therapeutics letter
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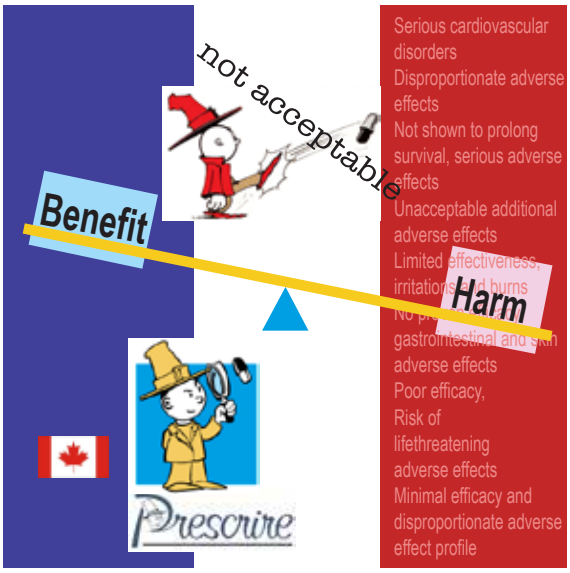
THERAPEUTICS INITIATIVE Evidence Based Drug Therapy

Drugs to avoid

In two previous Therapeutics Letters we presented *Clinical Pearls from Prescrire International*.[1,2] Prescrire is one of a small number of drug bulletins in the world, which reports on prescription drugs and is completely independent of industry influence. The front page of Prescrire International states, "Funded by subscribers. No advertising, no grants, no shareholders." The inside jacket documents the large number of contributors and the processes whereby they prevent conflicts: "Members of the Prescrire Editorial Staff sign a yearly declaration of absence of conflicts of interest, in accordance with Prescrire's 'Non merci…' Charter."

In April 2017 Prescrire published their latest "Drugs to avoid: 2017 update".[3] This update represents an assessment, based on a rigorous procedure, of the harm-benefit balance of drugs and indications. This fifth annual review of drugs to avoid includes all medicines examined by Prescrire between 2010 and 2017 and authorized in the European Union. It identifies 91 drugs that are more harmful than beneficial. The full 10-page version is freely available.[4]



The Tables provided here include only the drugs on the Prescrire list that are currently available in Canada. The Tables also include the indications, a summary of the reasons to avoid and Prescrire's suggestions of better alternatives. For ease of reference we have divided the list into drugs prescribed for prevention (Table 1) and drugs prescribed for treatment (Table 2).

Table 1: Drugs to avoid prescribed for prevention

Drug (Brand)	Indication	Reason(s) to avoid	Better alternative(s)
Aliskiren (Rasilez)	High blood pressure	Not shown to reduce cardiovascular events	Thiazides, ACE inhibitors
Bezafibrate (Bezalip)	Elevated lipids	Not shown to reduce cardiovascular events	Gemfibrozil
Fenofibrate (Lipidil)	Elevated lipids	Not shown to reduce cardiovascular events	Gemfibrozil
Dronedarone (Multaq)	Anti-arrhythmic	Less effective than amiodarone	Amiodarone
Ivabradine (Lancora)	Heart failure	Toxicity such as myocardial infarction and severe bradycardia; no advantages	Beta blockers
Olmesartan (Olmetec)	High blood pressure	Possible sprue-like enteropathy	Other angiotensin receptor blockers
Gliptans: Alogliptan (Nesina), Linagliptan (Trajenta), Saxigliptan (Onglyza), Sitagliptan (Januvia)	Type 2 diabetes	Unfavorable adverse effect profile such as anaphylaxis and pancreatitis	Metformin, sulfonylureas
Flozins: Canagliflozin (Invokana), Dapagliflozin (Forxiga)	Type 2 diabetes	Adverse effects such as hypotension and genital infections	Metformin, sulfonylureas
Pioglitazone (Actos)	Type 2 diabetes	Adverse effects such as heart failure and bone fractures	Metformin, sulfonylureas
Orlistat (Xenical)	Weight loss	No long-term effectiveness; adverse effects such as severe diarrhoea and malnutrition	Diet and exercise
Denosumab (Prolia)	Osteoporosis	Modest efficacy; disproportionate adverse effects such as back pain and serious infections	Weight bearing exercise

