



# **Best Medicines Coalition**

**Submission to the  
Standing Committee on Health  
on the Common Drug Review**

**May 9, 2007**

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**Introduction: Canadian Patients Review CDR Effectiveness**

The Best Medicines Coalition (BMC) is a national group of organizations representing millions of Canadians living with or affected by chronic disease. With a mission to ensure access to the best evidence-based medicines for Canadians, BMC's members support implementation of a national system to achieve this goal. Likewise, the BMC is steadfast in its goal that public bodies, including the Common Drug Review (CDR), deliver a service that addresses the needs of Canadian patients in an efficient, consistent and effective manner.

From a patient perspective, the CDR's stated goals of providing consistency and reducing duplication while maximizing resources are worthwhile and necessary. ***In practice, however, the CDR has emerged as a significant barrier to individuals requiring treatment access, tangibly and profoundly compromising the health outcomes of Canadian patients and failing to meet its stated goals.***

BMC has expressed its members' concerns since CDR's earliest days, as evidenced by the attached letter. At this time, the BMC appreciates the value of the Standing Committee on Health's work and commends its members for their proactive review of the CDR.

The following submission to the Standing Committee on Health presents four key questions about the CDR's performance, supported by issue outlines and case studies, which the BMC believes address the crux of patient concerns regarding the CDR:

- ***Are the CDR's recommendations based on sound pharmacoeconomic principles and best practices of medical care?***
- ***Has the CDR contributed to equal treatment access across the country?***
- ***Has the CDR had a positive impact on the efficiency at which drugs are reviewed and access provided?***
- ***Have the CDR's processes for review been fair, equitable, transparent and effective?***

**Key Question:**

***Are Common Drug Review recommendations based on best medical practices and sound pharmacoeconomic principles?***

**Issue Overview: *Failure to assess full impact***

CDR has not implemented an effective and appropriate method of incorporating pharmacoeconomic analysis and real world effectiveness into its considerations. As a result, treatments have been rejected which been shown to provide real value to patients, potentially proving to reduce overall treatment costs including hospitalization, surgery and inability to work.

**Supporting points:**

- Medications with fewer side effects also require fewer treatments to manage side effects and fewer physician visits, fewer hospital stays and fewer diagnostic tests, and thus a “Do Not List” recommendation for these drugs is not good pharmacoeconomics.
- This inability to incorporate a more comprehensive analysis or pharmacoeconomic review, using a range of evidence, has had negative results for patient populations who may rely on a range of medications or perhaps have complicating co-existing conditions, as the following case study demonstrates:

**Case Study: Viread® (tenofovir DF)**

Viread, an HIV/AIDS nucleoside reverse transcriptase inhibitor class drug (NRTI), entered the CDR process in February, 2004. Initially rejected because of cost, in 2006 Viread received a conditional recommendation as an alternative treatment for those who have adverse events or virological failure on other NRTIs, making it a second-line drug and therefore inaccessible to treatment-naïve patients. However, clinical data clearly shows that Viread provides better viral response, reduced virological failure rates, has less side effects and fewer cases of non-adherence than does the regimen currently considered to be the standard of care in HIV. Since HIV drugs must be taken in combination, pharmacoeconomic data was submitted showing that the combination 3TC, AZT and efavirenz had statistically and significantly more adverse side effects such as anemia and lipodystrophy than did the combination of tenofovir, 3TC and efavirenz. The patient impact of such side effects include the need to take more drugs to battle anemia, cholesterol increases, or insulin resistance, procedures like hump reductions, non-adherence, and treatment failure, all leading to increased drug and healthcare system costs. Meanwhile, the only possible side effect from Viread (1-3% of cases) is a potential kidney function impact. Its therapeutic value lead the four richest provinces in Canada (B.C., Ontario, Alberta and Québec) to ignore CDR’s recommendation and list Viread without conditions. Québec, not a CDR participant, consults clinical and patient experts and weighs quality of life and social impacts in decision-making, stated the following in its approval letter: “The data shows that combinations of antiretrovirals that include tenofovir demonstrate efficacy that is at least equivalent to other first-line antiretroviral combinations for patients with HIV who have never received antiretrovirals. This combination also appears to have a safety profile that leads to fewer patients abandoning treatment. This is in addition to the known benefits of tenofovir: a single daily dose, which reduces the problems caused by forgetting a dose and improves treatment compliance; low potential for drug interactions...; and improved safety in regard to the lipid profile and lipodystrophy.”

