress UI	82% were significantly improved, 8% were moderately improved and 10% remained unchanged. Post-operative complications necessitating device removal included migration seen in 8% of patients and urethral erosion in 3.5% of patients

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Percutaneous tibial nerve stimulation	Vandoninck, 2003[213]	To determine the safety and efficacy of percutaneous peripheral afferent nerve stimulation for treatment of refractive overactive bladder and/or pelvic floor dysfunction.	53	90.20	Not reported	Percutaneous Tibial Nerve Stimulation: 12 sessions	12 weeks	Patients older than 18 years with documented urgency, frequency, and/or pelvic floor dysfunction resulting in a mean frequency of at least 10 voids/day and/or 3 voids/night. In all these patients, all traditional therapy had failed.	Dependent on baseline conditions, treatment with the percutaneous device in the acute treatment phase (12 weeks) resulted in at least a 25% reduction or improvement in daytime frequency for 55.2% of patients having 10 or greater voids per day ($p<0.05$), an average 25% reduction or improvement in mean daytime voiding frequency ($p<0.05$), an average 22% reduction or improvement in mean 24-hour voiding frequency ($p<0.05$) and an average 70% reduction, that is "mean daytime frequency defined as the mean number of voids greater than 10 per patient per day" ($p<0.05$). Overall, treatment with the device resulted in an average 21% reduction or improvement in mean nighttime voiding frequency ($p<0.05$). Overall, patients had a 35% reduction or improvement in daytime and night time urgency incontinence or leak episodes during the 12-week treatment ($p<0.05$). 71% patients were

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Percutaneous tibial nerve stimulation	Vandoninck, 2003[214]	To evaluate urodynamic changes after percutaneous tibial nerve stimulation (PTNS) for the treatment of complaints related to overactive bladder syndrome and to search for urodynamic-based predictive factors	90	74.44	75	Percutaneous Tibial Nerve Stimulation: 12 sessions	Not reported	Patients with overactive bladder syndrome (defined as urgency, frequency, and/or urgency incontinence) were enrolled. For urgency and urgency incontinence, International Continence Society definitions were used. Urinary frequency was defined as eight voids or more per 24 hours.	The objective success rate was 56% (leakages/24 hours). Subjective success rate was 64%. Subjects without detrusor instabilities at baseline were 1.7 times more prone to respond to PTNS (odds ratio, 1.75; 95% confidence interval [CI], 0.67-4.6). The more the bladder overactivity was pronounced, the less these patients were found to respond to PTNS, the area under the receiver operating curve was 0.644 (95% CI, 0.48-0.804).

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Percutaneous tibial nerve stimulation	Govier, 2001[215]	To evaluate the effect of posterior tibial nerve stimulation for the treatment of urgency incontinence	35	71.43	100	Percutaneous Tibial Nerve Stimulation: 12 sessions	Not reported	Patients with symptoms of urgency incontinence	A total of 24 patients (69%) showed a reduction in incontinence episodes (primary outcome measure) of more than 50%; of these 24 patients, 16 had no leakage episodes. 22 patients (63%) reported a subjective success. Severity of incontinence and number of pads used, decreased more than 50% in 19 (54%) and 20 patients (57%), respectively.

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Percutaneous tibial nerve stimulation	Woolridge, 2009[216]	To evaluate the application of percutaneous tibial nerve stimulation, a minimally invasive neuromodulation therapy	53	98.11	79.25	Percutaneous Tibial Nerve Stimulation: 12 sessions of 30 minutes duration each	12 weeks	Patients with chronic OAB symptoms referred to a community-based, nurse practitioner-led continence practice; older than 18 years with documented urgency, frequency, and/or pelvic floor dysfunction resulting in a mean frequency of at least 10 voids/day and/or 3 voids/night.	Patients experienced a statistically significant average decrease in daytime voids of 27.9% from baseline (p <0.0001). Patients experienced an average 63.5% decrease in nighttime voids from baseline (p <0.0001). Thirty-seven of the 42 patients reporting incontinence at baseline (88%) improved with 59.5% (25 of 42) patients cured (such as reporting no incontinence episodes during the period of review for the study).

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
Percutaneous tibial nerve stimulation	Vandoninck, 2004[217]	To determine urodynamic changes and predictive factors in patients with voiding dysfunction who underwent 12 percutaneous tibial nerve stimulations	39	69.23	Not reported	Percutaneous Tibial Nerve Stimulation: 12 sessions of 30 minutes duration each	12 weeks	Patients with idiopathic non-obstructive voiding dysfunction; symptoms existed for a minimum of 6 months	In 13 out of 23 patients, more than 50% decrement in 24 hour total catheterized volume was obtained. Another eight subjects noticed a reduction of their 24 hour residual volume with more than 25%. Side effects: diarrhea, headaches, calf cramps, and low back pain were reported; one patient did not complete the treatment because of aggravating pre-existing heart rhythm problems. However, these adverse effects were considered not to be related to PTNS.

Appendix Table F26. Clinical outcomes after nonpharmacological treatments in nonrandomized studies (continued)

Intervention	Reference	Aim	Number	% Women	% with UI	Treatment	Duration	Population	Results
PFMT and electrical stimulation	Surwit, 2009[218]	The hypothesis of the study is that adding percutaneous tibial nerve neuromodulation with pelvic floor muscle rehabilitation is safe, and more successful than either therapy alone for the treatment of urgency incontinence	256	100	100	Eight traditional PFMR (Pelvic Floor Muscle Rehabilitation) twice a week with biofeedback, PFMT exercises, and electrical stimulation at 100 Hz, and then an additional 8 weekly electrical stimulations at 10 Hz, utilizing the Hollister Evadri bladder control system equipment.	8 weeks	Patients with both urgency incontinence and mixed (urgency and stress incontinence) were eligible for this prospective clinical trial	935 achieved a totally dry status and an OAB-V8 score of less than 8, three months after the completion of their treatment (The criteria for successful treatment was an absence of incontinent episodes (dry) and an OAB-V8 score less than 8, indicating no OAB). The remaining 7% patients had a median improvement in UI episodes of 84%. No patient improved less than 70%, and all felt that the treatment had significantly improved their quality of life. The urge continence patients had a 94% dry rate at three months, while the mixed incontinence patients had a 91% dry rate. There were no adverse side events.

Appendix Table F27. Pharmacological treatments for female UI

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Abrams, 1998[219] RCT Multinational N: 293	Men and women aged ≥18 years having urodynamically confirmed bladder overactivity, an increased frequency of micturition (≥8 micturitions/24h) and urgency incontinence (≥1 incontinent episode/24h) and /or urgency during a 2-week washout/run-in period	Clinically significant stress incontinence; detrusor hyper-reflexia; hepatic, renal or hematological disorders; symptomatic or recurrent urinary tract infection; bladder outlet obstruction; those receiving bladder training, electro stimulation therapy; those with an indwelling catheter or who were on intermittent catheterization; pregnant or nursing women; or women of childbearing age who were not using reliable contraception	tolterodine	oxybutynin	Pharmacia and Upjohn AB, Uppsala. Sweden	Not reported
Abrams, 2006[220] RCT UK N: 77	Men and women (aged >18 years) with a clinical diagnosis of idiopathic OAB with detrusor overactivity and two or more of the following OAB symptoms during the 2-week run-in period were enrolled: urinary frequency (7 or more micturitions/day), urgency incontinence (one or more episodes necessitating a change of clothing or pad), or urinary urgency (7 or more episodes preceding micturition/week)	Clinically significant hepatic, renal, or cardiac abnormalities; stress incontinence; evidence of untreated narrow angle glaucoma; urinary and gastric retention; bladder outlet obstruction >40 (Abrams-Griffiths number); indwelling catheter; recent urogenital surgery; and use of investigational drugs in the 30 days preceding the study	Propiverine 20 mg once daily or propiverine 15 mg three times daily or oxybutynin 5 mg three times daily	Placebo	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Abrams, 2008[47] Pooled N: 1,059	Pooled analysis of three RCTs: Women and men, age >18 years with reported symptoms of OAB for >6 months, 5–50 episodes of UI per week during the treatment-free or placebo run-in periods, together with an increased frequency of micturition (a mean of at least 8 voids per day) and urgency (a mean of at least one episode per day)	The presence of clinically significant stress UI (i.e., >1 episode of stress UI per week), BOO and/or a postvoid residual urine volume of >200 mL (as measured by pelvic ultrasound); contraindications to antimuscarinic therapy (e.g., uncontrolled narrow-angle glaucoma, urinary retention, gastric retention).	Darifenacin 7.5 mg and 15 mg once daily	Placebo	ACUMED® provided editorial and project management services for this manuscript. Funding for this was provided by Novartis Pharma AG.	Paul Abrams is a consultant to Novartis Pharma AG and Jasper Huels, Erhard Quebe- Fehling, Mohamed A. Omar and Michael Steel are all employees of Novartis Pharma AG.
Altan-Yaycioglu, 2005[221] RCT Turkey N: 52	Women with urodynamic diagnosis of overactive bladder	History of ocular disease or surgery; dry eyes, ocular surface disorders, glaucoma, or issues that could affect visual acuity or accommodation (such as cataract, macular degeneration, or history of ocular surgery)	2 mg tolterodine bid	5 mg oxybutynin tid	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Appell, 1997[222] Pooled N: 1,120	Pooled analysis of 4 RCTS: men and women with detrusor overactivity (phasic detrusor contraction with an amplitude ≥10 cm H2O); and urinary frequency (an average of 28 micturitions/24 hours) and urgency incontinence (an average of ≥1 incontinence episode/24 hours) or urinary frequency.	Clinically significant stress incontinence; hepatic or renal disease; recurrent urinary tract infections (UTIs); interstitial cystitis; uninvestigated hematuria or hematuria secondary to malignant disease; indwelling catheter or intermittent catheterization; treatment with any investigational drug in the 2 months prior to entry; previous treatment with tolterodine; electro stimulation therapy or bladder training within 14 days prior to entry or initiation during the study; treatment with any anti-cholinergic drug or any drug for urinary incontinence within 14 days prior to the baseline visit or initiation during the study; unstable dosage of any treatment with anticholinergic side effects of initiation of such treatment during the study; previously demonstrated serious side effects on oxybutynin; an average total voided volume >3,000ml/24 hours; and clinically significant voiding difficulty with risk of urinary retention.	Tolterodine 2 mg twice daily; tolterodine 1 mg twice daily; oxybutynin (5 mg three times daily)	Placebo	Not reported	Not reported
Appell, 2001[223] The OBJECT (Overactive Bladder: Judging Effective Control and Treatment) U.S. N: 378	Participants with overactive bladder who had between 7 and 50 episodes of urgency incontinence per week and 10 or more voids per 24 hours were included. Those with mixed stress and urgency incontinence were eligible if the majority of the leakage accidents were related to urgency	Urinary tract infection, interstitial cystitis, urinary tract obstruction, urethral diverticulum, bladder tumor, bladder stone were excluded, as were those who had delivered a baby or undergone pelvic, vaginal, or bladder surgery less than 6 months before study enrollment; participants with a post-void residual urine volume of more than 150ml at the time of screening; those at considerable risk of developing complete urinary	10 mg/d of extended-release oxybutynin	2 mg twice daily of tolterodine	ALZA Corporation, Mountain View, California	Dr Appell is an adviser, investigator, and speaker for ALZA Corporation and a speaker and investigator for Pharmacia Corporation. Dr Sand is an adviser, investigator, and speaker for ALZA Corporation and an

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
	incontinence.	retention if placed on an anti-muscarinic agent; those with clinically important medical problems or other organ abnormalities or pathologies for whom administration of extended-release oxybutynin or tolterodine would present undue risk (medically uncontrolled cardiovascular, pulmonary, gastrointestinal, renal, endocrine, neurological, autoimmune, hematological, urological, or psychiatric disorders; severely reduced hepatic function or renal impairment); subjects with hematuria, or a positive urine culture; those with narrow-angle glaucoma; obstructive uropathy; myasthenia gravis; pelvic organ prolapse to the hymenal ring; gastrointestinal conditions such as partial or complete obstruction, preexisting severe gastrointestinal narrowing (pathologic or iatrogenic), decreased gastrointestinal motility (paralytic ileus, intestinal atony, chronic and severe constipation), or risk of gastric retention; those who had taken an investigational drug within the previous month; those with known allergies or hypersensitivities to oxybutynin chloride, tolterodine tartrate, or components of the respective drugs; current alcohol or other drug abuse; women who were pregnant or breastfeeding; those who were not capable of following the study schedule or directions; and those who were not able to swallow the medication without chewing, crushing, biting, dividing, or				investigator for Pharmacia Corporation

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
		dissolving the capsule.				
Armstrong, 2005[224] RCT N: 790	Post hoc analysis of the OPERA study: Women 18 years and older, with urinary urgency incontinence (21–60 episodes/week), urinary urgency, and frequency (on average at least 10 voids per day); may have a history of prior treatment with an antimuscarinic drug for overactive bladder	Treatable genitourinary conditions that could cause incontinence, 2 postvoid residual urine volumes greater than 150 ml at the time of screening, significant risk of developing complete urinary retention, clinically significant medical condition that could put the patient at undue risk from anti-cholinergic effects, hematuria, uncontrolled narrow-angle glaucoma, obstructive uropathy, reduced gastrointestinal motility, or known hypersensitivity to the study medications.	Extended release oxybutynin 10 mg once daily	Extended release tolterodine 4 mg once daily	Not reported	Not reported
Armstrong, 2007[225] Pooled U.S.N: 1,168	OBJECT and OPERA trials: men and women 18 years of age and older with a diagnosis of overactive bladder with 7–50 episodes of urge UI/week in the OBJECT study and 21–60 episodes/week in the OPERA study	Reported previously[223, 226, 227]	Extended-release oxybutynin 10 mg qd	Extended-release tolterodine 4 mg qd; Immediate-release tolterodine 2 mg bid	This report was supported by Ortho Women's Health and Urology Division of Ortho Pharmaceutical, Inc.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Barkin, 2004[228] UROMAX Study Group. Canada N: 125	Men and women with UI (≥7 episode/week) and frequency (≥8 micturitions/day)	Postvoid residual volume >100 mL; unstable dosage of any drug with anticholinergic or diuretic/antidiuretic side effects; allergy or previous life-threatening side effects with anticholinergic/antispasmodic medications; primary diagnosis of stress UI; conditions contraindicating anticholinergic therapy; daily fluid intake >3L; hepatic/renal disease; diagnosed painful bladder syndrome; uninvestigated voiding difficulty with risk of urinary retention, uninvestigated hematuria, hematuria secondary to malignant disease; urinary tract infection (UTI) or history of recurrent UTI (>3 UTIs/year); indwelling catheter or bladder training within 14 days of screening; drug/alcohol abuse; untreated psychiatric conditions affecting completion of voiding diaries; chronic untreated constipation; bladder outlet obstruction; pregnancy or breastfeeding; failure to use reliable contraception in women of childbearing potential.	CR oxybutynin 15 mg every morning	IR oxybutynin 5 mg t.i.d.	Purdue Pharma	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Bent, 2008[229] RCT U.S. N: 588	Women, 19-85 years old with ≥4 incontinence episodes/week (at least one SUI and at least one UUI episode) for a minimum of three consecutive months prior to study entry	Treatment of UI by a specialist (a urologist, urogynecologist, gynecologist whose practice emphasized incontinence, continence nurse or advisor, or physiotherapist) within the past 5 years; an active urinary tract infection; the use of medication for UI within 3 months; any previous use of duloxetine; surgery within 6 months; pelvic organ prolapse greater than ICS Stage II; any non-pharmacological intervention (e.g., electrical stimulation, bladder training, continence devices) within 3 months; pelvic floor muscle training that had not been stable for 3 months or would not remain stable during the trial; and a major neurological lesion affecting lower urinary tract function.	Duloxetine 40 mg twice daily	Placebo	Eli Lilly and Company; Boehringer Ingelheim GmbH	Not reported
Birns, 2000[230] The Oxybutynin CR Clinical Trial UK N: 130	Outpatients of either sex, aged 18-76 years, with voiding problems which were currently stabilized on and tolerant to treatment with the referent drug, were recruited.	Patients with any medical condition for which anticholinergic medication is contraindicated or with a history of myasthenia gravis, glaucoma or functional or organic gastrointestinal obstructive disorders; patients with symptomatic UTIs, clinically significant BOO or symptoms of only nocturnal enuresis; female patients who were pregnant, lactating, or of child-bearing age and using adequate contraceptive measures.	oxybutynin - controlled release	oxybutynin	Funded by Leiras Oy and Pharmacia & UpJohn	NR

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Blom, 1995[231] RCT The Netherlands N: 19	19 ambulant elderly women (52 years and older) with confirmed urgency incontinence	History of breast and endometrial cancer, thromboembolic disorders, severe hypertension, cardiac failure, diabetes mellitus, peptic ulceration	1. Estradiol transdermal therapeutic system (0.05mg estradiol/day). 2. Estradiol transdermal therapeutic system (0.05mg estradiol/day) combined with naproxen 250mg tablets twice daily.	Placebo	CIBA, Isando, South Africa supplied Estraderm TTS and PHARMATEZ Pharmaceuticals. Lyndhurst, Johannesburg, South Africa supplied naproxen tablets	Not reported
Bodeker, 2010[232] Post-hoc N: 1,658	Men and women 18 years of age or older with urinary frequency (8 or more micturitions every 24 hours) plus urgency incontinence (5 or more episodes per week)	Subjects with a total daily urine volume of 2.8L or more, a mean micturition volume of more than 250mL, and/or a clinically significant bladder outlet obstruction (i.e., post void residual urine volume of more than 100mL); those with indwelling catheter or intermittent self-catheterization; urinary tract infection at the screening visit; interstitial cystitis and/or hematuria; contraindications to anticholinerigc therapy (e.g., untreated narrow-angle glaucoma, mechanical gastrointestinal stenosis, myasthenia gravis syndrome), tachycardiac arrhythmia, severe psychiatric illnesses, hypersensitivity to trospium or oxybutynin or one of the vehicle ingredients; participation in a bladder training or electro stimulation program, or in another study within the past 30 days.	Trospium chloride	Oxybutynin chloride	Dr. R .Pfleger GmbH (Bamberg, Germany) sponsored the parent study and the post hoc analysis	Rolf-Hasso Bodekar is paid consultant to Dr. R. Pfleger GmbH. Claudia Neumeister is Project Manager Clinical Research of Dr.R.Pfleger GmbH. Helmut Madersbacher and Michael Zellner declare that they have no competing interests to disclose

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Brubaker, 2008[233] Pelvic Floor Disorders Network. U.S. N: 43	Women at least 21 years with refractory urgency incontinence, detrusor overactivity incontinence and 6 or greater urgency incontinence episodes in 3 days	Not reported	BoNT-A (200 U)	Placebo	Grants from the National Institute of Child Health and Human Development	Not reported
Brunton, 2010[234] RCT N: 17,822	52 multicenter studies with data from 17,822 patients. All patients were at least 18 years of age	Not reported	Duloxetine	Placebo	Sponsored/ supported by Eli Lilly and Company and Boehringer Ingelheim, GmbH	Fujun Wnag, S.Beth Edwards, Antonio Crucitti, Melissa Ossana, Daniel Walker and Michael Robinson own stock in and are employees of Eli Lilly and Company. Stephen Brunton has acted as consultant for Eli Lilly and Company, Novo Nordisk and Amylin Pharmaceuticals, Inc.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Bump, 2003[103] Duloxetine Urinary Incontinence Study Group. U.S. N: 553	The Duloxetine Urinary Incontinence Study Group: Women aged 18–65 years with urinary incontinence of at least 3 months' duration. The case definition included a predominant symptom of stress urinary incontinence with a weekly incontinent episode frequency of at least four; the lack of predominant symptoms of enuresis or urge urinary incontinence; diurnal and nocturnal frequencies less than eight and less than three, respectively, on screening history; negative funnel infusion cystometry with a first sensation greater than 100ml and a bladder capacity of at least 400ml; and a positive fixed volume cough stress test and stress pad test (greater than 2g).	Prolapse stage II or greater; had a postvoid residual volume of 50 mL or more; were using any pharmacologic agent or device for urinary incontinence; had adopted or changed behavioral management for urinary incontinence within 3 months; or had a history of prior continence surgery.	Duloxetine 20 mg per day (20 mg once daily), duloxetine 40 mg per day (20 mg twice daily), duloxetine 80 mg per day (40 mg twice daily)	Placebo	This work was sponsored by Eli Lilly and Company. Dr. Bump and Dr. Yalcin are full-time employees of Eli Lilly and Company and hold stock and stock options in the company.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Bump, 2008[235] Pooled European countries N: 3,939	Women were >18 years with a clinical diagnosis of predominant SUI (an incontinence episode frequency, IEF of >7/week) identified with an identical, validated clinical algorithm that required a retrograde-filling bladder capacity of 400 mL and a positive cough-stress test and stress pad test. For study 4, the major diagnostic criteria were age >18 years and predominant SUI symptoms with an IEF >4/week and urine leakage most often associated with activity. Cohort B included 2,515 patients from not published RCT with predominant SUI that was defined as twice as many SUI episodes as urge UI episodes on the S/UIQ.	Not reported	Duloxetine 40-mg twice daily	Placebo	The studies and these analyses were sponsored by Eli Lilly and Company and by Boehringer Ingelheim GmbH.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Burgio, 2001[236] RCT N: 197	Older, community-dwelling women at least 55 years of age, ambulatory, with predominant urgency incontinence (the number of urge accidents had to exceed the number of stress and other accidents) at least twice per week and persisting for at least 3 months.	Continual leakage, postvoid residual urine volume greater than 200 ml, uterine prolapse past the introitus, narrow-angle glaucoma, unstable angina, decompensated congestive heart failure, history of malignant arrhythmias, or impaired mental status (MMSE score below 20).	Four clinic visits at 2-week intervals; biofeedback-assisted behavioral treatment implemented by nurse specialist, or drug treatment with oxybutynin chloride 2.5 mg of oxybutynin chloride three times a day	Placebo; self-monitoring (bladder diary), and therapist contact	Supported by Grants AG 08010	Not reported
Burgio, 2000[237] RCT analysis U.S. N: 197	Older, community dwelling women with urgency incontinence at least twice per week (the number of urge accidents had to exceed the number of stress accidents) and persisting for at least 3 months; urodynamic evidence of bladder dysfunction (detrusor instability during filling or provocation or maximal cystometric capacity of 350ml or less).	Continual leakage, postvoid residual urine volume >200ml, uterine prolapse past the introitus, narrow-angle glaucoma, unstable angina, decompensated congestive heart failure, history of malignancy arrhythmias, or impaired mental status (MMSE score <20).	Oxybutynin chloride individually titrated from 2.5 mg to 15 mg daily	2.5 to 5mg t.i.d./ Placebo	Supported by Grants AG 08010	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Burgio, 1998[238] RCT U.S. N: 197	Adults with at least 2 urge accidents per week on the 2-week baseline bladder diary, and urgency incontinence had to be the predominant pattern (the number of urge accidents had to exceed the number of stress accidents). Also, there had to be urodynamic evidence of bladder dysfunction (detrusor instability filling or provocation or maximal cystometric capacity of ≤350ml).	Continual leakage, postvoid residual urine volume >200 mL, uterine prolapse past the introitus, narrow-angle glaucoma, unstable angina, decompensated congestive heart failure, history of malignant arrhythmias, or impaired mental status (MMSE score <20).	Oxybutynin chloride, possible range of doses, 2.5 mg daily to 5.0 mg 3 times daily	Behavioral Training: biofeedback-assisted PFMT/ placebo	Grants AG08010	Not reported
Burgio, 2008[239] Fitzgerald, 2008[240] Zimmern, 2010[241] Urinary Incontinence Treatment Network. U.S. N: 307	The BE-DRI (Behavior Enhances Drug Reduction of Incontinence) trial: at least 7 episodes of incontinence in the diary, persistent incontinence for at least 3 months, no current use of antimuscarinic or other medications that could affect UI, and no evidence that incontinence was secondary to neurologic or other systemic diseases	Age <21 years; pregnancy, plan to become pregnant in the next 8 months, or declining medically acceptable birth control; <6 months postpartum delivery or other termination after 20 weeks of gestation; inability to contract pelvic floor muscles during evaluation; participated in a formal behavioral therapy program of >2 months in the past 2 years; reported continual leakage or always being damp; hypersensitive to study drug (extended-release tolterodine); systemic disease known to affect bladder function (e.g., Parkinson's disease, multiple sclerosis, spina bifida, or spinal cord injury or trauma); currently using catheter to empty bladder; postvoid residual volume >150ml; treatment for pelvic organ prolapsed with pessary <3 months; incontinence, vaginal,	Tolterodine tartrate (extended-release capsules), 4 mg/day + behavioral intervention: teaching pelvic floor muscle control and exercises; behavioral strategies to diminish urgency, suppress bladder contractions, and prevent both stress and urge	Tolterodine tartrate (extended-release capsules), 4 mg/day	Grant support by the National Institute of Diabetes and Digestive and Kidney diseases. Additional support, including provision of study drugs and funding, was contributed by Pfizer	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
		bladder, or prolapse surgery in the past 6 months; urethral diverticulum, current or repaired; previous augmentation cystoplasty or artificial sphincter; neuromodulation for pelvic indications; currently using anticholinergic agents, cholinergic agonists, tricyclic antidepressants, or duloxetine-must have discontinued use for ≥4 weeks; currently using diuretics with dosage change in past 3 months; uncontrolled medical problem (e.g., poorly controlled diabetes or decompensated congestive heart failure); history of bladder or pelvic cancer or pelvic radiation therapy; glaucoma, with or without ophthalmologist clearance; gastric retention (by medical history); non-ambulatory (may use assisted device); and participation in another intervention trial that might influence the results of the trial.				

