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THERAPEUTICS INITIATIVE Evidence Based Drug Therapy

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# What is the Common Drug Review?

A federal government process within Health Canada licenses prescription drugs for market access in Canada. Multiple provincial, territorial, and federal (i.e. Armed Services, First Nations) drug benefit plans must decide which of these prescription drugs are eligible for public payment. Until 2002, each public plan decided on payment independently with input from different expert groups that evaluated drug benefit and harm. For example, for the past 12 years, the TI has been one of the expert groups providing this input in BC. Differences in evaluations of drug benefit and harm led, at times, to differences in payment decisions. **In 2002, in an attempt to standardize input to public drug plan listing decisions, the Ministers of Health established a national Common Drug Review (CDR) process for new brand name drugs.** The CDR is administered by the Canadian Agency for Drugs and Technologies in Health (CADTH, www.cadth.ca). This Letter briefly describes the CDR process and excerpts 4 drug examples.

## What does the CDR do?

The CDR attempts to answer the following questions for a drug newly licensed in Canada:

- How does it compare with alternatives?
- Which patients will it benefit?
- Will it deliver value for money?

The CDR conducts a standardized, rigorous, and reproducible systematic review of the clinical evidence and a critique of a pharmaco-economic evaluation submitted by the manufacturer. Expert teams of physicians, pharmacists, health economists, clinical experts, information specialists and other consultants prepare these reviews. The reviewers are located across Canada (including the TI) and at CADTH, and each reviewer must sign a Conflict of Interest disclosure statement.

The CDR process is an improvement from past reviews as it often benefits from access to unpublished, confidential manufacturer and Health Canada data. However, this improved access has led manufacturers to invoke proprietary rights to prevent public access to the complete CDR review. The CDR is submitted to the drug manufacturer for comment or challenge, before discussion at a Canadian Expert Drug Advisory Committee (CEDAC) meeting. **Ultimately, CEDAC makes a recommendation for or against formulary listing, with an easy to read rationale for the decision.**


This is posted and openly available on the CDR website, www.cadth.ca/index.php/en/cdr, which also provides a detailed description of the process, full committee memberships and conflict disclosures. **Provincial/territorial drug benefit plans are not obliged to accept these recommendations, however most plans follow the 'Do not list' recommendation.**

## CEDAC decisions - 4 drug examples Excerpts from the CDR website*

**PREGABALIN (Lyrica®):** is approved in Canada for management of neuropathic pain associated with diabetic peripheral neuropathy (DPN) or post-herpetic neuralgia (PHN).[1]

**Recommendation:** The CEDAC recommends that pregabalin not be listed.

**Reasons for the recommendation:**

**1.** ...With the exception of 1 randomized controlled trial (RCT) in painful DPN, that included amitriptyline as a comparator, all 12 trials were placebo controlled and of relatively short duration (≤13 weeks). The lack of RCTs comparing pregabalin to other therapies makes it very difficult to determine the relative efficacy and safety of pregabalin.

**4.** The rate of discontinuation due to adverse effects was 11.4% for pregabalin and 5.1% for placebo. Adverse effects that most frequently led to discontinuation of pregabalin include dizziness, somnolence, confusion, peripheral edema, ataxia, and asthenia.

* For brevity not all available information could be provided here.

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**5.** There are other treatment options for patients with painful DPN and PHN, including narcotic and non-narcotic agents. In the one RCT in painful DPN that compared placebo, pregabalin 600 mg daily and amitriptyline 75 mg daily, amitriptyline caused statistically significant improvement in pain control compared to placebo whereas pregabalin did not. In this trial there was no statistically significant difference in pain control between pregabalin and amitriptyline.
**6.** Pregabalin costs are higher than tricyclic antidepressants...

**ATOMOXETINE (Strattera®):** is an inhibitor of norepinephrine re-uptake approved by Health Canada for the treatment of attention deficit hyperactivity disorder (ADHD) in children 6 years of age and over, adolescents and adults. It is indicated as part of a program that includes psychological, educational and social measures.[2]
**Recommendation:** The CEDAC recommends that atomoxetine not be listed.
**Reasons for the recommendation:**
**1.** In RCTs, atomoxetine has been shown to be more effective than placebo for ADHD symptoms. However, atomoxetine has not been proven superior to methylphenidate products. There are no published studies that assess the efficacy of atomoxetine in patients who have not responded to methylphenidate or dexamphetamine.
**4.** The cost of atomoxetine is higher than the cost of methylphenidate products or dexamphetamine, particularly if taken more than once per day.