**Issue Overview: Relatively high rejection rates**

The CDR's rate of rejection of the drugs it reviews is unreasonably high, especially regarding novel or first in class, innovative treatments. The CDR is effectively denying treatment to Canadians with serious, life-threatening diseases, despite evidence that shows that many of these medications save lives, provide significant therapeutic advance and treat unmet needs.

**Supporting points:**

- CDR has given a “do not list” recommendation to 52 per cent of all products it has reviewed, a rate which lags far behind most international jurisdictions and Québec (which does not participate in CDR).
- Among life-altering biologic treatments, 75 per cent have been given “no” recommendations, with 100 per cent of first in class biologics being rejected.
- CDR recommendations lag far behind international comparators. In a study examining 50 CDR-reviewed drugs, CDR recommended listing of only 26 compared to 41 and 40 for Sweden and Switzerland respectively. Are all of these other jurisdictions wrong?
- More choice does not mean more cost. Total drug expenditure per capita in Sweden is about 46% less than in Canada (340\$/capita against 634\$/capita respectively in current CAD PPP) and in Switzerland it is about 21% less than in Canada (498\$/capita against 634\$/capita respectively in current CAD PPP).
- If Canada continues on this route, the result will be an outdated list of drugs approved for use. No innovative drugs will be available due to their higher cost. CDR's approach will also create a stagnant research and development environment in Canada.

Please consult the attached chart for details of all drugs reviewed by CDR to date, CDR's recommendations and provincial listings.

**Issue Overview: Biased review approach**

The CDR review process is flawed and inherently biased against treatments that offer the opportunity for patients to experience the most dramatic gains. The CDR's almost exclusive reliance on evidence of large, traditional clinical trials, involving results with large numbers of patients over a long period of time, effectively shuts out treatments for rare diseases among specialized populations.

**Supporting points:**

- Treatments which are being used effectively around the world are being rejected in Canada because CDR is unwilling to accept surrogate or non-traditional markers, short study durations, and innovative comparators.
- For example, if CDR criteria had been applied to the early HIV/AIDS drugs, none would have been approved. At the time, there was no proof of clinical benefit, only reductions in CD4 counts which no one knew for sure would lead to better survival. Most of the early AIDS patients would have died. Likewise, life-altering biologic treatments for rheumatoid arthritis would likely not have been given a positive recommendation had the CDR reviewed (see case study on page four).
- Other review bodies have effectively addressed this: Health Canada understands this issue, and has implemented the “Notice of Compliance with Conditions” (NOC/C) designation for breakthrough drugs, or those drugs that do not have a viable product for comparison. In these cases an NOC/C is given to the drug and the manufacturer must undertake further trials. Health Canada's proposed Progressive Licensing program is another example of this acknowledgement of the evolving nature of knowledge related to drugs.

- The following case studies provide real life examples where the CDR's flawed review process lead to rejections of treatments showing strong, previously unavailable outcomes.

**Case Study: Nexavar® (sorafenib)**

Nexavar is the first drug for kidney cancer introduced in the past ten years and the manufacturer initiated a large, randomized, controlled trial with advanced stage patients. More than 900 patients who had failed prior systemic therapy were randomized to receive Nexavar or placebo. Before trial completion, interim results showed Nexavar doubled progression-free survival and improved overall survival by 56 per cent over placebo. As is usual, ethical practice, the placebo group was offered Nexavar, effectively halting the trial before long-term survival data were collected. The FDA supported the change in protocol. Health Canada understood this and approved Nexavar on the basis of the data collected. However, the CDR gave Nexavar a negative recommendation because of the lack of the long-term survival data and also because of cost. Kidney cancer patients who do not have access to private insurance are now denied access to this life saving therapy.