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Burgio, 2010[242] RCT N: 64	Community dwelling women with urgency predominant incontinence. Incontinence for 3 or more months, no formal behavioral therapy, an average of 2 or more urgency incontinence episodes per week on bladder diary, number of urgency incontinence episodes exceeding other types and cystometric evidence of bladder dysfunction (detrusor overactivity or reduced bladder capacity)	Not reported	Pelvic Floor Muscle training +Urge suppression techniques +Oxybutynin	Oxybutynin	Supported by a grant from the Department of Veterans Affairs, Veterans Health Administration, Rehabilitation Research and Development Service, and the Female Veterans Project, Birmingham/ Atlanta Geriatric Research Education and Clinical Center, Birmingham VA Medical Center	Kathryn Burgio has financial interest and/or other relationship with Pfizer and Astellas; Patricia Goode has financial interest and/or other relationship with Pfizer; Holly Richter has financial interest and/or other relationship with Xanodyne, Pfizer and Astellas; Theodore Johnson has financial interest and/or other relationship with Aventis, Yamanouchi, Ortho McNeil, Boehringer Ingelheim, Johnson & Johnson and Pfizer
But, 2010[243] SOLIDAIR N: 77	Women with OAB symptoms	Not reported	solifenacin	darifenacin	Funded by a research grant from Astellas, Europe	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Cardozo, 2010[244] RCT followed by open-label Multinational N: 2,758	Women aged ≥18 years with SUI, defined by either urodynamic evaluation within 12 months before study entry without intervening continence surgery or significant change in symptoms, or by episodes of SUI confirmed by question 1 of the validated Stress/Urgency incontinence Questionnaire(S/UIQ). In addition, eligible patients had at least twice as many SUI episodes as urgency incontinence episodes as defined by question 2 of the S/UIQ and an average of ≥7 incontinence episodes	Pregnancy; alcohol abuse; active or chronically recurring urinary tract infection; presence of ureteric, bladder, urethral or rectal fistula; uncorrected congenital abnormality leading to incomplete emptying or advanced pelvic organ prolapse (stage III or IV by ICS POP-Q criteria); active or chronic hepatitis A, B or C; previous urinary incontinence surgery; or any other condition that, in the opinion of the investigator, precludes evaluation of response to duloxetine hydrochloride. Patients were not allowed to be on a medication regimen that included diuretics where dose and/or frequency were unstable, nor did they allow taking other medications that were demonstrated to be effective for SUI. Subjects who regularly performed pelvic floor muscle exercises could not change their exercise regimen during the course of the study and subjects who did not perform pelvic floor exercises were not permitted to start during the study.	duloxetine	Placebo	Sponsored by Eli Lilly and Company and by Boehringer Ingelheim GmbH	L.C. has disclosed being in receipt of funding for research, lecturing, and/or advice/consultancies from Astellas, Pfizer, UCB Pharma, Plethora, cook, Organon, Bioxell, and Sanofi-Aventis. R.L. is a member of European and German advisory boards and speaker in Lilly-sponsored congresses or training sessions. S.V., A.B., M.M., L.V. and Y.D.Z. are employed by Eli Lilly and Company and potentially own stock and/or hold stock options in the company
Cardozo, 2006[244] Pooled N: 3,298	Men and women at least 18 years of age with a mean of >8 micturitions/day; >1 incontinence episode/day; >1 urgency episode/day	Reported previously52	Solifenacin 5 mg; solifenacin 10mg	Placebo	Grant from Yamanouchi Pharmaceutical Co., Ltd., Tokyo, Japan.	Not reported
Cardozo, 2004[245] RCT Australia, Canada, the	Women aged 18–75 years with severe stress urinary incontinence defined with both urodynamic and severity criteria. Pure	Not reported	Duloxetine (40 mg twice daily for 4 weeks, escalating to 60 mg twice daily	Placebo	This work was sponsored by Eli Lilly and Company and Boehringer	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Netherlands, and the K N: 109	urodynamic stress incontinence was defined as a predominant complaint of stress urinary incontinence and the finding of urodynamic stress incontinence without detrusor overactivity and with normal compliance on an urodynamic study within 6 months of enrollment. All urodynamic diagnoses conformed to the standards of the International Incontinence Society. Severity criteria included both 1) that the subject have at least 14 incontinence episodes per week and 2) that she had scheduled her continence surgery after having discussed all other reasonable options for stress urinary incontinence with her physician. Intrinsic sphincteric deficiency was defined as urodynamic stress incontinence with a maximum straining urethral axis less than 20o, maximum urethral closure pressure less than 20cm H2O, or Valsalva leak-point pressure less than 60 cm H2O.		for another 4 weeks)		Ingelheim.	

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Cardozo, 2004[51] RCT N: 911	Men and women 18 years old or older with symptoms of OAB (including urinary frequency with urgency and/or urgency incontinence) for 3 months or more with an average micturition frequency of >8 times/day, with >3 episodes of urgency and/or >3 episodes of UI during the 3-day micturition period.	Reported previously[52]	Solifenacin 5 mg, solifenacin 10 mg	Placebo	Not reported	Not reported
Cartwright, 2011[246] RCT UK N: 96	Adult women attending as new or followup patients between October 2006 and December 2007, with at least a 3-month history of OAB symptoms, with or without urgency urinary incontinence, were invited to participate. This included patients with mixed urinary incontinence symptoms, unless previous urodynamics had demonstrated isolated urodynamic stress incontinence.	History of hypersensitivity to oxybutynin or a previous transdermal skin patch; pregnancy or breastfeeding, voiding difficulties (flow rate <15 mL/s, or post void residual >50mLs), current UTI, or one of a number of medical complaints contraindicating anticholinergic treatment as detailed in the Summary of Product Characteristics for the licensed drug Kentera, including narrow-angle glaucoma and myasthenia gravis. Participants could be naive to anticholinergic treatment, previous anticholinergic users or current anticholinergic users, provided that they discontinued other anticholinergic agents at study entry. Participants taking any contraindicated medication listed in the Summary of Product Characteristics, or any other medication for incontinence, including duloxetine, were also excluded.	Oxybutynin	Placebo	Unrestricted educational grant from UCB Pharma	Rufus Cartwright is a study investigator funded by UCB Pharma and has a financial relationship with a competitor of the mentioned product; Sushma Srikishna and Dudley Robinson were both funded by UCB Pharma and have a financial relationship with a competitor of the mentioned product; Linda Cardozo is a paid consultant for, and was funded by, UCB Pharma, and has a financial relationship with a competitor of the mentioned product.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Castro, 2008[247] RCT Brazil N: 118	Women with proven urodynamic stress urinary incontinence and no detrusor overactivity; positive cough stress test; and >3g leakage measured by a pad test with a standardized bladder volume (200ml). All subjects had symptoms of SUI with an average of at least 3 stress incontinence episodes a week	Patients with chronic degenerative diseases that would affect muscular and nerve tissues, advanced genital prolapses, pregnancy, active or recurrent urinary tract infections, vulvovaginitis, continence surgery within one year, patients with cardiac pacemakers, patients with intrinsic sphincteric deficiencies identified by the Valsalva leak point pressure<=60cm H2O measurement in the sitting position with a volume of 250ml in the bladder and/or by the measurement of a urethral closure pressure<=20cm H2O in the sitting position at maximum cystometric capacity.	Pelvic Floor Muscle Training/ electrical stimulation/ vaginal cone	No treatment	Not reported	Not reported
Castro-Diaz, 2007[248] Duloxetine Dose Escalation Study Group. 8 countries N: 516	Duloxetine Dose Escalation Study Group: women ≥18 years old with symptoms of predominant SUI using the validated Stress/Urgency incontinence Questionnaire (S/UIQ), with ≥7 SUI episodes per week and at least twice as many SUI episodes as urge UI episodes, urodynamic diagnosis of incontinence within the 6 months of study entry or an average daytime voiding interval >2 hours, a nocturnal voiding frequency ≤2 per day and a positive cough stress test.	Continence surgery within 6 months or pharmacological treatment for symptoms of overactive bladder within 14 days of visit 1, pelvic organ prolapse beyond the hymen and previous participation in a duloxetine clinical trial.	Duloxetine 40 mg BID for 8 weeks, duloxetine 40 mg daily for 2 weeks escalating to 40 mg BID for 6 weeks, duloxetine 20 mg BID for 2 weeks escalating to 40 mg BID for 6 weeks	Placebo	This study was sponsored and funded by Eli Lilly and Company and by Boehringer Ingelheim GmbH	Commercial or other associations that might pose a conflict of interest: Drs. Voss, Yalcin and Bump are full-time employees of Lilly Research Laboratories and Eli Lilly and Company.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Chancellor, 2001[249] RCT U.S. N: 36	Subjects were healthy men and women who were within 15% of ideal weight for height and had no clinically relevant abnormalities, as determined by medical history, physical examination, blood chemistry, complete blood count, urinalysis, and electrocardiography.	Clinically significant medical problems, glaucoma, obstructive uropathy, partial or complete obstruction or narrowing of the gastrointestinal tract, paralytic ileus, intestinal atony, colitis, or myasthenia gravis; male subject with hemoglobin levels <13 g/dL and female subjects with hemoglobin levels <11.5 g/dL; subjects using prescription medications (except for estrogen replacement or birth control) within 14 days before start of the study; known allergies to the study drugs; who had smoked tobacco within the past 3 months, or who drank ≥2 ounces of alcoholic beverages per day or >40 ounces of caffeine-containing beverages per day.	ER-oxybutynin 10mg, tolterodine 2mg, IR-oxybutynin 5mg	Placebo	This study was sponsored by ALZA Corporation, Mountain View, California.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Chancellor, 2008[250] The ABLE trial U.S. N: 395	Male and female patients >18 years old with symptoms of OAB for at least 6 months; >8 micturitions on average per day, >2 episodes of UUI on average per day and/or >2 episodes of urgency on average per day	Use of any drug that could affect bladder function within 2 weeks prior and during the study, participation in any formal bladder-training program within 30 days of screening, predominant stress urinary incontinence and any bladder or neurological condition that could affect urinary bladder function or in which use of anti-cholinergic drugs was contraindicated.	Darifenacin with voluntary up-titration from 7.5 mg once daily (qd) to 15 mg qd and Behavioral Modification Program: brochures on modification of diet and daily habits; training in a primary physician's office about pelvic muscle exercises and urgency control techniques including timed voiding, dietary modifications and Kegel-type exercises.	Darifenacin with voluntary up-titration from 7.5 mg once daily (qd) to 15 mg qd	Funding for this study was provided by Novartis Pharmaceuticals Corp., who was involved in study design, data collection and analysis.	Michael Chancellor has no potential conflicts of interest within International Journal of Clinical Practice guidelines for financial disclosure.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Chancellor, 2010[251] Post-hoc U.S. N: 1,156	Male or female patients aged ≥18 years with OAB for ≥6 months; required to have urinary frequency (an average of ≥10 toilet voids per day); symptoms of urgency (at least 1 "severe" urgency severity rating associated with a toilet void per 3 days, as measured by the Indevus Urgency Severity Scale [IUSS]); and an average of ≥1 urge urinary incontinence (UUI) episode per day, as recorded in a baseline 3-day patient urinary diary	Total void volume of >3000mL per day, stress incontinence, insensate continence; history of neurogenic bladder; significant renal disease; urinary tract infections; and bladder obstructions	Trospium chloride XR	Placebo	Not reported	Dr. Oefelein-Director: Allergan; Dr. Chancellor-Consultant, Speaker honorarium, trial participant: Allergan
Chapple, 2005[252] RCT U.S. N: 65	Men and women aged 18–75 years with cystometric evidence of detrusor overactivity within the previous 6 months, either idiopathic or neurogenic (secondary to a neurological lesion present for >12 months), with >2 associated symptoms (average of >7 micturitions/day, >7 episodes of urgency/week, >1 urgency incontinence episode/week necessitating change of clothing or pads).	Previous bladder surgery for detrusor overactivity; bladder stones; treatment with diuretics, antimuscarinic, tricyclic antidepressants or digoxin within the previous 2 weeks; stress and mixed incontinence, unless detrusor overactivity was the principal urodynamic observation and the patient was experiencing normal recommended limits, contraindications to anticholinergics (e.g. untreated or narrow angle glaucoma, bladder outlet obstruction).	Darifenacin immediate release (IR) 2.5 mg three times a day ; darifenacin controlled release (CR) 15 mg once daily (q.d.); darifenacin CR 30 mg q.d.	Oxybutynin 2.5 mg t.i.d.; oxybutynin 5 mg t.i.d.; oxybutynin 5 mg t.i.d.	Pfizer Inc	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Chapple, 2007[253] RCT Belgium, Bulgaria, Czech Republic, Estonia, France, Germany, Hungary, Italy, the Netherlands, Poland, Romania, Russia, Spain, Sweden, Ukraine, the United Kingdom, South Africa, Australia, and New Zealand N: 1,135	Men and women with OAB symptoms with urinary urgency for >6 months and >3 UUI episodes per 24 hours (symptoms were recorded in a 3-day diary).	Pregnancy ;non adequate contraception throughout the trial; lower urinary tract pathology that could, in the investigator's opinion, be responsible for urgency or incontinence (e.g., genuine stress incontinence, bladder stones, interstitial cystitis urothelial tumors), pelvic prolapse of grade III or higher, clinically relevant bladder outlet obstruction, polyuria (>3 l per 24 hours), symptomatic or recurrent urinary tract infections, or postvoid residual (PVR) urine volume >100 ml; currently receiving treatment, were treated within 2 weeks of screening visit with antimuscarinic agents, were treated within the past 4 weeks with electro stimulation for bladder training, or had an active urinary tract infection or an underlying neurological disease responsible for their OAB; cardiac arrhythmia and/or unstable angina or a QT interval >500 ms.	Tolterodine ER 4 mg, fesoterodine 4 mg, fesoterodine 8 mg	Placebo	Schwarz BioSciences GmbH and Pfizer Inc	Professor Chapple is a consultant/ investigator/speaker for Astellas (Yamanouchi), Pfizer Inc, Novartis, and Schwarz BioSciences GmbH, and has acted as a consultant for UCB. Professor Van Kerrebroeck is an investigator and lecturer for Astellas

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Chapple, 2008[254] RCT analysis N: 1,135	Men and women aged ≥18 years with OAB syndrome for ≥ 6 months; urinary frequency (≥8 voids/24 hours), and urinary urgency (≥6 episodes during the 3-day diary period) or UUI (≥3 episodes during the 3-day diary period, and at least moderate bladder problems on a six-point Likert scale.	The presence of lower urinary tract pathology that could, in the investigator's opinion, be responsible for urgency or UI (e.g. significant stress UI, urolithiasis, interstitial cystitis, urothelial tumors); pelvic organ prolapse grade >III; clinically relevant BOO; a postvoid residual urine volume of >100 mL; polyuria (>3 L/24 hours); symptomatic or recurrent UTIs; current treatment with antimuscarinic agents; a neurogenic cause for OAB; clinically relevant arrhythmia, unstable angina, or a QT interval of >500 ms; and current treatment, or treatment within the past 4 weeks, with electro stimulation or bladder training.	Fesoterodine 8 mg, tolterodine ER 4 mg	Placebo	Schwarz BioSciences GmbH and Pfizer Inc.	Philip E. Van Kerrebroeck and Christopher R. Chapple are study investigators funded by the sponsor, and Joseph T. Wang and Marina Brodsky are Employees of the sponsor.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Chapple, 2007[255] RCT U.S., Poland, South Africa, Hungary, Sweden, UK and Germany N: 400	Men and women >65 years of age with OAB for at least 6 month with >1 urge UI/day and >10 micturitions/day	Dependent toileting, dependent diary completion, taking drugs that can affect bladder function or external urethral sphincter, total daily volume >3000ml, mean volume/micturition >300ml, clinically significant stress UI or bladder outlet obstruction (postvoid residual volume >100ml); marked cystocele, stage 3 or 4 pelvic prolapse; participation in bladder training program or electrical stimulation therapy within 3 months of screening; intermittent urinary tract infection, clinically significant congenital or acquired disorder of the urinary tract, chronic pain syndrome or other clinically significant medical conditions including cognitive impairment, uncontrolled severe hypertension, uncontrolled severe heart failure, recent myocardial infarction, or uncontrolled thyroid disease.	Darifenacin (7.5 mg once daily for 2 weeks, then optional titration to 15 mg daily)	Placebo	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Chapple, 2005[256] Pooled N: 1,059	Men and women aged ≥18 years with symptoms of OAB for ≥6 months, and capable of independent toileting, with 5–50 episodes of incontinence per week during the run-in period, and a high voiding frequency (a mean of ≥8 voids/24 hours) and urgency (a mean of ≥1 episode/24 hours); women of childbearing potential required to use an adequate method of contraception throughout the study; those taking hormone–replacement therapy had to have received such therapy for ≥2 months before entering the study; those receiving long-term therapy with diuretics, antihypertensive medications, benzodiazepines or antihistamines had to be taking a stable dose before study recruitment, with no plans to change treatment during the study; and patients on bladder training program were not to modify or discontinue their training during the course of the study.	Initiation of a bladder training; pregnancy and lactation; clinically significant stress incontinence (i.e.>1 episode of stress incontinence per week), BOO and/or a postvoid residual urine volume of > 200 mL (as measured by pelvic ultrasonography); clinically important medical problems that would interfere with the patient's participation in the study; patients with interstitial cystitis, severe constipation (two or fewer bowel movements per week), hematuria or intermittent UTI; cystocele or other clinically significant pelvic prolapsed; patients with an indwelling catheter and those who practiced intermittent self-catheterization; urogenital surgery in the previous 6 months; patients with contraindications to antimuscarinic therapy (e.g., uncontrolled narrow-angle glaucoma, urinary retention, gastric retention); history of alcohol/drug abuse; and known hypersensitivity to study medication.	Darifenacin 7.5 mg or 15 mg/day	Placebo	The studies were funded by Pfizer Inc.	All authors are investigators in the study and/or have acted as consultants to Pfizer or Novartis.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Chapple, 200725761[258] U.S. Food and Drug Admin[257] STAR study group N: 1,177	The STAR study :men and women aged at least 18 years who had OAB symptoms (including urinary frequency, urgency or urgency incontinence) for 3 months or more; with an average of >8 micturitions/day; >1 incontinence episode/day, or an average of >1 urgency episode/day.	Stress incontinence or mixed incontinence where stress was predominant (mixed incontinence was allowed otherwise) and patients with a neurological cause of abnormal detrusor activity.	Solifenacin 5 mg	Tolterodine ER 4 mg	Grant from Yamanouchi Pharmaceutical Co, Ltd (now Astellas Pharma Inc). Tokyo, Japan.	Professor Chapple is a consultant, investigator, and speaker for Astellas Pharma Inc (Yamanouchi), Pfizer, Novartis, and Schwarz, and has acted as a consultant to UCB.
Chapple, 2006[259] RCT Multinational N: 3,032	Outpatient men and women, at least 18 years of age, with symptoms of OAB. During a baseline 3-day micturition diary period, patients were required to report a mean of ≥8 micturitions per 24 h ,and either a mean of ≥1 incontinence episode per 24 h or a mean of ≥1 urgency episode per 24 h.	Patients with at least one on-treatment efficacy assessment	Solifenacin 5mg or 10mg	placebo	Funded by an educational grant from Astellas.	Christopher Chapple is an investigator/ consultant for Pfizer, Astellas, Schwarz Pharma, Novartis and UCB Pharma. Linda Cardozo receives money for consultancy and/or advisory work, or research or lecturing from Astellas, Lilly/Boehringer Ingelheim, UCB Pharma, Pfizer, Gynecare, Plethora and Cook. William D.Steers is an investigator/consultant for Sanofi, Pfizer, Lilly and Astellas. Fred E.Govier has nothing to disclose

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Chapple, 2004[260] RCT Multinational N: 225	Men and women aged 18-80 years were eligible to enter the study if they had idiopathic detrusor overactivity (defined in this study as phasic contractions of ≥10 cmH20, assessed by filling cystometry) within 6 months of study initiation; a mean of ≥8 voids/24h for 3 days and ≥3 episodes of incontinence or urgency during the 3-day urinary diary period before randomization	Neurogenic detrusor overactivity, significant outlet obstruction, urinary retention, urodynamic stress incontinence, bladder stones, UTI, interstitial cystitis, previous or current malignant disease of the pelvic organs, previous pelvic radiation, and diabetic neuropathy; those taking concomitant anticholinergic medications, or had known or suspected hypersensitivity to anticholinergic medications or lactose; pregnant or lactating women and those not taking approved contraception methods	Solifenacin	Tolterodine and placebo	Not reported	Not reported
Chapple, 2004[261] RCT Multinational N: 728	Not reported	Not reported	Fesoterodine	Placebo	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Chapple, 2004[52] RCT Not reported N: 1,081	Men and women aged>=18 years with symptomatic OAB (including urgency, urgency incontinence, or frequency) for >=3 months. After run-in period patients had to have had an average frequency of >=8 voids/24 hours and have experienced at least 3 episodes of urgency and/or three episodes of incontinence during the 3-day voiding diary period.	Significant BOO, a postvoid residual volume of >200mL, incontinence for which stress was determined to be the predominant factor, presence of a neurological cause for detrusor muscle overactivity, evidence of UTI or bladder stones, previous pelvic irradiation, or previous or current malignant disease of the pelvic organs, any medical condition contraindicating the use of antimuscarinic medication (including narrow-angle glaucoma and urinary or gastric retention), nonpharmacological treatment for OAB including electro stimulation therapy or start of a bladder training program during the 2 weeks before or during the study, diabetic neuropathy, use of drugs intended to treat incontinence, use of any drugs with cholinergic or anticholinergic side-effects, and participation in a clinical trial within 30 days before the study entry; pregnant or nursing women, women of child-bearing potential intending to become pregnant during the study or who were not going to use reliable contraceptive methods.	Solifenacin 5mg and 10mg	Tolterodine 2mg twice daily or placebo	Yamanouchi Pharma Co., Ltd, Tokyo, Japan	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Chompootaweep, 1998[262] RCT Thailand N: 40	40 postmenopausal women with urogenital symptoms related to estrogen deficiency.	Thromboembolic disorders, severe liver diseases, estrogen-dependent tumors, high blood pressure (diastolic >100mm/Hg), those who had received oral estrogen in the 3 months before the study.	Combined contraceptive intravaginal 1 pill/week at bedtime with 250mg levonorgestrel +30mg ethinyl estradiol.	Intravaginal conjugated estrogen cream (1g=0.625mg conjugated equine estrogens) at bedtime, 3/week in week 1, 2/week in week 2, and then 1/week for 6 weeks	Grant from the Rhatchada-Pisakessompoj Fund, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Choo, 2008[263] RCT Korea N: 357	Men and women aged ≥18 years with symptoms of OAB for ≥3months; average frequency of ≥8 voids per 24h and experienced at least three episodes of urgency or three episodes of urgency incontinence during the 3-day voiding diary period.	Clinically significant bladder outlet obstruction, a PVR volume of >200ml, incontinence for which stress was determined to be the predominant factor, presence of a neurological cause for detrusor muscle overactivity, evidence of urinary tract infection or bladder stones, previous pelvic irradiation, or previous or current malignant disease in the pelvic organs, any medical condition contraindicating the use of antimuscarinic medication(including narrow angle glaucoma and urinary or gastric retention), non-pharmacological treatment for OAB including electro stimulation therapy or start of a bladder training program during the 2 weeks before or during the study, diabetic neuropathy, use of drugs intended to treat incontinence, use of any drugs with cholinergic or anitcholinergic side effects and participation in a clinical trial within 30 days before study entry; women of child-bearing potential who were pregnant or nursing, intending to become pregnant during the study, or who were not using reliable contraceptive methods.	solifenacin 5mg/10mg	tolterodine 4mg	Research grant from Astellas Pharma Inc., Tokyo, Japan	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Chu, 2009[264] RCT U.S. N: 672	Men and women aged ≥18 years with a diagnosis of OAB made by an investigator based on symptoms (urinary frequency, urgency, or urgency incontinence); had to record a mean of >=8 micturitions per 24 hours plus a mean of ≥1 incontinence episode per 24hours and/or a mean of ≥1 urgency episode per 24 hours	Stress urinary incontinence or mixed urinary incontinence in which stress was predominant (mixed incontinence was otherwise allowed), a neurologic cause of detrusor overactivity, urinary retention, grade III/IV prolapse with cystocele, and recurrent or active urinary tract infection; patients with abnormal findings on 12-lead ECG or abnormal laboratory findings. Women of childbearing potential were required to have a negative serum pregnancy test at screening and to use a medically acceptable form of contraception during study participation	Solifenacin	Placebo	Funded and sponsored by Astellas Pharma Inc., Tokyo, Japan	No

