ODPRN ONTARIO DRUG POLICY RESEARCH NETWORK

Drugs for the Treatment of Overactive Bladder (OAB) Syndrome

FINAL SYSTEMATIC REVIEW REPORT

March 2016

Conflict of Interest Statement

No study members report any affiliations or financial involvement (e.g., employment, consultancies, honoraria, stock options, expert testimony, grants or patents received or pending, or royalties) that may present a potential conflict of interest in the overactive bladder (OAB) Drug Class Review

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Study Team

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Contributions

The review authors would like to thank Nazmun Nahar, David Beking and Clemence Ongolo Zogo for their contributions to this review.

Note

Some details are censored in this report so as not to preclude publication. Publications (when available) and/or final unpublished reports will be available on the ODPRN website (www.odprn.ca).

Executive Briefing

- This report assessed the current evidence regarding the comparative efficacy and safety of pharmacotherapies in the treatment of overactive bladder (OAB) syndrome through a systematic review and Bayesian network meta-analysis.

- Previously published evidence syntheses are limited in scope, outcomes or statistical comparisons. Most focus on the anticholinergic agents compared to placebo or each other, and more recent reviews including newer pharmacotherapies such as mirabegron report a limited number of outcomes. The availability of comprehensive, high-quality comparative evidence on all approved pharmacologic treatments available in Canada is lacking; as such, previously published evidence syntheses were updated and expanded to form the evidence base for a comprehensive review of efficacy and safety outcomes reported in randomized controlled trials.

- Outcomes assessed for efficacy were frequency of micturitions, nocturia, urgency and incontinence episodes over a 24 hour period, and patient quality of life.

- Outcomes assessed for safety were dry mouth, constipation, arrhythmia, withdrawals (all-cause, due to adverse events, or due to a lack of clinical response).

- The pharmacotherapies reviewed were compared with each other or no therapy (placebo). Dual therapy with anticholinergic and β3- adrenoceptor agonists was also considered, as were comparisons to onabotulinumtoxin A (Botox). Outcomes were assessed at 12 weeks (frequency of micturitions and incontinence episodes over a 24 hour period) and end of study (all other outcomes).

- The systematic review located a total of 101 unique randomized controlled trials (RCTs) reported in 168 publications. A total of 79 unique RCTs reported outcomes of interest.

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Executive Summary

Research Questions

RQ1. What is the current evidence for the comparative efficacy and safety of pharmacologic treatments for overactive bladder (OAB) syndrome?

RQ2. Does the efficacy or safety of pharmacologic treatments for OAB syndrome vary depending on sex (male or female), age (≥65, 65 to 75, ≥75) or in those previously treated with an anticholinergic medication?

Methods

The strategy for building and analyzing the evidence base for the pharmacotherapies for OAB syndrome consisted of three fundamental steps based on a predefined protocol:

1. To expedite evaluation of the existing evidence base, multiple relevant existing systematic reviews of randomized controlled trials (RCTs) were identified through a broad search of the literature. Three reviews were selected and all included RCTs were screened de novo to confirm their eligibility.

2. A comprehensive search of published and grey literature sources to update the existing systematic reviews and ensure coverage for all pharmacotherapies of interest back to database inception. Search results were deduplicated against the results of the previous systematic reviews.

3. Meta- and Bayesian network meta-analyses were conducted involving the pharmacological treatments for OAB syndrome in a network for each of the outcomes specified a priori.

Systematic Review of Efficacy and Safety

In brief, this review highlights the current evidence on the comparative efficacy and safety of pharmacologic treatments in the management of adults with overactive bladder syndrome.

Over 1,300 titles and abstracts were screened for eligibility by two independent reviewers. Following review of full text articles, 168 publications reporting 101 unique RCTs were included. Of those, 88 RCTs reported outcomes of interest to this review.

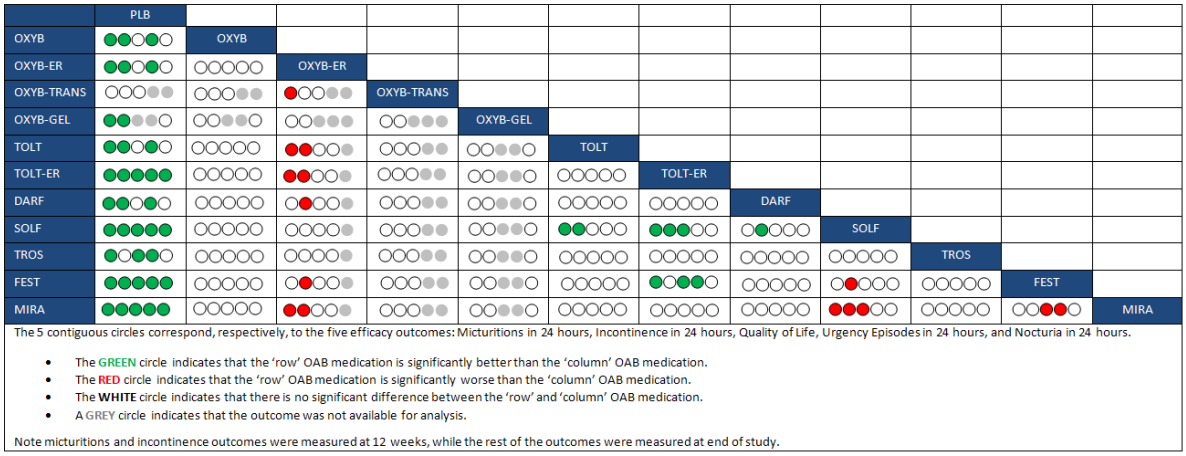
Studies reporting outcomes of interest were published between 1997 and 2015. The total number of participants in each study ranged from 18 to 2,417. RCTs included in the analyses were all parallel design, except for a single crossover study which reported data for the first period. Study duration ranged from 2 to 52 weeks, although median study duration was 12 weeks. Study participants were predominantly female (range 50 to 100%) and had varying treatment experience with anticholinergic agents. Mean age ranged from 40.2 years to 75.3 years.

Bayesian Network Meta-Analyses

Bayesian network meta-analyses were conducted for five efficacy and seven safety outcomes.

Results from the Bayesian network meta-analyses for efficacy are summarized in Exhibit 1.

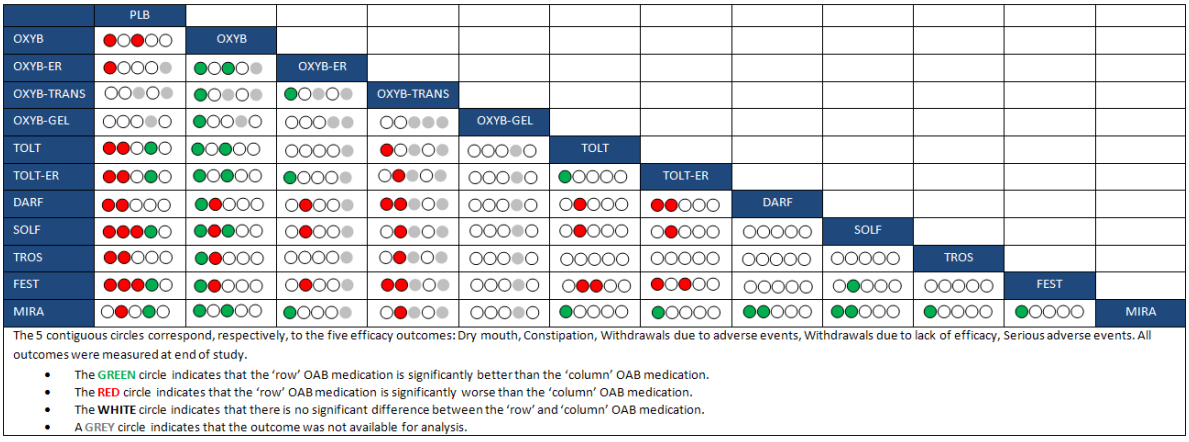
Exhibit 1: Summary of efficacy results from the Bayesian Network meta-analyses.



OXYB=immediate release oxybutynin, OXYB-ER=extended-release oxybutynin, OXYB-TRANS=transdermal oxybutynin, OXYB-GEL=oxybutynin gel, TOLT=tolterodine, TOLT-ER= extended-release tolterodine, DARF=darafenicin, SOLF=solifenacin, TROS=trospium, FEST=fesoterodine, MIRA=mirabegron.

Results from the Bayesian network meta-analyses for safety are summarized in Exhibit 2.

Exhibit 2: Summary of safety results from the Bayesian Network meta-analyses.



OXYB=immediate release oxybutynin, OXYB-ER=extended-release oxybutynin, OXYB-TRANS=transdermal oxybutynin, OXYB-GEL=oxybutynin gel, TOLT=tolterodine, TOLT-ER= extended-release tolterodine, DARF=darafenicin, SOLF=solifenacin, TROS=trospium, FEST=fesoterodine, MIRA=mirabegron.

The results of these analyses show that most treatments are generally more effective than no treatment, and that certain pharmacologic treatments may be superior to other agents at relieving symptoms of OAB syndrome, but which treatments vary by outcome. Results confirm that anticholinergic agents can increase dry mouth and constipation, which may contribute to discontinuation, but that there are no differences amongst the pharmacologic treatments for the risk of serious adverse events.

Systematic Review

Objective

To determine the comparative clinical efficacy and safety of pharmacologic treatments for overactive bladder (OAB) syndrome in adults through a systematic review and Bayesian network meta-analysis.

Research Questions

RQ1. What is the current evidence for the comparative efficacy and safety of pharmacologic treatments for overactive bladder (OAB) syndrome?

RQ2. Does the efficacy or safety of pharmacologic treatments for OAB syndrome vary depending on sex (male or female), age (≥65, 65 to 75, ≥75) or in those previously treated with an anticholinergic medication?

Methods

The strategy for building and analyzing the evidence base for the overactive bladder agents consisted of three fundamental steps based on a predefined protocol posted online for stakeholder feedback. First, to expedite evaluation of the existing evidence base, existing systematic reviews of pharmacologic treatments for OAB syndrome including RCT evidence were identified through a broad search of the literature. Priority was given to recent (previous 5 years) systematic reviews that closely matched the current review in scope, inclusion and exclusion criteria and provided transparency of methods (to confirm that systematic review steps were followed), search strategy and analysis. Following a thorough screening and assessment, three reviews were selected to form the evidence base for this review.[1-3] Following that, we carried out an update of the available randomized evidence using a de novo search of the published and grey literature for the outcomes specified in the protocol back to database inception. Results from the three existing systematic review were excluded or deduplicated from the updated search. Third, meta- and network meta-analyses were conducted involving the pharmacologic treatments for OAB syndrome in a network for each of the outcomes specified a priori.

Search Strategy

The search strategy was developed and tested through an iterative process by an experienced medical information specialist in consultation with the review team. The database searches were executed on August 15, 2015. Using the OVID platform, we searched Ovid MEDLINE®, Ovid MEDLINE® In-Process & Other Non-Indexed Citations, and

Embase. We also searched the CENTRAL database in Cochrane Library on Wiley.

Strategies utilized a combination of controlled vocabulary (e.g., “Urinary Bladder, Overactive”, “Muscarinic Antagonists”, “Flavoxate”) and keywords (e.g., overactive bladder, antimuscarinics, urispas). Vocabulary and syntax were adjusted across databases. We used a validated randomized controlled filter to focus results. No date or language restrictions were used but overlap with a previously conducted systematic review (used as our starting point) was removed. Animal-only and opinion-pieces were removed from the results.

We also searched for completed trials using ClinicalTrials.gov and the World Health Organization’s ICTRP search portal.

Specific details regarding the strategies appear in Appendix A.

Study Eligibility and Selection Criteria

The systematic review included randomized controlled trials (RCTs) that compared at least two overactive bladder agents to placebo or no treatment in adult patients diagnosed with OAB syndrome. Comparisons to onabotulinumtoxin A were also considered, as were combinations of mirabegron and any anticholinergic agent.

Studies were selected for inclusion in the systematic review based on the selection criteria presented in Exhibit 3. Health Canada-approved doses and daily maximums for all pharmacotherapies were used. Details are reported in Appendix C.

Exhibit 3. Inclusion and exclusion criteria for randomized controlled trials.

Study Population	Adults (aged 18 years or older) with overactive bladder as diagnosed by a health care professional and having symptoms of urgency, frequency, nocturia, or urgency incontinence*.
Interventions	OAB treatments currently available in Canada[a]: • Anticholinergic (antimuscarinic) agents - oxybutynin (generics, Ditropan XL, Oxytrol, Gelnique) - tolterodine (Detrol, Detrol LA) - darifenacin (Enablex) - solifenacin (Vesicare) - trospium (Trosec) - fesoterodine (Toviaz) - flavoxate (Urispas)[†] • β_3- adrenoceptor agonists: - mirabegron (Myrbetique) Combination therapy (mirabegron + an anticholinergic agent dual therapy)[b]

Comparisons	• Placebo • Neurotoxin: onabotulinumtoxin A (Botox) • Any of the OAB treatments or combinations explicitly listed above	
Outcomes	Efficacy	Safety

	• Urinary frequency (24 hrs)
	• Incontinence (24 hrs)
	• Urgency Episodes (24 hours)
	• Nocturia
	• Quality of Life
		• Dry Mouth
		• Constipation
		• Arrhythmia
		• Withdrawals
		  • All-cause
		  • Due to adverse events
		  • Due to efficacy
		• Serious Adverse Events

Index Node	Placebo	
Study types	Randomized controlled trials[c]	
Exclusions	• Non-pharmacologic therapies • Other treatments not listed above (e.g., estrogen, tricyclic antidepressants) • Non-randomized or observational studies • Primary studies published only in abstract format • Patients with neurologic conditions or cancer	

a All formulations approved in Canada including immediate- and extended-release, gel and transdermal patches.
b Accepted only combinations of mirabegron and another anticholinergic drug.
c No limitations on sample size or follow-up duration. Cross-over trials were eligible for inclusion and included in the analyses provided that data for the first period was reported separately and by treatment group.

Data Extraction and Management

All information was extracted using a standardized data abstraction form. Abstraction included 1) characteristics of trial participants including, inclusion and exclusion criteria; 2) type of intervention including dose, duration and co-medication 3) results of the clinical safety and efficacy outcomes of the intervention. All extracted data were checked for accuracy by two independent review authors.

The original, primary publication for each unique study included was used for data extraction, except where multiple publications for a single RCT were found. Multiple publications for a unique RCT (e.g. supplemental online appendices, companion publications reporting additional outcomes or populations from the original study) were handled by extracting the most recently adjudicated data for each outcome specified in the protocol.

Studies included from existing evidence syntheses went through de novo data extraction process following identical methods and procedures as articles identified in the literature

search of bibliographic databases. Data from all studies, regardless of source, were abstracted into a single data sheet.

Efficacy Data

Data were extracted for five efficacy outcomes (urinary frequency, or micturitions, incontinence, urgency episodes, nocturia, and quality of life) at two time points – 12 weeks and end of study. Data were extracted for micturitions, incontinence, urgency episodes and nocturia for a 24 hour reporting period. Where longer time periods were reported (e.g., micturitions per seven days), data were translated back to 24 hours.

Safety Data

Data were extracted for seven safety outcomes (dry mouth, constipation, withdrawals [all, due to adverse events, and due to lack of efficacy], serious adverse events, and arrhythmia*) at the end of study. Safety outcomes were analyzed using the number of participants who received the study drug. If not reported, the number randomized to the treatment group was used.

Risk of Bias Assessment of Included Studies

The Cochrane Collaboration's Risk of Bias (ROB) tool was applied to each of the included studies in this review. The ROB tool is a two-part instrument addressing six specific domains (namely sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and 'other issues' which we identified as source of funding). Each domain includes one or more specific entries in a 'risk of bias' table, and a form was created in line with the Cochrane Collaboration's ROB template: the first part involves describing what was reported to have happened in the study; and the second part involves assigning a judgment relating to the risk of bias for that entry by answering a pre-specified question about the adequacy of the study in relation to the entry, including a judgment of 'LOW' risk of bias, 'HIGH' risk of bias and 'UNCLEAR' or unknown risk of bias. Two entries were considered for the domain 'blinding' for assessments of outcomes that were subjective or objective.

For each unique RCT, information for the quality appraisal was first obtained from the original publication, but additional relevant study literature was also used to conduct the assessment, including where available: design and rationale documents, companion study publications, protocols, published comments on the study and contact with investigators.

Data Synthesis and Analysis

The study and patient characteristics for the included studies were presented narratively and summarized to accompany the synthesized data.

When data were available, sufficiently similar, and of sufficient quality, network meta-analysis (NMA) methods were used to synthesize the evidence from the included RCTS reporting outcomes for the overactive bladder agents of interest using WinBUGS software (MRC Biostatistics Unit, Cambridge, UK).[4] Model fit for Bayesian analyses was based on the Deviance Information Criterion (DIC) and comparison of residual deviance to number of

unconstrained data points.[5-11] Selection of the model/measure depended on the outcome of interest and the availability of data. Heterogeneity across trials in terms of patient characteristics, trial methodologies, and treatment protocols was carefully assessed. We also considered sensitivity analyses including removal of studies from the network of therapies that were not scored as being of high quality. We formally and informally assessed consistency between direct and indirect evidence by comparing direct estimates obtained from pair-wise meta-analysis with estimates from the Bayesian network meta-analysis. Model diagnostics including trace plots and the Brooks-Gelman-Rubin statistic were also assessed to ensure model convergence. At least two chains were fit in WinBUGS for each analysis, each employing at least 40,000 iterations, with a burn-in of at least 20,000 iterations.[12,13]

For continuous outcomes, the effect size was expressed in terms of the mean difference (MD) when change scores from the same scale were analyzed together (e.g., cognition) and standardized mean difference (SMD) when change scores from a variety of scales were pooled together for analyses. Effect estimates for dichotomous outcomes are reported using odds ratios with 95% credible intervals.