**Case Study: Lyrica® (pregabalin)**

Lyrica is the first and only approved medication for neuropathic pain associated with diabetic peripheral neuropathy and post herpetic neuralgia. Although not life-threatening, these conditions are debilitating for patients, often the elderly. A range of other treatments are used, with poor patient response and side effects requiring additional medications and drug interactions. Based on the same studies sent to CDR, Lyrica was deemed safe and effective by Health Canada, FDA, EMEA, and many other regulatory authorities in the world. Its safety is supported by the experience of 9,000 patients receiving Lyrica in studies and 17 months of post-marketing experience in Europe. In January, 2006, CDR issued its recommendation to the public drug plans to not reimburse Lyrica, based on their assessment that there is insufficient scientific and cost-effectiveness evidence. The CDR recommendation has left these patient untreated and perhaps directed towards using medications unapproved by Health Canada for neuropathic pain management.

**Case Study: Enbrel® (etanercept) and Remicade® (infliximab)**

Before the advent of biologic therapies to treat difficult cases of rheumatoid arthritis, sufferers relied on ineffective medications to help their pain and progressive disability. For many, inability to walk, extended hospital stays, and surgeries kept them from living independently, supporting their families and contributing to society. Starting in 2000, innovative biologic treatments, such as Enbrel and Remicade, started to become available, and in many cases treatment essentially gave patients their life back, relieving them from pain and further disability. These biologics were introduced pre-CDR, but recently CADTH's Health Technology Assessment program issued a report inferring that these treatments are not cost effective, citing a trial which showed a small to moderate clinical outcome. Patients who are now able to work and live full lives strongly disagree with this assessment, and urge decision-makers to incorporate a broader scope of evidence, including real world experience.

**Key Question:**

***Has the Common Drug Review contributed to equal treatment access across the country?***

**Issue Overview: *Inconsistent access and duplicated services******Inconsistent access***

CDR has failed at achieving its mandated goals of building consistency. Provincial uptake of CDR decisions remains disparate, as the chart below demonstrates. A patchwork environment where a CDR “no” most often means “no” to provincial listing and a CDR “yes” means “maybe” to provincial listing.

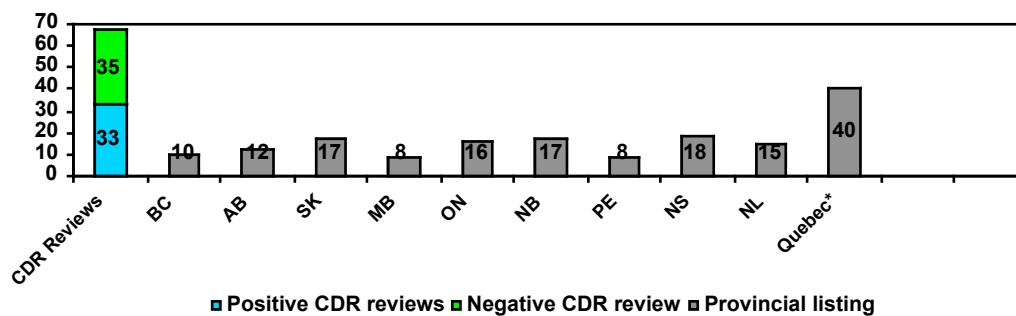
***Supporting points:***

- A number of drugs have been given positive provincial formulary listing, despite a negative CDR recommendation. For example, CDR gave Fosavance®, for osteoporosis, a “do not list” recommendation but it has been listed in Ontario, based on that province’s review of a broader range of evidence.
- Even when CDR gives a positive recommendation, provinces are still conducting their own reviews and sometimes declining listing for those drugs. For example, Spiriva®, for Chronic Obstructive Pulmonary Disorder, is listed across the country but not in B.C., so patients there are denied access, sometimes leaving them to rely on 24-hour oxygen.
- Québec has refused to join CDR since its inception. In addition, Ontario will soon no longer be following CDR recommendations for breakthrough drugs, but has promised a review of those drugs within three to four months of Health Canada approval.

***Duplicated services******Supporting points:***

- Not one provincial drug decision-making body has been disbanded since the creation of the Common Drug Review. Furthermore, each of the six federal drug programs has also continued to retain their own formulary committees.
- Provinces continue to conduct independent reviews, despite the substantial federal and provincial investment in the CDR. The CDR budget has grown to \$5.1 million annually (up from \$2 million at its inception in 2003 in part because of its recently expanded mandate to review new indications for previously approved drugs), with two-thirds coming from the provinces and one-third from the federal government. In addition, provincial budgets are still in place, or are expanding, to undertake their own reviews. For instance, Ontario has just done a significant overhaul of its drug review process, involving significant investment, including the creation of a separate breakthrough drug process as mentioned above.