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Corcos, 2006[265] Uromax Study Group Canada N: 237	Men and women (aged ≥18 years) with UUI	A screening postvoid residual urine volume of >100 mL; allergy/serious side-effects with anticholinergic medications; primary diagnosis of stress UI; conditions contraindicating anticholinergic therapy; hepatic/renal disease; interstitial cystitis, hematuria secondary to malignancy; recurrent UTI (more than three/year); indwelling catheter/bladder training within 14 days of screening; drug/alcohol abuse; untreated psychiatric conditions affecting participation; pregnant/nursing women; and women of childbearing potential not using reliable contraception. A urine sample was collected and analyzed at the first study visit. Confirmed UTI at study entry was treated, and initiation of the washout/baseline period followed confirmation of absence of bacteria. Use of pharmacotherapy for UUI was terminated at or before the baseline evaluation (if applicable).	Daily dose of 5, 10, and 15 mg controlled-release oxybutynin	Daily dose of 5, 10 and 15 mg controlled-release oxybutynin	Purdue Pharma	J. Corcos, A. Patrick, C. Andreou and R. Casey are study investigators funded by sponsor; P. Miceli is a paid consultant/writer; and A. Darke, J. Reiz and Z. Harsanyi are sponsor employees.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Corcos, 2011[266] Fesoterodine Assessment and Comparison Versus Tolterodine (FACT)Study Group N: 1,022	Men and women aged>=18 years with symptoms of OAB 9self-assessed) for >=3 months before screening and a mean of >=1 UUI episode per 24 hours and >=8 micturitions per 24 hours reported in 3-day bladder diaries completed at baseline.	Not reported	Fesoterodine	placebo	Funded by Pfizer Inc.	Jacques Corcos is a consultant and investigator for Pfizer Inc., Astellas Pharma, Inc., Allergan, Inc, Johnson & Johnson, Inc, and Paladin Labs inc. Javier C. Angulo has no disclosures. Alan D. Garely is a consultant and speaker for Covidien and a speaker for Astellas and Pfizer Inc. Marin Carlsson, Jason Gong, and Zhonghong Guan are employees of Pfizer Inc. and hold stock in the company. The peer reviewers on this manuscript have disclosed that they have no relevant financial relationships.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Davila, 2001[267] Transdermal Oxybutynin Study Group. N: 76	Men or women 18 years or older with a history of urge or mixed urinary incontinence with a predominance of urge symptoms, previously diagnosed with motor urge urinary incontinence and had symptomatic improvement during a minimum of 6 weeks of oral oxybutynin; a minimum of 3 incontinent episodes daily, and a greater than 30% increase after 2 week washout from current treatment.	Allergy to oxybutynin, intolerability of transdermal system, current pregnancy or lactation, overflow incontinence secondary to underactive or non-contractile detrusor or outlet obstruction, impaired bladder compliance, including tonic increase in pressure greater than 15 cm. water during filling cystometry, or current medical conditions or pharmacological therapies that could contribute to or cause urinary incontinence; medical conditions that could be worsened by oxybutynin.	Transdermal system with 1.3 mg. oxybutynin daily + oral placebo	Oral capsules with 2.5 mg. oxybutynin + transdermal placebo	Watson Laboratories, Inc.	Not reported
Dessole, 2004[268] RCT Italy N: 88	88 postmenopausal women with incontinence confirmed by the direct visualization of loss of urine from the urethra during the standard stress test and by urodynamic investigation.	Estrogen treatment, anatomical lesions of the urogenital tract, detrusor over activity and abnormal maximal cystometric capacity; presence of severe systemic disorders, thromboembolic diseases, biliary lithiasis, previous breast or uterine cancer, abnormal uterine bleeding, and body mass index of 25 kg/m2 or higher.	Intravaginal estriol ovules: 1 ovule/day (1mg) for 2 weeks and then 2 ovules/ week for 6 months.	Placebo: vaginal sup-positories	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Diokno, 2003[227] Chu, 2005[269] Anderson, 2006[270] OPERA (Overactive bladder: Performance of Extended Release Agents) trial U.S. N: 790	OPERA (Overactive bladder: Performance of Extended Release Agents):Women with OAB, aged 18 years and older, who documented 21 to 60 UUI episodes per week and an average of 10 or more voids per 24 hours; predominant urge UI; with or without history of prior treatment with an anticholinergic drug for OAB.	Treatable genitourinary conditions that could cause incontinence, 2 postvoid residual urine volumes shown by ultrasonography to exceed 150 mL; pronounced risk of developing complete urinary retention, clinically important medical problems that would put a participant at undue risk of anticholinergic effects, hematuria, uncontrolled narrow-angle glaucoma, obstructive uropathy, reduced gastrointestinal motility, and known hypersensitivity to the study medications.	Extended-release formulations of oxybutynin at 10 mg/d	Tolterodine at 4 mg/d	ALZA Corporation, Mountain View, California, and Ortho-McNeil Pharmaceutical, Raritan, NJ	Dr. Diokno is a medical consultant for Ortho-McNeil Pharmaceutical. Dr. Appell is on the Medical Advisory Board of Ortho-McNeil Pharmaceutical, Watson Pharmaceuticals, Inc, and Indevus Pharmaceuticals, Inc. Dr. Sand is an investigator/advisor for Pharmacia Corporation. Dr. Dmochowski is a consultant for Ortho-McNeil Pharmaceutical. Dr. Kell is a full-time employee of ALZA Corporation, a subsidiary of Johnson & Johnson; she owns Johnson & Johnson stock and has Johnson & Johnson stock options.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Dmochowski, 2002[271] Transdermal Oxybutynin Study Group. U.S. N: 520	Male and female patients at least 18 years old with a history of overactive bladder, with or without neurological disease, 10 or more urge urinary incontinent episodes/week, with pure urgency or a predominant urgency UI, 56 or more voids and an average recorded voided volume of 350 ml. or less.	Incontinence related to chronic illness, anatomical weakness/abnormalities or concomitant medications, lower urinary tract surgery in the previous 6 months; a diagnosis of interstitial cystitis, urethral syndrome, painful bladder syndrome and overflow urinary incontinence; alcohol/drug abuse within the previous year; known hypersensitivity to oxybutynin, similar compounds or transdermal medications; active skin disorder; narrow-angle glaucoma or shallow anterior chamber evident on physical examination; and excessive consumption of caffeine, defined as greater than 5 cups of caffeine–containing beverages daily.	1.3, 2.6, or 3.9 mg Oxybutynin twice weekly to the abdomen	Placebo twice weekly to the abdomen	Not reported	All authors have financial interest and/or other relationships with Watson Pharmaceuticals; Roger R. Dmochowski has financial interest and/or other relationship with Lilly, Surx, Alza, Pharmacia, Bioform, and Genyx; Norman Zinner has financial interest and/or other relationship with Bayer, Lilly, Abbott, Praecis, Pharmacia, Interneuron, Alza, Amgen, AstraZeneca, and Roche; Marc Gittelman has financial interest and/or other relationship with Alza, Interneuron, Yamanouchi, Merck, Pfizer, Seprecor, Otsulta, Glaxo, Pharmacia, Praecis, Synthelabo, and Vivus; Sydney Lyttle has financial interest and/or other relationship with PPD Development.
Dmochowski, 2008[272]	Men and women aged 18 years or older with OAB of	Total voided volumes greater than 3000 mL/day or a mean volume	Trospium chloride 60 mg	Placebo	Esprit Pharma and Indevus	Dr. Dmochowski has acted as a consultant

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
RCT U.S. N: 564	6 months' or longer duration with symptoms of urinary frequency (a mean of 10 or more toilet voids per day), urgency (1 or more episodes of severe urgency associated with a toilet void), and UUI (a mean of 1 or more UUI episodes per day).	voided/void greater than 250 mL; predominantly stress, insensate, or overflow incontinence; history of neurogenic bladder, indwelling or intermittent catheterization, significant renal disease (defined as serum creatinine greater than 1.5 mg/dL), uninvestigated hematuria or urinary tract infection during screening, or a history of more than 3 urinary tract infections in the previous 12 months; other bladder pathologies, including clinically significant retention (defined as postvoid residual urine volume greater than 100 mL), cancer, and interstitial cystitis.	once daily		Pharmaceuticals Inc.	for Esprit Pharma, Indevus Pharmaceuticals Inc, Allergan, Novartis, Pfizer, and Watson; Dr Sand has acted as a consultant for Esprit Pharma, Indevus Pharmaceuticals Inc, Ortho, Allergan, Watson, GSK, Astellas, and Schwarz Pharma. In addition, Dr Sand has also been an investigator in clinical trials for Esprit Pharma, Indevus Pharmaceuticals Inc, Ortho, Allergan, Watson, and Astellas, and has participated in meetings for Esprit Pharma, Indevus Pharmaceuticals Inc, Ortho, Allergan, Watson, GSK, and Astellas; Dr Zinner has acted as a consultant for Esprit Pharma, Indevus Pharmaceuticals Inc, Novartis, Watson, Eli Lilly, GSK, Allergan, Astellas, and Medtronic. In addition, Dr Zinner has also been an investigator on clinical trials for

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
						Esprit Pharma, Indevus Pharmaceuticals Inc, Novartis, Watson, GSK, Allergan, and Astellas, and has participated in meetings for Esprit Pharma, Indevus Pharmaceuticals Inc., Eli Lilly, and Astellas; Dr. Staskin has acted as a consultant for Esprit Pharma, Indevus Pharmaceuticals Inc, Ortho-McNeil, Novartis, Watson, Pfizer, and Astellas.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Dmochowski, 2005[273] Pooled U.S. N: 241	Pooled analysis of RCTs: men and women with urge or mixed urinary incontinence with a predominance of urge symptoms with >10 urgency incontinence episodes/week and 56 or more micturitions (>8 micturitions per day). For study 2 patients had to have a beneficial response to previous anticholinergic OAB treatment, at least 4 incontinence episodes, 24 or more voids, and a mean void volume of 350 mL or less over 3 days.	Postvoid residual volume >250 mL; abnormal physical, laboratory, or ECG examination; lower urinary tract surgery within preceding 6 months; an active dermatologic disorder; known narrow–angle glaucoma; shallow anterior chamber, evident on physical examination (study 1 only); hypersensitivity to oxybutynin or other anticholinergic medications; hypersensitivity to transdermal drug delivery systems; history of overflow incontinence caused by underactive or acontractile detrusor or outlet obstruction; failure to complete urinary diary during washout period; recent (within 1 year) alcohol and/or drug abuse; inability to maintain nonpharmacological urinary; incontinence management program during study; consumption of 5 or more cups of caffeinated beverages per day; use of medications that affect detrusor activity; use of medications that interfere with oxybutynin or tolterodine (study 2 only).	3 dosages of oxybutynin-TDS 1.3 mg/d, 2.6 mg/d, or 3.9 mg/d for 12-week (double-blind)+ 12-week (open-label)+ 28-week (open-label extension)	Placebo	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Dmochowski, 2003[274] Transdermal Oxybutynin Study Group. U.S. N: 361	Men and women at least 18 years of age taking current pharmacologic treatment for OAB with beneficial response to the pre-study treatment; four or more urge urinary incontinent episodes, with pure urge or a predominance of urge episodes, 24 or more voids, and an average recorded urinary void volume of 350 mL or less.	History of lower urinary tract surgery in the previous 6 months and a diagnosis of interstitial cystitis, urethral syndrome, painful bladder syndrome, and overflow urinary incontinence.	Transdermal oxybutynin 3.9 mg/day or oral tolterodine 4 mg/day	Placebo	Watson Pharma	R.R. Dmochowski, P.K. Sand, N.R. Zinner, M.C. Gittelman, and G.W. Davila are study investigators funded by, and members of the medical advisory board, the sponsor. S.W. Sanders is an employee of the sponsor.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Dmochowski, 2003[275] Duloxetine Urinary Incontinence Study Group Canada and the U.S. N: 683	Non-pregnant women 18 years and older with a clinical diagnosis of bothersome SUI at least 3 months in duration, with predominant symptom of SUI with 7 or greater stress incontinent episodes weekly; daytime voiding frequency less than 8 times daily, nocturnal frequency less than 3 times daily and no predominant urgency incontinence symptoms. After filling a positive cough stress test and stress pad test were required. This clinical algorithm has been demonstrated to predict urodynamic stress incontinence with 92% accuracy.	Inability to tolerate retrograde bladder filling to 400 ml or who had a first sensation of bladder filling at less than 100 ml; treatment with other antidepressants.	80 mg duloxetine daily	Placebo	Supported by Eli Lilly and Co.	Roger Dmochowski has financial interest and/or other relationship with Lilly Pharmaceuticals, Watson Pharmaceuticals, Ortho McNeil and Indevus Pharmaceuticals; John Miklos, Ilker Yalcin and Richard Bump have financial interest and/or other relationship with Eli Lilly; Peggy Norton has Financial interest and/or other relationship with Eli Lilly, Pharmacia and Pfizer; Norman Zinner has Financial interest and/or other relationship with Lilly, Watson, Kyowa and Schwarz Pharmaceuticals.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Dmochowski, 2007[276] RCT U.S. N: 1,015	Post hoc analysis of RCT: men and women aged ≥18 years and reported symptoms of urinary frequency (≥ 8 voids/24 hours) and UUI (≥5 episodes/week) for ≥6 months.	Significant hepatic or renal disease, current or recurring UTI, stress UI, clinically relevant BOO, indwelling catheter or intermittent self-catheterization, and any condition for which antimuscarinic treatment was contraindicated; taking any anticholinergic drug or treatment for OAB and those who showed a mean of 200 mL/void or total daily of 3000 mL.	Tolterodine-ER (4 mg once daily)	Placebo	Pfizer Inc	Dr. Dmochowski is an advisor to Pfizer. Dr Kreder is a speaker for Astellas, Lilly, Merck, Novartis, and Pfizer; serves as a paid consultant to Astellas, Lilly, and Pfizer; receives research support from Lilly, Merck, and Pfizer; and holds stock options from Merck. Dr MacDiarmid is a speaker for Pfizer, Ortho-McNeil, Esprit, Astellas, Watson, and Novartis; he is a paid consultant to Pfizer, Ortho-McNeil, Esprit, Astellas, and Watson. Martin Carlsson and Zhonghong Guan are employees of Pfizer Inc.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Dmochowski, 2010[277] RCT Multinational N: 313	Men and women 18 to 85 years old with symptoms of idiopathic OAB with UUI for 6 or more months who were not adequately treated with anticholinerigc therapy (defined as inadequate response or intolerable side effects) were included in the study following informed consent. At baseline patients were required to have 8 or more UUI episodes a week, with no more than 1 incontinence-free day, and an average of 8 or more micturitions daily.	Patients using clean intermittent catheterization, history or evidence of pelvic or urological abnormalities, or diseases affecting bladder function, treatment for 2 or more UTIs within 6 months, or 24-hour total urine volume void greater than 3, 000ml or postvoid residual urine volume greater than 200ml at screening	Onabotulinumtoxin A	Placebo	Supported by Allergen, Inc.	Roger Dmochowski has financial interest and/or other relationship with Allergen, Pfizer, Astellas, and Contura; Christopher Chapple has financial interest and/or other relationship with Pfizer, Allergen, Astellas, Novartis, Ono, and Recordati; Victor Nitti has financial interest and/or other relationship with Allergen, Astellas, Coloplast, Ethicon, Medtronic, Pfizer, Serenity, Uroplasty and Watson; Michael Chancellor, Catherine Thompson, Grace Daniell, Jihao Zhou and Cornelia Haag-Molkenteller have financial interest and/or other relationship with Allergen; and Karel Everaert has financial interest and/or other relationship with Allergen and Medtronic

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Dorschner, 2000[278] RCT N: 107	Men and women older than 60 years of age with urgency, urgency incontinence, or mixed urge-stress incontinence, >1 episode of UI/day and micturition volume <300ml/micturition	Acute urinary tract infections, mechanical or functional bladder-emptying disorders, residual urine >20% of voided volume by ultrasound, micturition volume >300ml in uroflow, renal insufficiency, concomitant medications interfering with the drug studied (neurotropic/ musculotropic spasmolytics, centrally acting muscle relaxants, psychopharmacological agents or drugs for the treatment of Parkinson's disease, anti-arrhythmic), serious life threatening cardiovascular diseases (myocardial infarction within the previous 3 months, unstable coronary heart disease, implanted cardiac pace-maker, decompensated myocardial insufficiency, tachycardia or bradycardia at rest, second-or third-degree atrio-ventricular block, complete bundle branch interventricular heart block, chronic atrial fibrillation and ventricular extrasystoles Lown IVb in the pre-study ECG monitoring.	Propiverine (15 mg t.i.d.)	Placebo	Grant provided by Apogepha	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Drutz, 1999[279] RCT U.S. and Canada N: 277	Age ≥18 years; all female patients were to be postmenopausal, surgically sterile, or using an adequate contraceptive method before and during the study; evidence of detrusor overactivity on subtracted cystometry (phasic detrusor contraction with an amplitude ≥10cm H2O), along with urinary frequency (≥8 micturitions on average per 24 hours) and either urgency incontinence (≥1 incontinence episode on average per 24 hours), as confirmed by micturition diaries during the run-in period, and/or urinary urgency.	Clinically significant stress incontinence as determined by the investigator during a cough stress test maneuver; hepatic or renal disease; any disease which the investigator thought made the patient unsuitable for inclusion; recurrent urinary tract infections; interstitial cystitis; uninvestigated hematuria or hematuria secondary to malignant disease; indwelling catheter or intermittent catheterization; treatment with any investigational drug in the 2 months prior to entry; previous treatment with tolterodine; electro-stimulation therapy or bladder training within 14 days prior to entry or initiation during the study; treatment with any anticholinergic drug, or any drug for urinary urgency incontinence within 14 days prior to the baseline visit or initiation during the study; unstable dosage of any treatment with anticholinergic adverse effects or initiation of such treatment during the study; previously demonstrated serious adverse effects on oxybutynin average total voided volume/24 hours of >3000 ml; or clinically significant voiding difficulty with risk of urinary retention (such as residual volume >200 ml or urine flow rate <10ml/s).	Tolterodine 2mg b.i.d. or oxybutynin 5mg t.i.d.	Placebo	The study was funded by Pharmacia & Upjohn AB, Uppsala, Sweden	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
DuBeau, 2005[280] RCT analysis Europe (Denmark, Finland, Ireland, Norway, Sweden, and United Kingdom) N: 854	Women aged >18 years with urge-predominant mixed incontinence (>5 episodes of urge UI per week), urinary frequency (mean > voids per 24 hours), and urgency (strong and sudden need to urinate), together with stress incontinence symptoms.	Any contraindication to antimuscarinic therapy (narrow angle glaucoma, urinary retention, gastric retention, allergy, or hypersensitivity); treatment within 2 weeks of randomization with any anticholinergic drug, or any drug for UI (excluding stable doses of estrogen and alpha-adrenergic agonists); interstitial cystitis, uninvestigated hematuria, bladder outlet obstruction, indwelling or intermittent catheterization; urinary tract infection during the run-in period or greater than three times in the last year; hepatic or renal dysfunction; use of inhibitors of cytochrome P450 3A4 isoenzymes; 24-hour urine volume >3L; significant renal or hepatic dysfunction; pregnancy, lactation, or childbearing potential without use of adequate contraception; and behavioral therapy for UI within 4 weeks of initial study visit.	Tolterodine 4 mg once daily	Placebo	Pfizer	Not reported
Duckett, 2007[281] RCT U.S. N: 222	Women with a diagnosis of urodynamic stress incontinence, with mixed USI and detrusor overactivity if they were predominantly complaining of moderate/severe stress incontinence	Women not assessed with cystometry and women who declined drug therapy were excluded from further analysis.	Duloxetine 40 mg twice a day	None	Not reported	Not reported
Enzelsberger, 1995[282] RCT Austria N: 52	52 women complaining of frequency (more than five times per 12 hours), nocturia (more than twice per night) and urgency.	Women with urodynamically assessed genuine stress incontinence and with neurologic disorders.	Oxybutynin	Placebo	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Flynn, 2009[283] RCT N: 22	Overactive bladder refractory to anticholinergic medications (at least 1 anticholinergic medication and behavioral modifications must have failed), multiple daily incontinence episodes and a 24-hour pad weight of 100 gm or greater; subjects with coexisting severe OAB and mild stress incontinence were allowed to enter the study; demonstrate willingness and ability to perform self-catheterization, and have negative urine culture.	Low leak point pressures, increased post-void residual volume or neurological etiologies; gross fecal incontinence or an absent detrusor contraction on pressure flow.	Cystoscopic administration of botulinum-A toxin 200 U and 300 U	Placebo	Supported by National Institutes of Health National Institute on Aging Grant #R21 AG25490-01.	Cindy L. Amundsen has financial interest and/or other relationship with Pfizer; George D. Webster has financial interest and/or other relationship with Lifetech and AMS.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Foote, 2005[284] Pooled N: 317	Men and women with symptoms of OAB for at least 6 months and capable of visiting a toilet unaided with 5–50 episodes of incontinence per week, along with elevated micturition frequency (mean 8 voids/24 hours) and urgency (mean 1 episode/ 24 hours).	Clinically significant stress incontinence (i.e. 1 episode of stress incontinence per week); bladder outlet obstruction and/or post-void residual urine volume >200 ml; concomitant medical problems that would interfere with the patient's participation in the study; severe constipation (2 bowel movements per week); hematuria, intermittent urinary tract infection, cystocele or other clinically significant pelvic prolapse; use of an indwelling catheter or intermittent self-catheterization; urogenital surgery in the previous 6 months; contra-indications to antimuscarinic therapy (e.g.,. uncontrolled narrow-angle glaucoma, urinary retention or gastric retention); and a history of alcohol/drug abuse or known hypersensitivity to study medications; treatment with potent cytochrome P450 (CYP) 3A4 inhibitors (e.g., ketoconazole), opioids (or other drugs that could cause significant constipation), non-study antimuscarinic agents or other drugs with significant anticholinergic effects (e.g. tricyclic antidepressants); concomitant treatment with CYP2D6 inhibitors such as cimetidine, fluoxetine and paroxetine; initiation of bladder-training program was not permitted during the study.	Darifenacin 7.5 mg or 15 mg once daily	Placebo	The studies were funded by Pfizer Inc. Preparation of the manuscript was supported by an educational grant from Novartis Pharma AG.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Franzen, 2010[285] RCT Sweden N:72	Women ≥18 years of age with urgency/urgency incontinence presenting to the gynecology/urology outpatient clinics; had symptoms for at least 3 months, had increased frequency of micturition (at least 8 micturitions per 24 hours), had a mean volume of urine voided per micturition of not more than 200ml, and had a total urine volume per 24 hours of less than 3,000ml during a 48-hour bladder diary.	Persistent urinary tract infection, post-void volume greater than 150ml, history of neurological disease or dementia, pregnancy, contraindications to anticholinergic therapy, and cardiac pacemaker; if they had used tolterodine or any other anticholinergic drugs in order to treat urgency/urgency incontinence during the last 2 months or had received electrical stimulation treatment within the last 3 years.	Electrical stimulation	Tolterodine	Not reported	None
Freeman, 2003[286] RCT analysis Europe, North America, Australia, and New Zealand N: 1015	Tolterodine Study Group (secondary analysis): men and women at least 18 years old with urinary frequency (eight or more micturitions per 24 hours) and urgency incontinence (five or more episodes per week) irrespective of whether they had received prior antimuscarinic therapy and the outcome of that treatment.	Stress incontinence, total daily urine volume greater than 3 L, any contraindications to antimuscarinic treatment, significant hepatic or renal disease, symptomatic or recurrent urinary tract infections, interstitial cystitis, hematuria or bladder outlet obstruction, electro-stimulation or bladder training, indwelling catheter, or intermittent self-catheterization; pregnancy or nursing; any treatment for overactive bladder, including use of anticholinergic drugs or drugs that inhibit cytochrome P450 3A4 isoenzymes, within 14 days preceding randomization.	Tolterodine extended release 4 mg	Placebo	Pharmacia Corporation, Peapack, New Jersey	Investigator fees were paid by Pharmacia into the research funds of the authors and used to employ research staff, fund research, and purchase equipment. None of the authors own stock in Pharmacia or hold stock options.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Gahimer, 2007[287] Duloxetine exposures integrated safety database U.S.A. N: 23,983	Reported previously for 64 pooled studies	Not reported	Duloxetine 20-120 mg/day	None	Eli Lilly	Not reported
Ghei, 2005[288] RCT N: 20	Men and women 18 to 80 years old with urodynamic detrusor overactivity unresponsive to oral antimuscarinic agents willing to use intermittent self-catheterization.	Known bladder malignancies, previous bladder surgery, active urinary tract infections, known major drug allergies, major urethral access problems and children; anticholinergics during the study period were not permitted.	Botulinum toxin B (5,000 IU diluted up to 20 ml) intravesically	Placebo	Not reported	The trial was independent of industry sponsorship and involvement.
Ghoniem, 2005[289] Duloxetine/ Pelvic Floor Muscle Training Clinical Trial Group. The Netherlands, UK and U.S. N: 201	Women 18 to 75 years old with SUI; urodynamic stress incontinence and no detrusor overactivity on studies within 6 months before entry (36 subjects) or a positive cough stress test and normal micturition frequency (less than 8 voids daily) at entry (165 subjects). All subjects had predominant symptoms of SUI with an average of at least 2 stress incontinent episodes daily.	Advanced pelvic organ prolapse, active or recurrent urinary tract infections, and continence surgery within 1 year, current device or pharmaceutical incontinence treatment, prior hip fracture or replacement and any prior formal PFMT with a continence nurse or physical therapist.	40 mg duloxetine twice daily plus imitation PFMT (duloxetine only), duloxetine plus PFMT (combined treatment), placebo plus PFMT (PFMT only). PFMT groups received 30 minutes of instruction and feedback initially and 15 minutes of re-instruction	Placebo plus imitation PFMT (no active treatment)	Supported by Eli Lilly and Company and Boehringer Ingelheim.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Goode, 2002[290] RCT U.S. N: 105	Patients had to average at least two urge accidents per week documented in the 2-week bladder diary, and urgency incontinence had to be the predominant pattern (the number of urge accidents had to exceed the number of stress and other accidents). Also, there had to be urodynamic evidence of bladder dysfunction (DI during filling or provocation or bladder capacity of 350 mL or less).	Continual leakage, postvoid residual urine volume greater than 200 mL, uterine prolapse past the introitus, narrow-angle glaucoma, unstable angina pectoralis, decompensated congestive heart failure, history of malignant arrhythmias, or impaired mental status (Mini-Mental State Examination score <20).	Behavioral treatment	Oxybutynin treatment 2.5mg three times a day, placebo	Grants AG 08010 and K00431 from the National Institute on Aging to Dr. Burgio	Not reported
Goode, 2004[291] RCT analysis U.S. N: 197	Subjects were community-dwelling women aged ≥55 years who were recruited to a university based continence clinic through professional referrals and advertising. They had urgency incontinence or mixed incontinence with urge as the predominant pattern. All patients were ambulatory and not demented. They had urodynamic evidence of bladder dysfunction, either detrusor overactivity or a maximal cystometric capacity ≥350 mL.	Not reported	Behavioral therapy	Oxybutynin 2.5mg/day to 5mg t.i.d. or Placebo	NIH Grant	Patricia S. Goode has been a paid consultant to Alza, Eli Lilly, Pharmcia, and Yamanouchi

