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Update on New Drugs

Health Canada approved 51 new molecular entities/significant biologicals in 2013. [1] Although this may seem like a lot, many of these drugs are for the treatment of various cancers, or approved as notice of compliance (NOC w/ conditions), and so may not necessarily be seen in community pharmacy. Also, many of these drugs are considered "me-too" drugs and do not differ significantly from previously approved drugs in the same class. This leaves a handful of drugs that are first in class drugs and available through wholesalers, meaning they are likely to show up in community pharmacy practice, if not already there.

Drug	Indication	Safety	Efficacy	Place in therapy	Cost
Fibristal ™ (ulipristal) **Selective Progesterone Receptor Modulator (SPRM)** [2]	Treating moderate to severe signs and symptoms of uterine fibroids in women of reproductive age eligible for surgery. Treatment is limited to three months (study patients had planned surgeries after three months of ulipristal use). [2,3,4] US indication: emergency contraception [5] MOA: Partial antagonist at progesterone receptors, which reduces fibroid size by inhibiting fibroid cellular proliferation and inducing apoptosis.[2] Ulipristal is structurally similar to mifepristone, but has less antiglucocorticoid activity, providing a potential advantage for long-term use. [4]	Avoid with: oral contraceptive pills or progestin only pills [2] strong CYP3A4 inducers/inhibitors [2] women who are pregnant, breast feeding, have genital bleeding of unknown etiology or for reasons other than uterine fibroids, or have cancer of the breast, cervix, uterus, or ovaries [2] **Adverse reactions**: >10%: endometrial thickening (reversible) [2] 1-10%: fatigue, nausea, dizziness, hot flush [2] Compare to leuprolide: favourable side effect profile (fewer hot flashes, less profound suppression of estradiol levels, less osteoporotic concerns) [6]	Compared to leuprolide: non-inferior for control of bleeding [7] no initial steroidal flare quicker amenorrhea induction (7-10 days for ulipristal; 21 days for leuprolide) [7] less effective than leuprolide in decreasing fibroid volume, but may have a more prolonged volume reduction after treatment discontinuation [7]	Canadian Drug Expert Committee (CDEC) recommends to list with conditions: maximum duration of treatment is three months; patient is under the care of an OB/GYN; AND, the drug plan costs of ulipristal acetate do not exceed the drug plan costs for the comparator leuprolide acetate. [8] Surgery (especially hysterectomy) is the predominating treatment for uterine fibroids, therefore ulipristal may be used prior to surgery to relieve symptoms and reduce fibroid sizes. [6,7]	$422.69/34d (once daily oral tablet)[10]

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Fycompa™ (perampanel) **Antiepileptic Drug (AED);** **Glutamate Receptor Antagonist**[11]	Adjunctive therapy for partial-onset seizures in adults not satisfactorily controlled with conventional therapy. [11] MOA: Selective, non-competitive antagonist of ionotropic-AMPA-glutamate receptors on post-synaptic neurons; thereby reducing neuronal excitation. Full mechanism is unknown. [11]	Monitor for serious psychiatric and behavioural reactions (aggression and hostility) during titration and at higher doses (12mg/day) [11,12] Avoid with CYP3A4 inducers and levonorgestrel containing oral contraceptives (interactions with CYP3A4 inhibitors not specified) [11] Start at a higher dose (4mg) with concomitant enzyme inducing (EI) AEDs (carbamazepine, phenytoin) (2mg initial dose without EI AEDs) [11] Potential for abuse [11] **Adverse reactions**: ≥5%: dizziness, somnolence, fatigue, headache, weight gain, gait disturbances [11]	Reduction in seizure frequency compared to placebo when used adjunctively (median change of -26.3% vs -21.0% after 28 days, perampanel 8mg vs. placebo) [12] Commonly tested with carbamazepine, valproic acid, lamotrigine, levetiracetam, and oxcarbazepine. [12] No head-to-head trials	CDEC recommends to list with conditions: patients are currently receiving two or more AEDs, less costly AEDS are ineffective or inappropriate, and patients are under the care of a physician experienced in treating epilepsy. [13] This places permampanel as add-on therapy after at least two other AEDs used concomitantly have been tried.	$348.55/34d (once daily oral tablet) [10]
Myrbetriq™ (mirabegron) **Beta-3 adrenergic agonist** [14]	Treatment of overactive bladder with symptoms of urgency, urgency incontinence, and urinary frequency. [14] MOA: Selective β_3 agonist, causing relaxation of the bladder smooth muscle and an increase in bladder capacity. [14,15]	Avoid in uncontrolled hypertension (≥180 +/- ≥110mmHg) and pregnancy [14] Caution with chronic kidney disease, narrow TI 2D6 drugs (increases plasma concentrations of CYP2D6 substrates), digoxin (increases digoxin AUC), and QT prolonging drugs (additive effect) [14] May cause urinary retention [14] **Adverse reactions**: 1-10%: hypertension, tachycardia, dry mouth, constipation [14]	Reduces mean number of micturition and incontinence episodes (one to two fewer per 24 hours) [16] Volume voided per micturition significantly improved versus placebo (11mL/micturition) [16]	No head-to-head trials Suggested to use after failure or intolerance to other antimuscarinic drugs (e.g. oxybutynin, tolterodine) (due to potential for serious adverse effects, high costs, and lack of long-term data) [17] CDEC is currently reviewing its recommendation.	$64.18 /34d (once daily oral tablet) [10]
Tecfidera ™ (dimethyl fumarate) **Fumarac acid derivative; systemic immuno-modulator** [18]	Monotherapy for the treatment of relapsing-remitting multiple sclerosis (MS). [18] MOA: Activates the Nuclear factor Nrf2 pathway, which is involved in the cellular response to oxidative stress. It also has demonstrated anti-inflammatory effects. Exact mechanism for effect in MS is unknown. [18]	May decrease lymphocyte count, elevate liver enzymes, and cause proteinuria; monitor CBCs, liver enzymes, and urinalyses [18] Avoid live vaccines, nephrotoxic drugs, and other immunomodulators [18] **Adverse reactions:** flushing (35%), gastrointestinal (N/V/D; 48%), infections Compared to glatiramer: Adverse reaction rates similar - 94% for dimethyl fumarate (flushing and GI)	Reduces relapse rates (NNT=6) [19] May delay progression of disability [19] Compared to glatiramer and placebo: No significant reductions in disability progression vs placebo for either drug [19] Significantly greater number of patients relapse-free after two years vs placebo (ARR=18% and 11%, dimethyl fumarate and glatiramer) [20]	CDEC recommends to list with conditions: - Patients contraindicated to, or have failed to respond to adequate courses of at least one interferon beta-1b formulation AND glatiramer acetate [20]; AND, - The patient is under the care of a neurologist experienced in the diagnosis and management of MS. [20]	$2265.76 per 34 days (twice daily oral capsule) [10] Tecfidera™ is not cost-effective [20] **Glatiramer:** $1384.88 per 30 days (once daily SQ injection)

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