Overactive Bladder *Medications*

Overactive bladder (OAB) is a symptom complex, affecting approximately 15% of the adult population. Symptoms include urgency *(urgent sensation to empty the bladder)*, usually with frequency *(8 or more void per 24h)* and nocturia (one or more void during the night), with or without urge incontinence *(leakage of urine usually associated with a sudden urge to urinate)*. Diagnosis is mainly clinical, and includes a thorough questionnaire and a focused physical exam (abdominal, neurological, pelvic in females and rectal in males) to eliminate other related conditions. Treatments include behavioral counseling *(fluid intakeand bladder habits)*, pelvic floor exercises *(contraction of muscles around the outlet of the bladder)*, pharmacological treatment and surgical options.

We will limit our discussion to pharmacological treatment of this condition. Many products are available to treat OAB, including many who have been recently approved in Canada. They act by blocking nerve receptors at the bladder muscle level. Most of them are called anticholinergics because they block the release of acetylcholine at the junction of nerves and bladder muscle fibers, hence diminishing bladder contractions. Unfortunately, these products don't act only at the bladder level but also on other organs where acetylcholine plays a role. This is how they produce side effects called «anticholinergic side effects» that include dry mouth, constipation, blurred vision and some degree of cognitive impairment. Side effects are proportional to the product blood level. Some products *(IR: immediate release formulation)* are rapidly absorbed and eliminated, producing high blood levels for a short period of time hence producing more side effects and requesting multiple daily administrations. Other products *(PR: prolonged release formulation)* are absorbed more steadily, hence producing a more stable blood concentration with sustained efficacy and fewer side effects, and they require only daily dosing. Some other products are absorbed through the skin and may cause even fewer side effects. In addition to differences in absorption, some are more selective for bladder receptors and less active on other organs cholinergic receptors, hence producing fewer side effects.

The following list includes all products approved to treat this condition in Canada as of January 2012. Cost coverage of these products varies according to provincial drug reimbursement (formularies) programs and private insurance programs.

Ditropan and generics (Oxybutynin IR)

Ditropan has been available in Canada for 30 years, and many generics products are available. These compounds contain Oxybutynin (a non selective anticholinergic) in an immediate release formulation with proven efficacy over placebo. It is available in 2.5 and 5 mg tablets and requires up to 4 daily administrations. Maximum daily dosage is 20 mg. It is also available in liquid formulation. It is recommended to start with a low dosage (2.5 mg) two or three times a day and to increase progressively to maximum dosage. Drug compliance is poor at maximum dosage due to anticholinergic side effects, including confusion and cognitive impairment in elderly. The majority of patients discontinue by 6 months due to side effects. It is on the drug reimbursement program in every province.

Urispas and generics (Flavoxate IR)

Urispas has been available in Canada for over 15 years, and generics are available. These compounds contain flavoxate *(a non selective anticholinergic)* in an immediate release formulation and efficacy over placebo has not been proven at dosage recommended in Canada. It is available in 200 mg tablets and requires administration three times a day. Maximum daily dosage is 600mg. It is well tolerated at recommended dosage, but efficacy is poor. Compliance is poor due to lack of efficacy. It is on the drug reimbursement program in some provinces.

Detrol (Tolterodine IR)

