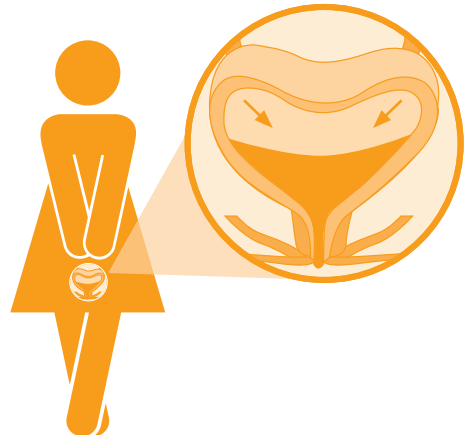


Why did we do this review?

The Ontario Drug Policy Research Network (ODPRN) conducted multiple studies on the efficacy, safety and accessibility of medications used in the treatment of overactive bladder using multiple research methods as part of an initiative to modernize the public drug formulary in Ontario.



What is overactive bladder (OAB)?

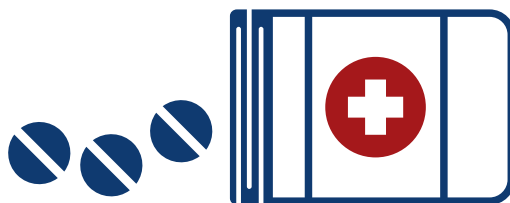
- Overactive bladder is a health condition characterized by problems in bladder storage that causes a sudden urge to urinate; in some patients this may result in unintentional urine loss (incontinence). It is a common condition that is more prevalent in the elderly.

Drugs used to treat OAB

- Anticholinergics (also known as antimuscarinics) are the main drug class used to treat OAB; there are six of them available in Canada and their listing and formulations on public drug plans vary, some also have generic versions available.
- Mirabegron is another drug, from a different drug class, that is being increasingly used. It became available in March 2013.

- In Ontario, only a small proportion of patients are tried on oxybutynin first, before other products, despite this being a part of the criteria for Limited Use coverage.

- Oxybutynin is the intended first choice for treatment but only small proportions, approximately 15%, of patients are tried on this drug first (it is not even the most commonly used agent in Ontario).



Name	Listing/Public plan coverage in Ontario
Trospium	• Limited Use
Darifenacin	• Limited Use
Mirabegron	• Limited Use
Fesoterodine	• Limited Use
Oxybutynin	<ul style="list-style-type: none"> • Immediate release (IR) is General Benefit • Patch is available through the Exceptional Access Program • Generic versions available for IR formulation • Oxybutynin gel and oxybutynin extended release are currently not available
Solifenacin	<ul style="list-style-type: none"> • Limited Use • Generic versions available
Tolterodine	<ul style="list-style-type: none"> • Limited Use • Generic versions available

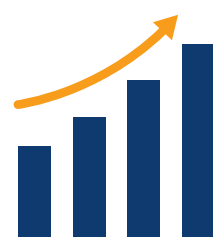
Why review drugs used to treat OAB?



There is concern that the side effects of anticholinergics, including risk of falls and effects on cognition, may be harmful in the elderly population.



With the introduction of generic products and their lower costs, an updated cost-effectiveness analysis was needed.



New agents have been recently introduced (e.g., mirabegron) and are being increasingly used.

Overall, the drugs have similar efficacy but have varying differences in safety outcomes.

	Safety		Efficacy
	Severity of dry mouth	Severity of constipation	Reduction in symptoms
Oxybutynin (IR)	●●●	●●●	●●●
Mirabegron	●●●	●●●	●●●
Solifenacin	●●●	●●●	●●●
Tolterodine	●●●	●●●	●●●
Placebo	●●●	●●●	●●●

●●● least severe
 ●●● most severe

●●● least effective
 ●●● most effective

- Please note that the diagram is based on relative comparisons, and it is meant to illustrate a ranking rather than a metric of magnitude of 'better' or 'worse'

Utilization

73,000+

Publicly-funded OAB medication users in 2014 in Ontario.



A relatively high proportion of users of oxybutynin discontinued use or switched to a different drug within 6 months after initiation (24-26%), compared to other drug groups (14% or less).