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Gupta, 1999[292] RCT Scotland N: 13	Subjects must have been at least 40 years of age, within 20% of the Metropolitan Life Insurance Table ideal weight for height value, normotensive with no clinically significant postural hypotension, and using a birth control method if premenopausal.	Volunteers were excluded for known sensitivity to any anti cholinergic drug; recent (or planned) medication usage other than estrogen replacement therapy or birth control pills; recent alcohol, caffeine, or investigational drug use; history of drug abuse; a positive urine drug screen; or recent smoking.	Three 5 mg OROS® oxybutynin chloride tablets at 0700 every day for 4 days	IR oxybutynin 5 mg t.i.d. 4 days	Not reported	Not reported
Gupta, 1999[293] Pooled N: 187	Women and men with urge urinary incontinence or mixed urinary incontinence with clinically significant urge components who were known to be responsive to anticholinergic treatment of urinary incontinence but who might have discontinued such treatment because of side effects. Patients were allowed to enroll if they had at least six urge urinary incontinence episodes per week (based on off-medication run-in patient urinary diary results) and could distinguish between urge and non-urge episodes.	Not reported	Oxybutynin XL (Ditropan XL) 5 to 30mg once daily	Oxybutynin - immediate release 5mg once/twice/ thrice or four times a day	Not reported	Not reported
Gousse, 2010[294] RCT U.S. N:60	Patients with refractory idiopathic overactive bladder symptoms	Not reported	Botulinum toxin Type A	Botulinum toxin Type A	Funded by Allergan Inc., USA	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Haab, 2006[295] RCT analysis N: 719	Successful completion of previous 12-week darifenacin studies without major protocol violation; few concomitant medications, a maximum darifenacin dose of 7.5 mg for patients taking potent inhibitors of cytochrome P450 3A4 and patients with moderate hepatic impairment (Child Pugh B); adequate contraception ; ability to complete patient diaries independently; capable of independent toileting.	Reported previously[43,296]	Patients received darifenacin CR 7.5 mg irrespective of previous study treatment, for the first 2 weeks of the extension followed by self-selected individualized dosing: patients were permitted to increase their dose to 15 mg or decreased from 15 to 7.5 mg.	None, all patients received darifenacin	Funded by Pfizer, Inc. and Novartis Pharma AG. Preparation of this manuscript was supported by an educational grant from Novartis Pharma AG and editorial and project management services were provided by ACUMED®.	F. Haab is a consultant for Novartis and Astellas and is a study investigator funded by sponsor; J. Corcos, P. Siami and P. Dwyer are study investigators funded by sponsor; J. Corcos is also a member of the board of sponsor; M. Steel, F. Kawakami and K. Lheritier are employees of sponsor; W. Steers is a paid consultant to sponsor and is a study investigator funded by sponsor.
Haab, 2005[297] RCT analysis N: 1,633	Solifenacin Study Group: Patients completing treatment in the two previous RCTs <14 days prior to extension-study; with symptoms of OAB (including urinary frequency, urgency, or urgency incontinence) for >3 months, with >8 micturitions /day, either >1 urgency episode or >1 incontinence episode/day.	Clinically significant outflow obstruction, postvoid residual urine >200 ml, persistent or recurrent urinary tract infection, bladder stones, chronic interstitial cystitis, previous pelvic irradiation or previous or current malignant disease of the pelvic organs, and any medical condition contraindicating the use of anticholinergic medication (including narrow-angle glaucoma and urinary or gastric retention); pregnancy or nursing, or intention to become pregnant during the study, or unreliable method of contraception.	Solifenacin 5 mg daily for 4 weeks, after which a flexible dosing regimen based on patient satisfaction (5 mg or 10 mg)	No control	Grant from Yamanouchi Pharmaceutical Co., Ltd., Tokyo, Japan.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Haab, 2004[296] RCT N: 561	Men and women 19–88 years old, 85% females with symptoms of OAB for at least 6 months with urgency incontinence (5-50 episodes per week); frequency of micturition (a mean of >8 voids per 24 hours); and urgency (a strong desire to void at least once per day). Those who did not benefit from other antimuscarinic agents or participated in previous double-blind studies of darifenacin were eligible for inclusion in the intervening period was >4 months.	Contraindications to the use of antimuscarinic drugs (e.g. uncontrolled narrow-angle glaucoma, urinary or gastric retention), clinically significant stress incontinence (more than one episode per week), clinically significant bladder outlet obstruction and/or a post-void residual volume >200 ml, genitourinary conditions that could cause urinary symptoms, recent urogenital surgery, or hepatic disease; bladder training program while in the study; known hypersensitivity to the study medication.	Darifenacin controlled-release tablets 3.75 mg; 7.5 mg or 15 mg/day	Placebo	The study was funded by Pfizer Inc. Preparation of the manuscript was supported by an educational grant from Novartis PharmaAG. Editorial and project management services were provided by Thomson ACUMED	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Halaska, 2003[298] RCT Austria, Bulgaria, Czechoslovakia, Germany, Russia and Spain N: 358	Men and women >18 years of age with urge syndrome (undue frequency of micturition, nocturia, overwhelming urge, wetting), urgency incontinence, urgency incontinence as one component of mixed incontinence, or urgency incontinence due to a neurological condition (detrusor hyperreflexia) as confirmed using urodynamic measurements.	Absolute tachycardia; closed-angle glaucoma; myasthenia gravis; severe arteriosclerosis of the cerebral vessels; stress incontinence; undue frequency of micturition due to heart failure, renal failure or diuretic therapy; bladder outlet obstruction; acute urinary tract infection at the beginning of the trial; hiatus hernia in combination with reflux esophagitis; stenoses in the gastrointestinal tract; megacolon; colonic ulceration; allergy or intolerance towards atropine, OXY, TCI or other constituents of the trial medication; concurrent medication with anticholinergics, tricyclic or tetracyclic antidepressants, alpha-blockers or beta-sympathomimetics within the last 7 days before starting the trial; urological or gynecological operations within the last 3 months before starting the trial; serious illnesses or conditions which would preclude participation in any clinical trial (malignant neoplasms, alcoholism, drug misuse); pregnancy or lactation; participation in any other study.	Trospium chloride (20 mg twice daily) or	Oxybutynin (5 mg twice daily).	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Herschorn, 2004[299] RCT N: 138	Male and female adults older than 50 years of age with OAB symptoms (urinary urgency, frequency >8 micturition/day, nocturia >2/night) with or without urge UI who would benefit from tolterodine administration (according to physician's opinion).	Stress UI only, abnormal cognitive function, non English speakers; interstitial cystitis, acute urinary tract infections, taking investigational drug.	Tolterodine combined with an education intervention: printed information and an explanation about OAB, medication use, and behavioral treatments (kegel exercise, bladder stretching, fluid regulation). Previously trained nurse or physician provided education.	Tolterodine alone	Pharmacia Corporation and Pfizer	Not reported
Herschorn, 2010[300] VECTOR Canada N:132	18 years old or older with OAB symptoms (more than 1 urgency episode per 24 hours and 8 micturitions or greater per 24 hours)	Significant stress incontinence, active urinary tract infection or another significant lower urinary tract pathology, clinically significant outflow obstruction, urinary retention and the use of concomitant tricyclic antidepressants, α-blockers, 5α-reductase inhibitors or anti-Parkinson's disease agents	solifenacin 5mg	Oxybutynin IR 5mg thrice daily	Not reported	Sender Herschorn has financial interest and/or other relationship with Astellas, Pfizer, Allergan, American Medical Systems, Jonhson &Johnson and Coloplast; Lynn Stothers has financial interest and/or other relationship with Astellas Canada, Merck, Urodynamix, Allergan, UBC; Kevin Carlson has financial interest and/or other relationship with Astellas Canada,

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
						Pfizer Canada, GlaxoSmithKline, American Medical Systems, BR Capital Inc. and Health Education United Partnership Inc.; Blair Egerdie has financial interest and/or other relationship with Astellas Canada, Amgen, Bayer, Protox Therapeutics and Pfizer; Jerzy Gajewski has financial interest and/or other relationship with Astellas Canada, Allergan, Pfizer, Sanofi-Aventis, Johnson & Johnson and Medtronic; Peter Pomerville has financial interest and/or other relationship with Astellas Canada, Aeterna Zentralis, American Medical Systems, Amgen, AstraZeneca, Dendreon, Eli Lilly, Ferring, Pfizer, Protox Therapeutics, Spectrum Uromedica, Bioniche Inc., Sanofi-Aventis, GlaxoSmithKline, Schering Plough,

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
						Amgen, and Abbott; Jane Schulz has financial interest and/or other relationship with Astellas, Gynecare, Pfizer and Triton; Sidney Radomski has financial interest and/or other relationship with Astellas Canada, Pfizer, Bayer and Lilly; Harold Drutz has financial interest and/or other relationship with Astellas, Lilly, Pfizer, Calldion, Gynecare, Troton and Watson; Jack Barkin has financial interest and/or other relationship with Astellas, GlaxoSmithKline, Merck, AstraZeneca and Pfizer; Fran Paradiso-Hardy has financial interest and/or other relationship with Astellas Pharma Canada

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Herschorn, 2008[301] RCT Multinational N: 617	≥18 years of age; mean of ≥8 micturitions per 24 hours and ≥3 episodes of urgency or urgency urinary incontinence (UUI) in a 3-day bladder diary before randomization; experienced OAB symptoms for ≥3 months and at least moderate problems associated with their most bothersome OAB symptom, as reported on the OAB Bother Rating Scale	Patients who received any drug used to treat UUI or OAB within 14 days before the study treatment period	Tolterodine-ER	Placebo	Funded by Pfizer Inc	Sender Herschorn has served as an advisory board member for Pfizer Inc. and as a study investigator sponsored by Pfizer Inc., Astellas Pharma Inc., Johnson & Johnson, Sanofi Aventis, and Allergan Inc. John Heesakkers has no conflict of interest to declare. David Castro-Diaz has served as a study investigator sponsored by Pfizer Inc. Joseph Wang, Marina Brodsky and Zhonghong Guan are employed by Pfizer Inc.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Hill, 2006[42] Darifenacin Study Group. N: 439	Male and female patients, aged >18 years, with urgency incontinence (>10 episodes over 14 days), high micturition frequency (mean of >8 eight voids per day), and urinary urgency (a strong desire to void on average at least once per day) for at least 6 months, regardless of previous antimuscarinic treatment.	Clinically significant stress incontinence, bladder outlet obstruction or a postvoid residual urinary volume >200 ml; local pathology that could cause urinary symptoms (e.g., interstitial cystitis, bladder stones), severe constipation (≤2 bowel movements per week), history of intermittent urinary tract infections; those who had undergone urogenital surgery within the previous 6 months, or cystoscopy in the previous 30 days; patients with indwelling catheter or using intermittent self-catheterization; presence of clinically significant systemic disease; patients who intended to start a bladder-training program during the study, or had contraindications to antimuscarinic therapy; pregnant and lactating women; no concomitant treatment with drugs (including drugs with significant anticholinergic effects), opioids, hormone replacement therapy (unless taken for >2 months), and drugs known to be significant inhibitors of cytochrome P450 2D6 or 3A4 isoenzymes (cimetidine, fluoxetine, ketoconazole, nitraconazole, etc.).	Oral Darifenacin (Novartis Pharma AG, Basel, Switzerland) once-daily 7.5, 15, 30 mg	Placebo	The study was funded by Pfizer Inc.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Ho, 2010[302] RCT Taiwan N: 75	Male or female patients aged ≥18 years; informed consent willing and able to complete the micturition diary correctly; OAB symptoms, including urinary frequency, urgency, or urgency incontinence, had persisted for ≥3 months; and having frequency, defined as ≥8 micturitions per 24 hours	Pregnant and lactating women or those who intended to become pregnant during the study; clinically significant bladder outflow obstruction (such as women with bladder outlet obstruction); significant post-void residual volume (>200mL); genuine stress incontinence; evidence of symptomatic urinary tract infection, chronic inflammation, bladder stones, previous pelvic radiation therapy, or previous or current malignant disease of the pelvic organs; patients with any medical condition that contraindicated the use of antimuscarinic medication; uncontrolled narrow angle glaucoma, urinary or gastric retention, or any other medical condition that, in opinion if the investigator, contraindicated the use of antimuscarinic	Solifenacin	Tolterodine	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Holtedahl, 2000[303] RCT analysis Norway N: 87	Women 50-74 years of age reporting two or more leakage episodes per month.	Reported previously[304]	Estriol and pelvic floor exercise for all patients, plus bladder training and maximal electrical stimulation in patients with urge, vaginal long-term electrical stimulation in patients with stress, and all elements in patients with mixed incontinence.	Estriol and pelvic floor exercise (for all patients, plus bladder training and maximal electrical stimulation in patients with urge, vaginal long-term electrical stimulation in patients with stress, and all elements in patients with mixed incontinence	The Norwegian Medical Association Fund no. 1, Odd Berg Medical Research Fund, Finnmark County Research Fund, Medicon A/S, Organon A/S, Coloplast A/S, SABA Mo¨lnlycke A/S, and LIC Hygiene A/S.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Holtedahl, 1998[304] RCT Norway N: 90	Women, 50-74 years of age with regular incontinence (>2 leakage episodes per month) diagnosed during gynecological examinations, with positive pad test, or self reported in 48 hour chart.	Cardiac pacemaker, dementia, medical conditions that would prevent following the protocol.	Local estrogen in vagitories or jelly plus physiotherapy and electro-stimulation	Usual care	Financial and material (pads, estriol) support from The Norwegian Medical Association Fund no. 1, Odd Berg Medical Research Fund, Finnmark County Research Fund, Medicon A/S, Organon A/S, Coloplast A/S, SABA Mo¨ lnlycke A/S, LIC Hygiene A/S.	Not reported
Homma, 2006[305] RCT analysis Japan N: 637	Adult patients with OAB syndrome and having experienced urgency incontinence one or more times a day on average with urinations eight or more times a day during the preceding week.	22 patients were excluded from full-analysis-set for the following reasons: (1) non-OAB patients (n =8), (2) not treated (n = 2), (3) no efficacy data after randomization (n =11), (4) duplicated enrollment (n =1).	Three sizes of oxybutynin transdermal patch (26, 39, and 52 cm2) were used	Placebo	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Homma, 2004[306] RCT Japan and Korea N: 293	Men and women aged ≥20 years were eligible for inclusion if they had symptoms of OAB for ≥6 months and urinary urgency, urinary frequency (≥8 micturitions/ 24 hours), urgency incontinence (≥5 episodes/week) as assessed by micturition diaries during the wash-out/run-in period. Patients were recruited solely on the basis of their OAB symptoms, irrespective of whether they had received prior antimuscarinic treatment and irrespective of their response to such therapy.	Demonstrable stress incontinence, total daily urine volume >3L, average volume voided/ micturition >200 ml, significant hepatic or renal disease, any contraindication for anticholinergic treatment (e.g., uncontrolled narrow-angled glaucoma, urinary retention, or gastric retention), symptomatic or recurrent urinary tract infection, interstitial cystitis, hematuria or bladder outlet obstruction, an indwelling catheter or intermittent self-catheterization, electro-stimulation or bladder training within 14 days before randomization or expected to commence during the study period.	Tolterodine ER 4 mg once daily	Oxybutynin 3 mg three times daily, placebo	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Homma, 2003[307] Japanese and Korean Tolterodine Study Group Korea and Japan N: 608	Men and women aged >20 years with symptoms of urinary urgency, urinary frequency (> 8 voids/24 hours), urgency incontinence (>5 episodes/ week) and symptoms of OAB for >6 months were eligible for inclusion. Patients were recruited based solely on their symptoms of OAB, irrespective of whether they had received previous antimuscarinic treatment and irrespective of their response to such therapy.	Demonstrable stress incontinence; total daily urine volume of >3 L; average volume voided/ void of >200 mL; significant hepatic or renal disease; any contraindication to anticholinergic treatment, e.g. uncontrolled narrow-angled glaucoma, urinary retention or gastric retention; symptomatic or recurrent UTI; interstitial cystitis; hematuria or BOO; an indwelling catheter or intermittent self-catheterization; and electro-stimulation or bladder training within 14 days before randomization or expected to commence during the study period; pregnant or nursing women and women of childbearing potential not using reliable contraception.	Tolterodine 4mg capsules once daily	Oxybutynin 3mg tablets three times daily, placebo	This study was supported by a grant from Pharmacia Corporation.	Not reported
Hurley, 2006[308] Viktrup, 2007[309] Pooled Africa, Australia, Europe, North America, and South America N: 2,188	1,913 women with SUI who participated in four controlled clinical trials of duloxetine vs. placebo. All had predominant SUI were enrolled using a clinical algorithm validated to be 90.2% predictive for urodynamic SUI.	Subjects who received lower doses of duloxetine (20 or 40 day, n = 275) in the phase 2 trial. Active substance abuse disorder within the 5 years prior to study entry; regular consumption of 21 or more alcoholic drinks per week; use of monoamine oxidase inhibitors or antidepressants within 14 days prior to study entry; a current diagnosis of a voiding abnormality or significant diseases of the genito-urinary tract; a history of urogenital cancer; symptomatic arrhythmia despite antiarrhythmic medication; uncontrolled angina, or a significant abnormality on electrocardiogram (ECG) at screening; any active cardiac ischemic condition, including myocardial infarction within 6 months	Duloxetine (80 mg per day).All subjects were given the option to continue taking duloxetine in open-label extensions of these studies. Those randomized to duloxetine 80 mg per day in the phase 2 studies were dose escalated over the first 2 weeks from 20 mg twice daily	Placebo	This work was sponsored by Eli Lilly and Company and Boehringer Ingelheim.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
		prior to study entry; uncontrolled or poorly controlled hypertension; an active seizure disorder; unstable diabetes mellitus; a spinal cord lesion, multiple sclerosis, or neurological abnormality that affected the lower urinary tract; a history of severe allergies requiring emergency medical treatment or multiple adverse drug reactions; and . active or chronic hepatitis A, B, or C.	for the first week to 30 mg twice daily for the second week before taking 40 mg twice daily. At the end of the active-treatment phase, subjects had their duloxetine dose tapered over 2 weeks (30 mg twice daily for the first week and 20 mg twice daily for the second week) before duloxetine was discontinued.			
Ishiko, 2001[310] RCT Japan N: 73	73 women with postmenopausal stress incontinence.	Urge or mixed incontinence	Combination of estriol (1 mg/day) and pelvic floor muscle exercise	Pelvic floor muscle exercise	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Jackson, 1999[311] RCT UK N: 67	Postmenopausal women with symptoms of urinary incontinence. If genuine stress incontinence was diagnosed, and the woman was more than 12 months post-menopausal and had not taken hormone replacement therapy in the previous 12 months, she was fully informed about her options for treatment as well as being offered recruitment to the clinical trial.	History of cancer of the endometrium, liver, or breast; endometrial thickness >4mm	Estradiol valerate 2mg/day	Placebo	Industry + grant	Not reported
Jacquetin, 2001[312] RCT Belgium and France N: 251	Male and female patients aged ≥18 years were eligible for inclusion in the study if they had urodynamically proven overactive bladder, and symptoms of urgency and/or urgency incontinence (≥1 incontinence episode/24 hours) with increased frequency of micturition (≥8 micturitions/24 hours) irrespective of prior treatment or treatment failure.	Significant stress incontinence; hepatic or renal disease; symptomatic or recurrent urinary tract infection; interstitial cystitis; hematuria; clinically significant voiding difficulty; patients receiving bladder training, electro-stimulation therapy or having an indwelling catheter or on intermittent catheterization; pregnant or nursing women, or women of childbearing age who were not using reliable contraception.	Tolterodine 1 or 2mg twice daily	Placebo	Pharmacia Corporation	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Johnson, 2005[313] RCT analysis U.S. N: 131	Participants had to report at least two accidents per week and to demonstrate the ability to complete an interpretable bladder diary that confirmed this frequency of urine loss. Urgency incontinence had to be the predominant pattern (urge accidents exceeded the number of stress and other accidents), with urodynamic evidence of bladder dysfunction. Two-channel supine water cystometry was performed to demonstrate detrusor instability (defined as urodynamic observation of involuntary detrusor contractions during the filling phase) or sensory urgency (defined as bladder capacity of less than 350 mL) for inclusion in the study.	Participants with continual leakage, elevated postvoid residual urine volume (4200 mL), narrow angle glaucoma, uterine prolapse past the vaginal introitus, unstable angina pectoris, decompensated congestive heart failure, or impaired mental status (MMSE score <20).	Behavioral training, drug treatment (oxybutynin IR titrated from 2.5 mg per day to 5.0 mg three times a day)	Placebo	Supported by grant from the National Institute on Aging. Dr. Johnson received additional support from the Emory University Center for Health in Aging. The John A. Hartford Foundation Southeast Center of Excellence in Geriatric Medicine and the Birmingham/ Alabama VA GRECC provided infrastructural support that enabled this inter-institutional collaboration.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Jonas, 1997[314] The International Study Group N: 242	Men or women >18 years and presenting with detrusor overactivity, defined as the existence of any phasic detrusor contraction with an amplitude of >10 cm H20 or the existence of one strong detrusor contraction that caused the end of the infusion, with frequency (> 8 micturitions/24 hours) in combination with urgency incontinence (>1 incontinence episode/24 hours), urinary urgency, or both.	Significant stress incontinence hepatic disease, defined as twice the upper limit of the reference range for liver function tests, renal disease, defined as twice the upper limit of the reference range for creatinine, any condition contraindicating anticholinergic therapy, recurrent urinary tract infections, interstitial cystitis, uninvestigated hematuria, or clinically significant voiding difficulty with risk of urinary retention; any anticholinergic treatment; using an indwelling catheter, history of electro-stimulation therapy or bladder training (last 14 days prior to the inclusion visit).Concomitant treatment with anticholinergic drugs or treatment with any agent for urinary urgency incontinence (with the exception of any estrogen treatment started at more than 2 months prior to entry) was not permitted in the 14 days prior to entry or during the study.	Tolterodine 1 or 2 mg b.i.d	Placebo	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Junemann, 2006[315] RCT Multinational N: 988	Patients with overactive bladder who met all of the following inclusion criteria were allowed to participate in the study: female and male patients >=18 years, voluntarily signed informed consent, at least 2 incontinence episodes within 3 days, and at least 10 micturitions within 24h	Stress incontinence; intermittent catheterization; neurogenic detrusor under- and overactivity; postvoid residual urine >=100ml; acute urinary tract infections; electro stimulation therapy, bladder training if performed within 4 weeks before run-in period of this study; anomalies of the lower genitourinary tract (e.g. ectopic ureters, fistulas, urethral stenosis); pre-existing medical contraindications for anticholinergics (e.g. obstruction of the bowel, toxic megacolon, severe colitis ulcerosa, bladder or intestinal atony, significant degree of bladder outflow obstruction where urinary retention could be anticipated, pollakiuria of cardiac or renal genesis, tachyarrhythmia, narrow-angle glaucoma, myasthenia gravis); cardiac insufficiency(New York Heart Association stage III/IV); multiple sclerosis; evidence of severe renal, hepatic or metabolic disorders; history of drug or alcohol abuse; concomitant medications known to have a potential to interfere with the study medication; pregnant or breastfeeding women, or women of childbearing potential without using any reliable contraceptive method	Propiverine hydrochloride IR	Propiverine hydro-chloride ER and placebo	Funded by Apogepha Arzneimittel GmbH	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Junemann, 2000[316] RCT N: 234	Patients with urge - syndrome (motor urge, sensory urge and combined motor urge and stress incontinence). Patients medical history and a urodynamic measurement (minimum one unstable detrusor contraction of 10 cm H2O or first desire to void at a bladder filling of <150ml) verified the diagnosis of urge-syndrome	Not reported	Trospium hydrochloride	Tolterodine and placebo	Not reported	Not reported
Junemann, 2005[317] RCT Bosnia, Czech Republic, Germany, Poland, Slovenia, United Kingdom N: 201	Men and women aged >18 years with overactive bladder, defined as at least one unstable detrusor contraction at a minimum of 10 cm H2O combined with an increased frequency of micturition (>8 micturitions/24 hours); sensoric urgency incontinence, defined as at least one incontinence episode/24 hours combined with increased frequency of micturition (>8 micturitions/24 hours).	Maximum cystometric bladder capacity 300 ml; post void residual >50 ml; acute urinary tract infection (>106 bacteria/ml urine); electro-stimulation therapy, bladder training if performed <4 weeks before run-in period of this study; intermittent catheterization; anomalies of the lower genitourinary tract (e.g. ectopic ureters, fistulas, urethral stenosis, etc.); operations of the lower urinary tract within the last 4 weeks; pre-existing medical contraindication for anticholinergics.	15 mg propiverine twice daily	2mg tolterodine twice daily	APOGEPHA Arzneimittel GmbH.	Not reported
Kaplan, 2010[318] RCT Multinational N: 2417	Subjects with OAB symptoms for >=months and recorded micturitions and >=1 urgency urinary incontinence episode per 24h in 3-day baseline diaries	Not reported	Fesoterodine	Tolterodine/ Placebo	Sponsored by Pfizer Inc.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Karademir, 2005[319] RCT Turkey N: 43	Patients with a >6-month history of overactive bladder symptoms and who had detrusor overactivity findings on urodynamic studies (UDS).	Urinary tract obstruction, urinary retention, a neurologic or metabolic disorder; any kind of intervention for urinary incontinence.	Stoller afferent neuro-stimulation (SANS) with low-dose anticholinergic (oxybutynin hydrochloride)	Stoller afferent neuro-stimulation (SANS)	Not reported	Not reported
Karram, 2009[320] Toglia, 2009[321] VENUS U.S. N: 739	Patients aged>=18 years with OAB (at least 1 urgency episode with or without incontinence and >=8 micturitions per 24 hours) for >=3 months	Presence of stress or stress-predominant mixed urinary incontinence, chronic inflammation or cystitis, and clinically significant bladder outlet obstruction	Solifenacin	Placebo	Research grant from Astellas Pharma US, Inc. and Glaxo-SmithKline	Marc Toglia discloses conflict of interest with Astellas Pharma US, Inc. and Ethicon Women's Health. Scott R. Serels discloses conflicts of interest with Astellas Pharma US, Inc., GlaxoSmithKline, and Takeda. Mickey Karram discloses conflict of interest with Allergan, Astellas Pharma US, Inc., Cooper, and Ehticon. Indrani Nandy discloses conflict of interest with GlaxoSmithKline. Masakazu Andoh discloses no conflict of interest. Raafat Seifeldin discloses conflict of interest with AStellas Pharma US, Inc. Sergio Forero-Schwanhaeuser discloses conflict of interest with GlaxoSmithKline