Meta-analyses were considered for efficacy and safety outcomes where data were insufficient to carry out NMA. Odds ratios and corresponding 95% confidence intervals were calculated for fixed or random effects models.

Results

Search Findings

A total of 1,941 citations were identified from the initial searches, 1,818 of which were found through searches of electronic databases and an additional 123 records identified from grey literature sources and the previous systematic reviews.[1-3] Following the removal of duplicate records, 1,378 unique citations were retrieved for screening.

Two reviewers independently reviewed the titles and abstracts of studies identified by the search strategy in a standardized method using electronic tools customized to the project in DistillerSR, an online systematic review software tool (ref). Use of the online tool by the review team maximizes efficiency in the review process and facilitates consistency across reviewers for literature screening, selection and data extraction. Of the 1,378 unique records screened, 364 citations were selected for full-text review by two independent reviewers. Any disagreements during this two-stage screening process were resolved through consensus.

Studies included in the existing systematic reviews, along with those excluded for unsuitable outcomes, were rescreened for eligibility using their full-text. Any uncertainties or disagreements between the two reviewers at any stage of the study selection process were resolved by discussion and, if required, consensus was reached with a third review author. Attempts were made to obtain all studies that meet the selection criteria in full-text format. Appendix B presents the search results, including reasons for exclusion of full-text publications.

Among the 364 articles that were retrieved for full-text review, a total of 168 articles[14-181] reporting 105 unique RCTs addressed the objective of the review and were selected for inclusion. A subset of 79 unique RCTs[19,20,26-31,34,35,38,40,41,43,45-52,55-61,63-66,68-71,73-78,84-86,88-90,92,94,96,99,101-104,108,110,111,114-117,123,124,128,130-133,135-137,141,144-147,150,152,161,163,165-167,171-175,179,180,182-187] reported outcomes of interest and were eligible for evidence synthesis.

Included Studies

A list of included studies is presented in Appendix E. Excluded studies and those that could not be located during the expedited timeline of this review are listed in Appendix D.

Study and Patient Characteristics

A total of 79 unique RCTs reported in 121 articles[19,20,26-31,34,35,38,40,41,43,45-52,55-61,63-66,68-71,73-78,84-86,88-90,92,94,96,99,101-104,108,110,111,114-117,123,124,128,130-133,135-137,141,144-147,150,152,161,163,165-167,171-175,179,180,182-187] described outcomes of interest. Included RCTs were published between 1997 and 2015, and the total number of participants in each study ranged from 18 to 2,417 (Exhibit 4). RCTs included in the analyses were all parallel design, except for one crossover study which reported data for the first period. Study duration ranged from 2 to 52 weeks, although median study duration was 12 weeks (Exhibit 5). Detailed study and patient characteristics are presented in Appendix G.

Exhibit 4. Summary of Study Characteristics

Publication Status	Unique RCTs	79
Study Design	Parallel	78 (99%)
	Crossover	1 (0.1%)
	Placebo control (+/- active control)	55 (70%)
	Active control	23 (29%)
Country	Single	41 (51%)
	Multinational	38 (48%)
Sponsors	Industry	57 (72%)
	Not reported	20 (25%)
Year of Publication	Range: 1997 to 2015	
Randomized Sample Size	Range: 18 to 2,417	
Study Duration	Range: 2 to 52 weeks	

For n=79 unique RCTs reporting outcome data

Study participants were predominantly female (range 50 to 100%) and had varying treatment experience with anticholinergic agents. Mean age ranged from 40.2 years to 75.3 years. OAB syndrome characteristics were often not described in detail.

Exhibit 5. Summary of Patient Characteristics

Mean age	Range: 40.2 to 75.3	
% Female	Range: 50 to 100%	
% Treatment Experienced	Range: 38 to 100%	
Duration of Symptoms	Range: <6 to 121.2 months	
Diagnosis/OAB Type	Urge	17
	Mixed	15
	Stress	1
	OAB	45
Adherence (%)	Range: 52 to 98% <50% reported adherence	

Detailed trial and study characteristics are provided in Appendix G.

Risk of Bias Assessments

Risk of Bias assessments were carried out on the 79 unique RCTs reporting study outcomes. Of these, 10 studies had at least 1 domain at high risk of bias. The domains with a high risk of bias were generally the blinding of subjective outcomes, or that there was incomplete data addressed for efficacy or safety. With the exception of 5, all RCTs had at least one domain with an unclear risk of bias. Unclear risk of bias in most of the RCTs was related to the extremely poor reporting of allocation concealment and sequence generation.

Full results from the ROB assessment are presented in Appendix F.

Network Meta-Analyses

Network meta-analyses were conducted for the following efficacy outcomes: micturitions, incontinence, quality of life, urgency episodes and nocturia. Evidence networks for micturitions and incontinence were analysed at 12 weeks, and all other outcomes at end of study. Results in this report are based on the random effects model. Subsequent publications, or the unfinished final report, will present findings for micturitions and incontinence at end of study, along with the detailed results from both the random and fixed effects models, and all checks of model assumptions.

Efficacy

Micturitions in 24 Hours

- All agents were superior to placebo except for the oxybutynin transdermal formulation.
- When compared head-to-head, extended-release oxybutynin was superior to transdermal oxybutynin, tolterodine, extended-release tolterodine and mirabegron.
- Solifenacin was superior to tolterodine, extended-release tolterodine and mirabegron.
- The evidence network included 49 RCTs[19,27,31,35,45,47,48,51,58,61,64-66,68,70,76,78,89,90,92,94,96,99,101-105,108,110,111,114,116,117,128,130-132,136,141,144,145,147,149,150,152,161,163,166,167,174,180] and a total of 39,119 adults with OAB syndrome.

Incontinence Episodes in 24 Hours

- All agents were superior to placebo except for the oxybutynin transdermal formulation and trospium.
- When compared head-to-head, extended-release oxybutynin and solifenacin were superior to tolterodine, extended-release tolterodine, darifenacin, fesoterodine, and mirabegron.
- The evidence network included 40 RCTs[27,31,35,41,46,57,58,61,65,66,68,73,78,92,96,99,101-104,110,111,115-117,131,144,145,150,152,161,163,166,167,174,180,183] and a total of 30,959 adults with OAB syndrome. Urge and total incontinence episodes were considered for this outcome.

Quality of Life

- Extended-release tolterodine, solifenicin, trospium, fesoterodine and mirabegron significantly improved quality of life when compared with placebo.

- When compared head-to-head, extended-release tolterodine significantly improved quality of life compared to solifenacin and fesoterodine.
- Solifenacin and fesoterodine were superior to mirabegron.
- No studies reported quality of life outcomes for the oxybutynin gel formulation.
- The evidence network included 26 RCTs[56,64,89,99,111,115,117,122,128,131-133,135,136,141,144,145,147,150,152,161,166,167,183] and a total of 22,888 adults with OAB syndrome.

Urgency Episodes

- All agents significantly reduced mean urgency episodes when compared to placebo.
- When compared head-to-head, only one comparison showed statistically superior efficacy. Fesoterodine significantly reduced mean urgency episodes when compared to mirabegron.
- No studies reported urgency episode outcome data for the oxybutynin gel or transdermal formulations.
- The evidence network included 43 RCTs[55,56,60,64-66,68,70,76,78,89,90,94,96,99,102-104,111,114-117,122,128,130-132,135,136,141,144,145,147,150,152,161,166,167,172,174,180] and a total of 35,051 adults with OAB syndrome.

Nocturia

- Extended-release tolterodine, solifenicin, fesoterodine and mirabegron significantly reduced nocturia when compared with placebo.
- No differences were seen amongst the OAB agents when they were compared head-to-head.
- The evidence network included 30 RCTs[65,68,73,76,78,86,90,94,96,102,103,110,111,115,117,122,128,130-132,136,141,144,145,166,167,172,174,180] and a total of 27,671 adults with OAB syndrome.

Safety

Network meta-analyses were conducted for the following safety outcomes: Dry mouth, constipation, withdrawals due to adverse events, all-cause withdrawals, withdrawals due to a lack of efficacy, and serious adverse events.

Dry mouth

- All agents had significantly higher proportion of patients with dry mouth, except for transdermal oxybutynin, oxybutynin gel and mirabegron when compared to placebo.

- When compared head-to-head, all agents were superior to immediate-release oxybutynin.
- Mirabegron was superior to all agents except the transdermal and gel formulations of oxybutynin.
- Extended-release tolterodine was superior to darifenicin, tolterodine, extended-release oxybutynin and fesoterodine.
- The evidence network included 67 RCTs[26-31,34,35,40,41,45-48,51,56,57,60,61,64-66,68,70,73,74,78,86,90,94,96,99,101-104,108,110,111,114,115,117,122,128,130-133,135,136,141,144,145,147,150,152,161,163,166,167,172-174,180,182,183] and a total of 43,707 adults with OAB syndrome.

Constipation

- All agents had a significantly higher proportion of patients with constipation compared to placebo except the oxybutynin formulations, including immediate- and extended-release, transdermal and gel.
- When compared head-to-head, oxybutynin (including immediate- and extended-release, transdermal but not gel formulations) were generally superior to the other agents, with few exceptions.
- Mirabegron and tolterodine were superior to darifenacin, solifenacin, and fesoterodine.
- The evidence network included 53 RCTs[26,28-30,41,45-48,56,57,60,61,64-66,68,70,73,78,86,90,94,96,99,101,102,108,110,111,114,115,117,122,128,131-133,136,144,145,147,150,152,161,163,166,167,174,180,182,183] and a total of 37,876 adults with OAB syndrome.

All-cause withdrawals

- All agents were no different than placebo except for immediate-release oxybutynin which had significantly more withdrawals and extended-release tolterodine which had significantly fewer withdrawals.
- When compared head-to-head, all agents had significantly less withdrawals than immediate-release oxybutynin, with the exception of trospium and the oxybutynin gel formulations.
- Mirabegron, immediate-release tolterodine and solifenacin had significantly fewer withdrawals than fesoterodine.
- The evidence network included 64 RCTs[26-31,35,40,41,45-48,51,56,57,60,61,64-66,68,73,76,78,86,90,94,96,99,101-104,108,110,111,114-117,122,128,130-132,135,136,141,144,145,147,150,152,161,163,166,167,172-174,180,182,184] and a total of 42,715 adults with OAB syndrome.

Withdrawals due to adverse events (WDAE)

- All agents were no different than placebo except for immediate-release oxybutynin, solifenacin and fesoterodine which had significantly higher WDAE.
- Extended-release oxybutynin, tolterodine, extended-release tolterodine, solifenacin and mirabegron had significantly fewer WDAE compared to immediate-release oxybutynin.
- Fesoterodine had significantly more WDAE when compared to tolterodine and extended-release tolterodine.
- The evidence network included 64 RCTs[26-31,35,40,41,45-48,51,56,57,60,61,64-66,68,73,76,78,86,90,94,96,99,101-104,108,110,111,114-117,122,128,130-132,135,136,141,144,145,147,150,152,161,163,166,167,172-174,180,182,184] and a total of 42,974 adults with OAB syndrome.

Withdrawals due to lack of efficacy

- Tolterodine, extended-release tolterodine, solifenicin, fesoterodine and mirabegron had significantly fewer withdrawals due to a lack of efficacy when compared to placebo.
- No differences amongst the OAB agents were found when they were compared head-to-head
- The evidence network included 44 RCTs[28,40,41,47,52,56-58,60,61,64-66,70,76,78,89,99,101,103,104,114,115,117,122,128,130-132,135,136,141,144,145,147,150,152,161,163,166,167,174,180,182] and a total of 34,899 adults with OAB syndrome.

Serious adverse events

- No differences amongst the agents when compared head-to-head or to placebo.
- The evidence network included 36 RCTs[27,29,31,35,38,45-48,51,60,61,68,78,89,103,104,110,111,115,117,122,132,136,141,144,145,147,150,152,161,166,167,174,180,182] and a total of 28,827 adults with OAB syndrome.

Data Excluded from Evidence Networks

Studies reporting incomplete outcome data or where outcome data were reported in a way that did not allow for their inclusion in the evidence networks will be narratively summarized in publication(s) or unfinished final reports. The number of studies that were excluded from the evidence networks is reported in Exhibit 3.

Exhibit 6. Number of studies excluded from evidence networks.

	Studies Excluded (n)
EFFICACY OUTCOME	
Micturitions	2
Incontinence	1
Urgency Episodes	1
Quality of Life	0
Nocturia	2
SAFETY OUTCOME	
Dry Mouth	
Constipation	4
All-cause Withdrawals	7
Withdrawals due to Adverse Events	4
Withdrawals due to Lack of Efficacy	2
Serious Adverse Events	4

A note about arrhythmia

- The following outcomes were considered for the assessment of cardiac arrhythmia in adults with OAB syndrome: sick sinus syndrome, sinus tachycardia, atrial fibrillation, paroxysmal atrial tachycardia, supraventricular tachycardia, ventricular tachycardia, bradycardia, premature atrial contractions, premature ventricular contractions, long QT syndrome/QT prolongation, torsades de pointes, bundle branch re-entry ventricular tachycardia, palpitations.
- Data were reported as events or persons with events. At the time of this report, analyses for this outcome were not complete.
- Final results will be posted as an addendum to this report on the ODPRN website (www.odprn.ca).

A note about dual therapy

A number of included studies reported dual therapy with mirabegron and solifenacin. Results for this pharmacotherapy combination are still under investigation due to some statistical anomalies that arose during analyses. Dual therapy generally had similar efficacy to mirabegron and solifenicin alone, and showed no statistically significant benefit over monotherapy. Safety results for dual therapy generally mirrored those of solifenicin.

Subgroups

The following subgroups were considered: sex (male or female), age (≥65, 65 to 75, ≥75) and those previously treated with an anticholinergic medication. At the time of this report, subgroup data where evidence networks were possible were still being analysed. Final results will be published or provided in the unfinished final report. Exhibits 4 and 5 detail the studies

available for each efficacy and safety subgroup, and the method of synthesis that will be used. Subgroups where no data were available are also noted.

Exhibit 7. Studies available for subgroups: Efficacy outcomes

Efficacy Outcome	Subgroup	Studies (n)	Synthesis Type	Treatments Included
Micturitions	**<65 years**	7	NMA	PLB, TOLT-ER, OXYB, SOLF, TOLT, MIRA, FEST
	65 to 75 years	2	MA	PLB, FEST
	> 75 years	2	MA	PLB, FEST
	Treatment experienced	3	NMA	PLB, SOLF, MIRA, OXYB-TRANS, TOLT
	Treatment naïve	1	N	PLB, TOLT, MIRA
	Women	14*	NMA	PLB, TOLT-ER, DARF, SOLF, OXYB, OXYB-ER, OXYB-GEL, OXYB-TRANS, FEST
	Men	1	N	PLB, FEST
Incontinence	**<65 years**	3	NMA	PLB, TOLT, SOLF, TOLT-ER
	65 to 75 years	--	--	--
	> 75 years	--	--	--
	Treatment experienced	3*	NMA	PLB, SOLF, MIRA, OXYB-TRANS, TOLT-ER, OXYB, TOLT,
	Treatment naïve	1	N	PLB, TOLT, MIRA
	Women	10	NMA	PLB, TOLT-ER, OXYB, OXYB-ER, OXYB-GEL, OXYB-TRANS, DARF
	Men	--	--	--
Urgency Episodes	**<65 years**	3	NMA	PLB, SOLF, MIRA, TROS, TOLT, TOLT-ER
	65 to 75 years	1	N	PLB, FEST
	> 75 years	1	N	PLB, FEST
	Treatment experienced	1	N	SOLF, MIRA
	Treatment naïve	--	--	--
	Women	5*	NMA	PLB, TOLT-ER, DARF, SOLF, TOLT, OXYB, OXYB-ER,
	Men	1	N	PLB, FEST
Quality of Life	**<65 years**	4	NMA	PLB, TOLT-ER, TOLT, TROS, SOLF
	65 to 75 years	1	N	PLB, FEST
	> 75 years	1	N	PLB, FEST
	Treatment experienced	2	N	PLB, TOLT-ER, MIRA, SOLF, OXYB-TRANS
	Treatment naïve	--	--	--

Efficacy Outcome	Subgroup	Studies (n)	Synthesis Type	Treatments Included
	Women	7	NMA	PLB, TROS, TOLT-ER, TOLT, DARF, SOLF, OXYB, OXYB-ER, OXYB-TRANS
	Men	1	N	PLB, TROS
Nocturia	**<65 years**	1	N	OXYB, TOLT
	65 to 75 years	1	N	PLB, FEST
	> 75 years	1	N	PLB, FEST
	Treatment experienced	1	N	SOLF, MIRA
	Treatment naïve	--	--	--
	Women	3	N	PLB, OXYB, OXYB-GEL, TOLT, DARF, SOLF
	Men	--	--	--

***** Single additional study unable to be included in the evidence network. Results will be summarized narratively.
--=No studies reported.
N=narrative only, NMA=network meta-analysis, MA=meta-analysis, OXYB=immediate release oxybutynin, OXYB-ER=extended-release oxybutynin, OXYB-TRANS=transdermal oxybutynin, OXYB-GEL=oxybutynin gel, TOLT=tolterodine, TOLT-ER= extended-release tolterodine, DARF=darafenicin, SOLF=solifenacin, TROS=trospium, FEST=fesoterodine, MIRA=mirabegron.