Users of OAB medications in Ontario

Average age 73 years old



66.9%
diagnosed with OAB

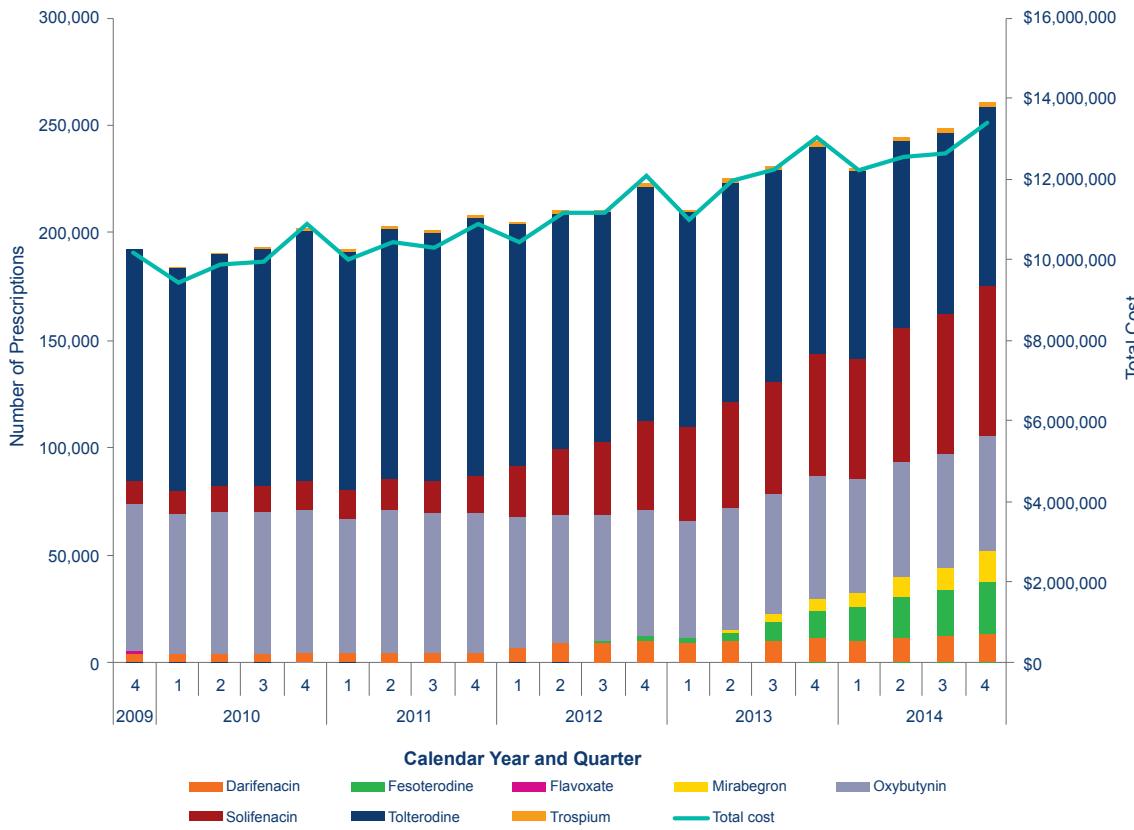


38.8%
were males



4.1%
lived in long-term care

Total number of prescriptions and cost for OAB medications dispensed in Ontario through the public drug plan



By end of 2014, tolterodine was the most prescribed, followed by solifenacin, oxybutynin, fesoterodine, mirabegron, darifenacin, and then trospium

Cost



Solifenacin is the most cost-effective therapy for OAB.



However if solifenacin fails, then oxybutynin (immediate release) is the next best option.

Reimbursement option

Use of oxybutynin IR or solifenacin or tolterodine ER as initial therapy, all other currently listed OAB medications Limited Use

Rationale:

- Oxybutynin IR, solifenacin and tolterodine ER are considered first line therapy based on arguments of efficacy, safety and cost-effectiveness.
- Physician participants prefer using long-acting agents, such as solifenacin and tolterodine ER. This option provides initial treatment choices for solifenacin.
- At current prices, mirabegron, fesoterodine, trospium, darifenacin, oxybutynin ER, transdermal oxybutynin, oxybutynin gel and tolterodine IR are not cost-effective. If price of tolterodine IR is reduced to 25% of brand-name price, this drug may also become cost-effective.

Other recommendation



No listing is recommended for oxybutynin extended release (Ditropan XL)

- Oxybutynin ER does not provide any advantages over other currently available OAB medications for patients unable to swallow.
- At current prices, oxybutynin ER is not cost effective.



For patients unable to swallow, we recommend listing oxybutynin gel (Gelnique) under the Exceptional Access Program

- Oxybutynin gel is better than placebo but no more effective than other OAB medications; as well, fewer patients experience dry mouth with oxybutynin gel than with other agents. Oxybutynin gel provides an option for patients unable to swallow oral medications.



All anticholinergics, including oxybutynin, should have a Therapeutic Note, cautioning about the use of these drugs in the elderly.

- This note should be added for all anticholinergic agents used for management of OAB (including oxybutynin IR). The therapeutic note does not apply to mirabegron, a beta-3 adrenoceptor agonist.