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Kelleher, 2006[322] RCT U.S. N: 3,032	Pooled analysis of 4 RCTs: men and women at least 18 years of age with either MUI or UUI based on their history and the results of a cough test; a mean of ≥8 micturitions per 24 hours in addition to a mean of ≥1 incontinence episode per 24 hours or a mean of ≥1 urgency episode per 24 hours during the baseline 3-day micturition diary period.	Predominant stress UI.	5 mg solifenacin once daily, 10 mg solifenacin once daily	Placebo	Not reported	Not reported
Kelleher, 2002[323] RCT U.S. N: 1,015	Male and female patients aged 18 years or older with urinary frequency (average of ≥8 micturitions/24 hours over a 7-day period), urgency incontinence (≥5 episodes/week), and symptoms of OAB for at least 6 months.	Other types of bladder dysfunction, with diseases that may have affected urinary output.	Tolterodine extended-release (ER) 4 mg once/day, or tolterodine immediate-release (IR) 2 mg twice daily	Placebo	Pharmacia Corporation	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Kelleher, 2008[324] Pooled analysis U.S. N: 1,971	Men and women aged ≥18 years with OAB syndrome for ≥6 months; patients had to report at least moderate problems related to their bladder condition on a six-point Likert scale	Presence of lower urinary tract pathology that could, in the investigator's opinion, be responsible for urgency or UI (e.g. significant stress UI, interstitial cystitis, urothelial tumors); pelvic organ prolapse grade ≥III; clinically relevant BOO; a post void residual urine volume of >100mL; polyuria (>3L/24h); symptomatic or recurrent UTI; current treatment with antimuscarinic agents; a neurogenic cause of OAB; clinically relevant arrhythmia, unstable angina, or a QTcB interval of >500ms; and current treatment, or treatment within the past 4 weeks, with electro stimulation or bladder training	Fesoterodine	Tolterodine/ Placebo	Funded by Schwarz BioSciences GmbH and Pfizer Inc	Con J.Kelleher is an Advisor to Astellas and Novartis and a Lecturer for Pfizer. Andrea Tubaro is a paid Consultant and study investigator funded by the sponsor. Joseph is an employee of the sponsor
Khullar, 2004[325] RCT UK N: 854	Women 18 years or older with urge-predominant mixed incontinence, including urgency incontinence (five or more episodes per week), urinary frequency (eight or more micturitions on average in 24 hours), and urgency in combination with stress incontinence irrespective of the use of previous antimuscarinic treatment.	Pure stress urinary incontinence; predominant stress urinary incontinence; a total daily urine volume greater than 3 L; suspected or documented hepatic or renal dysfunction; symptomatic urinary tract infection; interstitial cystitis, uninvestigated hematuria, or clinically significant bladder obstruction; any contraindication to antimuscarinic treatment; and any nonsurgical treatment for incontinence within 4 weeks of the first study visit; treatment within 2 weeks before randomization with any drug for incontinence (except estrogen therapy started more than 2 months before the first visit); agonist or potent inhibitors of cytochrome P450 3A4 isoenzymes; pregnancy, lactation, or inadequate contraception.	Tolterodine tartrate extended-release (ER) 4 mg	Placebo	Pfizer Inc	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Khullar, 2008[326] Pooled U.S. N: 1,674	Pooled analysis of two RCTs: men and women 18 years of age or older with OAB syndrome for 6 or more months; urinary frequency (8 or more micturitions per 24 hours) and urinary urgency (6 or more episodes during the 3-day diary period) or UUI (3 or more episodes during the 3-day diary period).	Presence of lower urinary tract pathology that could, in the investigator's opinion, be responsible for urgency or incontinence (for example, significant stress incontinence, urolithiasis, interstitial cystitis, urothelial tumors); pelvic organ prolapse grade III or higher; clinically relevant bladder outlet obstruction; postvoid residual urine volume greater than 100mL; polyuria (more than 3L/24 hours); symptomatic or recurrent urinary tract infections; current treatment with antimuscarinic agents; a neurogenic cause of OAB symptoms; clinically relevant arrhythmia, unstable angina, or a QTcB interval greater than 500 ms; current treatment, or treatment within the past 4 weeks, with electro-stimulation or bladder training during the past 4 weeks.	Fesoterodine 4 mg, or fesoterodine 8 mg	Placebo	Schwarz BioSciences GmbH and Pfizer Inc	Dr. Vik Khullar has been a consultant and investigator in clinical trials by Pfizer Inc. Drs. Eric Rovner and Roger Dmochowski have served as consultants and investigators on clinical trials sponsored by Pfizer Inc. Dr. Victor Nitti has been a consultant and lecturer sponsored by Pfizer Inc. Joseph Wang and Dr. Zhonghong Guan are employed by Pfizer Inc.
Kinchen, 2005[327] RCT Not reported N: 451	Ambulatory women with symptoms of SUI 18 years of age or older, >1 episode per week of urinary incontinence due to activities such as coughing, sneezing, lifting, and exercising. Women had to have experienced stress symptoms for >3 months but may have predominant symptoms of urgency incontinence	Pregnancy, breastfeeding, having an active urinary tract infection, participation in a previous trial of duloxetine, or having conditions such as arrhythmias, poorly controlled or uncontrolled hypertension, liver disease, seizure disorders, or an unstable cardiac condition.	Duloxetine (40 mg b.i.d.) but dose adjustment was allowed	Placebo	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Kreder, 2003[328] RCT analysis N: 994	Age >18 years with OAB, diagnosed by a physician assessment based on self-reported symptoms with urinary frequency (>8 voids/24 hours) and either urgency or UI (>1 incontinence episode/24 hours).	Predominating stress UI; contraindications to antimuscarinic therapy; significant hepatic or renal disease; symptomatic UTI or history of recurrent UTI; hematuria or interstitial cystitis; significant voiding difficulty with risk of urinary retention; and bladder training, electro stimulation therapy, or having an indwelling catheter or an intermittent catheterization, women with reproductive potential; pregnancy or nursing; concomitant treatment for OAB (other than estrogen-replacement therapy started at least 2 months before study commencement) and use of anticholinergic agents.	Tolterodine 1 mg twice daily for 4 weeks, after which the dose could be increased to 2 mg twice daily (and subsequently reduced to 1 mg if necessary), based on the patient's response	None. Outcomes were compared among patients with urge UI vs. mixed UI	Pharmacia Corporation.	Not reported
Lackner, 2008[329] RCT U.S. N: 50	Nursing home resident for at least 3 months; aged ≥65; not residing in a subacute, transitional care, or rehabilitation unit of the nursing home; not enrolled in hospice; bladder incontinence (Minimum Data Set 2.0 score of 1–4); no indwelling catheter; able to swallow medication intact and obtained permission from potential participants or their designated proxies for chart review by the NP; Mini-Mental State Examination score of 5–23; Global Deterioration Scale score of 3–6; ≥1	Terminal illness; bed-bound; non-communicative; delirium (Confusion Assessment Method feature 1 (acute onset) and 2 (inattention) plus feature 3 (disorganized thinking) or 4 (altered level of consciousness)); Lewy body dementia; history of ≥3 urinary tract infections in previous year or current infection; postvoid residual urine volume ≥150 mL (bladder ultrasound); urethral diverticulum; bladder tumor or stone; severe pelvic organ prolapse or vaginitis; genitourinary surgery within past 6 months; hepatic disease; severe cardiovascular disease; myasthenia gravis; spinal cord injury; bowel movement <every 3 days; history of gastrointestinal obstruction or decreased motility; current drug therapy for urinary incontinence;	Extended release oxybutynin 5mg once daily	Placebo	Funded by a research grant from Ortho-McNeil Pharma-ceutical, Raritan, New Jersey. ALZA Corporation, Mountain View, California, supplied oxybutynin extended-release (Ditropan XL) 5-mg tablets and matching placebo tablets.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
	symptom or sign of urge urinary incontinence (≥4 micturitions or wet checks or requests to toilet within an 8-hour period of prompted voiding schedule on 2 consecutive days (8:00 a.m. to 4:00 p.m.); nocturia or nocturnal enuresis >2 times per night; staff observation that incontinence occurs on way to toilet or resident reports urgency; or medical record documentation of detrusor overactivity or urgency); Medication adherence rate ≥80% during the week before screening.	current use of acetylcholinesterase inhibitor or bisphosphonate; investigational drug, systemic or ophthalmic cholinomimetic drug, or gastrointestinal antispasmodic within 2 weeks before trial.				
Landis, 2004[330] RCT North America, Europe and Australia/New Zealand. N: 1529	Men and women 18 years old or older with urinary frequency (8 micturitions or greater per 24 hours), urgency incontinence (5 episodes or greater a week) and symptoms of overactive bladder for 6 months; severe incontinence defined as 21 episodes or greater per week at baseline irrespective of prior antimuscarinic treatment and response to such treatment.	Reported previously[331]	4 mg tolterodine ER once daily	Placebo	Pharmacia Corporation, Peapack, New Jersey	J. Richard Landis has financial interest and/or other relationship with Alza Pharmaceuticals, Pharmacia and Bristol-Myers Squibb; Eboo Versi has financial interest and/or other relationship with Pharmacia.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Lee, 2002[332] RCT South Korea N: 228	Male and female subjects aged ≥18 years with symptoms of overactive bladder for ≥6 months were eligible for enrolment in the study. Symptoms, as measured by micturition diaries, were defined as urinary urgency and frequency (≥8 micturitions on average per 24 hours), with or without urgency incontinence. Patients were enrolled exclusively on the basis of symptoms (i.e. urodynamics was not performed), irrespective of whether they had received prior antimuscarinic therapy.	Significant stress incontinence; women of childbearing age who were not using reliable contraception; pregnant or nursing women; treatment with any drug with known anticholinergic side-effects in the in the 2 weeks prior to the study; significant renal or hepatic disease; any contraindication to antimuscarinic therapy (e.g. narrow-angle glaucoma, urinary or gastric retention, known hypersensitivity to tolterodine or oxybutynin); symptomatic acute or recurrent urinary tract infection; interstitial cystitis or hematuria; bladder outlet obstruction; and patients receiving bladder training, electro-stimulation therapy or having an indwelling catheter or on intermittent catheterization.	Tolterodine 2mg bid	Oxybutynin 5mg bid	Grant from Pharmacia	Not reported
Lee, 2010[333] Propiverine study on overactive bladder including urgency data Korea N: 264	Men and women aged ≥18 years who had self-reported symptoms of OAB for ≥3months; average urinary frequency of ≥10 voids/24h and urgency of two or more episodes/24h defined as 'moderate to severe' in the Indevus Urgency Severity Scale during the 3-day voiding diary period before randomization	Clinically significant stress urinary incontinence (more than one episode per week); genitourinary conditions that could cause OAB symptoms, such as UTI; and contraindications to the use of antimuscarinic drugs	Propiverine hydrochloride 60 mg/d	Placebo	Sponsored by Jeil Pharma-ceutical Co. Ltd., Seoul, Korea	NR

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Lehtoranta, 2002[334] RCT Finland N: 9	Female or male patients aged 18–75 years were recruited to the study. They had to have a history of urgency or urgency incontinence and cystometrically proven detrusor hyperreflexia or instability according to the ICS criteria (International Continence Society).	Stress incontinence and pure nocturnal enuresis	Oxybutynin 5mg/30ml three times daily	Placebo 30ml of sterile saline	Not reported	Not reported
Leung, 2002[335] RCT Hong Kong N: 106	Age ≥18 years; a diagnosis of overactive bladder confirmed by urodynamic test (phasic detrusor contraction with an amplitude ≥15cm H2O) in accordance with ICS criteria; urinary frequency (an average of ≥8 voids/24 hours), urgency or urgency incontinence (an average of ≥1 incontinence episode/24 hours); and willing to give written informed consent.	A diagnosis of genuine stress incontinence; clinically significant voiding difficulty (maximum flow rate <10 mL/s with a residual volume of >200 mL); recurrent or acute UTIs; require intermittent catheterization or an indwelling catheter; uninvestigated hematuria or bladder cancer; currently on treatment for an overactive bladder or on anticholinergic medications; presence of psychiatric disease or cognitive impairment, as shown by their history or an abnormal Mini Mental State Examination; clinically significant cardiac, hepatic, renal or hematological disorders, as shown by their history; the presence of contraindications for antimuscarinic agents; pregnant or lactating women and women of childbearing age who were not using reliable contraception.	Tolterodine 2mg twice daily	Oxybutynin 5mg twice daily	Financial Assistance from Pharmacia Limited	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Lin, 2008[336] RCT Taiwan N: 121	Non-pregnant women 20 years of age and older with predominant symptoms of SUI during the last 3 months with an average of ≥1 incontinent episode/day, positive cough stress test after filling the bladder, daytime voiding frequency ≤8 voids daily, nocturnal frequency ≤ 2 voids daily and no predominant urgency incontinence symptoms.	Inability to tolerate retrograde bladder filling to 400 mL or who had a first sensation of bladder filling at ≤100 mL. Concomitant medications including urinary continence promoting drugs, antidepressants, drugs for obesity (including over the counter appetite suppressants and diet pills), and illicit drugs.	80 mg duloxetine (40 mg twice daily)	Placebo	This study was supported by Eli Lilly and Company and Boehringer Ingelheim.	Not reported
Lipton, 2005[337] RCT N: 129	Male and female volunteers 65 years or older with a score of 10 or less on the Short Orientation Memory and Concentration Test,12 which is a short version of the Blessed Information-Memory Concentration (no clinical dementia).	A diagnosis of clinical dementia, depression or any other medical, psychological or social condition that would impair participation in the study, clinically significant or unstable hematological, renal, hepatic or cardiac disease, or the use of cimetidine, psychotropic drugs, anticholinergic drugs, antihistamines or other drugs known to affect cognitive function; severe drug allergy or contraindications to antimuscarinic therapy (e.g., narrow angle glaucoma, significant urinary outflow obstruction or obstructive bowel disease); treatment with another investigational drug within the previous 3 months.	Darifenacin controlled release (3.75, 7.5 or 15 mg once daily), darifenacin immediate-release (5 mg 3 times daily)	Placebo	Supported by Pfizer, Inc. and an educational grant from Novartis Pharma AG.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Lose, 2000[338] RCT Denmark N: 254	251 women reporting at least one bothersome lower urinary tract symptom after spontaneous or surgical post menopause	Known or suspected estrogen-dependent neoplasia or mammary, ovarian (endometroid) or corpus uteri malignancies, vaginal bleeding, clinically significant liver diseases, acute or intermittent porphyria, uterovaginal prolapse II-III, sex hormone treatment within the last 6 months, vaginal irritation other than atrophy derived or signs of vaginal ulceration; participation in clinical trials within last 3 months prior to inclusion	Estradiol-releasing ring, 7.5mg estradiol.	Estriol pessaries 0.5 mg every second day	Not reported	Not reported
MacDiarmid, 2005[339] Pooled U.S. N: 420	Men and women with UUI or mixed incontinence with a predominating urge component; with at least 6 (studies 1 and 3) or 7 (study 2) UUI episodes weekly when unmedicated; with known response to oxybutynin in study 1 or to anticholinergic medications in study 2.	Reported previously[40,340-342]	ER oxybutynin was initiated at 5 mg daily and adjusted in 5 mg increments at intervals of approximately 1 week until continence was achieved	None	Grant from ortho-McNeil Pharma-ceutical, Inc.	Not reported
Madersbacher, 1999[343] RCT U.S. N: 366	History of urgency or urgency incontinence, a maximum cystometric bladder capacity of ≤300 ml, age ≥18years and body weight ≥45kg	Detrusor hyperreflexia, postoperative (bladder) incontinence, intravesical obstruction, a postvoid residual urine of >15% of the maximal cystometric bladder capacity, acute UTIs, angina pectoris, glaucoma, megacolon, clinically relevant cardiac, renal or hepatic dysfunctions, tachy/dysrhythmias, frequency or nocturia due to heart or renal insufficiency, or overt cerebral sclerosis.	Propiverine 15mg three times a day	Oxybutynin 5mg twice a day, placebo three times a day	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Malhotra, 2010[344] RCT U.S. N: 261	Healthy subjects aged 45-65 years with a body mass index between 19 and 32kg/m2(inclusive); had no clinically relevant abnormal findings on the physical examination, ECG, blood pressure, pulse rate, medical history, or clinical laboratory results at the eligibility assessment visit and were characterized as extensive metabolizers for CYP2D6	Medical history of any serious disease of the internal organs or of the central nervous system; a history or presence of urinary retention, obstructive disturbance of bladder emptying, micturition disturbance, nocturia, or pollakiuria, for example, prostatic hyperplasia, or urethral stricture; a history of ischemic heart disease or a positive diagnostic cardiac stress test within 12 weeks before the start of the trial; a supine systolic blood pressure of<100mg or>160mmHg or a supine diastolic blood pressure of >95mmHg; a supine pulse rate of <50bpm or >100bpm; and any clinically relevant changes in ECG such as second-or third-degree AV block, or prolongation of the QRS interval to >110ms, the PR interval to >240ms, or QTc(Bazett's correction, machine read) to >480ms	Fesoterodine 4mg/28mg	Placebo	Funded by Schwarz BioSciences GmbH and Pfizer Inc.	Bimal Malhotra and Kuan Gandelman are employees of Pfizer Inc., New York, NY, U.S.A. Nolan Wood was an employee of Pfizer Inc., Sandwich, Kent, UK at the time the study was conducted. Richard Sachse is an employee of Schwarz BioSciences, Monheim, Germany
Malone-Lee, 2009[345] RCT UK N: 307	Male and female subjects aged ≥18 years with urinary frequency (defined as an average of ≥8 voids/24 hours, measured over a 7-day period) and urgency (with or without UUI), symptoms of OAB for ≥6 months before randomization, with no significant stress UI and adequate contraception.	Mean volume voided of >300 mL/void or a mean total volume of urine >3000 mL/24 hours; significant hepatic or renal disease, symptomatic UTI, diagnosed interstitial cystitis, un-investigated hematuria, or clinically significant BOO; anticholinergic drugs or other treatments for OAB in the 14 days before randomization; known hypersensitivity to tolterodine-ER or any of its recipients; oral cytochrome P450 3A4 inhibitors (e.g. macrolide antibiotics), and electro-stimulation or bladder retraining in the 3 months before randomization.	Tolterodine-ER (4 mg capsule od)	Placebo	Pharmacia (now Pfizer Ltd)	James Malone-Lee has received travel expenses for attending professional conferences from Pharmacia & Upjohn and Pfizer Inc, and has served as a consultant and received research funds from Pfizer Inc.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Malone-Lee, 2001[346] RCT United Kingdom, France, and the Republic of Ireland N: 177	Older men and women (age ≥65 years) with symptoms of urinary urgency, increased frequency of micturition (≥8 micturitions/24 hours), and/or urgency incontinence (≥1 episode/24 hours).	Significant stress incontinence, urinary outflow obstruction, urinary retention (as determined by palpation after voiding), symptomatic urinary infection, interstitial cystitis, unexplained hematuria, use of urinary catheterization or electro-stimulation, hepatic and renal disease with biochemical markers twice the upper limit of the normal reference range, concomitant antimuscarinic medication, previous treatment with tolterodine, and exposure to any other investigational drug in the preceding 2 months.	Tolterodine 1 mg or 2 mg twice daily	Placebo	Pharmacia & Upjohn AB	Not reported
Mattiasson, 2009[61] SOLAR62 Multinational N: 643	Men or women aged >=18 years with OAB symptoms were eligible if they gave written informed consent, were capable of completing a simplified bladder training regimen correctly, and were willing and able to complete a voiding diary correctly	Patients should not have received non-drug treatment for OAB, including electro stimulation therapy and pelvic floor exercises, in the 4 weeks before starting the study, or during the study except for those randomized to receive bladder training instructions. Patients were also excluded if they had received cognitive bladder training in the previous 6 months, or if they intended to commence bladder training other than the study regimen during the study.	Simplified Bladder training + Solifenacin	Solifenacin 5mg or 10mg	Research Grant from Astellas Pharma Europe Ltd.	Anders Mattiason: Astellas, Ferring: Pfizer; Alberto Masala: Astellas, Angelini Group; Richard Morton and John Bolodeoku: employees of Astellas