Exhibit 8. Studies available for subgroups: Safety outcomes

Safety Outcome	Subgroup	Studies (n)	Synthesis Type	Treatments Included
Constipation	**<65 years**	6*	NMA	PLB, TOLT-ER, FEST, OXYB-ER, TOLT, SOLF
	65 to 75 years	3[†]	MA	PLB, FEST, OXYB-ER, TOLT
	> 75 years	4[§]	MA	PLB, FEST, OXYB-ER, TOLT-ER, MIRA
	Treatment experienced	2	N	OXYB-ER, TOLT-ER, SOLF, MIRA
	Treatment naïve	1	N	OXYB-ER, TOLT-ER
	Women	15[a]	NMA	PLB, OXYB-ER, TOLT, TOLT-ER, FEST, OXYB, DARF, SOLF, OXYB-GEL, OXYB-TRANS
	Men	2	NMA	PLB, FEST, TOLT-ER
Dry mouth	**<65 years**	11[∞]	NMA	PLB, TOLT-ER, FEST TOLT, OXYB-ER, OXYB, SOLF
	65 to 75 years	3[†]	MA	PLB, FEST, OXYB-ER, TOLT
	> 75 years	4[§]	MA	PLB, FEST, OXYB-ER, TOLT-ER, MIRA
	Treatment experienced	3**	NMA	OXYB-ER, TOLT-ER, SOLF, MIRA
	Treatment naïve	1	N	OXYB-ER, TOLT-ER

Safety Outcome	Subgroup	Studies (n)	Synthesis Type	Treatments Included
	Women	18[ß]	NMA	PLB, TOLT-ER, OXYB, OXYB-ER, OXYB-GEL, OXYB-TRANS, DARF
	Men	2	NMA	PLB, FEST, TOLT-ER
All cause withdrawals	**<65 years**	9	NMA	PLB, TOLT, TOLT-ER, OXYB, SOLF
	65 to 75 years	--	--	--
	> 75 years	1	N	PLB, FEST
	Treatment experienced	3**	NMA	OXYB-ER, TOLT-ER, SOLF, MIRA
	Treatment naïve	1	N	OXYB-ER, TOLT-ER
	Women	20*	NMA	PLB, OXYB, OXYB-ER, OXYB-GEL, TOLT, TOLT-ER, FEST, DARF, SOLF
	Men	1	N	PLB, FEST, TOLT-ER
Withdrawals due to AE	**<65 years**	6	NMA	PLB, TOLT-ER, OXYB, TOLT TOLT, SOLF
	65 to 75 years	1	N	PLB, FEST
	> 75 years	2	N	PLB, FEST, TOLT-ER, MIRA
	Treatment experienced	3**	NMA	OXYB-ER, TOLT-ER, SOLF, MIRA
	Treatment naïve	1	N	OXYB-ER, TOLT-ER
	Women	15*	NMA	PLB, TOLT, TOLT-ER, FEST, OXYB, DARF, SOLF, OXYB-ER, OXYB-GEL
	Men	1	N	PLB, FEST, TOLT-ER
Withdrawals due to a lack of efficacy	**<65 years**	4	NMA	PLB, TOLT-ER, TOLT, SOLF
	65 to 75 years	1	MA	PLB, FEST
	> 75 years	1	MA	PLB, FEST
	Treatment experienced	3**	NMA	OXYB-ER, TOLT-ER, SOLF, MIRA
	Treatment naïve	1	N	OXYB-ER, TOLT-ER
	Women	12*	NMA	PLB, TOLT, TOLT-ER, OXYB, SOLF, DARF, OXYB-ER, OXYB-TRANS
	Men	1	N	PLB, FEST, TOLT-ER
Serious Adverse Events	**<65 years**	3	NMA	PLB, TOLT-ER, TROS
	65 to 75 years	1	N	PLB, FEST
	> 75 years	2	N	PLB, FEST, MIRA, TOLT-ER
	Treatment experienced	1	N	SOLF, MIRA
	Treatment naïve	--	--	--
	Women	5	NMA	PLB, TOLT, TOLT-ER, OXYB-GEL, DARF
	Men	--	--	--

* Single additional study unable to be included in the evidence network. Results will be summarized narratively.
† Only PLB and FEST will contribute to the meta-analysis, a single study of OXYB-ER and TOLT will be summarized narratively.
§ Only PLB and FEST will contribute to the meta-analysis, two additional studies of TOLT-ER versus MIRA and TOLT-ER versus OXYB-ER will be summarized narratively.
∞ Two additional studies involving OXYB, TOLT, TROS and PLB are not included in the evidence network. Results will be summarized narratively.
** One of the studies does not connect to the evidence network of OXYB-ER, TOLT-ER and OXYB. Results for SOLF and MIRA will be summarized narratively.
a Three studies involving OXYB, TOLT, TROS, PLB and DARF are not included in the evidence network. Results will be summarized narratively.
ß Four studies involving OXYB, TOLT, TROS, OXYB-ER, DARF and PLB are not included in the evidence network. Results will be summarized narratively.

--=No studies reported.
AE=adverse event, N=narrative only, NMA=network meta-analysis, MA=meta-analysis, OXYB=immediate release oxybutynin, OXYB-ER=extended-release oxybutynin, OXYB-TRANS=transdermal oxybutynin, OXYB-GEL=oxybutynin gel, TOLT=tolterodine, TOLT-ER= extended-release tolterodine, DARF=darafenicin, SOLF=solifenacin, TROS=trospium, FEST=fesoterodine, MIRA=mirabegron.

Conclusions

On the whole, the available evidence relating to the comparative efficacy and safety of pharmacologic treatments for the management of adults with overactive bladder symptoms is generally of limited quality, with a large proportion of studies disclosing financial support or affiliation with the pharmaceutical industry, and a high or unclear rating across many risk of bias domains. Although there are limitations in the evidence base, there is still applicability to the Canadian decision making context. Anticholinergic agents are generally efficacious for treatment of the symptoms of overactive bladder; however, common adverse events such as dry mouth and constipation necessitate alternative treatment options, either by novel dosage formats (e.g. transdermal or gel) for existing medications, or through agents from novel drug classes like the β3-adrenergic agonist, mirabegron.

Results of this review are comparable to those in previous reviews for the anticholinergic agents and for mirabegron. Previous reviews rarely evaluate the newer dosage formats of oxybutynin. Nabi et al. (2006)[3] compared anticholinergic agents to placebo and found differences in both incontinence and micturitions in 24 hours favouring overactive bladder agents. A subset of overactive bladder agents in this review (extended-release tolterodine, solifenacin, fesoterodine and mirabegron) modestly improved quality of life scores compared to placebo, a finding noted in the 2006 Cochrane systematic review. Maman et al. also demonstrated using network meta-analysis that mirabegron had similar efficacy to most of the anticholinergic/antimuscanarinic agents, but a lower proportion of patients who experience dry mouth.[2] Solifenicin was also superior to most agents, including mirabegron, for 24-hour micturitions and urgency incontinence episodes in previous reviews[1,2] and confirmed in this review.

This review confirms that many of the agents for overactive bladder are at a high risk of discontinuation in the first two years due to a lack of efficacy[188] . Although mirabegron is a treatment option for those who do not respond or tolerate anticholinergic agents, this review

shows that that mirabegron is no different than the anticholinergic agents in this respect.

Limitations

This review has provided a comprehensive overview of the efficacy and safety of the currently available overactive agents in Canada. Although we followed a rigorous methodology, turnaround time for this review was rapid (less than four months) and limitations are important to discuss. Due to time constraint, we were unable to review evidence pertaining to outcomes that may be of importance to patients, such as cognitive impairment and cardiac risk. We were unable to complete the assessment of arrhythmia in time for publication; however, we will post findings once they are available (www.odprn.ca). Although the evidence in this review showed no statistically significant differences in serious adverse events amongst the overactive bladder agents, the RCTs included in this review were relatively short in duration (median 12 weeks). Large, comparative RCTs with a lengthy duration of follow-up are required to fully elucidate the risk of serious adverse events in patients with overactive bladder, especially those at high risk like the elderly. Additionally, a comprehensive systematic review including both randomized and non/quasi-randomized evidence may better suit the evaluation of important safety outcomes.

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187. Anderson RU, MacDiarmid S, Kell S, Barada JH, Serels S, Goldberg RP. Effectiveness and tolerability of extended-release oxybutynin vs extended-release tolterodine in women with or without prior anticholinergic treatment for overactive bladder. International Urogynecology Journal 2006;17:502-11.

188. Tubaro A, De Nunzio C. Words of wisdom. Re: Comparative efficacy and safety of medical treatments for the management of overactive bladder: a systematic literature review and mixed treatment comparison. European urology 2014;65:1220-1.

Appendix A: Search Strategy

The following is the search strategy used in Ovid interfaces MEDLINE and EMBASE to identify RCTs of pharmacologic treatments for OAB syndrome.

Overactive Bladder
Final Strategies
2015 Aug 15

OVID

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>, Embase <1974 to 2015 August 14>
Search Strategy:
---

1 Urinary Bladder, Overactive/ (10805)
2 Urinary Incontinence, Urge/ (5095)
3 ((overactive adj2 (bladder* or detrusor*)) or (urina* adj2 (incontinen* or frequen*)) or (urge adj2 incontinen*) or (detrusor adj2 dyssynergia) or (bladder adj1 irritat*) or DESD).tw,kw. (66538)
4 or/1-3 (70360)
5 Cholinergic Antagonists/ (30119)
6 (((cholinergic* or acetylcholine) adj2 (antagonist* or blocker*)) or anticholinergic* or anti cholinergic* or AChR inhibitor* or cholinolytic*).tw,kw. (31310)
7 Muscarinic Antagonists/ (13988)
8 ((muscarinic* adj2 (antagonist* or blocker*)) or antimuscarinic* or anti muscarinic* or muscarinolytic*).tw,kw. (16198)
9 Adrenergic beta-3 Receptor Agonists/ (1251)
10 ((adrenergic adj1 (beta3 or "beta-3") adj2 agonist*) or (adrenoreceptor* adj1 (beta3 or "beta 3") adj2 agonist*) or (adrenergic adj2 receptor agonist*)).tw,kw. (4492)
11 (solifenacin or vesicare or vesikur or vesiker or vesitirim or ym53705 or "ym 53705" or ym905 or "ym 905").tw,kw. (1297)
12 (tolterodine or detrusitol or detrol or "detrol la" or pnu200583 or "pnu 200583" or unidet or urotrol).tw,kw. (2348)
13 (mirabegron or betanis or betmiga or myrbetique or sc211912 or "sc 211912" or YM178 or "YM-178").tw,kw. (513)
14 (darifenacin or darifenacine or enablex or emselex or uk88525 or "uk 88525").tw,kw. (821)
15 (fesoterodine or "spm 907" or spm907 or toviaz).tw,kw. (524)
16 (oxybutynin or anturol or "apo-Oxybutynin" or contimin or cystonorm or cystrin or delifon or ditropan or diutropin or dresplan or dridase or driptane or esoxybutynin or frenurin or gelnique or "gen-oxybutynin" or iliaden or kentera or "kl 007" or kl007 or lenditro or "lyrinel XL" or "mutum cr" or nefryl or "novo-oxybutynin" or "nu-oxybutyn" or "oxyb AbZ" or oxyban or oxybugamma or oxybutinin or obuton or oxymedin or oyrobin or oxytrol or "PMS-oxybutynin" or pollakis* or renamel or reteven or ryol or spasyt or tavor or tropan or uricont or uroflax or urotrol or zatur).tw,kw. (4534)
17 (trospium or ceris or spasmolyt or trospi or uraplex or urato or regurin or flotros or sanctura or tropez or tosec or spasmex or "spasmo-lyt" or "spasmo-rhoival" or "spasmo-urgenin" or spasmolyt or spasmourgenin).tw,kw. (907)
18 Flavoxate/ (861)
19 (flavoxate or "ak 123" or ak123 or baduson or bladderon or bladuril or cleanxate or "dw 61" or dw61 or flavate or "flavo-spa" or flavorin or fucotin or genurin or harnin or spagerin or spasdic or spasuret or tonlin or urispas or uronid or uropeace or uroxate or voxate or yungken).tw,kw. (540)
20 or/5-19 (82343)
21 4 and 20 (9106)
22 (controlled clinical trial or randomized controlled trial).pt. (494451)
23 clinical trials as topic.sh. (177811)
24 (randomi#ed or randomly or RCT$1 or placebo*).tw,kw. (1604197)
25 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (319109)
26 trial.ti. (334413)
27 or/22-26 (2031352)
28 21 and 27 (2263)
29 exp Animals/ not (exp Animals/ and Humans/) (8643168)
30 28 not 29 (2248)

31 (comment or editorial or interview or news).pt. (1610240)
32 (letter not (letter and randomized controlled trial)).pt. (1844622)
33 30 not (31 or 32) (2214)
34 exp Urinary Bladder, Overactive/ (13005)
35 exp Urinary Incontinence, Urge/ (5824)
36 ((overactive adj3 bladder*) or (urge adj3 incontinence) or (detrusor adj3 dyssynergia) or urinary frequency or bladder irritation or DESD).mp. (32389)
37 or/34-36 (32389)
38 exp Muscarinic Antagonists/ (113938)
39 (solifenacin or Vesicare or Vesikur or Vesiker or Vesitirim).mp. (2011)
40 (tolterodine or Detrusitol or Detrol or Detrol LA).mp. (4075)
41 (mirabegron or YM-178 or Betanis).mp. (670)
42 (darifenacin or Enablex or Emselex).mp. (1475)
43 (fesoterodine or Toviaz).mp. (769)
44 (oxybutynin or Ditropan or Lyrinel XL).mp. (6332)
45 (propiverine or Detrunorm).mp. (1693)
46 (trospium or Regurin or Flotros or Sanctura or Tropez or Trosec or Spasmex).mp. (1568)
47 or/38-46 (118764)
48 Randomized controlled trials as Topic/ (181983)
49 Randomized controlled trial/ (790575)
50 Random allocation/ (153158)
51 Double blind method/ (259156)
52 Single blind method/ (41894)
53 Clinical trial/ (1356984)
54 exp Clinical Trials as Topic/ (457996)
55 or/48-54 (2162939)
56 (clinic$ adj trial$1).tw. (570178)
57 ((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw. (318490)
58 Placebos/ (307612)
59 Placebo$.tw. (397014)
60 Randomly allocated.tw. (42679)
61 (allocated adj2 random).tw. (1560)
62 or/56-61 (1170604)
63 55 or 62 (2632332)
64 Case report.tw. (521399)
65 Letter/ (1809539)
66 Historical article/ (323989)
67 Review of reported cases.pt. (0)
68 Review, multicase.pt. (0)
69 or/64-68 (2637131)
70 63 not 69 (2562018)
71 37 and 47 and 70 (3034)
72 limit 71 to (humans and yr="2000 -Current") (2677)
73 ("20130621" or "20130622" or "20130623" or "20130624" or "20130625" or "20130626" or "20130627" or "20130628" or "20130629" or "20130630" or 201307* or 201308* or 201309* or 201310* or 201311* or 201312* or 2014* or 2015*).dc. (2425891)
74 72 and 73 (72)
75 72 not 74 (2605)
76 33 not 75 (890) [OVERLAP WITH MAMAN, REMOVED]
77 76 use prmz (370)
78 overactive bladder/ (13005)
79 detrusor dyssynergia/ (2779)
80 urinary urgency/ (4428)
81 urge incontinence/ (5824)
82 urinary frequency/ (5127)
83 bladder irritation/ (722)