**CICLESONIDE (Alvesco®):** is a corticosteroid that is approved for use by inhalation in the prophylactic management of steroid-responsive bronchial asthma in people 18 years of age and older.[3]
**Recommendation:** The CEDAC recommends that ciclesonide be listed.
**Reasons for the recommendation:**
**1.** Ciclesonide is similar in efficacy to other inhaled corticosteroids in patients with asthma.
**2.** The cost of ciclesonide is similar to other inhaled corticosteroids.
**Summary of Committee Considerations:**
...In general, ciclesonide was similar to fluticasone (10 RCTs), budesonide (3 RCTs), and beclomethasone (3 RCTs) with respect to several measures of pulmonary function...
...There were no statistically significant differences in the overall incidence of serious adverse events or adverse events in any of the RCTs comparing ciclesonide with other inhaled corticosteroids...

**TERIPARATIDE (Forteo®):** is a recombinant human parathyroid hormone that has been approved by Health Canada for the following indications:
• The treatment of postmenopausal women with severe osteoporosis who are at high risk of fracture or who have failed or are intolerant to previous osteoporosis therapy.
• To increase bone mass in men with primary or hypogonadal severe osteoporosis who have failed or are intolerant to previous osteroporosis therapy.[4]
**Recommendation:** The CEDAC recommends that teriparatide not be listed.
**Reasons for the recommendation:**
**1.** One RCT compared teriparatide with placebo in postmenopausal women. It showed a decrease in vertebral and non-vertebral (but not hip) fracture rates in teriparatide-treated patients. However, an exclusion criterion for the trial was the use of drugs that alter bone metabolism within the previous 2 to 24 months.
**3.** No RCTs, using the Health Canada approved dose, provided evidence that teriparatide decreases fracture rates in men.
**4.** No evidence is available to support teriparatide's efficacy for patients who continued to fracture due to severe osteoporosis despite adequate anti-resorptive therapy...
**5.** No evidence was provided to demonstrate that teriparatide is cost-effective in any patient group. Teriparatide costs $9,700 per patient per year...

*Of note: Both published and unpublished data were reviewed and taken into consideration in making the above four recommendations.*

## Summary

The Common Drug Review is a standardized process whereby the relative therapeutic and cost effectiveness of new brand name drugs is reviewed for government drug plans across Canada. The full drug reviews are used by CEDAC to develop listing recommendations and rationales for the recommendations, available on the CDR website: **www.cadth.ca/index.php/en/cdr**. At the present time full drug reviews are not open to the public.

**References**

1. CEDAC Final Recommendation on Reconsideration and Reasons for Recommendation. Pregabalin (Lyrica - Pfizer Canada Inc.). January 25, 2006. http://www.cadth.ca/media/cdr/complete/cdr_complete_Lyrica_Jan26-06.pdf *(accessed January 14, 2007)*
2. CEDAC Final Recommendation on Reconsideration and Reasons for Recommendation. Atomoxetine (Strattera - Eli Lilly Canada Inc.) September 28, 2005. http://www.cadth.ca/media/cdr/complete/cdr_complete_Strattera_2005Sept28.pdf *(accessed January 14, 2007)*
3. CEDAC Final Recommendation and Reasons for Recommendation. Ciclesonide (Alvesco - Altana Pharma Inc.) December 20, 2006. http://www.cadth.ca/media/cdr/complete/cdr_complete_Alvesco_Dec-20-06.pdf *(accessed January 14, 2007)*
4. CEDAC Final Recommendation on Reconsideration and Reasons for Recommendation. Teriparatide (Forteo - Eli Lilly Canada Inc.) December 22, 2004. http://www.cadth.ca/media/cdr/complete/cdr_complete_Forteo_2004Dec22.pdf *(accessed January 14, 2007)*

The draft of this Therapeutics Letter was submitted for review to 40 experts and primary care physicians in order to correct any inaccuracies and to ensure that the information is concise and relevant to clinicians.