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Table 2: Drugs to avoid prescribed for treatment

Drug (Brand)	Indication	Reason(s) to avoid	Better alternative(s)
Domperidone	Vomiting, upper GI hypomotility	Cardiac dysrhythmias	Metoclopramide
Prucalopride (Resotran)	Chronic idiopathic constipation	Uncharacterized adverse effect profile	Other laxatives
Moxifloxacin	Bacterial infections	Serious toxicity such as liver and cardiac disorders	Ciprofloxacin, Ofloxacin
Donepezil (Aricept), Galantamine (Reminyl), Rivastigmine (Exelon), Memantine	Alzheimer's and other dementias	Minimal efficacy; disproportionate adverse effects such as severe vomiting and syncope	Support from caregivers and family
Alemtuzumab (Lemtrada), Natalizumab (Tysabri), Teriflunomide (Aubagio)	Multiple sclerosis	Disproportionate adverse effects such as infections and liver damage	Interferon beta
Olaparib (Lynparza)	Advanced ovarian cancer	Not shown to prolong survival; serious adverse effects	Appropriate supportive care
Trabectedin (Yondelis)	Ovarian cancer, soft-tissue sarcoma	No tangible efficacy; severe adverse effects such as diarrhoea and liver damage	Appropriate supportive care
Duloxetine (Cymbalta)	Depression	Unacceptable risk of cardiac and liver toxicity	Other antidepressants
Citalopram (Celexa), Escitalopram (Cipralex)	Depression	Risk of QT prolongation	Other antidepressants
Venlafaxine (Effexor)	Depression	Risk of cardiac disorders	Other antidepressants
Bupropion (Zyban)	Smoking cessation	Risk of neuropsychiatric disorders	Nicotine
Oral or Nasal Decongestants: Pseudo-ephedrine, Naphazoline, Phenylephrine	Allergic or viral rhinitis	Serious cardiovascular disorders	Conservative measures
Omalizumab (Xolair), Mepolizumab (Nucala)	Severe asthma, chronic idiopathic urticaria	Disproportionate adverse effects	Corticosteroids
Nintedanib (Ofev)	Idiopathic pulmonary fibrosis	No survival benefit; serious liver damage and thromboembolism	Symptomatic treatment
NSAIDs: Celecoxib (Celebrex), Diclofenac (Voltaren), Ketoprofen, Piroxicam	Pain and inflammation	Unacceptable additional adverse effects such as myocardial infarction and skin reactions	Acetaminophen, Ibuprofen, Naproxen (lowest dose for shortest period)
Glucosamine	Osteoarthritis	Not effective; rare allergic reactions	Appropriate exercise
Capsaicin topical	Pain	Limited effectiveness; irritations and burns	Other analgesics
Methocarbamol (Robaxin)	Muscle relaxant	No proven efficacy; gastrointestinal and skin adverse effects	Acetaminophen
Quinine	Muscle cramps	Poor efficacy; risk of life-threatening adverse effects	Regular stretching

Prescrire's conclusions

- **"91 authorised drugs more dangerous than beneficial"**
- "This review lists drugs that have an unfavourable harm-benefit balance in all their authorized indications, in other words drugs that should be removed from the market on account of their toxicity."

From a Canadian perspective the good news is that 44 (48%) of the 91 drugs to avoid are available in Europe and are not available in Canada.

ERRATUM: We have removed cyclosporine eye drops (Restasis) from Table 2. The Prescrire article refers to Ikervis, a 0.1% cyclosporine solution. Restasis is a 0.05% cyclosporine solution.

References

1. Therapeutics Initiative. *Clinical pearls from Prescrire*. Therapeutics Letter. 2006 (Oct-Dec); 60:1-2.
2. Therapeutics Initiative. *Clinical pearls from Prescrire*. Therapeutics Letter. 2012 (Jan-Mar); 85:1-2.
3. Prescrire Editorial Staff. *Drugs to avoid: 2017 update*. Prescrire Int 2017; 26 (181):108-111.
4. Prescrire Editorial Staff. *Towards better patient care. Drugs to avoid in 2017*. Rev Prescrire 2017; 37 (400): 137-148.

The draft of this Therapeutics Letter was submitted for review to 65 experts and primary care physicians in order to correct any inaccuracies and to ensure that the information is concise and relevant to clinicians.

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