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Mattiasson, 2003[347] Tolterodine Scandinavian Study Group Sweden, Norway and Denmark N: 501	Men and women aged ≥18 years with symptoms of urinary frequency (≥8 micturitions/24h on average) and urgency (a strong and sudden desire to urinate), with or with no urgency incontinence. Women of child-bearing potential were required to be using a reliable birth control method to enter the study	Any contraindication to antimuscarinic therapy; use of electro stimulation therapy or behavioral therapy within the previous 3 months; patients with an indwelling catheter or on intermittent catheterization; pregnancy and lactation; and use of anticholinerigc agents or concomitant treatment for an overactive bladder (other than estrogen replacement therapy started at least 2 months before study commencement)	Tolterodine + Simplified Bladder training	Tolterodine	Supported by Pharmacia Corporation	Not reported
Milani, 1993[348] RCT Milan N: 50	Women over 18 years of age with motor or sensory urgency	Severe illness, overt neurological diseases, acute or chronic urinary tract infections or obstructive diseases, pregnancy, taking concomitant medication which could affect urinary symptoms, continence or bladder function.	Flavoxate was 1 200 mg (400 mg t.i.d.)	Oxybutynin 15 mg (5 mg t.i.d.)	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Millard, 1999[349] RCT Sweden N: 316	Male and female patients 18 years old or older with cystometrically proved detrusor overactivity (idiopathic instability or detrusor hyperreflexia, or uninhibited phasic detrusor contractions with an amplitude of 10 cm. water or greater) and average urinary frequency of 8 or more voids per 24 hours; urgency incontinence (an average of 1 or more incontinence episodes per 24 hours on the frequency volume chart) and/or urinary urgency.	Inadequate contraception; demonstrable stress incontinence (fluid escaping from the external urethral orifice during coughing when the bladder was stable), clinically significant voiding difficulty (maximum flow rate less than 10 ml. per second with post-void residual volume greater than 200 ml.), proved recurrent urinary tract infection, interstitial cystitis, uninvestigated hematuria or any bladder cancer; catheterization, indwelling catheterization , hepatic or renal disease, or narrow angle glaucoma, electro-stimulation therapy or bladder training, any primarily anticholinergic drug initiated 14 days before or at any time during the study, an unstable dose of any treatment with anticholinergic side effects; average total voided volume of greater than 3,000 ml/24 hours, or treatment with any investigational drug during or 2 months before the study.	1 or 2 mg. tolterodine twice daily	Placebo	Pharmacia and Upjohn AB	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Millard, 2004[350] Duloxetine UI Study Group N: 458	Women aged ≥18 years with a clinical diagnosis of troublesome SUI of at least 3 months' duration with the predominant symptom of SUI with ≥7 incontinent episodes per week. An 'episode' was defined as an easily noticed leakage of urine that wet a pad or clothing and occurred with a physical stress such as coughing, sneezing or exercising. Patients also needed to report a diurnal frequency of <9 per day, nocturnal frequency of and the absence of predominant symptoms of urgency incontinence. In addition, objective testing was used to confirm normal bladder capacity and the sign of SUI. With the patient supine the bladder was filled with saline at 100 mL/min with no pressure measurements; positive cough-stress test (visualization of urine leakage concurrent with a cough) and a positive stress pad test (leakage of >2.0 g) (clinical algorithm has a sensitivity of 92% for urodynamic stress incontinence).	Inability to tolerate filling to 400 mL were excluded, as were those who experienced a first sensation of bladder filling at <100 mL, or who had no sensation at any time during the filling	Duloxetine 40 mg twice daily	Placebo	Sponsored by Eli Lilly and Company and Boehringer Ingelheim.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Moore, 1990[351] RCT N: 53	Patients with involuntary detrusor contractions >30cm H2O during the filling phase of cystometry	Those with neurological and other urological disorders; patients with coexistent genuine stress incontinence, low compliance bladder, bacterial or interstitial cystitis, age greater than 75 years or previous treatment with oxybutynin	Oxybutynin hydrochloride	Placebo	Tillots Laboratories provided oxybutynin and placebo tablets	NR
Naglie, 2002[352] RCT U.S. N: 86	Men and women 65 years or older with a history, physical exam and urodynamic findings consistent with urgency incontinence, and at least 4 documented episodes of urinary incontinence on a 5-day voiding record.	An indwelling or condom catheter, or intermittent catheterization; a clinical history of stress urinary incontinence; a history of >2 urinary tract infections per year; insulin dependent diabetes; spinal cord pathology; symptomatic orthostatic hypotension, congestive heart failure or ventricular arrhythmia; taking any calcium channel blocker; cognitive impairment; evidence of bladder cancer; cystoscopic or urodynamic evidence of outlet obstruction; post-void residual urine volume >100 cc or more than trivial urinary leakage occurring with coughing/straining in the sitting or standing position; unable to complete a 5-day voiding record during the run-in period.	30 mg. nimodipine twice daily	Placebo	Research grant from the Physicians' Services Incorporated	Not reported
NCT00269750[55] RCT U.S. N: 105	Men and women, age 40 to 75, with urge or mixed UI provided that stress UI was not the predominant manifestation of mixed UI. Patients who were currently taking immediate-release oxybutynin (Ditropan), hyoscyamine, or propantheline, or who had taken Ditropan® in the past for urge or mixed UI.	Not reported	Oxybutynin chloride ER	Oxybutynin chloride IR	ALZA Corporation	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
	Patients who had taken and discontinued Ditropan® for urge or mixed UI should not have discontinued due to failure of efficacy; patients who had at least six urge UI episodes per week recorded on the Run-in Diary after washout of anticholinergic medications. Patients who were able to differentiate incontinent episodes associated with urgency from incontinent episodes not associated with urgency when recording incontinent episodes in the diary. The Run-in Diary after washout of all anticholinergic medications must have demonstrated that the number of urgency incontinent episodes per week was greater than the number of incontinent episodes not associated with urgency per week.					

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
NCT00168454[53] RCT U.S. N: 313	Must be between 18-85 years old; must have been diagnosed by his/her doctor with overactive bladder at least 6 months ago; must weigh at least 50 kg (110 lbs); must be willing and able to record information regarding bladder function into a diary (provided); and must be willing and able to complete the entire course of the study	Cannot currently be cathetered as a way to control incontinence and must not have used botulinum toxin type A or any other botulinum toxin previously for any condition	Botulinum toxin Type A	Placebo	Sponsored by Allergan, Inc.	Principal Investigators are not employed by the organization sponsoring the study.
NCT00444925[56] RCT Multinational N: 1,712	Adult overactive bladder (OAB) patients who present with OAB symptoms, including urinary frequency ≥ 8 per day and urgency urinary incontinence ≥1 per day	Patients with conditions that would contraindicate for fesoterodine use, e.g., hypersensitivity to the active substance (fesoterodine) or to peanut or soya, urinary retention, and gastric retention; patients with significant hepatic and renal disease or other significant unstable diseases; and OAB symptoms caused by neurological conditions, known pathologies of urinary tract, etc.	Fesoterodine	Tolterodine/ Placebo	Sponsored by Pfizer Inc.	Principal Investigators are not employed by the organization sponsoring the study.
NCT00536484[57] RCT U.S. N: 883	Adults 18 years and older; overactive bladder symptoms for greater than or equal to 3 months; mean urinary frequency of greater than or equal to 8 micturitions per 24 hours in bladder diary; and mean number of urgency episodes greater than or equal to 3 per 24 hours in bladder diary.	Known etiology of OAB (e.g., neurogenic, local urinary tract pathology); previous history of acute urinary retention requiring catheterization or severe voiding difficulties in the judgment of the investigator, prior to baseline; and unable to follow the study procedures, including completion of self-administered bladder diary and patient reported outcome questionnaires.	Fesoterodine	Placebo	Sponsored by Pfizer Inc.	Principal Investigators are not employed by the organization sponsoring the study.
NCT00178191[54] RCT	Adults 21 years and older; must have completed a	Children (< 21 years old), pregnant women and prisoners; history of	Botulinum toxin Type A	Placebo	Sponsored by University of	Principal Investigators are not employed by

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
U.S. N: 28	routine evaluation of incontinence (urodynamics, bladder diaries, and pad weights) through the urogynecology clinic within 3 months of the screening visit; symptoms of urgency incontinence associated with leakage on bladder diary; 24-hour pad weight >100 cc's (volume requiring multiple daily diaper changes); absence of a bladder infection or other condition that could explain urinary leakage; absence of stress incontinence or a cough leak point pressure >100 cm H2O on cystometry (this correlates with mild stress incontinence); failed anticholinergic therapy; willingness and ability to perform intermittent clean catheterization (due to the risk of prolonged urinary retention from Botox); the ability and willingness to return for surveillance evaluations; a negative urine pregnancy test if at risk for pregnancy; and competent to give signed consent and complete all of the study measures.	carcinoma of the bladder; absence of a measurable detrusor contraction on a pressure flow micturition study; a foreign body in the bladder or other correctable etiology for the UUI; prior documented resistance to Botox; gross fecal incontinence (due to confounding effects on pad weights and counts); known allergy to lidocaine or related compounds (used for local analgesia); known allergy to or inability to take both Bactrim DS or Ciprofloxacin (used for urinary tract infection prophylaxis); current use of an aminoglycoside or preparing for general anesthesia within 1 week (risk of synergetic effects); and known neurologic conditions such as Parkinson's disease, myasthenia gravis, multiple sclerosis, autonomic dysfunction, Lambert-Eaton syndrome, Amyotrophic Lateral Sclerosis or other neurologic disorder that may impact urinary function or the effect of Botox.			Rochester, New York, U.S.A.	the organization sponsoring the study.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Nitti, 2007[353] RCT U.S. N: 836	Men and women 18 years or older with OAB syndrome for 6 months or greater, including urinary frequency (8 micturitions or greater per 24 hours) and urinary urgency (6 episodes or greater during the 3-day diary period) or UUI (3 episodes or greater during the 3-day diary period).The amended inclusion criterion required 3 or greater UUI episodes in 3-day diary; at least moderate bladder problems on a Likert scale that was almost identical to the patient perception of bladder condition.	Positive pregnancy test and non adequate contraception throughout the trial; lower urinary tract pathology that could in the opinion of the investigator be responsible for urgency or incontinence, such as significant stress incontinence, urolithiasis, interstitial cystitis or urothelial tumors; pelvic organ prolapse grade III or greater; clinically relevant bladder outlet obstruction; PVR volume greater than 100 ml; polyuria (greater than 3 l/24 hours); symptomatic or recurrent urinary tract infections; current treatment with antimuscarinic agents; a neurogenic cause of OAB; clinically relevant arrhythmia, unstable angina or a corrected QT interval (Bazett's formula) of greater than 500 milliseconds; or current treatment or treatment within the last 4 weeks with electro-stimulation or bladder training.	4 mg fesoterodine or 8 mg fesoterodine once daily	Placebo	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Norton, 2002354 Sahai, 2006[355] Duloxetine Urinary Incontinence Study Group. U.S. N: 553	Women aged 18 to 65 years with a predominant symptom of stress urinary incontinence for at least 3 months with ≥4 incontinent episodes per week (easily noticeable leakage of urine that wets a pad or clothing and occurs with a physical stress such as coughing, sneezing, or exercising); urinary diurnal frequency ≤7 per day, nocturnal frequency ≤2 per day; both a positive cough stress test, visualization of urine leakage concurrent with a cough) and leakage of >2.0 g.	Predominant symptoms of enuresis or urgency incontinence, and no previous continence or prolapse surgical procedure, inability to tolerate the filling, who had a first sensation of bladder filling at <100 mL, or who had no sensation at any time during the filling.	Duloxetine at one of three doses (20 mg/d, n = 138 women; 40 mg/d, n = 137 women; or 80 mg/d, n = 140 women)	Placebo	Supported by Eli Lilly and Company.	Not reported
Ozdedeli, 2010[356] RCT Turkey N: 35	35 female patients who presented to the University Departments of Urology and Physical Medicine and Rehabilitation for urgency incontinence and had overactive bladder or mixed incontinence with predominantly overactive bladder symptoms	History of pelvic surgery, a neurological deficit or peripheral neuropathy that may cause neurogenic bladder, presence of a medical condition that may preclude anticholinergic drug use, pregnancy or suspicion of pregnancy, cardiac pacemaker, genitourinary infection or hemorrhage, deterioration in cognitive or intellectual functions, anatomical abnormality that hinders the use of vaginal probe, and post-voiding residual volume >100mL	Trospium hydrochloride	Electrical stimulation	Not reported	Not reported
Peters, 2009[357] MacDiarmid, 2010358The Overactive Bladder Innovative	The Overactive Bladder Innovative Therapy trial : ambulatory men and women with OAB symptoms, with or without a history of previous	OAB pharmacotherapy within the previous month, primary complaint of stress urinary incontinence, demonstrated sensitivity to tolterodine or its ingredients, pacemakers or implantable	Weekly percutaneous 30-minute tibial nerve stimulation	4 mg daily extended-release tolterodine with a subsequent	Supported by Uroplasty Inc.	Kenneth Peters has financial interest and/or relationship with Medtronic Inc., Advanced Bionics, Boston Scientific,

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Therapy U.S. N: 100	anticholinergic drug use, with at least 8 voids per 24 hours	defibrillators, excessive bleeding, urinary or gastric retention, nerve damage or neuropathy, uncontrolled narrow angle glaucoma, positive urinalysis for infection or pregnancy, or current pregnancy or planning to become pregnant during the trial		decrease to 2 mg daily if intolerability was experienced		Allergan, Pfizer, Celegene and Trillium Therapeutics; Scott MacDiarmid has financial interest and/or other relationship with Watson, Pfizer, Astellas, Allergan, Novartis and Uroplasty; Leslie S. Wooldridge has financial and /or relationship with Astellas, Uroplasty and Watson; Eric Rovner has financial and/or relationship with Novartis, Astellas, Allergan, Contura, Solace, Tengion and Pfizer; Steven Siegel has financial and/or relationship with Medtronic, American Medical Systems, Uroplasty, Uromedica, North Central Section of the American Urological Association, and Society for Urodynamics and Female Urology; SU.S.A. B. Tate has financial and/or relationship with C.R. Bard; Peter

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
						Rosenblatt has financial and/or relationship with Pfizer; Brian A. Feagins has financial and/or relationship with Medtronic, American Medical Systems, Novartis, Astellas, Uroplasty and Boston Scientific.
Pontari, 2010[359] RCT U.S. N: 20	Female gender, age 18 years or older, with symptoms of urinary frequency of at least 8 voids per day for at least 6 months	Stress incontinence, total daily volume greater than 3 L, significant hepatic or renal disease, symptomatic or recurrent urinary tract infections, concomitant sacral neurostimulation therapy, claustrophobia with magnetic resonance imaging, bladder outlet obstruction, self-catheterization, post-void residual volume greater than 100 ml, women who pregnant or nursing, or women of child bearing potential not using reliable contraceptive methods, or any neurological condition which may contribute to bladder dysfunction such as multiple sclerosis.	Tolterodine	Placebo	Supported by an educational grant form Pfizer	Michel Pontari has financial interest and/or relationship with Pfizer, Sanofi and Endo Pharmaceuticals

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Rentzhog, 1998[360] RCT Multinational N: 81	Men and women aged 18-75 years; presence of symptoms of urinary urgency, increased frequency of micturition (at least 8 micturitions per 24 hours) and/or urgency incontinence (at least one episode of incontinence per 24 hours) during a 1-week pre-study run-in period. All eligible patients should have had urodynamically confirmed detrusor instability (defined as a phasic increase in detrusor pressure in the presence of typical symptoms) and a maximum urinary flow rate (Q max)of >=15mL/s (patients with a lower Qmax were eligible for inclusion provided there was no evidence of clinically significant bladder outlet obstruction), either sterile urine or clinically insignificant bacteriuria, and normal routine laboratory tests	Stress incontinence or detrusor hyperreflexia; clinically significant cardiac, hepatic, renal or hematological disorders; patients with contraindications to antimuscarinic agents; and pregnant or lactating women and women of childbearing age who were not using reliable contraception.	Tolterodine	Placebo	Pharmacia and Upjohn AB, Uppsala. Sweden	NR
Richter, 2010[361] ATLAS N: 446	Women at least 18 years old with symptoms of stress only or stress-predominant mixed-incontinence symptoms.	Not reported	Behavioral therapy	Pessary or pessary+ behavioral therapy	Grants from the Eunice Kennedy Shriver National Institute of Child Health	Dr. Burgio is a consultant for Pfizer (New York) and on the advisory board for Astellas (Deerfield, IL). Dr. Brubaker is a Research Consultant

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
					and Human Development; National Institute of Diabetes and Digestive and Kidney Diseases, and National Institutes of Health Office of Research on Women's Health	for Pfizer (New York, NY) and a Research Investigator for Allergan (Irvine, CA). Dr. Zyczynski has performed contract research for Johnson and Johnson (New Brunswick, NJ). Dr. Lukacz is a consultant for Pfizer (New York, NY), Medtronic (Minneapolis, MN) and Watson Pharmaceuticals (Corona, CA). She has served on the speaker's bureau for Novartis (Basel, Switzerland) and Proctor and Gamble (Cincinnati, Ohio). She has been a consultant and proctor for Intuitive Surgical Corporation (Sunnyvale, CA),and she has been an editor First Consult. Dr. Schaffer is on the Speaker's bureau and National Advisory Board of Astellas/ GlaxoSmithKline (Deerfield, IL; Philadelphia, PA) and on the Specialty Surgeons Advisory Board of Cadence

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
						Pharmaceuticals (San Diego, CA)
Rios, 2007[362] RCT U.S. N: 58	Women clinically diagnosed with urgency incontinence and proven urodynamic DO for at least 6 months prior to the study	The use of anticholinergics or tricyclic antidepressants in the last 2 months, neurologic conditions, urinary tract infection, pelvic prolapses (greater than grade 2), history of pelvic radiation or bladder tumor, poor bladder wall compliance, and detrusor underactivity.	Single intravesical dose of 100 ml of resiniferatoxin 50 nM	Single intravesical dose of 100 ml placebo	Departments of Urology of the Federal University of Sao Paulo, Paulista School of Medicine and Hospital do Servidor Publico Estadual de Sao Paulo.	Not reported
Robinson, 2007[363] The Tamsulosin Study Group Multinational N: 364	Women aged 18-75 years with symptoms of OAB (urinary urgency and frequency, with or without urgency incontinence) for >=3 months; patients must have recorded a mean of at least eight voids/24h in the previous 3 days and one or more of the following during the 3-day period)at least 3 episodes of urinary urgency incontinence; or at least three episodes of urgency	Stress incontinence or mixed incontinence where stress symptoms were predominant and women with neurogenic DOA	Tolterodine	Placebo	Funded by Astellas	Gerben Terpstra and John Bolodeoku are both employees of the sponsor
Rogers, 2009[364] Rogers, 2008365 RCT U.S. N: 413	Heterosexual women ≥18 years with OAB symptoms for ≥3 months; mean of ≥8 micturitions per 24 hours, including ≥0.6 UUI episodes and ≥3 OAB micturitions (i.e. micturitions associated with at least a moderate	One subject in the tolterodine group with an extreme increase in the number of UUI episodes per 24 hours from baseline to week 12 was identified as an influential outlier and was excluded from all efficacy analyses	Tolterodine-ER	Placebo	Funded by Pfizer Inc.	Zhanna Jumadilova, Franklin Sun, Jon Morrow and Zhonghong Guan have disclosed that they are employed by Pfizer Inc. Rebecca Rogers has disclosed that she received

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
	degree of urgency), in a 5-day bladder diary at baseline; subjects also reported being in a stable, sexually active relationship (self-defined) for ≥6 months and having at least some moderate problems related to their bladder condition on the Patient Perception of Bladder Condition scale.					speaker honoraria and research funding support from Pfizer Inc., and has served a consultant for Pfizer Inc. She has also disclosed that she serves on the advisory board for American Medical Systems. Gloria Bachmann has disclosed that she has served as a consultant and received research funding support from Astellas Pharma Inc., Wyeth, and other pharmaceutical companies. Harriett Scraper has disclosed that she has received speaker honoraria from Pfizer Inc., Astellas Pharma, Inc., and Watson Inc. All peer reviewers receive honoraria from CMRO for their review work. Peer reviewer 1 has disclosed that he/she is on the speakers' bureau of Watson Pharmaceuticals. Reviewer 2 has no relevant financial relationships

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Rogers, 2009[366] RCT U.S. N: 202	Sexually active women (≥18 years) reported OAB symptoms for ≥3 months, mean of ≥8 micturitions per 24 hour, including ≥0.6 UUI episodes and ≥3 OAB micturitions (i.e., micturitions associated with at least a moderate degree of urgency), in 5-day bladder diaries at baseline; reported being in a stable sexually active relationship (self-defined) with a male partner for ≥6 months; and indicated at least "some moderate problems" related to their bladder condition on the Patient Perception of Bladder Condition questionnaire.	Reported previously[365] Women who did not complete active treatment in the original study, women who were randomized to placebo were excluded from the analysis.	Tolterodine extended release 4 mg/day	Placebo for 12 weeks, none for 24 weeks	Pfizer Inc	Gloria Bachmann: Grant/Research Support: Astellas, Wyeth, Bayer, Duramed, Pfizer, Boehringer-Ingelheim, Roche, Merck, QuatRx, Bionovo, Glaxo Smith Kline, Femme Pharma, Hormos, Covance, Novartis, Johnson & Johnson, Boston Scientific, Novonordisk

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Rogers, 2008[366] RCT U.S. N: 413	Women (aged ≥18 years) with a mean of greater than or equal to eight micturitions, ≥0.6 UUI episodes, and greater than or equal to three OAB micturitions (i.e., micturitions associated with moderate or severe urgency or UUI) per 24 hours with at least "some moderate problems" on the Patient Perception of Bladder Condition Questionnaire; with OAB symptoms for ≥3 months and to have been in a stable, sexually active relationship (self-defined) with a male partner for ≥6 months.	Stage ≥3 pelvic organ prolapse, history of lower urinary tract surgery, lifelong sexual dysfunction unrelated to lifelong UUI, or predominant stress UI.	Tolterodine ER (4 mg)	Placebo	Pfizer Inc	Not reported
Rudy, 2006[367] RCT U.S. N: 658	Female and male patients aged 18 years or older with OAB symptoms for at least 6 months; a minimal urinary frequency average of >10 toilet voids/day, symptoms of urgency (i.e., at least one "mild," "moderate," or "severe" urgency severity rating under the "degree of urgency," associated with "toilet void" events); >7 urge urinary incontinence episodes/week	Predominately stress, insensate, or overflow UI; neurogenic bladder disorders, significant renal disease, uninvestigated hematuria, and urinary tract infection at washout or more than twice during the prior year; significant bladder outlet obstruction defined as a postvoid residual volume >100 mL and in the clinical judgment of the investigator; using any anticholinergic drug or other drug therapy for OAB within 21 days before randomization, history of bladder surgery	Trospium chloride 20 mg twice daily	Placebo	Indevus Pharma-ceuticals	D. Rudy, K. Cline, R. Harris, K. Goldberg, and R. Dmochowski are study investigators funded by the sponsor

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Rudy, 2006[34] RCT analysis U.S. N: 658	Men and women ≥18 years old with OAB symptoms for ≥6 months, a minimum urinary frequency of 70 toilet voids per 7 days (i.e. mean ≥10 voids/day), and symptoms of urgency; with at least seven UUI episodes/week	Predominately stress, insensate, or overflow; neurogenic bladder disorders, significant renal disease, uninvestigated hematuria, >2 UTIs during the previous year; significant BOO, concurrent anticholinergic drug use or other drug therapy for OAB within 21 days before randomization, bladder surgery within 6 months, cancer, interstitial cystitis, diuretic use, estrogen therapy, and non-pharmacological bladder therapy that were not part of a stable, long-term program.	Trospium chloride 20 mg twice daily	Placebo	Indevus Pharma-ceuticals	Not reported
Rufford, 2003[368] RCT England N: 40	Postmenopausal women (>1 year at menopause) with the 'urge syndrome'; with estradiol <150pmol/l in women after hysterectomy with no contraindication for estrogen therapy.	Medication treatment of urge syndrome, diuretics, HRT, history of diabetes, endometrial thickness >4mm urinary tract infection, pelvic masses and urogenital prolapse.	25mg 17 beta-estradiol implant subcutaneous tissue.	Placebo	Educational grant from Organon	Not reported
Salvatore, 2005[369] RCT UK N: 96	Over a period of 1 year women with urinary symptoms referred to the Urogynecology Department of the King's College Hospital in London were recruited into this study. Women with urinary symptoms and having a videourodynamic diagnosis of detrusor overactivity or low bladder compliance and who signed an informed consent.	Not reported	Oxybutynin 2.5 mg twice a day to a maximum dose of 5 mg three times a day over a period of 6 weeks,	Oxybutynin 5 mg to increase oxybutynin to a maximum dose of 5 mg three times a day over a period of 6 weeks.	Not reported	Not reported
Sand, 2009[370]	Men and women ≥18	Lower urinary tract pathology that	Fesoterodine 4	Placebo	Schwarz Bio-	Peter Sand is an