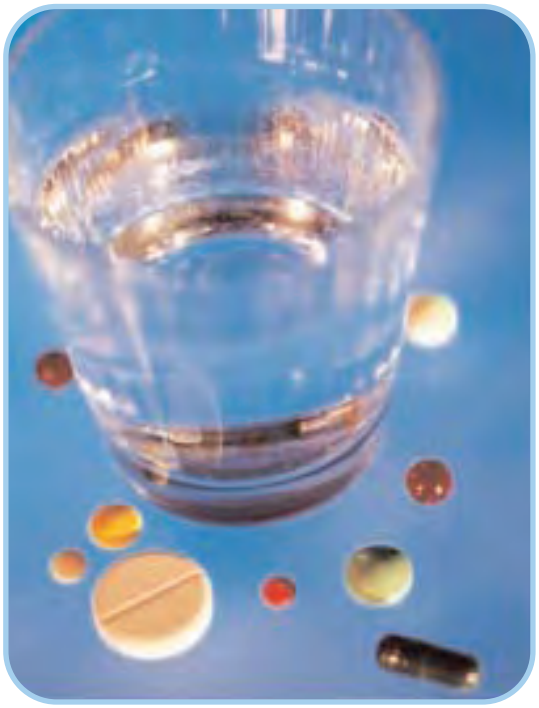
Introduced in Canada in late 1990s. Detrol contains tolterodine *(a non selective anticholinergic)* in an immediate release formulation with proven efficacy over placebo. Equivalent efficacy against Oxybutynin IR has been proven, but with a better side effect profile, especially dry mouth. It is available in 1 and 2 mg tablets, and requires twice a day dosing. Maximum daily dosage is 4 mg. It is recommended to start with maximal dosage *(2 mg twice a day)* and to decrease if needed to 1 mg once or twice a day. Drug compliance is acceptable at maximum dosage but anticholinergic side effects may limit compliance. In case of hepatic or renal impairment, maximum dosage should be reduced to 1mg twice a day. Precaution is recommended if using with cardiac antiarrythmic drugs. It is on the drug reimbursement program in some provinces.

Detrol LA (Tolterodine PR)

Introduced in Canada in 2001. Detrol LA contains tolterodine in a prolonged release formulation *(beaded capsule controlled release)* with proven efficacy over placebo. Better efficacy and improved tolerability have been documented when compared to regular Detrol. It is available in 2 and 4 mg tablets, and requires a single daily administration. Detrol LA 4 mg has been shown relatively similar to Ditropan XL 10 mg regarding efficacy and side effects *(opera trial)*. Maximum daily dosage is 4 mg. It is recommended to start with maximal dosage (4 mg) and to decrease if needed to 2 mg. Drug compliance is acceptable at maximum dosage but anticholinergic side effects may limit compliance. In case of hepatic or renal impairment, maximum dosage should be reduced to 2mg once a day. Precaution is recommended if using with cardiac antiarrythmic drugs. It is on the drug reimbursement program in some provinces.

Ditropan XL (Oxybutynin PR)

Introduced in Canada in 2001. Ditropan XL contains Oxybutynin in a prolonged release formulation *(expulsion by osmotic pressure with Oros technology)* with proven efficacy over placebo. Better efficacy and improved tolerability has been documented when compared to regular Ditropan. It is available in 5 and 10 mg tablets, and requires a single daily administration. Ditropan XL 10 mg has been shown relatively similar to Detrol LA 4 mg regarding efficacy and side effects. Maximum daily dosage is 30 mg, taken once a day. It is recommended to start with a 10mg dosage and if needed to decrease to 5 mg or increase to 30 mg. Drug compliance is acceptable at 10 mg dosage but anticholinergic side effects may limit compliance. Some patients with severe OAB conditions will tolerate increase in dosage up to 30 mg. It is on the drug reimbursement program in some provinces.



Oxytrol (Oxybutynin TDS)

Introduced in Canada in 2002. Oxytrol contains Oxybutynin in a transdermal delivery system that avoids first pass hepatic metabolism. Efficacy has been proven over placebo. Efficacy is equivalent to Detrol LA 4 mg but with less dry mouth. Skin irritation occurs in 15-20% of patients. It is available in patches of 36 mg liberating 3.9 mg by day. Patches must be applied twice weekly. Maximum dosage is 3.9 mg per day and this is the only recommended drug regimen. Drug compliance is good but skin irritation may limit compliance. It is on the drug reimbursement program in some provinces.