84 ((overactive adj2 (bladder* or detrusor*)) or (urina* adj2 (incontinen* or frequen*)) or (urge adj2 incontinen*) or (detrusor adj2 dyssynergia) or (bladder adj1 irritat*) or DESD).tw,kw. (66538)
85 or/78-84 (76176)
86 cholinergic receptor blocking agent/ (26297)
87 (((cholinergic* or acetylcholine) adj2 (antagonist* or blocker*)) or anticholinergic* or anti cholinergic* or AChR inhibitor* or cholinolytic*).tw,kw. (31310)
88 muscarinic receptor blocking agent/ (6897)
89 ((muscarinic* adj2 (antagonist* or blocker*)) or antimuscarinic* or anti muscarinic* or muscarinolytic*).tw,kw. (16198)
90 beta 3 adrenergic receptor stimulating agent/ (845)
91 ((adrenergic adj1 (beta3 or "beta-3") adj2 agonist*) or (adrenoreceptor* adj1 (beta3 or "beta 3") adj2 agonist*) or (adrenergic adj2 receptor agonist*)).tw,kw. (4492)
92 solifenacin/ (1512)
93 (solifenacin or vesicare or vesikur or vesiker or vesitirim or ym53705 or "ym 53705" or ym905 or "ym 905").tw,kw. (1297)
94 tolterodine/ (3114)
95 (tolterodine or detrusitol or detrol or "detrol la" or pnu200583 or "pnu 200583" or unidet or urotrol).tw,kw. (2348)
96 mirabegron/ (436)
97 (mirabegron or betanis or betmiga or myrbetique or sc211912 or "sc 211912" or YM178 or "YM-178").tw,kw. (513)
98 darifenacin/ (1136)
99 (darifenacin or darifenacine or enablex or emselex or uk88525 or "uk 88525").tw,kw. (821)
100 fesoterodine/ (583)
101 (fesoterodine or "spm 907" or spm907 or toviaz).tw,kw. (524)
102 oxybutynin/ (4923)
103 (oxybutynin or anturol or "apo-Oxybutynin" or contimin or cystonorm or cystrin or delifon or ditropan or diutropin or dresplan or dridase or driptane or esoxybutynin or frenurin or gelnique or "gen-oxybutynin" or iliaden or kentera or "kl 007" or kl007 or lenditro or "lyrinel XL" or "mutum cr" or nefryl or "novo-oxybutynin" or "nu-oxybutyn" or "oxyb AbZ" or oxyban or oxybugamma or oxybutinin or obuton or oxymedin or oyrobin or oxytrol or "PMS-oxybutynin" or pollakis* or renamel or reteven or ryol or spasyt or tavor or tropan or uricont or uroflax or urotrol or zatur).tw,kw. (4534)
104 trospium chloride/ (1218)
105 (trospium or ceris or spasmolyt or trospi or uraplex or urato or regurin or flotros or sanctura or tropez or tosec or spasmex or "spasmo-lyt" or "spasmo-rhoival" or "spasmo-urgenin" or spasmolyt or spasmourgenin).tw,kw. (907)
106 flavoxate/ (861)
107 (flavoxate or "ak 123" or ak123 or baduson or bladderon or bladuril or cleanxate or "dw 61" or dw61 or flavate or "flavo-spa" or flavorin or fucotin or genurin or harnin or spagerin or spasdic or spasuret or tonlin or urispas or uronid or uropeace or uroxate or voxate or yungken).tw,kw. (540)
108 or/86-107 (78572)
109 85 and 108 (9907)
110 randomized controlled trial/ or controlled clinical trial/ (1014917)
111 exp "clinical trial (topic)"/ (159208)
112 (randomi#ed or randomly or RCT$1 or placebo*).tw,kw. (1604197)
113 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (319109)
114 trial.ti. (334413)
115 or/110-114 (2202850)
116 109 and 115 (2680)
117 exp animal experimentation/ or exp models animal/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (39477100)
118 exp humans/ or exp human experimentation/ or exp human experiment/ (30539607)
119 117 not 118 (8939137)
120 116 not 119 (2672)
121 editorial.pt. (879934)
122 letter.pt. not (letter.pt. and randomized controlled trial/) (1840192)
123 120 not (121 or 122) (2635)
124 exp overactive bladder/ or exp detrusor dyssynergia/ (15352)
125 exp urinary urgency/ or exp urge incontinence/ (9514)
126 exp urinary frequency/ (5127)
127 exp bladder irritation/ (722)
128 ((overactive adj3 bladder*) or (urge adj3 incontinence) or (detrusor adj3 dyssynergia) or DESD).mp. (26257)
129 or/124-128 (31968)

130 exp solifenacin/ or exp tolterodine/ or exp mirabegron/ or exp darifenacin/ or exp fesoterodine/ or exp oxybutynin/ or exp propiverine/ or exp trospium chloride/ (8588)
131 (solifenacin or Vesicare or Vesikur or Vesiker or Vesitirim).mp. (2011)
132 (tolterodine or Detrusitol or Detrol or Detrol LA).mp. (4075)
133 (mirabegron or YM-178 or Betanis).mp. (670)
134 (darifenacin or Enablex or Emselex).mp. (1475)
135 (fesoterodine or Toviaz).mp. (769)
136 (oxybutynin or Ditropan or Lyrinel XL).mp. (6332)
137 (propiverine or Detrunorm).mp. (1693)
138 (trospium or Regurin or Flotros or Sanctura or Tropez or Trosec or Spasmex).mp. (1568)
139 exp muscarinic receptor blocking agent/ (64195)
140 or/130-139 (70226)
141 Clinical trial/ (1356984)
142 Randomized controlled trial/ (790575)
143 Randomization/ (153158)
144 Single blind procedure/ (20778)
145 Double blind procedure/ (125136)
146 Crossover procedure/ (43978)
147 Placebo/ (273773)
148 Randomi?ed controlled trial$.tw. (219975)
149 Rct.tw. (28629)
150 Random allocation.tw. (2745)
151 Randomly allocated.tw. (42679)
152 Allocated randomly.tw. (3919)
153 (allocated adj2 random).tw. (1560)
154 Single blind$.tw. (29231)
155 Double blind$.tw. (284659)
156 ((treble or triple) adj blind$).tw. (906)
157 Placebo$.tw. (397014)
158 Prospective study/ (703212)
159 or/141-158 (2686933)
160 Case study/ (1799050)
161 Case report.tw. (521399)
162 Abstract report/ or letter/ (1899117)
163 or/160-162 (3846799)
164 159 not 163 (2617474)
165 129 and 140 and 164 (2836)
166 limit 165 to (human and yr="2000 -Current") (2518)
167 ("20130621" or "20130622" or "20130623" or "20130624" or "20130625" or "20130626" or "20130627" or "20130628" or "20130629" or "20130630" or 201307* or 201308* or 201309* or 201310* or 201311* or 201312* or 2014* or 2015*).dd. (3511617)
168 166 not 167 (2165)
169 123 not 168 (1334) [OVERLAP WITH MAMAN, REMOVED]
170 169 use oemezd (1008) [EMBASE RECORDS]
171 77 or 170 (1378) [MEDLINE AND EMBAES RECORDS]
172 remove duplicates from 171 (1118) [TOTAL UNIQUE RECORDS]
173 172 use prmz (360) [MEDLINE UNIQUE RECORDS]
174 172 use oemezd (758) [EMBASE UNIQUE RECORDS]

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Cochrane Library

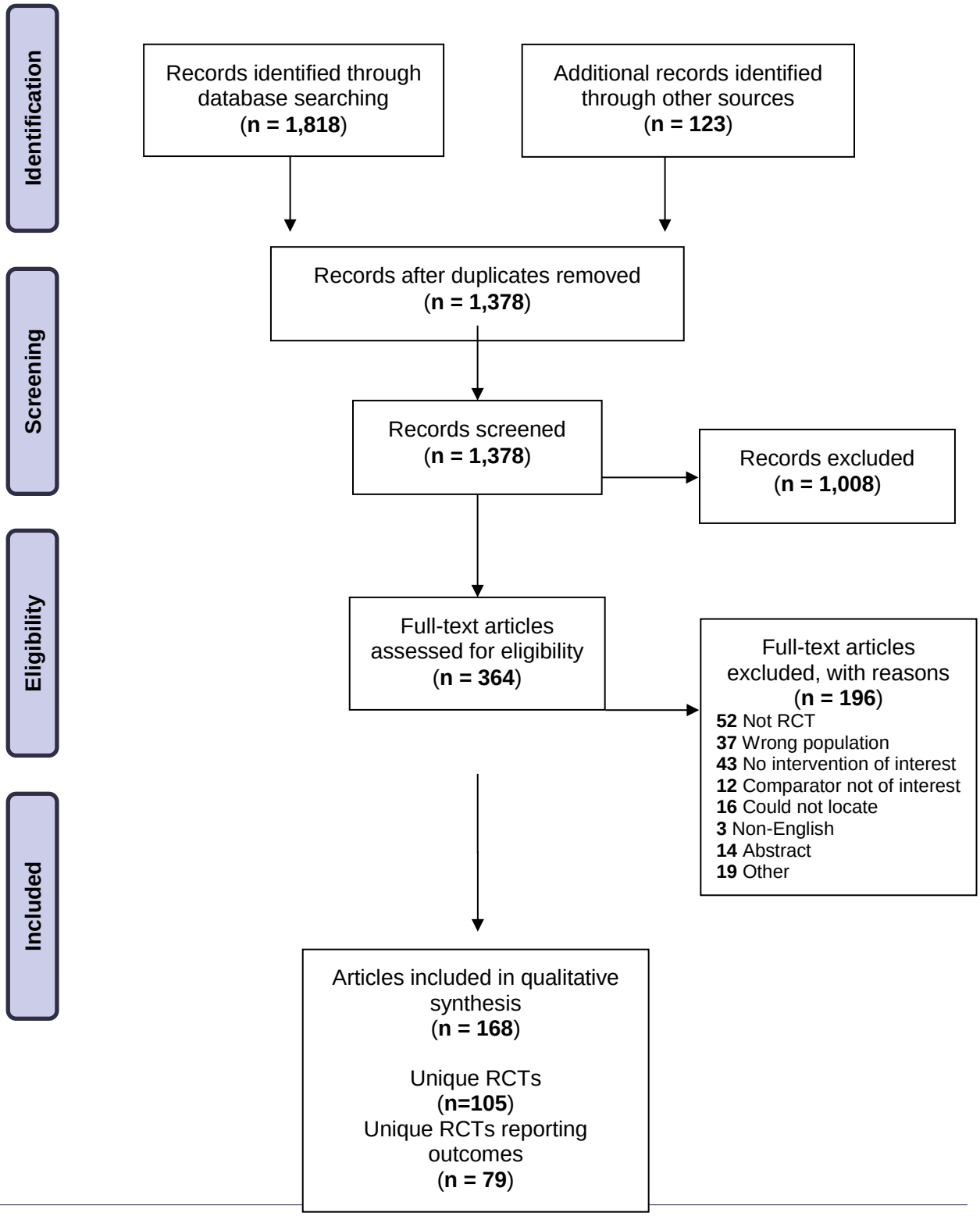
Search Name: Overactive Bladder - University of Ottawa Heart Institute - Maman Overlap Removed
Date Run: 15/08/15 13:12:44.226
Description: 2015 Aug 15

ID	Search	Hits
#1	[mh "Urinary Bladder, Overactive"]	339
#2	[mh "Urinary Incontinence, Urge"]	86
#3	((overactive near/2 bladder*) or (overactive near/2 detrusor*) or (urina* near/2 incontinen*) or (urina* near/2 frequen*) or (urge near/2 incontinen*) or (detrusor near/2 dyssynergia) or (bladder near/1 irritat*) or DESD):ti,ab,kw	4749
#4	#1 or #2 or #3	4749
#5	[mh ^"Cholinergic Antagonists"]	312
#6	((cholinergic* near/2 antagonist*) or (cholinergic* near/2 blocker*) or (acetylcholine near/2 antagonist*) or (acetylcholine near/2 blocker*) or anticholinergic* or (anti next cholinergic*) or (AChR next inhibitor*) or cholinolytic*):ti,ab,kw	2406
#7	[mh "Muscarinic Antagonists"]	613
#8	((muscarinic* near/2 antagonist*) or (muscarinic* near/2 blocker*) or antimuscarinic* or (anti next muscarinic) or muscarinolytic*):ti,ab,kw	1156
#9	[mh "Adrenergic beta-3 Receptor Agonists"]	18
#10	(((adrenergic next (beta3 or "beta-3")) near/2 agonist*) or (adrenergic near/2 (receptor next agonist*))):ti,ab,kw	189
#11	(solifenacin or vesicare or vesikur or vesiker or vesitirim or ym53705 or "ym 53705" or ym905 or "ym 905"):ti,ab,kw	259
#12	(tolterodine or detrusitol or detrol or "detrol la" or pnu200583 or "pnu 200583" or unidet or urotrol):ti,ab,kw	498
#13	(mirabegron or betanis or betmiga or myrbetique or sc211912 or "sc 211912" or YM178 or "YM-178"):ti,ab,kw	102
#14	(darifenacin or darifenacine or enablex or emselex or uk88525 or "uk 88525"):ti,ab,kw	78
#15	(fesoterodine or "spm 907" or spm907 or toviaz):ti,ab,kw	146
#16	(oxybutynin or anturol or "apo-Oxybutynin" or contimin or cystonorm or cystrin or delifon or ditropan or diutropin or dresplan or dridase or driptane or esoxybutynin or frenurin or gelnique or "gen-oxybutynin" or iliaden or kentera or "kl 007" or kl007 or lenditro or "lyrinel XL" or "mutum cr" or nefryl or "novo-oxybutynin" or "nu-oxybutyn" or "oxyb AbZ" or oxyban or oxybugamma or oxybutinin or obuton or oxymedin or oyrobin or oxytrol or "PMS-oxybutynin" or pollakis* or renamel or reteven or ryol or spasyt or tavor or tropan or uricont or uroflax or urotrol or zatur):ti,ab,kw	588
#17	(trospium or ceris or spasmolyt or trospi or uraplex or urato or regurin or flotros or sanctura or tropez or tosec or spasmex or "spasmo-lyt" or "spasmo-rhoival" or "spasmo-urgenin" or spasmolyt or spasmourgenin):ti,ab,kw	138
#18	[mh Flavoxate]	14
#19	(flavoxate or "ak 123" or ak123 or baduson or bladderon or bladuril or cleanxate or "dw 61" or dw61 or flavate or "flavo-spa" or flavorin or fucotin or genurin or harnin or spagerin or spasdic or spasuret or tonlin or urispas or uronid or uropeace or uroxate or voxate or yungken):ti,ab,kw	45
#20	{or #5-#19}	4487
#21	(#4 and #20)	1149
#22	[mh "Urinary Bladder, Overactive"]	339
#23	[mh "Urinary Incontinence, Urge"]	86
#24	(overactive near/3 bladder*) or (urge near/3 incontinence) or (detrusor near/3 dyssynergia) or (urinary frequency) or (bladder irritation) or DESD	4147
#25	#22 or #23 or #24	4147
#26	[mh "Muscarinic Antagonists"]	613
#27	solifenacin or Vesicare or Vesikur or Vesiker or Vesitirim	257
#28	tolterodine or Detrusitol or Detrol or Detrol LA	527
#29	mirabegron or YM-178 or Betanis	97
#30	darifenacin or Enablex or Emselex	89
#31	fesoterodine or Toviaz	154
#32	oxybutynin or Ditropan or Lyrinel XL	471
#33	propiverine or Detrunorm	127
#34	trospium or Regurin or Flotros or Sanctura or Tropez or Trosec or Spasmex	150
#35	(#26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34)	1737
#36	(#25 and #35) Publication Year from 2000 to 2012	725
#37	#21 not #36	467

CENTRAL - 440

Appendix B: Results of Search

Flow diagram of the selection process for potentially relevant studies.



Appendix C: Health Canada-approved Doses of pharmacotherapies for overactive bladder syndrome

For the pharmacotherapies for overactive bladder syndrome, RCTs reporting the following daily dosing regimens were included:

NAME	PRODUCT NAME	DOSAGE FORM	STRENGTH	RECOMMENDED DAILY DOSE	MAXIMUM DOSE	TIME NEEDED TO ASSESS EFFICACY
oxybutynin	**GENERIC**	Tablet, syrup	1, 2.5, 5 mg (1 mg/mL syrup)	5 mg BID or TID	5 mg, 4 times daily (20 mg)	Not reported in product monograph
	DITROPAN XL	extended-release tablet	5, 10 mg	5 or 10 mg QD	30 mg/day	Not reported in product monograph
	OXYTROL	Transdermal system	36 mg (3.9 mg/day system)	One 3.9 mg/day system applied twice weekly (every 3 to 4 days) (abdomen, hip or buttock)	Not reported in product monograph. Assume same as recommended daily dose.	Not reported in product monograph
	GELNIQUE	Gel	100 mg/gram	contents of one sachet (each gram of gel containing 100 mg) applied QD	Not reported in product monograph. Assume same as recommended daily dose.	Not reported in product monograph
tolterodine	**DETROL**	tablet	1, 2 mg	2 mg BID (1 mg BID acceptable)	4 mg/day	2 weeks minimum, additional benefit may be seen at 8 weeks
	DETROL LA	extended-release capsule	4 mg	4 mg QD	4 mg QD	Not reported in product monograph, however, RCTs mentioned were 12

NAME	PRODUCT NAME	DOSAGE FORM	STRENGTH	RECOMMENDED DAILY DOSE	MAXIMUM DOSE	TIME NEEDED TO ASSESS EFFICACY
						weeks
darifenacin	**ENABLEX**	extended-release tablet	7.5, 15 mg	7.5 mg QD	15 mg QD	Not reported in product monograph, however, RCTs mentioned were 12 weeks
fesoterodine	**TOVIAZ**	extended-release tablet	4, 8 mg	4 mg QD	8 mg QD	Not reported in product monograph, however, RCTs mentioned were 8 to 12 weeks
trospium	**TROSEC**	tablet	20mg	20 mg BID	Not reported in product monograph. Assume 20 mg BID is max.	Not reported in product monograph, however, RCTs mentioned were 26 and 52 weeks
flavoxate	**URISPAS**	tablet	200 mg	--	--	--
solifenacin	**VESICARE**	tablet	5 mg and 10 mg	5 mg QD	10 mg QD	4 wks
mirabegron	**MYRBETIQUE**	extended-release tablet	25 mg and 50 mg	25 mg QD	50 mg QD	8 weeks

For comparisons of pharmacotherapies to *onabotuinumtoxin a* intradetrusor injection:

NAME	PRODUCT NAME	DOSAGE FORM	STRENGTH	RECOMMENDED DOSE	MAXIMUM DOSE	TIME NEEDED TO ASSESS EFFICACY
onabotulinumtoxinA	**BOTOX**	Injected solution	50, 100 and 200 Allergan units per vial	100 Units/10 mL, re-injection after approximately 24 weeks (but ballpark around that time OK) but no sooner than 3 months	Not Reported	2 weeks min, best around 8 weeks. Treatment effects last approximately three months, following which the procedure can be repeated indefinitely.