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Pooled U.S. N: 1,971	years of age who reported OAB symptoms for ≥6 months and demonstrated urinary frequency (≥8 micturitions per 24 hours) and either urinary urgency (≥6 total episodes) or UUI (≥3 total episodes) in 3-day bladder diaries at least moderate bladder problems on a six-point Likert scale: "My bladder causes me no problems (0), very minor problems (1), minor problems (2), moderate problems (3), severe problems (4), or very severe problems (5)."	could (in the investigator's opinion) be responsible for urgency or incontinence, significant pelvic prolapse (grade III or higher), clinically relevant bladder outlet obstruction, polyuria (>3 L/24 hours), symptomatic or recurrent urinary tract infections, postvoid residual volume >100 mL, and recent treatment with an antimuscarinic agent.	or 8 mg, or tolterodine extended release (ER) 4 mg		Sciences GmbH and Pfizer Inc.	advisor for Astellas, Allergan, American Medical Systems, Boston Scientific, Coloplast, Glaxo-SmithKline, Ortho McNeil, Pfizer Inc, and Watson Pharma; an investigator for Allergan, Boston Scientific, Ortho McNeil, Pfizer Inc, and Watson Pharma and a speaker for Allergan, Astellas, GlaxoSmithKline, Ortho McNeil, and Watson Pharma. Jon Morrow and Tamara Bavendam are employees of Pfizer Inc. Dana Creanga is a consultant for Pfizer Inc. Victor Nitti is an investigator for Schwarz Pharma, a consultant and lecturer for Pfizer Inc and Novartis, a consultant and investigator for Allergan, a consultant for Astellas, an advisor for Watson Pharma, Serenity Pharmaceuticals, and Coloplast Corp, and a lecturer for American Medical Systems.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Sand, 2004[226] RCT U.S. N: 276	Participants with overactive bladder who had ≥7 and ≤50 urgency incontinence episodes/ week and ≥10 voids/24 hours were included.	Those with mixed stress and urgency incontinence were eligible if the majority of the leakage accidents were related to urgency incontinence. Participants with other causes of incontinence (e.g. urinary tract infection, interstitial cystitis, urinary tract obstruction, urethral diverticulum, bladder tumor, bladder stone) were excluded, as were those who had delivered a baby or undergone pelvic, vaginal or bladder surgery fewer than 6 months before study enrollment. Participants with a postvoid residual urine volume of >150 ml at the time of screening were also excluded. In addition, those with clinically significant medical problems, or other organ abnormalities or pathologies for whom the administration of extended-release oxybutynin chloride or tolterodine tartrate would present an undue risk (medically uncontrolled cardiovascular, pulmonary, gastrointestinal, renal, endocrine, neurological, autoimmune, hematological, urological or psychiatric disorders, significantly reduced hepatic function or renal impairment) were excluded. Participants with hematuria or a positive urine culture, those with uncontrolled narrow-angle glaucoma, obstructive uropathy, myasthenia gravis, pelvic organ prolapse to the hymeneal ring, gastrointestinal conditions such as partial or complete obstruction, pre-existing severe	ER Oxybutynin Chloride	Tolterodine Tartrate	ALZA Corporation, Mountain View, California	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
		gastrointestinal narrowing (pathologic or iatrogenic), decreased gastrointestinal motility (paralytic ileus, intestinal atony, chronic and severe constipation), or those at risk of gastric retention, were excluded. Subjects were recruited regardless of whether or not they had received prior treatment and regardless of their response to prior anticholinergic therapy. Any medications used for the treatment of overactive bladder, or medications with anticholinergic activity used to treat other conditions, had to be discontinued at screening. Participants who had taken an investigational drug within the last month or had known allergies or hypersensitivities to oxybutynin chloride, tolterodine tartrate, or components of the respective tablets were excluded. Participants with current drug or alcohol abuse, female participants who were pregnant or breastfeeding, and participants who were not capable of following the study schedule or directions were excluded. Those who were not able to swallow the medication without chewing, crushing, biting, dividing or dissolving the capsule were also excluded.				
Sand, 2009[371] Dmochowski, 2010[372] Pooled N: 989	Subgroup analysis of women aged ≥18 years with OAB of ≥6 months' duration with urinary urgency (≥1 severe urgency severity rating on the validated Indevus	Predominantly stress, insensate, or overflow incontinence (as determined by investigators), demonstrable renal or urinary disorders including neurogenic bladder disorders, significant renal disease, uninvestigated hematuria, current or	Trospium ER (60-mg capsules)	Placebo	Allergan, Inc. and Endo Pharma-ceuticals (formerly Indevus Pharma-	Peter K. Sand, MD, serves as an advisor and speaker for Allergan, Inc., Astellas Pharma US, Inc., Pfizer, Ortho-McNeil, Colplast, and

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
	urgency severity scale); urinary frequency (average ≥10 voids/day, occurring at any time of the 24-hour period); and pure urge or mixed urinary incontinence with predominant UUI, with an average of ≥1 UUI episode/day	a history of ≥3 episodes of urinary tract infection in the preceding year, bladder outlet obstruction, interstitial cystitis, or bladder cancer; subjects requiring long-term diuretic or estrogen therapy			ceuticals Inc.).	Watson Pharmaceuticals. Dr. Sand has received grants from Allergan, Inc., Astellas Pharma US, Inc., Boston Scientific, Pfizer, Ortho-McNeil, Watson Pharmaceuticals, and Antares Pharma. Roger R. Dmochowski, MD, has financial relationships with Allergan, Inc., Pfizer, Watson Pharmaceuticals, Novartis, and Astellas Pharma US, Inc. David R. Staskin, MD, serves as a consultant and lecturer for Allergan, Inc., Pfizer, Watson Pharmaceuticals, and Astellas Pharma US, Inc. Norman R. Zinner, MD, serves as a consultant, speaker, and/or for a clinical trial for Allergan, Inc., Actelion, Watson Pharmaceuticals, Pfizer, Novartis, Ferring Pharmaceuticals, and GlaxoSmithKline. Rodney A. Appell, MD

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
						(deceased), was on the advisory board for Pfizer, Boston Scientific, and Astellas Pharma US, Inc. Dr. Appell held stock in American Medical Systems. Dr. Appell served as an investigator for Allergan, Inc., Astellas Pharma US, Inc., Watson Pharmaceuticals, American Medical Systems, Boston Scientific, Solace Technology, Bulkamid, and Novasys Medical.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Sand, 2006[373] Sand, 2007[374] The Multicenter Assessment of Transdermal Therapy in Overactive Bladder with Oxybutynin trial U.S. N: 2,592	At least 18 years of age; have 1 or more symptoms of OAB (urge urinary incontinence, urgency, and/or frequency); be willing to discontinue any over-the-counter and/or prescription treatment for OAB for the duration of the study; be capable of completing Quality of Life Questionnaires without assistance; be willing and able to comply with the protocol; and for females of childbearing potential, have a negative urine pregnancy test and have used a medically acceptable contraceptive method.	Urinary retention or uncontrolled narrow-angle glaucoma or risk for these conditions; demonstrated hypersensitivity to oxybutynin or other components of the product; had 1 or more treatable conditions that might cause urinary incontinence or urgency (i.e., urinary tract infection, prostatitis, bladder tumor, bladder stone); had received an investigational product within 30 days prior to participation in this study; had been previously treated with transdermal oxybutynin; resided in long-term care facilities or nursing homes; or were judged by the investigator to be unsuitable for enrollment into the study	Transdermal oxybutynin 3.9 mg plus behavioral intervention of enhanced patient education	Transdermal oxybutynin alone	Supported by Watson Laboratories (Morriston, NJ)	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Sand, 2011[375] RCT U.S. N: 1,165	Male and female subjects experiencing OAB for ≥6 months who met the following criteria (based on a 3-day bladder diary) were enrolled: urinary frequency of ≥30 toilet voids in 3 days (i.e. mean ≥10 toilet voids per day); ≥1 'severe' urgency severity rating in 3 days (according to the Indevus Urgency Severity Scale); and pure urge urinary incontinence (UUI) or mixed urinary incontinence with predominant UUI, with ≥3 UUI episodes in 3 days (i.e. mean ≥1 UUI/day).	Not reported	Trospium	Placebo	Supported by Allergan, Inc., and Endo Pharma-ceuticals (formerly Indevus Pharma-ceuticals, Inc.),Watson, Pfizer, Astellas and GSK.	Michael G. Oefelein is an employee of the sponsor; Pamela I. Ellsworth is a consultant speaker for Pfizer, a speaker for Novartis and is on the speaker bureau for Allergan; Eric S. Rovner is a paid consultant to Allergan and is a study investigator funded by Allergan; David R. Staskin is a speaker for Allergen, Astellas, Pfizer and Watson, and is a paid consultant to Allergen, Astellas and Pfizer; Peter K. Sand is a an advisor, investigator and speaker for Allergan, Watson, Pfizer, Astellas and GSK.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Scarpero, 2011[376] RCT Multinational N: 890	Men and women who successfully completed double-blind treatment without meeting discontinuation criteria and did not experience any AE that, in the investigator's opinion, would jeopardize the subject's well-being upon continuation of treatment were eligible to participate in the open-label extension study.	Residual volume >200 mL, absolute corrected QT interval value >500ms or individual increase of >60 ms relative to the double-blind study baseline, those who had experienced any ongoing serious adverse effects during double-blind treatment that were treatment-related or of unknown origin, or had experienced an undercurrent illness that required termination of treatment.	Fesoterodine	None; extension of open-label study	Funded by Schwarz BioSciences GmbH and Pfizer Inc	Harriette Scarpero has been a consultant for AMS, Pfizer, and Watson and a speaker for Astellas and Watson. Con J. Kelleher has received educational funding for research from Pfizer and Astellas and is an advisor for Pfizer and Astellas. Peter K. Sand has been an advisor and speaker for Allergan, Astellas, GlaxoSmithKline, Ortho, Pfizer, and Watson and has received research grants from Allergan, Contura, Biofrom, Boston Scientific, Ortho, Pfizer, and Watson. Sandra Berriman, Tamara Bavendam, and Martin Carlsson are employees of Pfizer Inc. The peer reviewers on this manuscript have disclosed that they have no relevant financial relationships.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Schagen van Leeuwen, 2008[377] RCT Germany, France, the Netherlands, Spain, Sweden, Switzerland and South-Africa N: 265	Community-dwelling women of ≥65 years with symptoms of SUI or S-MUI for ≥3 consecutive months and ≥7 incontinence episodes per week as determined by the stress/urgency incontinence questionnaire S/UIQ; predominant stress UI with ≥50% of incontinence episodes had to be due to stress UI; post-void residual ≤100mL.	Language or significant cognitive barriers (modified mini-mental state exam score <80; >>4 urinary tract infections in the preceding year or a positive urine culture at visit 1, any nonpharmacological intervention (surgery, bulking agents, initiation of pelvic floor muscle training) for incontinence or prolapse within 3 months before study entry or throughout the study, increased suicidal risk (score ≥2 on question 9 of the Beck depression inventory), history of syncopal episodes, or hepatic dysfunction, defined as serum glutamate–pyruvate–transaminase (alanine aminotransferase) or glutamate–oxaloacetate–transaminase (aspartate aminotransferase) ≥3 times upper limit of normal (ULN) or bilirubin ≥1.5 times ULN.	Duloxetine 20 mg twice daily	Placebo	Funding was provided by Eli Lilly and Company, and Boehringer Ingelheim, GmbH	Not reported
Staskin, 2006[37] Pooled N: 3,298	Pooled analysis of 4 RCTs of men and women over 18 years with OAB (mean of ≥8 voids/24 hours, plus ≥1 incontinence episode or ≥1 urgency episode/24 hours) during the baseline 3- day voiding diary period.	Women with a history of stress-predominant UI, positive cough-provocation test; no baseline assessment or no episodes of the individual diary symptom during the baseline diary screening period.	Solifenacin 5mg; Solifenacin 10mg;	Placebo	Yamanouchi Pharma Inc.	D. Staskin is a consultant for Pfizer, Ortho- McNeil, Indevus, Watson, Astellas and Novartis; A. Te is an investigator for Sanofi- Aventis, Pfizer and NIH, and is a consultant for Sanofi-Aventis, Glaxo and Astellas. Source of funding: Astellas.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Staskin, 2007[45] Trospium Study Group. U.S. N: 601	Not reported	Not reported	Trospium chloride 60 mg/day	Placebo	Esprit Pharma and Indevus Pharma-ceuticals	Not reported
Staskin, 2004[378] RCT U.S. N: 658	Not reported	Not reported	Trospium chloride 20-mg twice daily	Placebo	Not reported	Not reported
Staskin, 2009[31] RCT U.S. N: 789	Men and women with OAB who were 18 years or older; urge or mixed UI with a predominance of urge UI episodes as well as a mean of 8 or more urinary voids per day and 4 or more urge UI episodes per day on a baseline 3-day bladder diary regardless of whether symptoms were of neurological origin. The bladder diary was to be independently completed by the patient. Patients needed to have a mean voided volume of 350 ml or less during a 2-day urine collection period and a postvoid residual volume of 250 ml or less on ultra-sonography or catheterization.	Potential participants were excluded from study based on criteria designed to rule out incontinence related to chronic illness, anatomical abnormality and concomitant medication.	OTG (oxybutynin chloride)	Placebo	Laboratory assessments were performed at Mayo Laboratory for Clinical Trials, Rochester, Minnesota	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Staskin, 2009[379] Post-hoc U.S. N: 1,165	Adult men and women with OAB of ≥6 months' duration with urgency and an average of ≥1UUI episode/day and ≥10 toilet voids/day, as assessed using 3 -day bladder diaries	Not reported	Trospium chloride	Placebo	Supported by Allergen, Inc. and Indevus Pharmaceuticals Inc.	Dr. Staskin has been an advisor and speaker for Allergen, Astellas Pharma, Pfizer and Watson. Professor Cardozo has received funding as a speaker, consultant or researcher from Astellas, Bioxell, Pfizer, Recordati, Rottapharm and Allergan within the last year
Staskin, 2009[49] P pooled analysis U.S. N: 1,165	Adults with OAB of ≥6 months' duration with urinary urgency (>=1 severe urgency severity rating/3 days on the validated Indevus Urgency Severity Scale), frequency (mean ≥10 voids/day), and UUI (mean of ≥1 UUI episode/day), as assessed using the 3-day bladder diaries. Subjects undergoing current pharmacological therapy for OAB eligible after a 7-day washout period prior to 3-day bladder diary data collection.	A mean total volume voided of >3000 mL/day; a mean voided volume of >250 ml/void; predominantly stress, insensate, or overflow incontinence; interstitial cystitis; bladder cancer; and a history of neurogenic bladder; clinically significant renal disease (defined as screening serum creatinine values >1.5mg/dL), urinary tract infection or clinically significant urinary retention (defined as postvoid residual urine volume >100mL); subjects who and been treated with or received trospium chloride in previous trials.	Trospium XR 60 mg once daily	Placebo	Supported by Allergan, Inc. and Endo Pharma-ceuticals Inc. (formerly Indevus Pharma-ceuticals, Inc.) Editorial support funded by Allergan, Inc.	David R. Staskin is a consultant and speaker for Allergan, Astellas, Pfizer, and Watson. Matt T. Resenberg receives grant/research support from Ortho-McNeil and Sanofi-Synthelabo and serves as a consultant for Ortho-McNeil, Sanofi-Sythelabo, Pfizer, GlaxoSmithKline, Endo Pharmaceuticals (formerly Indevus Pharmaceuticals), Lilly, and Novartis. He is also on the Speakers' Bureau for Ortho-McNeil, Endo Pharmaceuticals,

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
						GlaxoSmithKline, Pfizer, Lilly and AstraZeneca. Peter K.Sand is an advisor and speaker for Allergan, Astellas, Pfizer, Ortho, Colplast, and Watson. He has received grants from Allergan, Astellas, Boston Scientific, Pfizer, Ortho-McNeil, Watson, and Antares. Norman R. Zinner is a consultant, clinical trial investigator , and/or speaker for Allergan, Watson, Pfizer, Novartis, Ferring, GlaxoSmithKline and Astellas. Roger R. Dmochowski is a consultant for Allergan, Astellas, Novartis, Pfizer, and Watson.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Steers, 2005[43] RCT Canada, U.S. N: 395	Patients aged >18 years with symptoms of OAB for at least 6 months, capable of independent toileting. Irrespective of response to previous treatments patients had to have urgency incontinence (>5 episodes per week), voiding frequency (>8 voids per day), and urgency (a strong desire to void at least once per day). Adequate method of contraception throughout the study for young women.	Contraindications to anticholinergic therapy (e.g., uncontrolled narrow-angle glaucoma, urinary retention or gastric retention); clinically significant stress incontinence, BOO and/or a postvoid residual urinary volume (PVR) of >200 mL ; pregnancy and lactation; genitourinary conditions that could cause urinary symptoms; fecal impaction or severe constipation (two or fewer bowel movements per week); urogenital surgery within the previous 6 months; bladder biopsy in the previous 30 days; indwelling catheter and intermittent self-catheterization; clinically significant disease; bladder-training program during the study; concomitant treatment with anticholinergic or antispasmodic drugs (including drugs with significant anticholinergic effects, e.g., imipramine), opioids and other drugs known to cause significant constipation, hormone replacement therapy (unless taken for >2 months), and drugs known to be potent cytochrome P450 3A4 inhibitors (e.g., ketoconazole).	Darifenacin controlled-release tablets 7.5 mg	Placebo	This study was funded by Pfizer Inc.	Jacques Corcos is a member of the board of Sponsor; Georg Kralidis is an employee of Sponsor; Jenelle Foote is a study investigator funded by Sponsor.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Steers, 2007[380] Duloxetine OAB Study Group. Australia, Canada, U.S. N: 306	Duloxetine OAB Study Group: women aged ≥18 years and to be identified as having predominant symptoms of OAB for ≥3 consecutive months before study entry; no SUI, including a negative cough stress. The case definition for OAB: bothersome urinary urgency or urge UI+ abnormal voiding frequency (≥2 hours mean daytime voiding interval) documented by ≥2 days of recording of a screening urinary diary + urodynamic testing detected DOA or sensory urgency(urgent desire to void during the testing session in the absence of a DOA, with a maximum cystometric capacity of <400 mL, both with no SUI, including a negative cough stress test at MCC after the urethral catheter was removed.	A postvoid residual urine volume of >100 mL; a mean 24-hour total voided volume of < 3 L, documented on a 2-day frequency-volume chart ; a positive urine culture (>100 000 colony-forming units/mL) or four or more UTIs during the year before enrolment; the regular use of medications for OAB symptoms within a month of enrolment; any previous use of duloxetine; continence surgery within 6 months or any major surgery within 3 months of enrolment; pelvic organ prolapse greater than ICS Stage II; any nonpharmacological intervention (e.g., electrical stimulation, bladder training, continence devices) within 3 months of enrolment; and pelvic floor muscle training 3 months before the study.	Duloxetine (40-mg twice daily). After 4 weeks, the dose of duloxetine was increased to 60-mg twice daily	Placebo	Eli Lilly and Company and by Boehringer Ingelheim GmbH.	William D. Steers and Sender Herschorn are paid consultants and study investigators funded by the sponsor. Karl J. Kreder, Kate Moore and Kris Strohbehn are study investigators funded by the sponsor. Ilker Yalcin and Richard C. Bump are employees of Eli Lilly and company. Sponsored by Eli Lilly and Company and by Boehringer Ingelheim GmbH.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Swift, 2003[381] Tolterodine Study Group North America, Australia and New Zealand N: 1,235	Age 18 years or more with urinary frequency (≥8 micturitions/24 hours) and urgency incontinence (≥5 incontinence episodes/week), having had these symptoms of overactive bladder for 6 months or more whether or not they were treatment naïve, and irrespective of response to prior antimuscarinic therapy.	Demonstrable stress incontinence, total daily urine volume >3 L, any contraindications to antimuscarinic treatment, significant hepatic or renal disease (with biochemical markers twice the upper limit of the normal reference range), symptomatic or recurrent urinary tract infections (diagnosed by urinalysis), interstitial cystitis (diagnosed by clinical suspicion), hematuria or bladder outlet obstruction, current electro-stimulation or bladder training therapy, an indwelling catheter or intermittent self-catheterization; pregnant or nursing women; women of child-bearing potential not using reliable contraceptive methods; other treatments for overactive bladder, such as anticholinergic drugs, or drugs that inhibit cytochrome P450 3A4 isoenzymes were not permitted; treatment with an investigational drug in the 2 months prior to study entry was prohibited.	Tolterodine ER 4 mg capsules once daily, tolterodine IR tablets 2 mg twice daily	Placebo	This study was sponsored by a grant from Pharmacia Corporation.	Not reported
Szonyi, 1995[382] RCT N: 60	Outpatients of either sex aged over 70 with symptoms of urinary frequency, urgency and urgency incontinence were recruited. Patients had to be mobile, able to attend an outpatient department, able to keep a diary chart and willing to give consent.	Urinary infections at the time of recruitment, patients with severe hepatic or renal disease, glaucoma, or uncontrolled diabetes. Patients on concomitant anticholinergic therapy with imipramine were excluded.	Oxybutynin 2.5 mg twice daily	Placebo	Funded by Smith and Nephew Pharma-ceuticals Ltd.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Takei, 2005[383] Japanese Tolterodine Study Group. Japan N: 293	Eligible Japanese patients completing 12 weeks' treatment in a randomized, double-blind trial 20 continued with 12 months' open-label treatment with tolterodine ER 4 mg once daily, irrespective of (and without unblinding) the treatment received during the double blind study (tolterodine ER 4 mg capsules once daily [Detrol capsule, Detrusitol, Pharmacia Corporation, Peapack, NJ], oxybutynin 3 mg tablets three times daily [Pollakisu, Aventis Pharma Ltd, Tokyo, Japan] or placebo). The 12-week randomized study enrolled men and women aged ≥20 years with OAB symptoms including urinary urgency, urinary frequency (≥8 micturitions/24 h) and urgency incontinence (≥5 episodes/week) for ≥6 months. Patients were recruited based solely on OAB symptoms, irrespective of prior antimuscarinic treatment or their response to such therapy.	Demonstrable stress incontinence, total daily urine volume >3 L, average volume voided/micturition >200 mL, significant hepatic or renal disease, any contraindication for anticholinergic treatment, symptomatic or recurrent urinary tract infection, interstitial cystitis, hematuria or bladder outlet obstruction, indwelling catheter or intermittent self-catheterization, electro-stimulation or bladder training within 14 days before randomization or expected to commence during the study. Patients who were poorly compliant (missed >25% of prescribed medication), had an ongoing serious adverse event and pregnant or nursing women and women of childbearing potential not using reliable contraception were also excluded.	Tolterodine ER	Oxybutynin, Placebo	Pfizer Japan Inc	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Tapp, 1990[384] RCT N: 37	Postmenopausal women	Not reported	Oxybutynin 5mg four times daily	Placebo	Support from Tillots Laboratories	Not reported
Tincello, 2000[385] RCT UK N: 67	Urodynamically confirmed diagnosis of idiopathic detrusor instability.	All patients were screened for UTI using commercially available reagent test-strips before cystometry, and those with positive results were deferred until appropriate treatment had been given. Patients with a residual volume of ≥100mL and those with a maximum flow rate of <15mL/s were excluded.	Oxybutynin with salivary stimulant pastilles	Oxybutynin only	Drugs were supplied by Lorex Synthelabo and Thames Laboratories, Consolidated Chemicals, Wrexham, UK	Not reported
Thuroff, 1991[386] Study: RCT N: 169	15 years old and older complaining of symptoms of frequency, urgency and/or incontinence, in whom cystometry findings were related to detrusor hyperactivity, whether idiopathic (unstable detrusor) or neurogenic (detrusor hyperreflexia) in origin.	Pregnancy, congestive heart failure, severe renal/liver disease, myasthenia gravis, unable to swallow/uncooperative patient, hiatal hernia/reflux esophagitis, gastrointestinal tract obstruction, urinary tract obstruction, residual urine greater than 50ml, untreated urinary tract infection and hyperreflexia without urge.	Oxybutynin chloride	Placebo	Pharmacia Leo Therapeutics, Helsingborg, Sweden provided the pharmaceutical preparations used in this study	NR

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Toglia, 2010[387] Karram, 2009320 Post-hoc VENUS U.S. N: 739	Patients aged ≥18 years with OAB symptoms for ≥3 months	Reported previously[320]	Solifenacin	Placebo	Supported by Astellas Pharma US, Inc. and Glaxo-SmithKline	Dr. Toglia is a consultant and speaker for Astellas; Dr. Ostergard is a consultant and speaker for Astellas, GlaxoSmithKline, Novartis, Pfizer and Watson. Dr. Fakhoury is an employee of Astellas. Mr. Andoh and Dr. Hussain were employees of Astellas at the time the study was conducted and have no other conflicts of interest to disclose