Uromax (Oxybutynin PR)

Introduced in Canada in 2006. Uromax contains Oxybutynin in a prolonged release formulation (a cellulose matrix release technology) with proven efficacy over placebo. Better efficacy and improved tolerability has been documented when compared to regular Ditropan. It is available in 10 and 15 mg tablets, and requires a single daily administration. Maximum daily dosage is 20 mg. It is recommended to start with a 10mg dosage and if needed to increase to 15 mg. Drug compliance is acceptable at both 10 mg and 15 mg dosage but anticholinergic side effects may limit compliance. Some patients with severe OAB conditions will tolerate increase in dosage up to 20 mg. Cost and simplicity of use at higher dosage (15 mg) are the main advantages. It is on the drug reimbursement program in some provinces.

Vesicare (Solifenacine)

Introduced in Canada in 2006. Vesicare contains solifenacine *(a selective anticholinergic)* in an immediate release formulation with proven efficacy over placebo. Metabolism of solifenacine allows for daily administration without request for a prolonged release formulation. It is available in 5 and 10 mg tablets. At a starting dosage of 5 mg, efficacy and tolerability has been shown relatively similar to Detrol LA 4 mg, but at maximum dosage for both products, Vesicare has shown a better efficacy *(star trial)*. Its selectivity for bladder receptors (M3) may allow for a better tolerability especially in older patients. It is available in 5 and 10 mg tablets, and requires a single daily administration. Maximum daily dosage is 10 mg. It is recommended to start with a 5 mg dosage and if needed to increase to 10 mg. Drug compliance is acceptable at 5 and 10 mg dosage but anticholinergic side effects may limit compliance. It is on the drug reimbursement program in some provinces.

Enablex (Darifenacine)

Introduced in Canada in 2006. Enablex contains Darifenacine *(a selective anticholinergic)* in a prolonged release formulation with proven efficacy over placebo. It is available in 7.5 and 15 mg tablets and requires a single daily administration. Efficacy and tolerability has been shown superior to Ditropan and relatively similar to Detrol LA. Its high selectivity for bladder receptors (M3) may allow for a better tolerability especially in older patients. It has no cardiac side effect but may have more effect on bowels. Maximum daily dosage is 15 mg. It is recommended to start with a 7.5 mg dosage and if needed to increase to 15 mg. Drug compliance is acceptable at 7.5 and 15 mg dosage but anticholinergic side effects may limit compliance. It is on the drug reimbursement program in some provinces.

Trosec (Trospium)

Introduced in Canada in 2006. This product has been available in Europe for 25 years and is a market leader in some countries. Trosec contains Trospium chloride *(a quaternary amine with anticholinergic activity)* in an immediate release formulation with proven efficacy over placebo. It is available in 20 mg tablets and requires twice a day administration. Efficacy has been shown comparable to Ditropan, but with a better safety profile. Trospium doesn't cross the blood brain barrier, and doesn't have cardiac effect. Maximum daily dosage is 40 mg. It is recommended to start with at maximum dosage and to reduce to 20 mg once a day if needed. Drug compliance is acceptable at maximal dosage but anticholinergic side effects may limit compliance. In case of renal impairment, maximum dosage should be reduced to 20 mg once a day. It is on the drug reimbursement program in some provinces.

Gelnique (Oxybutynin chloride gel)

Introduced in Canada in 2012, Gelnique contains oxybutynin chloride in an alcohol based gel. Efficacy has been shown over placebo. It is available in individual sachets or packets and is applied to the shoulder, abdomen (stomach area) or thigh once a day. The gel is clear and dries quickly and because it is delivered transdermally (across the skin) it avoids the first pass metabolism by the liver. Drug compliance is very good and it has a low rate of anticholinergic side effects. It is supplied in cartons of 30 individual 1 gm sachets. It is under review by different provinces.

For more information about incontinence contact

The Canadian Continence Foundation

P.O. Box 417, Peterborough, Ontario K9J 6Z3

Tel: (705) 750-4600 • **Helpline:** 1-800-265-9575 • **Fax:** (705) 750-1770

Email: help@continence-fdn.ca • **www.continence-fdn.ca**