Appendix D: List of Excluded Studies

1. Tolterodine for overactive bladder. Med Lett Drugs Ther 1998;40:101.

2. Trospium chloride (Sanctura): another anticholinergic for overactive bladder. Obstetrics and gynecology 2005;105:431.

3. Erratum: Tolterodine and tamsulosin for treatment of men with lower urinary tract symptoms and overactive bladder: A randomized controlled trial (Journal of American Medical Association (November 15, 2006) 296, 19, (2319-2328)). Jama 2007;298:1864.

4. Anticholinergic drugs or botulinum toxin for urge incontinence? BMJ (Clinical research ed 2012;345:e6732.

5. Mirabegron. Aust Prescr 2014;37.

6. Aagaard JR. A comparison between the combination emepronium bromide/flavoxate and emepronium bromide in the treatment of detrusor instability. Urologia internationalis 1983;38:191.

7. Abrams P, Freeman R, Anderstrom C, Mattiasson A. Tolterodine, a new antimuscarinic agent: as effective but better tolerated than oxybutynin in patients with an overactive bladder. British journal of urology 1998;81:801-10.

8. Anderson RU, Mobley D, Blank B, Saltzstein D, Susset J, Brown JS. Once daily controlled versus immediate release oxybutynin chloride for urge urinary incontinence. OROS Oxybutynin Study Group. The Journal of urology 1999;161:1809-12.

9. Angulo JC. Cost effectiveness of fesoterodine and tolterodine for the treatment of overactive bladder with urge urinary incontinence in Spain and Finland. Clinical Drug Investigation 2014;34:297.

10. Astellas Pharma Europe BV. Study to Test the Efficacy and Safety of YM178 in Subjects With Symptoms of Overactive Bladder (Blossom). 2006.

11. Astellas Pharma I. Study to Test the Efficacy and Safety of the Beta-3 Agonist Mirabegron (YM178) in Patients With Symptoms of Overactive Bladder (SCORPIO). 2010.

12. Astellas Pharma I. Study to Test the Efficacy and Safety of the Beta-3 Agonist Mirabegron (YM178) in Patients With Symptoms of Overactive Bladder (ARIES). 2010.

13. Astellas Pharma I. A Study to Test the Efficacy and Safety of the Beta-3 Agonist Mirabegron (YM178) in Patients With Symptoms of Overactive Bladder (CAPRICORN). 2012.

14. Aydogmus Y, Sunay M, Arslan H, Aydin A, Adiloglu AK, Sahin H. Acupuncture versus solifenacin for treatment of overactive bladder and its correlation with urine nerve growth factor levels: a randomized, placebo-controlled clinical trial. Urologia internationalis 2014;93:437.

15. Bagger PV, Fischer-Rasmussen W, Hansen R. Emepronium carrageenate: clinical effects and urinary excretion in treatment of female urge incontinence. Scandinavian journal of urology and nephrology 1985;19:31.

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Appendix E: List of Included Studies

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Appendix F: Cochrane Risk of Bias Assessments

	First Author, year	Sequence generation	Allocation concealment	Blinding, objective outcomes	Blinding, subjective outcomes	Incomplete outcome data addressed - efficacy	Incomplete outcome data addressed - safety
1	**Kuo 2015**	Low	Low	Low	Unclear	Unclear	Low
7	**Kosilov 2015**	Unclear	Unclear	NA	Low	Low	Low
11	**Abrams 2015**	Unclear	Low	Low	Low	Low	Low
28	**Jafarabadi 2015**	Low	Unclear	NA	Unclear	Low	Low
38	**Kaplan 2014**	Unclear	Low	Low	Unclear	Low	Low
44	**Orri 2014**	Low	Low	Low	Low	High	High
46	**Aziminekoo**	Unclear	Unclear	Low	Unclear	Unclear	Unclear
68	**Chu 2009**	Low	Low	Low	Low	Low	Unclear
117	**Chapple 2014**	Unclear	Low	Low	Low	Low	Unclear
120	**Yamaguchi 2014**	Unclear	Unclear	Low	Unclear	Low	Low
132	**DuBeau 2014**	Unclear	Low	Low	Low	Unclear	Low
147	**Chapple 2013, p.1116**	Low	Low	Low	Low	Low	Low
158	**Chapple 2013, p.1447**	Unclear	Unclear	Low	Low	Low	Low
160	**Herschorn2013**	Unclear	Unclear	NA	Unclear	Low	Low
296	**Madersbacher 1999**	Unclear	Unclear	NA	Unclear	Low	Low
300	**Anderson 1999**	Unclear	Unclear	NA	Low	Low	Low
304	**MILLARD 1999**	Unclear	Unclear	Low	Unclear	Low	Low
306	**Drutz 1999**	Unclear	Unclear	Low	Low	Unclear	Unclear
308	**Burgio 1998**	Low	Unclear	NA	Low	Unclear	Unclear
312	**Abrams 1998**	Unclear	Unclear	Low	Low	Unclear	Unclear
314	**Rentzhog 1998**	Unclear	Unclear	Low	Low	Unclear	Unclear
318	**Jonas 1997**	Unclear	Unclear	Low	Unclear	NA	Low
368	**Batista 2015**	Unclear	Unclear	Low	Unclear	Low	Low
418	**Yamaguchi 2015**	Unclear	Unclear	Low	Low	Low	Low
715	**Dede 2013**	Unclear	Low	NA	Unclear	Unclear	Unclear
1119	**Chapple 2013, p.296**	Low	Low	Low	Unclear	Unclear	Unclear
1120	**Khullar 2013**	Low	Low	Low	Unclear	Low	Low
1152	**Weiss 2013**	Unclear	Low	Low	Low	Unclear	Low

	First Author, year	Sequence generation	Allocation concealment	Blinding, objective outcomes	Blinding, subjective outcomes	Incomplete outcome data addressed - efficacy	Incomplete outcome data addressed - safety
1153	**Nitti 2013**	Low	Unclear	Low	Unclear	Low	Low
1158	**Wagg 2013**	Low	Low	Low	Low	Unclear	Unclear
1558	**Dmochowski 2010**	Low	Low	Low	Unclear	Low	Low
1559	**Homma 2003**	Low	Unclear	Low	Low	Unclear	Unclear
1564	**Staskin 2009**	Unclear	Unclear	Low	Low	Low	Low
1570	**Chapple 2007**	Unclear	Unclear	NA	Low	Unclear	Unclear
1571	**Dmochowski 2003**	Unclear	Unclear	NA	Low	Low	NA
1574	**Herschorn 2009**	Low	Low	Low	Low	Low	Low
1575	**Chapple 2005**	Low	Low	Low	Low	Low	Low
1578	**But 2012**	Low	Unclear	NA	High	Low	Low
1579	**Halaska 2003**	Unclear	Unclear	Low	Unclear	Unclear	Unclear
1580	**Haab 2004**	Unclear	Low	Low	Low	Low	Low
1581	**Hill 2006**	Unclear	Unclear	Low	Low	Low	Low
1584	**Corcos 2005**	Unclear	Unclear	Low	Low	High	High
1585	**Versi 2000**	Low	Low	NA	Low	Low	Low
1588	**Herschorn 2008**	Unclear	Unclear	NA	Unclear	Low	Low
1592	**Choo 2008**	Unclear	Unclear	NA	Unclear	Low	Low
1601	**Rogers 2008**	Low	Unclear	NA	Unclear	Unclear	Unclear
1602	**Cardozo 2000**	Low	Unclear	Low	Unclear	Low	Low
1603	**Nitti 2007**	Low	Unclear	Low	High	Unclear	Unclear
1605	**Zinner 2006**	Unclear	Unclear	Low	Unclear	Low	Low
1615	**Homma 2006**	Unclear	Unclear	NA	Unclear	Unclear	Unclear
1618	**Rackley 2006**	Unclear	Unclear	NA	Unclear	NA	Low
1619	**Altan-Yaycioglu 2005**	Unclear	Unclear	NA	High	NA	Low
1625	**Moore 1990**	Unclear	Unclear	NA	Low	Unclear	NA
1630	**Appell 2001**	Unclear	Unclear	NA	Low	Low	Low
1631	**Diokno 2003**	Unclear	Unclear	Low	Low	Low	Low
1634	**Minassian 2007**	Unclear	Low	NA	High	Unclear	Unclear
1635	**Chapple 2004, p. 303**	Unclear	Unclear	NA	Unclear	Low	Low
1636	**Cardozo 2004**	Unclear	Unclear	NA	Unclear	Low	Low
1638	**Barkin 2004**	Unclear	Unclear	NA	Unclear	High	High
1639	**Yamaguchi**	Unclear	Unclear	NA	Unclear	Low	Low

	First Author, year	Sequence generation	Allocation concealment	Blinding, objective outcomes	Blinding, subjective outcomes	Incomplete outcome data addressed - efficacy	Incomplete outcome data addressed - safety
	2007						
1643	**Nitti 2009**	Unclear	Unclear	NA	Unclear	Low	Low
1646	**Ho 2010**	Unclear	Unclear	NA	High	Low	Low
1647	**Chapple 2004, p.71**	Unclear	Unclear	NA	Unclear	Low	Low
1648	**Kaplan 2010**	Low	Low	Low	Low	Low	Low
1650	**Herschorn 2010**	Low	Unclear	Low	Low	High	High
1651	**Van Kerrebroeck 2001**	Low	Unclear	Low	Low	Low	Low
1652	**Jacquetin 2001**	Unclear	Unclear	NA	Unclear	Low	Low
1654	**Malone-Lee 2001**	Unclear	Unclear	Low	Low	Unclear	Unclear
1655	**Lee 2002**	Low	Unclear	Low	Low	Low	Low
1656	**Malone-Lee 2001**	Unclear	Unclear	Low	Low	Unclear	Unclear
1658	**Sussman 2002**	Unclear	Unclear	NA	High	NA	Unclear
1659	**Khullar 2004**	Low	Low	NA	Low	Low	Low
1661	**Zinner 2004**	Unclear	Unclear	NA	Unclear	Unclear	Unclear
1674	**Dmochowski 2002**	Unclear	Unclear	NA	Low	Low	Low
1675	**Yamaguchi 2011**	Unclear	Unclear	Low	Low	Low	Low
1687	**Vardy 2009**	Low	Low	Low	Low	Low	Low
1689	**Chancellor 2000**	Low	Unclear	Low	Low	Low	Low
1691	**Leung 2002**	Low	Unclear	Low	Unclear	Low	Low