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
U.S. Food and Drug Admin[388] Cardozo, 2008[60] SUNRISE Multinational N: 865	Male of female aged ≥18 years, from whom written consent had been obtained, and who were willing and able to complete a voiding diary correctly; symptoms of OAB (including urinary frequency, urgency or urgency incontinence) for ≥3 months and three or more episodes of urgency with or without incontinence in the last 3 days	Not reported	Solifenacin	Placebo	Research grant from Astellas Pharma Europe Ltd.	Linda Cardozo: Astellas, Lilly, UCB Pharma, Pfizer, Gynecare, Plethora, Cook, Organon; Elke Heβdö rfer: Astellas, Pfizer, Bayer-Schering, Sanofi Aventis, Apogepha, Merckle Recordati, Lilly; Rodolfo Milani: Astellas, BARD, Recordati; Pedro Arano: Astellas; Luc Dewilde: Astellas,; Mark Slack: Astellas, Pfizer, Lilly, Johnson & Johnson, Boston Scientific; Ted Drogendijk, Mark Wright and John Bolodeoku: employees of Astellas
U.S. Food and Drug Administration, 2004[389] RCT U.S. N: 509	Male or female, 18 years and older, with symptoms of overactive bladder for at least 6 months prior to enrollment	Not reported	Trospium chloride	Placebo	Indevus Pharma-ceuticals, Inc.	Not reported
U.S. Food and Drug Administration, 2004[33] RCT U.S. N: 509	Male or female, 18 years and older, with symptoms of overactive bladder for at least 6 months prior to enrollment	Not reported	Trospium chloride	Placebo	Indevus Pharma-ceuticals, Inc.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
U.S. Food and Drug Administration, 2004[41] RCT Multinational N: 680	Male and female subjects, aged 18 years and older with symptoms of overactive bladder for at least 6 months. Subjects must exhibit all of the following symptoms of overactive bladder during the run-in period: 1) incontinence 2) frequency of micturition -at least 8 times per 24 hours, on average, over the run-in period 3) urgency -at least once per 24 hours, on average, over the run-in period	Not reported	Darifenacin	Placebo	Not reported	Not reported
U.S. Food and Drug Administration, 2004[390] RCT Multinational N: 562	Male and female subjects, aged 18 years and older with symptoms of overactive bladder for at least 6 months. Subjects must exhibit all of the following symptoms of overactive bladder during the run-in period: 1) incontinence 2) frequency of micturition -at least 8 times per 24 hours, on average, over the run-in period 3) urgency -at least once per 24 hours, on average, over the run-in period	Not reported	Darifenacin	Placebo	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
U.S. Food and Drug Administration, 2007[38] RCT U.S. N: 601	Patients currently undergoing OAB therapy at the time of enrollment were required to undergo 7-day wash-out period, followed by 3-day baseline urinary diary collection, prior to randomization. Patients not under OAB therapy could begin treatment after 3-days of baseline diary collection	Not reported	Trospium chloride ER	Placebo	Indevus Pharma-ceuticals, Inc.	Not reported
U.S. Food and Drug Administration, 2007[44] RCT U.S. N: 564	Patients currently undergoing OAB therapy at the time of enrollment were required to undergo 7-day wash-out period, followed by 3-day baseline urinary diary collection, prior to randomization. Patients not under OAB therapy could begin treatment after 3-days of baseline diary collection	Not reported	Trospium chloride ER	Placebo	Indevus Pharma-ceuticals, Inc.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
U.S. Food and Drug Administration, 1998[39] Anderson, 1999[340,341] Study: RCT OROS Oxybutynin Study Group U.S. N: 134	Female patients aged 40 years and older with urge urinary incontinence. Non-pregnant women determined to be in good health; patients with mixed urinary incontinence, provided that symptoms and/or signs of stress incontinence are not the predominant manifestation of UI and UUI episodes associated with urgency can be differentiated from urgency incontinence episodes not associated with urgency; normotensive, with or without hypertensive medication; no postural hypotension; patients who successfully completed the screening urinary diary for 7 days	Patients with known genitourinary conditions that may cause incontinence; those receiving any drugs that are considered effective in the treatment of incontinence less than the equivalent of 5 times the half-life of the drug and patients who have been treated with anticholinergic agents for urge UI and were found to be refractory to these agents	Oxybutynin as OROS-O5mg to 30mg/day based on achieved continence	Oxybutynin IR 5mg to 20mg/day based on achieved continence	ALZA Corporation Mountain View, California	M. Preik is an employee of Jansen-Cilag GmbH, Germany. A Albercht and M O'Connell are employees of ALZA Corp., U.S.A. R. Anderson is a stakeholder of Johson and Johson stock, is a member of the national advisory board for Ditropan XL, and also acts on behalf of the Speaker's Bureau of Ortho-McNeil.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Van Kerrebroeck, 2004[393] Duloxetine Urinary Incontinence Study Group. Belgium, Canada, Denmark, France, Germany, the Netherlands, Sweden and the United Kingdom N: 494	Women aged 24–83 years with predominant symptoms of stress urinary incontinence (according to clinical algorithm that was 100% predictive of urodynamic stress urinary incontinence), with >7 weekly incontinence episode, without predominant symptoms of urgency incontinence, normal diurnal and nocturnal frequencies, a bladder capacity >400 mL and both a positive cough stress test and positive stress pad test.	Inability to tolerate the filling to 400 mL or who experienced a first sensation of bladder filling <100 mL.	Duloxetine 40 mg BD	Placebo	Funded by Eli Lilly and Boehringer Ingelheim.	Dr Yalcin and Dr Bump are both full-time employees of Eli Lilly and hold stock and stock options in the company.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Van Kerrebroeck, 2001[394] Tolterodine Study Group. 167 centers in Australasia, Europe, and North America N: 1,529	Men and women with urinary frequency (eight or more micturitions every 24 hours) and urgency incontinence (five or more episodes per week) irrespective of whether they had received prior treatment and irrespective of their response to prior antimuscarinic therapy.	Demonstrable stress incontinence, total daily urine volume greater than 3 L, any contraindications to antimuscarinic treatment, significant hepatic or renal disease (biochemical markers twice the upper limit of the normal reference range), symptomatic or recurrent urinary tract infections, interstitial cystitis, hematuria or bladder outlet obstruction, current electro-stimulation or bladder training therapy, and indwelling catheter or intermittent self-catheterization, pregnancy, breastfeeding, unreliable contraceptive methods; other treatments for an overactive bladder such as anticholinergic drugs or drugs that inhibit cytochrome P450 3A4 isoenzymes; treatment with an investigational drug in the 2 months before study entry.	Tolterodine ER 4 mg once daily	Placebo	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Van Kerrebroeck, 2010[391] RCT 17 countries in Europe, South Africa, Australia, and New Zealand N: 417	Men and women were eligible to enroll in the open-label extension if they had completed the 12-week double-blind study without meeting discontinuation criteria and had not experienced an adverse event during double-blind treatment that, in the opinion of the investigator, would jeopardize their well-being upon continuation of treatment.	Any illness that required termination of treatment, a residual urine volume >200ml, an absolute corrected QT interval (QTc)>500 ms or an individual increase of >60 ms relative to baseline measurement in the double-blind study, or any ongoing serious AE during the double-blind study that was considered to be related to study medication or was of unknown origin.	Fesoterodine	None	Funded by Schwarz BioSciences GmbH and Pfizer Inc	Dr Van Kerrebroeck has been an investigator and lecturer for Astellas, Eli-Lilly, Ferring, Novartis and Pfizer Inc. John Heesakkers has been an investigator and lecturer for Astellas and lecturer for Astellas and Pfizer Inc. Sandra Berriman, Lalitha Padmanabhan Aiyer, Martin Carlsson and Zhongghong Guan are employees of Pfizer Inc. and hold stock in the company.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Vardy, 2009[392] VIBRANT U.S. N: 768	Eligible patients (aged ≥18 years) were required to have OAB symptoms for ≥3 months (≥8 micturitions and ≥1 urgency episode, with or without incontinence, per 24 hours) and a PPBC score ≥3.	Significant stress or stress-predominant mixed incontinence, recurrent urinary tract infection (UTI; ≥3 episodes within the past 3 months) or evidence of UTI at baseline, evidence of chronic urologic inflammation/interstitial cystitis or urinary/gastric retention.	Solifenacin	Placebo	Research grant from Astellas Pharma U.S. Inc. and Glaxo-SmithKline	Dr. Vardy is a consultant for Astellas Pharma US, Inc. and a speaker for Wyeth and BARD Urologic. Dr. Mitcheson is a study investigator for Pfizer, Novartis, Eli Lilly, Watson, and Antares; he is a speaker for GlaxoSmithKline. Dr. Forero-Schwanhaeuser is an employee of GlaxoSmithKline, and Drs. Marshall and He are employees of Astellas Pharma US Inc. Editorial support, including writing assistance, was provided by Linda A. Golstein, PhD, a medical writer at Envision Scientific Solutions and was funded by Astellas Pharma Global Development Inc. and GlaxoSmithKline
Vella, 2008[393] CT UK N: 228	Women with a diagnosis of urodynamic stress incontinence (USI) or mixed USI and detrusor overactivity.	Concurrent prolapse or contraindications to drug therapy	Duloxetine: 20 to 40 mg bid	None	Not reported	Jonathan Duckett has received funding to attend conferences from the makers of duloxetine.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Versi, 2000[40] Gleason, 1999[342] U.S. Food and Drug Administration, 1998[39] The Ditropan XL Study Group U.S. N: 226	Patients were included only if they had previously responded to treatment with anticholinerigc medications or to a trial of oxybutynin before enrollment.	Patients with clinically significant medical problems, a postvoid residual urine volume over 100 mL, or other conditions in which oxybutynin is contraindicated were excluded.	Controlled-release oxybutynin tablets containing 5 mg oxybutynin or a placebo were placed in identical hard gelatin capsules and packaged in cards that provided total doses of 5, 10, 15, and 20 mg.	Immediate-release oxybutynin tablets containing 5 mg oxybutynin or a placebo were placed in identical hard gelatin capsules and packaged in cards that provided total doses of 5, 10, 15, and 20 mg.	Grant from ALZA Corporation	Not reported
Von Holst, 2000[394] RCT Germany N: 186	Hysterectomized women age 40-65 years, with postmenopausal complaints, normal gynecological history and examination, serum estradiol <30pg/ml and follicle stimulating hormone >30IU/ml.	Use of sex hormones taken orally within the last 28 days; locally-applied sex hormones within the last 21 days or injectable sex hormones within the last 6 months.	7-day-Estradiol patch (1.5mg estradiol/week or 50mg estradiol/24 hours). All patients received active drug therapy (7-days). Estradiol patch) for a further 3 months (three cycles).	Placebo once-weekly	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Waetjen, 2005[395] RCT U.S. N: 417	Postmenopausal women age 60-80 years, with a uterus and at least 5 years after menopause, with normal bone mineral density for age (z score not below –2.0 at the lumbar spine).	Use of estrogen or progestin within 3 months of randomization or having unexplained uterine bleeding, endometrial hyperplasia or an endometrium 5mm or more in double-wall thickness, abnormal mammogram, breast cancer, a history of metabolic disease, cancer, coronary disease, cerebrovascular disease, uncontrolled hypertension, uncontrolled thyroid disease, liver disease, fasting triglycerides more than 300 mg/dL, or fasting glucose more than 180 mg/dL.	14mg of transdermal E2 per day.	Placebo	Grant from Berlex laboratories inc, Montville, NJ; Grant IND No. 98188 from the U.S. Food and Drug administration	Dr. Pinkerton is on the Berlex speaker's bureau
Wagg, 2006[400] Pooled analysis Not reported N: 1,045	Mean of ≥8 micturitions/24 hours and at least 1 of the following:1)a mean of ≥1 incontinence episode/24 hours; or 2)a mean of ≥1 urgency episode/24 hours	Patients with existing urinary tract dysfunction including postvoid residual volume of >150 or >200mL (depending on the trial), stress incontinence or mixed urinary incontinence with stress urinary incontinence predominating, neurologic dysfunction or injury affecting detrusor function or other lower urinary tract function, absolute urinary retention, grade III/IV prolapse with cystocele, recurrent or active urinary tract infection, bladder stones, current or previous bladder neoplasm, or history of interstitial cystitis; to discontinue any drug for treatment of urinary incontinence; use of anticholinergic or antimuscarinic agents only allowed only if receiving a stable dose; electro-stimulation, biofeedback, or bladder-training therapy not allowed during the study and not permitted during the 2 to 4 weeks immediately before the trials.	Solifenacin 5 or 10 mg	Placebo	Yamanouchi Pharma Co., Ltd, Tokyo, Japan	Dr. Wagg has received consultancy, lecture, and writing fees relating to OAB from Yamanouchi. Dr. Sieber is a member of the speaker's bureau for Yamanouchi and was also a principal investigator. Professor Wyndaele has no financial involvement with Yamanouchi

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Wang, 2006[396] RCT Taiwan N: 74	Age: 16 to 80 years; OAB for more than 6 months. No patients had taken anticholinergics or tricyclic antidepressants and none had been treated with pelvic floor muscle training, bladder training, or pelvic prolapse repair.	Pregnancy, neurologic disorders, diabetes mellitus, demand cardiac pacemaker or intrauterine device use, genital prolapse greater than Stage II of the International Continence Society grading system, a postvoid residual urine volume greater than 100 mL, overt urinary stress incontinence, a history of anti-incontinence surgery, and urinary tract infection.	Electrical stimulation (ES)	Oxybutynin, placebo	Grant from National Science Council, Taiwan.	Not reported
Wang, 2009[397] RCT Taiwan N: 73	Women with OAB for more than 6 months, and the symptom of urgency three times or more per day.	Treatment with anticholinergics or tricyclic antidepressants; treatment with pelvic floor or bladder training and pelvic prolapse repair, participation in prior trials; pregnancy, neurologic disorders, diabetes mellitus, demand cardiac pacemaker or intrauterine device use, genital prolapse greater than the International Continence Society (ICS) grading system stage II, overt urinary stress incontinence, a history of anti-incontinence surgery, urinary tract infection and patients receiving any OAB treatment during the 14-day washout/run-in period preceding randomization.	Vaginal electric stimulation (20 minutes per session, twice a week) or oxybutynin (2.5 mg) three times per day	Placebo three times per day	Grant from the National Science Council, Taiwan (NSC95-2314-B-182-062).	Not reported
Mazur, 1995[398] RCT N: 185	Men and women with urge urinary incontinence or urgency	Neurogenic bladder dysfunctions, urinary tract infections, gastrointestinal obstructions, cardiovascular diseases, potential pregnancy.	Propiverine hydrochloride 60 mg/d	Propiverine hydro-chloride 15, or 45 mg/d	Not reported	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Wein, 2007[399] RCT analysis Australia, Europe and North America N: 1,005	Men and women aged ≥18 years with symptoms of urinary frequency (≥8 voids/24 hours) and urgency UI (≥5 episodes/ week) for ≥6 months.	Stress UI, as determined by the investigator and confirmed by a cough provocation test; significant hepatic or renal disease, current or recurring UTI, clinically relevant BOO (defined by investigator's judgment based on a patient's history), indwelling catheter or intermittent self-catheterization, and any condition for which antimuscarinic treatment was contraindicated; anticholinergic drug or treatment for OAB during the 14-day washout/run-in period preceding randomization, and those with a mean micturition volume of 200 mL or total daily volume of 3 L on bladder diaries.	Tolterodine-ER (4 mg)	Placebo	Not reported	Alan J. Wein is a consultant to Astellas, Novartis, Pfizer and Indevus; Vik Khullar is a speaker and investigator for Pfizer on tolterodine; Joseph T. Wang and Zhonghong Guan are employees of Pfizer Inc.
Weinstein, 2006[400] DESIRE (Duloxetine Efficacy and Safety for Incontinence in Racial and Ethnic populations). U.S. N: 3,983	DESIRE Study Group: women >18 years old with stress urinary incontinence (>1 episode/week) or stress predominant mixed incontinence (frequency of stress at least twice higher than urge)	Prior treatment with monoamine oxidase inhibitors and duloxetine; depression; diabetic peripheral neuropathic pain	Duloxetine 40 mg twice daily	Not controlled trial	Funded by Eli Lilly and Boehringer Ingelheim.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Yalcin, 2006[401] Pooled U.S. N: 1,133	Women with SUI who were enrolled in two double-blind, controlled, randomized studies of duloxetine versus placebo having predominant SUI that was diagnosed using a clinical algorithm demonstrated to be 90.2% predictive of urodynamic stress.	Reported previously in individual studies	Duloxetine 80mg/day	Placebo	This study was sponsored by Eli Lilly and Company and Boehringer Ingelheim.	Not reported
Yalcin, 2004[402] the Duloxetine UI Study Group one phase 2 study in the US, and 3 phase 3 studies in 16 countries in Africa, Australia, Europe, and North and South America N: 1,913	Women with SUI of at least 3 months' duration predominant symptom of SUI with a weekly IEF >4 in phase 2 and IEF >7 in the 3 phase 3 studies, where an episode was defined as an easily noticeable leakage of urine that wet a pad or clothing, and that occurred with a physical stress such as coughing, sneezing, or exercising; the lack of predominant symptoms of enuresis or urge urinary incontinence, daytime frequency mL per minute, without pressure measurements; a positive cough stress test (visualization of urine leakage concurrent with a cough) and a positive stress pad test (leakage of >2.0 g).	Inability to tolerate filling to 400 mL; a first sensation of bladder filling <100 mL, or who had no sensation at any time during the filling; previous continence surgery.	All phase 3 studies included only duloxetine 40 mg bid as an active treatment. The phase 2 study included 3 duloxetine treatment groups (20 mg qd, 20 mg bid, and 40 mg bid); however, data from subjects taking duloxetine doses <40 mg bid were not included in the analyses to avoid any potential confounding effects of lower efficacy (duloxetine 40 mg bid has	Placebo	This work was sponsored by Eli Lilly and Company	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
			been demonstrated to be the optimum dose). Subgroup analysis was performed within each treatment group based on baseline incontinence severity.			
Yamaguchi, 2007[403] RCT Japan N: 1,593	Men and women aged ≥20 years and with symptoms of OAB reported for ≥6 months were eligible for screening and study enrolment. To be eligible for randomization after the 2-week placebo run-in period, patients had to report a mean number of voids/24 hr of ≥8, ≥3 episodes of urgency and/or ≥3 episodes of urgency incontinence during a 3-day voiding - diary period.	Significant BOO, an assessment based on measuring the postvoid residual urine volume; patients with a PVR of ≥100mL; presence of BOO symptoms assessed by investigators(who were all urologists); urinary retention, demonstrable stress incontinence, bladder stones, UTI, interstitial cystitis, previous or current malignant disease of the pelvic organs; those taking concomitant anticholinergic medications; known hypersensitivity to anticholinergic medications or lactose.	solifenacin 5mg or 10mg	Propiverine or placebo	Funded and sponsored by Astellas Pharma Inc.(formerly Yamanouchi Pharma-ceutical Co. Ltd), Tokyo, Japan	Osamu Yamaguchi and Eji Marui are consultants to Astellas Pharma
Zellner, 2009[404] RCT Germany N: 1,659	Male or female outpatients aged ≥18 years with urinary frequency ≥8 micturitions per day) and urgency incontinence (≥5 episodes per week), as verified in the micturition diary.	Patients were excluded if they did not complete the micturition diary correctly for 7 consecutive days to confirm that they met the inclusion criteria and to establish baseline symptoms and urgency severity before the entrance visit. Based on this diary, patients with a total daily urine volume ≥2.8 L (determined by	Oxybutynin Hydrochloride	Trospium Chloride	Dr. R. Pfleger GmbH (Bamberg, Germany) sponsored this study. Petra Schwantes, PhD, Biomedical	Petra Schwantes, PhD, Biomedical Services, assisted with the writing of this article; she received compensation from the sponsor. The authors have indicated that they

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
		total daily urine for 2 days, divided by 2), a mean micturition volume of >250 mL, and/or a clinically significant bladder outlet obstruction (i.e., postvoid residual urine volume of >100 mL, determined via sonography) were also excluded as were those with an indwelling catheter or intermittent self-catheterization. Those with other significant medical problems or urogenital conditions, including urinary tract infection at the screening visit (or before or at the entrance visit), interstitial cystitis and/or hematuria (as determined via urinalysis), contraindications to anticholinergic therapy (e.g., untreated narrow-angle glaucoma, mechanical gastrointestinal stenosis, myasthenia gravis syndrome), tachycardiac arrhythmia, severe psychiatric illnesses, or hypersensitivity to trospium chloride or oxybutynin or 1 of the vehicle ingredients, were also excluded. Patients who had participated in a bladder-training program, or in another study within 30 days before screening, were also prohibited, as were those undergoing electro stimulation programs. Further reasons for exclusion were alcohol and/or drug abuse, pregnancy, breastfeeding, and insufficient contraception among women of childbearing age.			Services, assisted with the writing of this article; she received compensation from the sponsor.	have no other conflicts of interest regarding the content of this article.

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Zinner, 2005[405] RCT U.S. N: 76	Males and non-pregnant (nor breastfeeding) females aged 18–85 years with urgency incontinence (>4 significant incontinent episodes per week, where significant was defined as leakage that would normally require a change of clothing or absorbent pad) and urinary frequency (≥8 voids per day, on average).	Neurogenic bladder or stress incontinence, contraindications to antimuscarinic therapy, previous bladder surgery, bladder stones (as demonstrated by pelvic x-ray or ultrasound), acute or chronic urinary tract infection, significant urinary outflow obstruction, and clinically significant concomitant disease; Patients intending to start or modify either an existing bladder training program or existing treatment with thyroid or estrogen hormone replacement therapy; those who had received treatment with drugs that affect bladder function/urine production in the previous 2 weeks.	Darifenacin controlled-release tablets 15 mg and 30 mg once/daily	Oxybutynin 5 mg three times daily, Placebo	Industry +Grant	Disclosure

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Zinner, 2008[406] CT N: 500	Men and women (>18 years of age) with OAB symptoms [an average of > 8 micturitions/ 24 hours]; >1 urgency episode/24 hours, with or without urgency urinary incontinence; >2 scores on the Patient Perception of Bladder Condition (PPBC) questionnaire; naive to darifenacin, dissatisfaction with previous oxybutynin ER or tolterodine ER administration after at least 1 week of taking these medications.	Mean daily urinary volume >3000 ml or a mean volume micturition of >300 ml (in micturition diary); clinically predominant and bothersome stress urinary incontinence, urinary retention, clinically significant bladder outlet obstruction, an indwelling catheter or intermittent self-catheterization; significant medical problems or urogenital conditions, including neurogenic bladder, cystocele or distal pelvic organ prolapse, frequent urinary tract infections (>3 over the preceding year) or urogenital surgery in the previous year or unexplained hematuria at screening; bladder-training program or any electro-stimulation therapy within 2 weeks prior to screening; pregnancy or inadequate contraception. Concomitant treatment with anticholinergics, antispasmodics, serotonin-noradrenalin-reuptake-inhibitors; cholinergic agonists, cholinesterase inhibitors (e.g. bethanecol, donepezil and rivastigmine), potent inhibitors of cytochrome CYP3A4 (e.g., ketoconazole, itraconazole, ritonavir, nelfinavir, clarithromycin and nefazadone), potent P-glycoprotein inhibitors (e.g. cyclosporine and verapamil), drugs with significant anticholinergic side effects (e.g. tricyclic antidepressants, selective-serotonin-reuptake-inhibitors and first generation antihistamines) or any other investigational drug.	Darifenacin 7.5 mg once daily (qd) for the first 2 weeks with voluntary up-titration to darifenacin 15 mg if the patient required additional efficacy, and treatment was well tolerated	Placebo	Funding for this study and for the editorial and project management services of ACUMED in the preparation of this manuscript were provided by Novartis Pharma AG.	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Zinner, 2006[407] RCT N: 445	Men and women aged >18 years with a history of OAB for >6 months and on average >1 urgency incontinence episodes/day; >8 micturitions/day; >4 urgency episodes/day and mean warning time of <15 minutes during 12 consecutive hours.	Stress urinary incontinence; marked cystocele or pelvic prolapse; those taking the following drugs in the 2 weeks prior to the screening visit: anticholinergic/antispasmodic drugs, or those with anticholinergic effects, cholinergic agonists, potent cytochrome P450 3A4 inhibitors, opioids and drugs that cause significant constipation; those who have contraindications to anticholinergic drugs, clinically significant bladder outlet obstruction, have the intention to start a bladder training program and an indwelling catheter or intermittent self-catheterization.	Darifenacin 15 mg controlled release qd	Placebo	This study was funded by Novartis Pharma AG	Not reported
Zinner, 2004[35] Trospium Study Group. U.S. N: 523	Male and female 18 years or older with OAB symptoms for at least 6 months; with urinary urgency, a minimum voiding frequency of 70 voids per week with at least 7 urgency incontinence episodes per week.	Predominantly stress UI, insensate or overflow in nature; with neurogenic bladder disorders, significant renal disease, uninvestigated hematuria and urinary tract infection at washout or more than twice during the prior year; significant bladder outlet obstruction (post-void residual volume >100 ml); concurrent use of any anticholinergic drug or other drug therapy for overactive bladder within 21 days before randomization, history of bladder surgery within 6 months before randomization, bladder cancer or interstitial cystitis; diuretic use, estrogen therapy and nonmedical bladder therapy that was not part of a stable, long-term program	20 mg trospium twice daily	Placebo	Indevus Corporation	Not reported

Appendix Table F27. Pharmacological treatments for female UI (continued)

Reference study, country, sample	Inclusion criteria	Exclusion criteria	Active	Control	Sponsorship	Conflict of interest
Zinner, 2002[408] RCT Europe, U.S., Canada, Australia, and New Zealand N: 1,015	Men and women aged 18 and older with urinary frequency (>8 micturitions/24 hours), urgency incontinence (>5 episodes per week), symptoms of overactive bladder for 6 months or more, and ability and willingness to complete micturition charts.	Stress incontinence; total daily urine greater than 3 L; significant hepatic or renal disease; symptomatic or recurrent urinary tract infections; interstitial cystitis, hematuria, or clinically relevant bladder obstruction; bladder training or electro-stimulation within 14 days before randomization; and indwelling catheter or intermittent self-catheterization, pregnancy and breastfeeding; unreliable contraceptive methods; treatments for overactive bladder (excluding estrogen treatment started more than 2 months before randomization), anticholinergic drugs, or potent inhibitors of cytochrome P450 3A4 isoenzymes.	Tolterodine ER 4 mg once daily	Placebo	Pharmacia Corporation	Not reported
Zinner, 2005[409] Pooled U.S. N: 1,157	Symptoms of urgency, an average of 10 or greater toilet voids daily and an average of 1 or greater UUI episode daily.	Reported previously[34, 35]	20 mg trospium chloride twice daily	Placebo	Indevus, Lilly, Pfizer, Watson, Bayer and Glaxo Smith Kline	Not reported