**CDR Listings by province**



(Data updated March, 2007. Numbers on bars indicate # of drugs listed. Note: Quebec does not participate in the CDR process.)

**Key Question:**

***Has the Common Drug Review had a positive impact on the efficiency with which drugs are reviewed and access provided?***

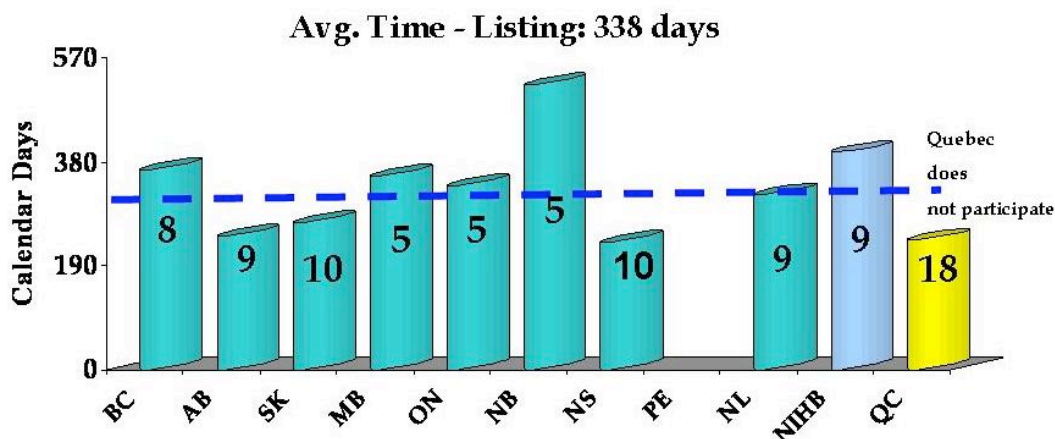
**Issue Overview: *Medicine delayed is medicine denied***

For patients, timely access to much needed medicines is critical, in some cases life-saving or necessary to halt disease progression and associated damage. The CDR's timelines for its own deliberations have remained consistent at 26 weeks. More importantly, Common Drug Review timelines are meaningless if provincial plans then add further weeks and months to conduct their own review processes, which can take an additional twelve months.

**Supporting points:**

- The CDR has effectively lengthened drug approval timelines by adding an additional level of scrutiny of 26 or more weeks.
- There is no collective performance commitment amongst the CDR and the participating drug plans to overall timeliness of their sequential processes, nor any commitment to monitor or improve total timelines.
- The CDR process has recently instituted a "priority review" process for breakthrough drugs. However, to date "priority review" status has not proven to speed up the process.
- The following chart demonstrates average timelines by province and a case study describing how one patient group awaits reviews is included.

**Time from CDR Submission until Participating Drug Plan  
Lists a Drug on their Formulary  
May 2004 - Dec 31 2005 (Calendar Days)**



iMAM® Brogan Inc. December 2005

**Case Study: Orenzia® (abatacept)**

A breakthrough biologic treatment for rheumatoid arthritis, Orenzia, is now listed on the CADTH web site as having submission received by CDR on October 26, 2006. On April 3, 2007, CDR completed its brief and has a meeting scheduled for April 18, 2007. If there are no attenuating circumstances, final approval or non-approval is expected on May 9, 2007. Provincial funding bodies will then begin their reviews, or they will have begun them simultaneously, a process, which according to usual practice will take, extended periods of time. Meanwhile, this treatment is already approved and in use in the United States and many other countries, while Canadian patients wait.

**Key Question:**

***Have the Common Drug Review's processes for review been fair, equitable, transparent and effective?***

**Issue Overview: *Transparency and accountability lacking***

The millions of Canadians who depend on drug listings have a right to know who is making decisions, how decisions are made and how they are accountable. From a patient perspective, the CDR process lacks transparency and is nearly impossible to navigate. Furthermore, patients who are most impacted by decisions have a right to be part of the decision-making process and rightfully should have access to an appeal process.