Appendix G: Characteristics of Reviewed Studies Reporting Outcomes

Study characteristics

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
1	**Kuo, 2015: p. 685 (Kuo 2015)**	Taiwan, Korea, China, India	≥ 18	Symptoms of OAB for ≥ 12 wk; ≥ 8 micturitions/24 hr; and ≥ 1 episode of urgency or urgency incontinence/24 hr, during a 3-day micturition diary period	12 wk	• Placebo (377) • TOLT-ER 4 mg/d (377) • MIRA 50 mg/d (372)
7	**Kosilov, 2015, p. 212**	Russia	> 65	Severe symptoms of overactive bladder (≥ 3 episodes of incontinence)	6 wk	• Placebo (59) •SOLF 10 mg/d (52 • MIRA 50 mg/d (63) • MIRA 50 mg/SOLF 10 mg/d (65)
11	**Abrams, 2015, p. 577**	Europe	≥ 18	≥ 8 micturitions/24 and 1 urgency episode or more per 24 h (with or without incontinence)	12 wk	• Placebo (81) • SOLF 5 mg/d (156) • SOLF 10 mg/d (78) • MIRA 25 mg/d (78) • MIRA 50 mg/d (79) • MIRA 25 mg/SOLF 2.5 mg/d (149) • MIRA 25 mg/SOLF 5 mg/d (144) • MIRA 25 mg/SOLF 10 mg/d (81) • MIRA 50 mg/SOLF 2.5 mg/d (149) • MIRA 50 mg/SOLF 5 mg/d (153) • MIRA 50 mg/SOLF 10 mg/d (81)
28	**Jafarabadi, 2015, p. 120**	Iran	>45	Urinary frequency ≥ 8 micturitions/24 h and urge incontinence (≥ 5 episodes/wk), idiopathic detrusor overactivity in the filling cystometry	12 wk	• OXYB 15 mg/d (151) • TOLT 4 mg/d (150)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
38	**Kaplan, 2014, p. 1065**	Europe, North America, Asia, and Africa	≥ 18	OAB symptoms for ≥ 6 mo, at least 'some moderate problems' reported on PPBC ≥2 to < 15 UUI episodes (Urinary Sensation Scale rating of 5) and ≥ 8 micturitions/24 h on a 3- day bladder diary; Only randomized patients with suboptimal response to 2-wk open-label trial of tolterodine ER 4 mg	12 wk	• Placebo (320) • FEST 4-8 mg/d (322)
44	**Orri, 2014, p. 190**	US	≥ 21	OAB symptoms for ≥ 3 months; ≥ 1 UUI episode/24 h and ≥ 8 micturitions/24 h in 3-day micturition diary	12 wk	• Placebo (6) • TOLT-ER 4 mg/d (12)
46	**Aziminekoo, 2014, p. 73 (Jafarabadi, 2015)**	Iran	NR	Documented over active bladder syndrome [urinary frequency (≥8 micturitions/24 h) plus urge incontinence (≥ 5 episodes/w)] with idiopathic detrussor overactivity in the filling cystometry	4 wk	• OXYB 15 mg/d (NR) • TOLT 4 mg/d (NR) (total no. randomized: 100)
68	**Chu, 2009, p. 405**	US	≥ 18	≥ 8 micturitions/24 h and ≥ 1 incontinence episode/24 h and/or a mean of ≥ 1 urgency episode/24 h during the screening period	12 wk	• Placebo (332) • SOLF 10 mg/d (340)
117	**Chapple, 2014, p. 418**	27 countries	≥ 18	OAB symptoms for ≥ 6 mo and ≥ 8 micturitions and ≥ 2 and ≥ 15 UUI episodes/24 h (Urinary Sensation Scale rating of 5) in a 3-day diary; at least some moderate problems on the PPBC	12 wk	• Placebo (402) • FEST 4 mg/d (806) • FEST 8 mg/d (804)
120	**Yamaguchi, 2014, p. 951**	Japan	≥ 20	OAB symptoms for ≥ 24 wk; ≥ 8 micturitions/24 h and ≥ 1 urgency episode/24 h and/or ≥ 1 urgency incontinence episode/24 h	12 wk	• Placebo (381) • TOLT-ER 4 mg/d (378) • MIRA 50 mg/d (380)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
132	**DuBeau, 2014, p. 395**	US	≥ 65	UUI symptoms for ≥ 3, 2–15 UUI episodes, ≥ 8 micturitions/24 h on baseline 3-day bladder diary; at least some moderate bladder related problem on the PPBC	12 wk	• Placebo (283) • FEST 4-8 mg/d (283)
147	**Chapple, 2013, p. 1116**	Europe	≥ 18	Urinary frequency and urgency with or without urgency incontinence for ≥ 3 months; ≥ 8 voids/24 hr; ≥ 3 episodes of urgency (grade 3 or 4), with or without incontinence, during the 3-day micturition diary period	4 wk	• Placebo (66) • TOLT-ER (66)
158	**Chapple 2013, p. 1447**	Europe	≥ 18	Symptoms of OAB for ≥ 3 months with ≥ 8 voids/24 h and ≥ 3 episodes of urgency (grade 3 or 4), with or without incontinence, during a 3-day micturition diary period at baseline	12 wk	• Placebo 169 • TOLT ER mg/d (85) • MIRA 25 mg/d (169) • MIRA 50 mg/d 169)
160	**Herschorn, 2013, p. 313 (Nitti 2014, p. 972; Nitti 2013, p. 619; Pavesi 2013, p. 866; Chapple 2015, p. 11; Castro-Diaz 2015, p. 1719; Chapple 2014, p. 1565, Wagg 2014, p. 666)**	Europe, NA	≥ 18	≥ 8 micturitions/24 h and ≥ 3 urgency episodes (grade 3 or 4 on Patient Perception of Intensity of Urgency Scale with or without incontinence	12 wk	• Placebo (433) • MIRA 25 mg/d (433) • MIRA 50 mg/d (440)
296	**Madersbacher, 1999, p. 646**	Austria	≥ 18	History of urgency or urge incontinence, a maximum cystometric bladder capacity of ≥ 300 mL	4 wk	• Placebo (72) • OXYB 10 mg/d (145)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
300	**Anderson, 1999, p. 1809**	US	NR	≥ 6 urge incontinence episodes/wk when not taking medication	NR	• OXYB 5-20 mg/d (52) OXYB-ER 5-30 mg/d (53)
304	**Millard, 1999, p. 1551**	Australia, US	≥ 18	cystometrically proved detrusor overactivity (idiopathic instability or detrusor hyperreflexia, or uninhibited phasic detrusor contractions with an amplitude of ≥ 10 cm) and average urinary frequency of ≥ 8 voids/24 h on the baseline frequency-volume chart; urge incontinence (≥1 incontinence episodes/24 h) and/or urinary urgency	12 wk	• Placebo (64) • TOLT 2 mg/d (123) • TOLT 4 mg/d (129)
306	**Drutz, 1999, p. 283**	US, Canada	≥ 18	Evidence of detrusor overactivity on subtracted cystometry (phasic detrusor contraction with an amplitude ≥ 10 cm H2O), along with urinary frequency (≥ 8 micturitions/24 h) and either urge incontinence (≥ 1 incontinence episode/24 h) and/or urinary urgency	12 wk	• Placebo (56) • OXYB 15 mg/d (112) • TOLT 4 mg/d (109)
308	**Burgio, 1998, p. 11995 (Goode 2002, p. 808; Burgio 2001, p. 46)**	US* (based on author affiliation)	≥ 55	≥ 2 urge incontinence/wk and persisting for ≥ 3 mo ; number of urge accidents had to exceed the number of stress accidents; urodynamic evidence of bladder dysfunction	8 wk	• Placebo (65) • OXYB 7.5-15 mg/d (67)
312	**Abrams, 1998, p. 801 (Appell 1997, p. 90)**	UK, Ireland, Sweden	≥ 18	Urodynamically confirmed bladder overactivity, ≥ 8 micturitions/24 h and urge incontinence (≥ 1 incontinent episode/24 h) and/or urgency during a 2-week washout/run-in period	12 wk	• Placebo (57) • OXYB 15 mg/d (118) • TOLT 4 mg/d (118)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
314	**Rentzhog, 1998, p. 42 (Appell 1997, p. 90)**	UK, Sweden	18-75	Symptoms of urinary urgency, increased frequency of micturition (≥ 8 micturitions/24 h) and/or urge incontinence (≥ 1 episode of incontinence/24 h) during a 1-week pre-study run-in period; urodynamically confirmed detrusor instability (a phasic increase in detrusor pressure in the presence of typical symptoms) and a maximum urinary flow rate of ≥ 15 mL/s	2 wk	• Placebo (13) • TOLT 2 mg/d (16) • TOLT 4 mg/d (14)
318	**Jonas, 1997, p. 144 (Appell 1997, p. 90)**	Germany, Austria, Sweden	≥ 18	Detrusor overactivity (phasic detrusor contraction, amplitude of > 10 cm H20 or 1 strong detrusor contraction that caused the end of the infusion); ≥ 8 micturitions/24 h in combination with urge incontinence (≥ 1 incontinence episode/24 h), urinary urgency, or both	4 wk	• Placebo (44) • TOLT 2 mg/d (99) • TOLT 4 mg/d (99)
368	**Batista, 2015, p. 167**	33 countries, inc. Can	≥ 18	Symptoms of OAB for ≥ 3 months, dissatisfaction with the efficacy of their last antimuscarinic	12 wk	• SOLF 5 mg/d (944) • MIRA 50 mg/d (943)
418	**Yamaguchi, 2015, p 84**	Japan	≥ 20	Average of ≥ 8 micturitions/24 h and ≥ 1 urgency episode and/or ≥ 1 urgency incontinence episode/24	12 wk	• Placebo (214) • MIRA 25 mg/d (211) • MIRA 50 mg/d (208)
715	**Dede, 2013, p. 511**	Turkey	NR	Urodynamic testing	6 wk	• OXYB 15 mg/d (30) • TOLT 2 mg/d (30) • TROS 40 mg/d (30)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
1119	**Chapple, 2013, p. 296 (Nitti 2014, p.972)**	Europe, US, Can, South Africa, Australia, New Zealand	≥ 18	Symptoms of OAB (urinary frequency and urgency with/without incontinence) for ≥ 3 mo; ≥ 8 voids/24 h during the 3-d micturition diary period; ≥ 3 episodes of urgency (grade 3 or 4) with/without incontinence during the 3-d micturition diary period	12 mo	• TOLT-ER 4 mg/d (813) • MIRA 50 mg/d (815)
1120	**Khullar, 2013: p. 283 (Khullar 2013, p. 45; Nitti 2014, p.972; Nitti 2013, p.619; Pavesi 2013, p. 866; Chapple 2015, p. 11; Castro-Diaz 2015, p. 1719; Chapple 2014, p. 1565; Wagg 2014, p. 666)**	Europe, Australia	≥ 18	Symptoms of OAB for 3 mo; including an average micturition frequency of ≥ 8 times per 24-h period and ≥ 3 episodes of urgency, with or without incontinence	12 wk	• Placebo (497) • TOLT-ER 4 mg/d (495) • MIRA 50 mg/d (497)
1152	**Weiss, 2013, 1396**	US	≥ 18	Nocturnal urgency for ≥ 3, and ≥ 8 micturitions/24 h, ≥ 3 urgency episodes per 24 h, and 2–8 nocturnal urgency episodes/24 h on bladder diary at screening	12 wk	• Placebo (487) • FEST 4-8 mg/d (476)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
1153	**Nitti, 2013, p. 1388 (Stratum A), (Nitti 2014, p. 972; Nitti 2013, p. 619; Pavesi 2013, p. 866; Chapple 2015, p. 11; Castro-Diaz 2015, p. 1719; Chapple 2014, p. 1565; Wagg 2014, p. 666)**	US, Can	≥ 18	OAB symptoms for ≥ 3mo; ≥ 8 micturitions/24 h and ≥ 3 urgency episodes (grade 3—severe urgency or grade 4—urge incontinence) with or without incontinence	12 wk	• Placebo (454) • MIRA 50 mg/d (442)
1153	**Nitti, 2013, p. 1388 (Stratum B) (Nitti 2014, p. 972; Nitti 2013, p. 619; Pavesi 2013, p. 866; Chapple 2015, p. 11; Castro-Diaz 2015, p. 1719; Chapple 2014, p. 1565; Wagg 2014, p. 666)**					

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
1158	**Wagg, 2013, p. 185 (Wagg 2015, p. 438)**	Austria, Belgium, Denmark, Finland, Germany, Israel, Italy, Norway, Portugal, Slovakia, Spain, Sweden, Switzerland, Turkey, UK	≥ 65	OAB symptoms for ≥ 3 mo, ≥ 8 micturitions and ≥ 3 urgency episodes/24 h on a 3-day bladder diary; moderate problems on the PPBC	12 wk	• Placebo (396) • FEST 4-8 mg/d (398)
1558	**Dmochowski, 2010, p. 62**	US	≥ 18	OAB symptoms for ≥ 3 mo before screening, ≥ 8 micturitions/24 h and ≥ 3 urgency episodes/24 h in a 3-day bladder diary at baseline, and at least some moderate problems on the PPBC	12 wk	• Placebo (448) • FEST 4-8 mg/d (448)
1559	**Homma, 2003, p. 741 (Homma 2004, p. 251)**	Japan, Korea	≥ 20	symptoms of urinary urgency, urinary frequency (≥8 voids/24 h), urge incontinence (≥5 episodes/wk) and symptoms of OAB for ≥ 6 mo	12 wk	• Placebo (122) • OXYB 9 mg/d (246) • TOLT-ER 4 mg/d (240)
1564	**Staskin, 2009, p. 1764 (Sand 2011, p. 145)**	US	≥ 18	Urge or mixed UI with a predominance of urge UI episodes as well as ≥ 8 urinary voids/d and ≥ 4 urge UI episodes/d regardless of whether symptoms were of neurological origin	12 wk	• Placebo (400) • OXYB-GEL 100 mg/d (389)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
1570	**Chapple, 2007, p. 1204 (Chapple 200, p. 1128; Cardozo 2010, p. 14; Herschorn 2010, p. 1149; Kraus 2010, p. 1350, Staskin 2010, p. 813; Khullar 2008, p. 839; Kelleher 2008, p. 56; Sand 2009, p. 827; Cardozo 2010, p. 816)**	International	≥ 18	8 micturitions per 24 h and either ≥ 6 urgency episodes or ≥ 3 UUI episodes per 24 h	12 wk	• Placebo (285) • TOLT-ER (290) • FEST 4 mg/d (272) • FEST 8 mg/d (288)
1571	**Dmochowski, 2003, p. 237 (Kelleher 2002, p. S608)**	US	≥ 18	≥ 4 urge urinary incontinent episodes, with either pure urge or a predominance of urge episodes, ≥ 24 voids, and an average recorded urinary void volume of 350 mL or less	12 wk	• Placebo (117) • OXYB-TRANS 3.9 mg/d (121) • TOLT-ER 4 mg/d (123)
1574	**Heschorn 2010, p. 58 (Herschorn 2014, p. 1023; Ginsberg 2013, p. 373)**	30 countries	≥ 18	Symptoms of OAB for ≥ 3 mo and ≥ 1 UUI episode/24 h and ≥ 8 voids/24 h reported in 3-day bladder diaries completed at baseline	12 wk	• Placebo (337) • TOLT-ER (690) • FEST 4-8 mg/d (685)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
1575	**Chapple, 2005, p. 464 (Chapple 2007)**	Europe	≥ 18	OAB symptoms (including urinary frequency, urgency or urge incontinence) for ≥ 3 mo: ≥ 8 micturitions/24 h; ≥ 1 incontinence episode/24 h, or ≥ 1 urgency episode/24 h during the 3-day voiding diary period.	12 wk	• TOLT-ER (607) • SOLF 5-10 mg/d (593)
1578	**But, 2012, p. 1347**	Slovenia	NR	Urgency intensity and urgency urinary incontinence of ≥ 3 on the Urgency Perception Scale and frequency of ≥ 1 urgency episode/d	12 wk	• DARF 7.5 mg/d (37) • SOLF 5 mg/d (40)
1579	**Halaska, 2003, p. 392**	Austria, Bulgaria, Czechoslovakia, Germany, Russia, Spain	≥ 18	Urodynamic measurements	52 wk	• OXYB 10 mg/d (90) • TROS 40 mg/d (268)
1580	**Haab, 2004, p. 420**	International	19-88	Urge incontinence (5-50 episodes/wk); frequency of micturition (≥8 voids/24 h); and urgency (a strong desire to void at least once/d	12 wk	• Placebo (164) • DARF 7.5 mg/d (229) • DARF 15 mg/d (115)
1581	**Hill, 2006, p. 239**	Belgium, Denmark, Israel, Norway, Poland, Sweden, Netherlands, UK	≥ 18	Urge incontinence (≥10 episodes over 14 d), high micturition frequency (≥8/d), and urinary urgency (a strong desire to void on average at ≥ 1/d)	12 wk	• Placebo (109) • DARF 7.5 mg/d (108) • DARF 15 mg/d (107)
1584	**Corcos, 2005, p. 520**	Canada	≥ 18	UI (≥ 1episodes/diary), plus either frequency (≥ 8 voids/d) or urgency (≥ 1 or more episodes/diary)	4 wk	• OXYB-ER 10 mg/d (77) • OXYB-ER (83)
1585	**Versi, 2000, p. 718**	US	NR	7-45 urge incontinence episodes/wk and ≥ 4 days of incontinence/wk during the placebo baseline period	12 wk	• OXYB 5-20 mg/d (115) • OXYB-ER 5-20 mg/d (111)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
1588	**Herschorn, 2008, p. 3513**	Can, Denmark, Germany, Italy, Netherlands, Norway, Poland, Spain, Sweden, Turkey, US	≥ 18	≥ 8 micturitions/24 h and ≥3 episodes of urgency or urgency urinary incontinence in a 3-day bladder diary	12 wk	• Placebo (207) • TOLT-ER 4 mg/d (410)
1592	**Choo, 2008, p. 1675**	Korea	≥ 18	≥ 8 voids per 24 h and at least 3 episodes of urgency or 3 episodes of urgency incontinence during the 3-day voiding diary period	12 wk	• TOLT 4 mg/d (118) • SOLF 5 mg/d (120) • SOLF 10 mg/d (119)
1601	**Rogers, 2008, p. 1551**	US	≥ 18	≥ 8 micturitions, ≥ 0.6 UUI episodes, and greater than or equal to ≥ OAB micturitions (moderate or severe urgency or UUI) per 24 h as recorded in 5-day bladder diaries at baseline	12 wk	• Placebo (211) • TOLT-ER 4 mg/d (202)
1602	**Cardozo, 2000, p. 659**	UK, Poland	18-70	Symptoms of detrusor instability confirmed by urodynamic diagnosis	3 wk	• Placebo (104) • TROS 40 mg/d (104)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
1603	**Nitti, 2007, p. 2488 (Cardozo 2010, p. 14; Herschorn 2010, p. 1149; Kraus 2010, p. 1350; Staskin 2010, p. 813; Khullar 2008, p. 839; Kelleher 2008, p. 56; Sand 2009, p. 827; Cardozo 2010, p. 816)**	US	≥ 18	OAB syndrome ≥ 6 mo, including urinary frequency (≥ 8 micturitions/24 h) and urinary urgency (≥ 6 episodes during the 3-day diary period) or UUI (≥ 3 episodes during the 3-day diary period). (Amended criteria during recruitment: ≥ 3 UUI episodes recorded in the 3-day diary at the end of the placebo run-in	12 wk	• Placebo (274) • FEST 4 mg/d (283) • FEST 8 mg/d (279)
1605	**Zinner, 2006, p. 119**	US	≥ 18	OAB for ≥ 6 mo and an average of ≥ 1 urge incontinence episodes/d; ≥ 8 micturitions/d; ≥ 4 urgency episodes/d and mean warning time of ≤ 15 min during 12 consecutive h	12 wk	• Placebo (229) • DARF 15 mg/d (216)
1615	**Homma, 2006, p. 228**	Japan	NR	OAB syndrome and having experienced urge incontinence ≥ 1 times/d on average with urinations ≥ 8 times/d during the preceding wk	12 wk	• Placebo (161)‡ • OXYB-TRANS 3.9 mg/d (164)
1618	**Rackley, 2006, p. 731**	US	≥ 18	OAB (≥ 8 micturitions/24 h and urgency with or without UUI) and nocturia (mean ≥ 2.5 nocturia episodes/night)	12 wk	• Placebo (421) • TOLT-ER 4 mg/d (429)
1619	**Altan-Yaycioglu, 2005, p. 588**	Turkey	22-60	Urodynamically proven detrusor over-activity	4 wk	• OXYB 15 mg/d (24) • TOLT 4 mg/d (28)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
1630	**Appell, 2001, p. 358 (Sand 2004, p. 243)**	US	NR	7-50 episodes of urge incontinence/wk and ≥ 10 voids/24 h	12 wk	• OXYB-ER 10 mg/d (185) • TOLT 4 mg/d (193)
1631	**Diokno, 2003, p. 687 (Chu 2005, p. 1849; Armstrong 2005, p. 247, Anderson 2006, p. 502)**	US	≥ 18	21-60 UUI episodes/wk and an average ≥ 10 voids/24 h	12 wk	• OXYB-ER 10 mg/d (391) • TLT-ER 4 mg/d (399)
1634	**Minassian, 2007, p. 726**	Canada	≥ 65	Symptoms of OAB including urgency, frequency, and nocturia as defined by the International Continence Society1; having mixed symptoms of OAB and stress urinary incontinence, with the former being the main presenting symptom	12 wk	• OXYB 7.5-15 mg/d (33) • OXYB-ER 5-10 mg/d (39)
1635	**Chapple, 2004 , p. 303 (Kelleher 2005, p. 81)**	International	≥ 18	≥8 voids/24 h and have experienced at least 3 episodes of urgency and/or 3 episodes of incontinence during the 3-day voiding diary period	12 wk	• Placebo (267) • TOLT 4 mg/d (266) • SOLF 5 mg/d (279) • SOLF 10 mg/d (269)
1636	**Cardozo, 2004, p. 1919 (Kelleher 2005, p. 81)**	International	≥ 18	≥ 8 voids/24 h and at least 3 episodes of urgency and/or 3 episodes of urinary incontinence during the 3-day micturition diary period	12 wk	• Placebo (301)‡ • SOLF 5 mg/d (299) • SOLF 10 mg/d (307)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
1638	**Barkin, 2004, p. 1026**	Canada	≥ 18	symptoms of OAB including urgency, frequency, and nocturia as defined by the International Continence Society; having mixed symptoms of OAB and stress urinary incontinence, with the former being the main presenting symptom	6 wk	• OXYB 5-20 mg/d (60) • OXYB-ER 15 mg/d (65)
1639	**Yamaguchi, 2007, p. 579**	Japan	≥ 20	symptoms of OAB ≥ 6 mo; mean ≥ 8 voids/24 h, ≥ 3 episodes of urgency and/or ≥ 3 episodes of urgency incontinence during a 3-day voiding-diary period	12 wk	• Placebo (406) • SOLF 5 mg/d (400) • SOLF 10 mg/d (385)
1643	**Nitti, 2009, p. 1268**	US	18-78	a urinary flow rate of ≥ 15 mL/s with a total volume of ≥ 100 mL during the baseline uroflowmetry; ≥ 8 voids/24 h, determined from recent medical history and confirmed on ≥ 5 days of the run-in phase; ≥ 3 within a 10-h period recorded on any single day of the run-in period; and ≥ 2 UUI episodes during the run-in period	8 wk	• Placebo (43) • FEST 4 mg/d (43) • FEST 8 mg/d (47)
1646	**Ho, 2010, p. 702**	Taiwan	≥ 18	urinary frequency, urgency, or urge incontinence, had persisted for ≥ 3 mo; have experienced ≥ 8 micturitions/24 hr	12 wk	• TOLT-ER 4 mg/d (36) • SOLF 5 mg/d (39)
1647	**Chapple, 2004, p. 71**	Europe	18-80	idiopathic detrusor overactivity (phasic contractions of ≥ 10 cm H2O, as assessed by filling cystometry)	4 wk	• Placebo (38) • TOLT 4 mg/d (37) • SOLF 5 mg/d (37) • SOLF 10 mg/d (35)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
1648	**Kaplan, 2010, p. 1432 (Herschorn 2014, p. 1023; Ginsberg 2013, p. 313)**	North America, South America, Europe, Asia, Africa	≥ 18	OAB symptoms for ≥3 mo and ≥ 1 UUI episode and ≥ 8 micturitions/24 h in 3-day bladder diaries at baseline	12 wk	• Placebo (480) • TOLT-ER 4 mg/d (974) • FEST 4-8 mg/d (963)
1650	**Herschorn, 2010, p. 1892**	Canada	≥ 18	> 1 urgency episode/24 h and ≥ 8 micturitions/24 h	8 wk	• OXYB,15 mg/d (64) • SOLF 5 mg/d (68)
1651	**Van Kerrebroeck, 2001, p. 414 (Swift 2003, p. 50; Freeman 2003, p. 605; Landis 2004, p. 752; Zinner 2002, p. 799, Kelleher 2002, p. S608)**	Australasia, Europe, NA	≥ 18	"...urinary frequency (≥ 8 micturitions every 24 hours), urge incontinence (≥ 5incontinence episodes/wk), and symptoms of an overactive bladder for 6 mo	12 wk	• Placebo (508) • TOLT 4 mg/d (514) • TOLT-ER 4 mg/d (507)
1652	**Jacquetin, 2001, p. 97**	Belgium, France	≥ 18	urodynamically proven overactive bladder, and symptoms of urgency and/or urge incontinence (≥ 1 incontinence episode/24 h) with increased frequency of micturition (≥ 8 micturitions/24 h)	4 wk	• Placebo (50) • TOLT 2 mg/d (97) • TOLT 4 mg/d (103)
1654	**Malone-Lee, 2001 p. 700**	UK, France, Ireland	≥ 65	Urgency, urinary frequency (≥ 8 micturitions/24 h), and/or urge incontinence (≥ 1 urge incontinence episode/24 h	4 wk	• Placebo (43) • TOLT 2 mg/d (61) • TOLT 4 mg/d (73)
1655	**Lee, 2002, p. 247**	South Korea	≥ 18	urinary urgency and frequency (≥ 8 micturitions on average per 24 h), with or without urge incontinence	8 wk	• OXYB 10 mg/d (116) • TOLT 4 mg/d (112)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
1656	**Malone-Lee, 2001 p. 1452**	UK, Ireland	≥ 50	symptoms of urinary frequency (≥ 8 voids/24 h) with urgency and/or urge incontinence (≥ 1 urge incontinence episode/24 h	10 wk	• (OXYB 4-10 mg/d (188) • TOLT 4 mg/d (190)
1658	**Sussman, 2002, p. 177**	US	≥ 18	Symptoms of urinary frequency and urgency (a strong and sudden need to urinate) with or without urge incontinence	8 wk	• TOLT-ER 2 mg/d (333) • TOLT-ER 4 mg/d (336)
1659	**Khullar, 2004, p. 269**	Europe	≥ 18	urge urinary incontinence (≥ 5episodes/wk), urinary frequency (≥ 8 micturitions on average/24 h), and urgency (a strong and sudden need to urinate) in combination with stress urinary incontinence	8 wk	• Placebo (285) • TOLT-ER mg/d (569)
1661	**Zinner, 2004, p. 2311 (Rudy 2006)**	US	≥ 18	OAB symptoms for at least 6 months; urinary urgency, a minimum voiding frequency of 70 voids/wk with at least 7 urge incontinence episodes/wk	12 wk	• Placebo (261) • TROS 40 mg/d (262)
1674	**Dmochowski, 2002, p. 580**	US	≥ 18	7-d urinary diary: ≥ 10 urge urinary incontinent episodes, with either pure urge or a predominance of urge episodes, ≥ 56 voids and an average recorded voided volume of 350 ml or less	12 wk	• Placebo (132) • OXYB-TRANS 3.9 mg/d (125)
1675	**Yamaguchi, 2011, p. 43 (Yokoyama 2014, p. 750)**	Japan, Taiwan, Korea, Hong Kong	≥ 20	≥ 1 UUI episodes and ≥ 8 micturitions/24 h during a 3-day diary period	12 wk	• Placebo (318) • FEST 4 mg/d (320) • FEST 8 mg/d (313)
1687	**Vardy, 2009, p. 1702 (Vardy 2011, p. 24)**	US	≥ 18	OAB symptoms for ≥ 3 months (≥ 8 micturitions and ≥ 1 urgency episode, with or without incontinence, per 24 h)	12 wk	• Placebo (318) • SOLF 5-10 mg/d (386)