- CDR's inflexible review model does not accommodate the need to involve a greater depth and variety of specialist experts, as would be the case in many therapeutic areas. For example, none of the CDR members appear to have special expertise in the complexities of HIV/AIDS. This becomes even more problematic given the CDR's insistence on "re-reviewing" safety and efficacy data rather than accepting TPD's analysis.
- Further, CDR does not consult clinicians with expertise in the field of the drug being reviewed.
- Patients have limited input into deliberations. It was only after intense lobbying and pressure that the CDR agreed to have two lay members on the CEDAC committee. However, it is stipulated that these individuals are not members of patient groups, and therefore may not reflect patient consensus or have the expertise to fully engage in the complex discussions.
- CDR does not consult patients who have knowledge about the use of these drugs in the real world.
- There is no effective appeal process for CDR recommendations, although manufacturers may request a "reconsideration" which is heard by the directorate, essentially the same body that issued the initial recommendation.
- To date all "reconsiderations" have been unsuccessful. There is no process in place for an independent or quasi-judicial review of such critically important decisions. Furthermore, healthcare providers or patients, who have the most at stake, have no avenue for appeal.
- The CDR does publish summaries of final recommendation on its web site. Information on how the committee arrived at its decision is not available, however, and this lack of transparency makes it impossible for patients to understand a negative recommendation.

### **Recommendations:**

It is clear that CDR has not been successful in meeting its mandated objectives, including reducing duplication and contributing towards a consistent national system of drug reimbursement. More importantly, the CDR has emerged as a significant barrier to patient access to innovative evidence-based medicines, including treatments that have been proven to be safe and effective, that improve quality-of-life and save lives.

#### ***Short Term Recommendation***

In the interests of Canadian patients, the BMC recommends that in the short term the Standing Committee on Health and other decision makers must take immediate measures to curtail the CDR in its present form, if possible placing a halt to further reviews and a moratorium on further broadening of its mandate.

#### ***Longer Terms Recommendations***

1. **Dismantle CDR as it is duplicative, costly and not value-added.** The provinces continue to make their own decisions and keep expert committees. From the money saved from CDR, give transfer payments to the provinces that do not have committees to create them. Ensure all committees meet minimum standards as follows:

- Comprehensive and progressive data analysis models, including pharmacoeconomic review, must be adopted which are broader and inclusive in nature, moving away from a narrow cost containment approach. These models must be designed to incorporate a wider definition of costs, including hospitalizations, surgeries and universal healthcare costs. In addition, post approval surveillance activities must be incorporated and enhanced.
- Models of pharmaceutical review must be flexible enough to facilitate, where appropriate, novel and innovative medicines, including those designed for rare disorders, those for previously unmet needs and where significant therapeutic advance is offered.
- Review processes must be further expedited and improved by involving thorough consultation of national and international experts in each therapeutic area.
- Patients, who are most impacted by decisions, must be significantly involved and consulted. In addition, broader stakeholder groups must participate in the process in a meaningful advisory capacity.
- Transparency and fairness must be integrated, allowing patients and other stakeholders a greater understanding of processes and rationale for actions. An appeal process must allow recourse on all decisions.

2. **If the Standing Committee on Health does not recommend dismantling CDR, it should recommend the creation of an independent working group to conduct a comprehensive review.** This working group should involve a full range of stakeholders, including Canadian patients, to completely overhaul CDR to meet its objectives, using the minimum standards set out above.

### **About the Best Medicines Coalition**

The Best Medicines Coalition is an alliance of organizations and individuals, representing those living with or affected by chronic disease or illness, who are concerned about drug review reform, treatment access, patient safety and general health policy development. With a broad mission of ensuring access to the best evidence-based medicines for Canadians, the BMC's specific goals are as follows:

- Accelerate reform of Canada's drug review and post-marketing surveillance systems to ensure that Canadians have timely access to the best medicines relative to other developed countries;
- Ensure the implementation of a pan-Canadian process that provides efficient, equitable access to the best evidence-based medicines for all Canadians
- Partner with governments and other relevant stakeholders to develop an effective model for the meaningful and equitable inclusion and participation of consumers/patients in Canada's drug review system and health policy development; and
- Further public awareness of relevant issues within the BMC Mission.