RefID	First author, Year (related publications)	Country	Included Ages	OAB Inclusion Criteria	Duration of Treatment	Included interventions (number randomized)
1689	**Chancellor, 2000 , p. 83 (Pliel 2000, p. 69)**	Europe, NA, Australia	≥ 18	urge incontinence (≥ 5 incontinence episodes/ wk) and urinary frequency (average of ≥ 8 micturitions/24 h); symptoms of overactive bladder for ≥ 6 months.	12 wk	• Placebo (508) • TOLT 4 mg/d (514)
1691	**Leung, 2002, p. 375, p. 375**	Hong Kong	≥ 18	OAB confirmed by urodynamic test (phasic detrusor contraction with an amplitude ≥ 15cm H2O) in accordance with ICS criteria; urinary frequency (≥ 8 voids/24 h), urgency or urge incontinence (≥ 1 incontinence episode/24 h)	10 wk	• OXYB 15 mg/d (53) • TOLT 4 mg/d (53)
1625	**Moore, 1990, p. 479 (Moore 1990, p. 486)**	UK	< 75	Involuntary detrusor contractions > 30 cm H20 during the filling phase of cystometry	NR	• Placebo (25) • OXYB 9 mg/d (28) CROSSOVER

PPBC=Patient Perception of Bladder Condition, OXYB = oxybutynin, OXYB-ER = extended release oxybutynin, OXYB-TRANS = transdermal oxybutynin, OXYB-GEL = gel oxybutynin, TOLT = tolterodine, TOLT-ER = extended release tolterodine, DARF = darifenacin, SOLF = solifenacin, TROS = trospium, FEST =fesoterodine, MIRA = mirabegron.

Cross-over studies with no first period data reported: Dmochowski 2014, Giannitsas 2004, Tapp 1990, Riva 1984, Zorzitto 1989, Chapple 2005, Zinner 2005.
No outcomes of interest reported: Gupta 1999

*If study location was not reported, location was inferred based on affiliation of first author.
†Co-medications as reported in the methods section as “permitted” or in the table of baseline characteristics.
‡No. randomized not reported; data is no. who received study drug.

Patient characteristics

RefID	First author, Year	Treatment (no. Randomized)*	Age Mean(SD) or [range]	Female (%)	Trt Experienced † (%)	Weight	Adherence‡ (%)	Duration of symptoms, mo, mean (SD) or [range]	Urge or mixed OAB qualifying diagnosis, %
1	**Kuo 2015**	• Placebo (377) • TOLT-ER 4 mg/d (377) • MIRA 50 mg/d (372)	55.3 (13.6) 53.9 (14.5) 54.3 (14.2)	70 64 68	52 51 52	61.4 (9.8) 61.7 (10.4) 61.8 (10.3)	98 98 98	58.3 (65.5) 57.8 (62.2) 62.2 (71.6)	Mixed: 17/17/19 Urge: 42/41/37
7	**Kosilov 2015**	• Placebo (59) •SOLF 10 mg/d (52 • MIRA 50 mg/d (63) • MIRA 50 mg/SOLF 10 mg/d (65)	71.2	NR	"All patients were treated with anti-muscarinic drugs … no less than one year prior to this study."	NR	NR	NR	NR

RefID	First author, Year	Treatment (no. Randomized)*	Age Mean(SD) or [range]	Female (%)	Trt Experienced † (%)	Weight	Adherence‡ (%)	Duration of symptoms, mo, mean (SD) or [range]	Urge or mixed OAB qualifying diagnosis, %
11	**Abrams 2015**	• Placebo (81) • SOLF 5 mg/d (156) • SOLF 10 mg/d (78) • MIRA 25 mg/d (78) • MIRA 50 mg/d (79) • MIRA 25 mg/SOLF 2.5 mg/d (149) • MIRA 25 mg/SOLF 5 mg/d (144) • MIRA 25 mg/SOLF 10 mg/d (81) • MIRA 50 mg/SOLF 2.5 mg/d (149) • MIRA 50 mg/SOLF 5 mg/d (153) • MIRA 50 mg/SOLF 10 mg/d (81)	54.6 (13.4) 54.2 (15.5) 55.0 (12.8) 55.2 (14.5) 53.4 (14.0) 55.8 (13.7) 55.0 (14.6) 56.5 (12.3) 53.7 (14.6) 54.1 (14.1) 55.5 (13.8)	67 66 68 68 67 67 66 64 67 66 67	50 47 38 55 49 50 45 54 44 47 50	NR	NR	48.5 (38.6) 62.9 (79.5) 53.5 (57.3) 60.6 (68.6) 57.3 (66.9) 56.7 (68.6) 55.8 (85.4) 65.8 (102.3) 57.0 (67.3) 57.8 (82.2) 58.0 (80.4)	Mixed: 11-17 Urge: 18-36
28	**Jafarabadi 2015**	• OXYB 15 mg/d (151) • TOLT 4 mg/d (150)	56.9 [46-75] 52.4 [45-78]	100	NR	NR	NR	NR	NR
38	**Kaplan, 2015**	• Placebo (320) • FEST 4-8 mg/d (322)	58.2 (13.2) 57.3 (13.4)	81 82	100	81.5 [45-156] 81.3 [45.0-194.1]	NR	6.6 [0.5-50.1]	NR
44	**Orri, 2014**	• Placebo (6) • TOLT-ER 4 mg/d (12)	46.2 [31-64] 48.4 [28-66]	100	NR	NR	NR	NR	NR
46	**Aziminekoo, 2014**	• OXYB-ER 15 mg/d (NR) • TOLT 4 mg/d (NR)	53 (12)	100	NR	NR	NR	NR	NR

RefID	First author, Year	Treatment (no. Randomized)*	Age Mean(SD) or [range]	Female (%)	Trt Experienced † (%)	Weight	Adherence‡ (%)	Duration of symptoms, mo, mean (SD) or [range]	Urge or mixed OAB qualifying diagnosis, %
68	**Chu, 2009**	• Placebo (332) • SOLF 10 mg/d (340)	58 (13) 59 (14)	83 80	33 42	81 (20.5) 82 (21.3)	NR	9 (10.2) yr 9 (10.3) yr	Mixed: 50/52 Urge: 49/47
117	**Chapple, 2014**	• Placebo (402) • FEST 4 mg/d (806) • FEST 8 mg/d (804)	59.6 [19-85] 58.8 [18-89] 59.8 [21–94]	82 82 80	NR	83.3 [36.0–172.4] 82.6 [42.2–197.0] 82.4 [43.1–163.6]	NR	8.4 [0.0–61.8] yr 7.1 [0.1–48.5] yr 7.3 [0.5–69.3] yr	NR
120	**Yamaguchi, 2014**	• Placebo (381) • TOLT-ER 4 mg/d (378) • MIRA 50 mg/d (380)	58.2 (14.18) 58.3 (13.69) 58.3 (13.88)	84 83 84	NR	55.3 (9.6) 56.5 (10.4) 55.1 (9.8)	>98	NR	Mixed: 25/25/29 Urge: 64/64/62
132	**DuBeau, 2014**	• Placebo (283) • FEST 4-8 mg/d (283)	75.3 [65-90] 74.8 [65-91]	84 80	NR	81.7 [47.1-158.7] 82.5 [47.2-147.4]	NR	NR	NR
147	**Chapple, 2013, p. 1116**	• Placebo (66) • TOLT-ER (66)	55.2 (13.3) 59.0 (13.3)	83 86	NR	NR	NR	NR	Mixed: 22/25 Urge: 45/46
158	**Chapple, 2013, p. 1447**	• Placebo 169 • TOLT ER mg/d (85) • MIRA 25 mg/d (169) • MIRA 50 mg/d 169)	57.1 (12.9) 56.6 (12.8) 57.2 (12.1) 56.9 (12.5)	91 81 88 89	NR	NR	>98	NR	Mixed: 31/28/26/28 Urge: 45/45/47/40

RefID	First author, Year	Treatment (no. Randomized)*	Age Mean(SD) or [range]	Female (%)	Trt Experienced † (%)	Weight	Adherence‡ (%)	Duration of symptoms, mo, mean (SD) or [range]	Urge or mixed OAB qualifying diagnosis, %
160	**Herschorn, 2013**	• Placebo (433) • MIRA 25 mg/d (433) • MIRA 50 mg/d (440)	58.2 (13.7) 58.5 (12.8) 60.3 (12.2)	70 68 69	~50	NR	NR	91.4 97.4 93.7	Mixed: 33/30/35 28/38/38
296	**Madersbacher, 1999**	• Placebo (72) • OXYB 10 mg/d (145)	47.6 (12.0) 50.3 (13.5)	94 93	NR	70.6 (12.3) 69.7 (11.8)	NR	Median 2.0 [0.2-40.0] yr median: 2.4 [0.1-40.0] yr	NR
300	**Anderson, 1999**	• OXYB 5-20 mg/d (52) • OXYB-ER 5-30 mg/d (53)	59.6 (10.0) 59.2 (10.6)	90 94	NR	NR	98 98	Most participants had been incontinent for ≥ 1 yr and about half had been incontinent ≥ 5 yr	NR
304	**Millard, 1999**	• Placebo (64) • TOLT 2 mg/d (123) • TOLT 4 mg/d (129)	60.5 (25-84) 60.1 (24-89) 60.2 (24-83)	66 78 77	NR	NR	NR	~50% had symptoms for > 5 yr	NR
306	**Drutz, 1999**	• Placebo (56) • OXYB 15 mg/d (112) • TOLT 4 mg/d (109)	62.1 [26–87] 66.3 [23–91] 63.0 [31–88]	80 72 81	NR	NR	NR	37-45% had symptoms > 5 yr	NR
308	**Burgio, 1998**	• Placebo (65) • OXYB 7.5-15 mg/d (67)	67.6 (7.6) 68.2 (7.5)	100	NR	NR	NR	12.7 (15.9) 9.8 (11.9)	Mixed: 52/51 Urge: 48/49

RefID	First author, Year	Treatment (no. Randomized)*	Age Mean(SD) or [range]	Female (%)	Trt Experienced † (%)	Weight	Adherence‡ (%)	Duration of symptoms, mo, mean (SD) or [range]	Urge or mixed OAB qualifying diagnosis, %
312	**Abrams, 1998**	• Placebo (57) • OXYB 15 mg/d (118) • TOLT 4 mg/d (118)	58 [6-78] 58 [21-80] 55[19-80]	75 75 77	75 60 52	NR	NR	NR	NR
314	**Rentzhog, 1998**	• Placebo (13) • TOLT 2 mg/d (16) • TOLT 4 mg/d (14)	58 59 56	78 63 86	NR	73 76 72	NR	NR	NR
318	**Jonas, 1997**	• Placebo (44) • TOLT 2 mg/d (99) • TOLT 4 mg/d (99)	57 [23-92] 59 [21-81] 57 [20-83	75 74 77	NR	NR	NR	NR	NR
368	**Batista, 2015**	• SOLF 5 mg/d (944) • MIRA 50 mg/d (943)	57.4 (13.6) 56.7 (14.3)	76 76	100	NR	NR	58.9 (68.8) 63.4 (79.8)	Mixed: 17/14 Urge: 41/41
418	**Yamaguchi, 2015**	• Placebo (214) • MIRA 25 mg/d (211) • MIRA 50 mg/d (208)	55.7 (12.9) 54.9 (13.6) 56.2 (13.6)	80 80 85	NR	56.04 (9.5) 55.81 (9.9) 56.70 (9.8)	>98	80.9 (85.1) 82.5 (77.4) 89.3 (84.0)	Mixed: 31/32/37 Urge: 60/60/55
715	**Dede, 2013**	• OXYB 15 mg/d (30) • TOLT 2 mg/d (30) • TROS 40 mg/d (30)	51.4 (10.8) 51.6 (9.8) 52.5 (10.9)	100	NR	NR	NR	NR	NR

RefID	First author, Year	Treatment (no. Randomized)*	Age Mean(SD) or [range]	Female (%)	Trt Experienced † (%)	Weight	Adherence‡ (%)	Duration of symptoms, mo, mean (SD) or [range]	Urge or mixed OAB qualifying diagnosis, %
1119	**Chapple, 2013**	• TOLT-ER 4 mg/d (813) • MIRA 50 mg/d (815)	59.6 (12.5) 59.2 (12.6)	74 74	NR; some patients previously participated in phase 3 MIRA/TOLT studies	NR	NR	83.8 (87.34) 87.4 (96.28)	Mixed: 26/29 Urge: 39/37
1120	**Khullar, 2013**	• Placebo (497) • TOLT-ER 4 mg/d (495) • MIRA 50 mg/d (497)	59.2 (12.30) 59.1 (12.89) 59.1 (12.36)	72 73 72	NR	NR	NR	76.9 (92.15) 76.3 (93.40) 78.7 (85.68)	Mixed: 21/22/23 Urge: 42/39/41
1152	**Weiss, 2013**	• Placebo (487) • FEST 4-8 mg/d (476)	57.5 (14.0) 58.0 (14.7)	66 68	26 26	NR	NR	8.0 [0.3–56.0] yr 7.5 [0.3–49.8] yr	NR
1158	**Nitti, 2013**	• Placebo (396) • FEST 4-8 mg/d (398)	72.8 (5.7) 72.6 (5.8)	52 54	NR	77.4 (13.4) 77.6 (14.5)	NR	7.0 [0.3-57.2] 7.4 [0.3-59.8]	NR
1558	**Dmochowski, 2010**	• Placebo (448) • FEST 4-8 mg/d (448)	60.1 (12.9) 59.7 (13.7)	83 83	~40% in each group	NR	NR	NR	NR
1559	**Homma, 2003**	• Placebo (122) • OXYB 9 mg/d (246) • TOLT-ER 4 mg/d (240)	58.4 (14.0) 57.9 (12.5) 61.2 (11.8)	69 73 68	NR	NR	94 93 98	NR	NR

RefID	First author, Year	Treatment (no. Randomized)*	Age Mean(SD) or [range]	Female (%)	Trt Experienced † (%)	Weight	Adherence‡ (%)	Duration of symptoms, mo, mean (SD) or [range]	Urge or mixed OAB qualifying diagnosis, %
1564	**Staskin, 2009**	• Placebo (400) • OXYB-GEL 100 mg/d (389)	59.3 (12.2) 59.5 (12.5)	88 91	NR	NR	91 91	97.4 (96.8) 106.6 (121.6)	NR
1570	**Chapple, 2007**	• Placebo (285) • TOLT-ER (290) • FEST 4 mg/d (272) • FEST 8 mg/d (288)	56.0 (13.7) 57.7 (14.6) 57.1 (13.2) 55.6 (14.1)	81 78 81 82	38-47% (includes 1 anticholinergic agent not of interest)	NR	NR	7.9 (9.6) yr 8.7 (10.1) yr 9.0 (11.2) yr 7.6 (8.4) yr	NR
1571	**Dmochowski, 2003**	• Placebo (117) • OXYB-TRANS 3.9 mg/d (121) • TOLT-ER 4 mg/d (123)	64.5 (12.3) 63.1 (12.0) 62.9 (13.5)	93 90 95	NR	NR	NR	Median 6.9 Median 5.5 Median 5.5	NR
1574	**Heschorn**	• Placebo (337) • TOLT-ER (690) • FEST 4-8 mg/d (685)	58.4 (13.7) 58.5 (13.2) 57.8 (12.8)	81 83 82	NR	NR	NR	7.3 [0.3–62.2] 6.9 [0.2–60.8] 7.1 [0.3–66.2]	NR
1575	**Chapple, 2005**	• TOLT-ER (607) • SOLF 5-10 mg/d (593)	56.4 56.5	88 85	NR	NR	NR	NR	NR
1578	**But, 2012**	• DARF 7.5 mg/d (37) • SOLF 5 mg/d (40)	54.8 (11.5)	100	NR	NR	NR	54 72	NR
1579	**Halaska, 2003**	• OXYB 10 mg/d (90) • TROS 40 mg/d (268)	52.2 [19–85] 54.2 [19–89]	87 85	NR	70.4 [50–90] 72.3 [50–120]	NR	NR	NR

RefID	First author, Year	Treatment (no. Randomized)*	Age Mean(SD) or [range]	Female (%)	Trt Experienced † (%)	Weight	Adherence‡ (%)	Duration of symptoms, mo, mean (SD) or [range]	Urge or mixed OAB qualifying diagnosis, %
1580	**Haab, 2004**	• Placebo (164) • DARF 7.5 mg/d (229) • DARF 15 mg/d (115)	56.5 [19-81] 57.7 [22-88] 56.6 [24-81]	84 85 87	NR	75.3 [49-144] 73.9 [42-128] 73.6 [45-119]	>86%	NR	NR
1581	**Hill, 2006**	• Placebo (109) • DARF 7.5 mg/d (108) • DARF 15 mg/d (107)	53.7 [21-85] 56.1 [23-88] 55.1 [24-82]	90 94 92	NR	NR	NR	NR	NR
1584	**Corcos, 2005**	• OXYB-ER 10 mg/d (77) • OXYB-ER 15 mg/d (83)	63.2 (12.6) 61.4 (13.2)	88 86	NR	NR	NR	NR	NR
1585	**Versi, 2000**	• OXYB 5-20 mg/d (115) • OXYB-ER 5-20 mg/d (111)	59.6 58.8	90 88	NR	79.0 78.0	NR	NR	NR
1588	**Herschorn, 2008**	• Placebo (207) • TOLT-ER 4 mg/d (410)	57 (14) 58 (13)	71 72	NR	NR	NR	NR	NR
1592	**Choo, 2008**	• TOLT 4 mg/d (118) • SOLF 5 mg/d (120) • SOLF 10 mg/d (119)	53.0 (12.2) 53.1 (10.5) 52.6 (12.7)	79 84 75	NR	59.1 (8.4) 59.6 (9.8) 60.2 (8.9)	NR	NR	NR
1601	**Rogers, 2008**	• Placebo (211) • TOLT-ER 4 mg/d (202)	47 (12) 49 (12)	100 100	NR	NR	NR	5 (6.5) yr 6 (8.0) yr	NR
1602	**Cardozo, 2000**	• Placebo (104) • TROS 40 mg/d (104)	47.0 (13.5)§ 46.3 (13.8)	57 67	NR	NR	NR	1.2 (4.0) yr 0.8 (2.2) yr	NR
1603	**Nitti, 2007**	• Placebo (274) • FEST 4 mg/d (283) • FEST 8 mg/d (279)	59 [24-88] 59 [21-85] 59 [23-91	74 76 78	54 49 53	NR	>96	9.8 (10.3) yr 9.1 (10.3) yr 10.1 (11.5) yr	NR

RefID	First author, Year	Treatment (no. Randomized)*	Age Mean(SD) or [range]	Female (%)	Trt Experienced † (%)	Weight	Adherence‡ (%)	Duration of symptoms, mo, mean (SD) or [range]	Urge or mixed OAB qualifying diagnosis, %
1605	**Zinner, 2006**	• Placebo (229) • DARF 15 mg/d (216)	59.1 [18-89] 59.1 [20-93]	88 86	NR	NR	NR	8.3 [0-58] yr 7.8 [0-45] yr	NR
1615	**Homma, 2006**	• Placebo (161) • OXYB-TRANS 3.9 mg/d (164)¶	63.3 (11.7) 62.7 (12.4)	72 81	NR	NR	NR	NR	NR
1618	**Rackley, 2006**	• Placebo (421) • TOLT-ER 4 mg/d (429)	59 (14) 58 (14)	50 52	NR	NR	NR	NR	OAB: 63/69
1619	**Altan-Yaycioglu, 2005**	• OXYB 15 mg/d (24) • TOLT 4 mg/d (28)	42.2 (11) 40.2 (10.7)	100 100	NR	NR	NR	NR	NR
1625	**Moore, 1990**	• Placebo (25) • OXYB 9 mg/d (28)	46.4 (12.4) 46.0 (11.7)	100 100	NR	NR	NR	8.9 (9.0) yr 7.5 (7.9) yr	NR
1630	**Appell, 2001**	• OXYB-ER 10 mg/d (185) • TOLT 4 mg/d (193)	58.6 (13.4) 59.6 (13.2)	82 84	40 38	NR	NR	NR	NR
1631	**Diokno, 2003**	• OXYB-ER 10 mg/d (391) • TLT-ER 4 mg/d (399)	60 60	100 100	46 48	NR	NR	NR	NR
1634	**Minassian, 2007**	• OXYB 7.5-15 mg/d (33) • OXYB-ER 5-10 mg/d (39)	73 (5) 75 (6)	100 100	NR	76 (14) 73 (14)	52 66	NR	Urge: 94/95 Stress:52/67
1635	**Chapple, 2004**	• Placebo (267) • TOLT 4 mg/d (266) • SOLF 5 mg/d (279) • SOLF 10 mg/d (269)	57.8 (13.7) 56.9 (12.8) 58.1 (13.4) 57.2 (13.4)	76 80 72 71	NR	72.6 (14.4) 74.8 (14.8) 74.6 (14.3) 75.5 (14.2)	NR	61.0 (83.9) 62.9 (82.5) 57.4 (60.5) 72.6 (105.4)	Mixed: 23/36/30/30 Urge: 70/56/64/61

RefID	First author, Year	Treatment (no. Randomized)*	Age Mean(SD) or [range]	Female (%)	Trt Experienced † (%)	Weight	Adherence‡ (%)	Duration of symptoms, mo, mean (SD) or [range]	Urge or mixed OAB qualifying diagnosis, %
1636	**Cardozo, 2004**	• Placebo (301)¶ • SOLF 5 mg/d (299) • SOLF 10 mg/d (307)	56.1 (13.3) 55.4 (13.8) 55.9 (14.2)	80 82 82	NR	74.1 (14.4) 74.1 (15.0) 74.6 (15.4)	NR	29.0 [5-327] 27.0 [4-383] 28.0 [4-314]	NR
1638	**Barkin, 2004**	• OXYB 5-20 mg/d (60) • OXYB-ER 15 mg/d (65)	60.6 (14.8) 58.0 (12.4)	90 91	NR	NR	NR	NR	NR
1639	**Yamaguchi, 2007**	• Placebo (406) • SOLF 5 mg/d (400) • SOLF 10 mg/d (385)	60.8 (12.5) 60.4 (13.3) 59.9 (13.0)	84 83 86	NR	56.2 (9.4) 56.3 (9.7) 57.1 (10.5)	NR	**	Mixed: 34/34/38 Urge: 62/61/57
1643	**Nitti 2009, Stratum A**	• Placebo (24) • FEST 4 mg/d (25) • FEST 8 mg/d (28)	57.1 (10.2) 52.3 (14.8) 53.3 (14.6)	75 76 89	NR	NR	NR	10.1 (9.5) yr 7.2 (5.4) yr 7.6 (5.7) yr	NR
1643	**Nitti 2009, Stratum B**	• Placebo (19) • FEST 4 mg/d (19) • FEST 8 mg/d (19)	56.5 (8.4) 56.0 (11.3) 58.0 (8.3)	89 100 89	NR	NR	NR	10.3 (9.0) yr 8.2 (6.4) yr 10.6 (12.3) yr	NR
1646	**Ho, 2010**	• TOLT-ER 4 mg/d (36) • SOLF 5 mg/d (39)	55.3 (15.7) 58.9 (15.1)	66 66	NR	60.5 (11.0) 63.4 (9.5)	NR	4.4 (4.9) 4.2 (6.2)	NR
1647	**Chapple, 2004**	• Placebo (38) • TOLT 4 mg/d (37) • SOLF 5 mg/d (37) • SOLF 10 mg/d (35)	[53-59]	60	NR	NR	NR	NR	NR

RefID	First author, Year	Treatment (no. Randomized)*	Age Mean(SD) or [range]	Female (%)	Trt Experienced † (%)	Weight	Adherence‡ (%)	Duration of symptoms, mo, mean (SD) or [range]	Urge or mixed OAB qualifying diagnosis, %
1648	**Kaplan, 2010**	• Placebo (480) • TOLT-ER 4 mg/d (974) • FEST 4-8 mg/d (963)	59.5 (13.2) 58.1 (13.8) 57.9 (13.5)	86 84 85	34 32 32	NR	NR	6.3 (7.2) yr 6.5 (7.3) yr 6.6 (7.7) yr	NR
1650	**Herschorn, 2010**	• OXYB,15 mg/d (64) • SOLF 5 mg/d (68)	61 [22-87]	78	NR	NR	≥ 80 ≥ 80	NR	NR
1651	**Van Kerrebroeck, 2001**	• Placebo (508) • TOLT 4 mg/d (514) • TOLT-ER 4 mg/d (507)	61 [22-93] 60 [22-92] 60 [20-89]	81 79 82	NR	NR	NR	NR	NR
1652	**Jacquetin, 2001**	• Placebo (50) • TOLT 2 mg/d (97) • TOLT 4 mg/d (103)	56 [19-89] 53 [18-85] 58 [21-88]	80 76 82	NR	NR	>80 >80 >80	33-45% had symptoms for > 5 yr	Urge: 76/77/73
1654	**Malone-Lee, 2001, p. 700**	• Placebo (43) • TOLT 2 mg/d (61) • TOLT 4 mg/d (73)	75 [66-88] 75 [65-92] 75 [62-92]	74 62 62	NR	NR	98 90 86	41-49% had symptoms for > 5 yr	Urge: 77/72/70
1655	**Lee, 2002**	• OXYB 10 mg/d (116) • TOLT 4 mg/d (112)	52 [20-86] 52 [27-82]	79 74	NR	NR	77 87	NR	NR

RefID	First author, Year	Treatment (no. Randomized)*	Age Mean(SD) or [range]	Female (%)	Trt Experienced † (%)	Weight	Adherence‡ (%)	Duration of symptoms, mo, mean (SD) or [range]	Urge or mixed OAB qualifying diagnosis, %
1656	**Malone-Lee, 2001, p. 1452**	• OXYB 4-10 mg/d (188) • TOLT 4 mg/d (190)	64.8 [50-90] 65.4 [49-87]	68 66	NR	NR	NR	33-40 % had symptoms for > 5 yr	NR
1658	**Sussman, 2002**	• TOLT-ER 2 mg/d (333) • TOLT-ER 4 mg/d (336)	63.8 (15.7) 63.4 (16.6)	73 76	NR	NR	NR	19-20% had symptoms for > 5 yr	Urge: 59/64
1659	**Khullar, 2004**	• Placebo (285) • TOLT-ER mg/d (569)	57.4 (13.8) 58.6 (13.1)	100 100	30 34	NR	NR	95-97% had symptoms for > 6 mo	Mixed: 100
1661	**Zinner, 2004**	• Placebo (261) • TROS 40 mg/d (262)	61.5 (SE 0.8) 63 (SE 0.8)	71 78	NR	NR	NR	NR	NR
1674	**Dmochowski, 2002**	• Placebo (132) • OXYB-TRANS 3.9 mg/d (125)	62.7 (13.1) 59.4 (14.5)	92 91	20 22	NR	≈90	9.1 (9.1) yr 9.9 (9.8) yr	NR
1675	**Yamaguchi, 2011**	• Placebo (318) • FEST 4 mg/d (320) • FEST 8 mg/d (313)	56.7 (13.5) 57.2 (14.2) 58.8 (13.4)	78 78 82	NR	57.6 (10.6) 57.2 (10.4) 57.9 (10.6)	NR	NR	NR
1687	**Vardy,**	• Placebo (318) • SOLF 5-10 mg/d (386)	60 (12) 59 (13)	84 81	NR	NR	NR	NR	NR

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1689	**Chancellor, 2000,**	• Placebo (508) • TOLT 4 mg/d (514)	61 [21-93] 60 [22-92]	81 79	NR	NR	95 95	NR	NR
1691	**Leung,**	• OXYB 15 mg/d (53) • TOLT 4 mg/d (53)	49 [43-57] 51 [44-67]	100 100	NR	NR	88 75	NR	NR

OXYB = oxybutynin, OXYB-ER = extended release oxybutynin, OXYB-TRANS = transdermal oxybutynin, OXYB-GEL = gel oxybutynin, TOLT = tolterodine, TOLT-ER = extended release tolterodine, DARF = darifenacin, SOLF = solifenacin, TROS = trospium, FEST =fesoterodine, MIRA = mirabegron, mo = months.

*Data for treatment arms not eligible for inclusion are not reported in this table.

†Treatment experienced reported as “antimuscarinic” or “anticholinergic” or as a specific drug of interest.

‡As defined by the study authors.

§Reported as “7.0 (13.5); inferred to be 47 years.

¶No. randomized not reported; data is no. who received study drug.

**Data reported in study by range; see original publication for details.