



Issues of Access to Cancer Drugs in Canada

**A Report for the
Canadian Cancer Action Network**

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Consultants to Healthcare

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Table of Contents

Executive Summary	iv
--------------------------	-----------

Part 1 How Are Cancer Drugs Approved in Canada?	
Introduction	2
Section 1 National Cancer Drug Approval Systems	3
1. Regulatory Approval: Health Canada	
2. Pricing Approval: The Patented Medicines Prices Review Board	
3. Cancer Drug Evaluation for Funding:	
a) Joint Oncology Drug Review	
b) Common Drug Review	
Section 2 Provincial Cancer Drug Approval Systems	8
1. Responsibility for Cancer Drugs by Province	
2. Cancer Drug Evaluation Process	

Part 2 Issues of Cancer Drug Access in Canada	
Issue 1 Why are some cancer drugs available in some provinces and not others?	13
1. Where Do Examples of Inequities Exist?	
2. Responsibility for Funding Cancer Drugs	
3. Differences in Provincial Drug Evaluation Processes	
4. Implications of Geographic Inequities for Cancer Patients	
Issue 2 How much does access depend on what a patient can afford to pay?	18
1. Why Do Canadians Need Prescription Drug Insurance?	
2. Which Canadians Need Insurance for Cancer Drug Costs?	

	<ul style="list-style-type: none"> 3. What Insurance Plans Are Available? 4. How Many Canadians Are Covered by Public and Private Plans? 5. How Good is Insurance Coverage? 6. Options for Private Payment of Unfunded Intravenous Cancer Drugs 7. Implications of Socioeconomic Inequities for Cancer Patients 	
Issue 3	<p>The impact on patients - what happens when people can't afford cancer drugs?</p> <ul style="list-style-type: none"> 1. Which Cancer Patients Are Vulnerable To High Drug Costs? 2. How Do Patients Cope When They Can't Afford Drugs? 	25
Issue 4	<p>How patient-centred are Canada's cancer drug access systems?</p> <ul style="list-style-type: none"> 1. How Easy Is It For Patients To Access The Drugs They Need? 2. How Responsive Is The System To Patients' Needs? 3. Appeals Processes And Transparency 	30
Issue 5	<p>Why are cancer drugs so expensive?</p> <ul style="list-style-type: none"> 1. Scope Of The Issue Of High Cancer Drug Prices 2. The High-Cost, High-Risk Drug Development Process 3. Recouping Investments 4. What Can Canada Do About High Cancer Drug Prices? 	33
Issue 6	<p>Where is the voice of the patient heard in the system?</p> <ul style="list-style-type: none"> 1. The Context of Public Involvement in Health Care Policy 2. Where Are Patients Currently Heard in the Canadian Cancer Drug Access System? 	37

Appendices

Appendix 1	National Cancer Drug Approval Systems	41
	<ol style="list-style-type: none"> 1. Regulatory Approval: Health Canada 2. Pricing Approval: Patented Medicines Prices Review Board 3. Cancer Drug Evaluation for Funding 	
Appendix 2	Provincial Cancer Drug Approval Systems	50
	<ol style="list-style-type: none"> 1. Comparison of Provincial Coverage for Supportive Care Drugs 2. Cancer Treatment Drug Approval Processes by Province 3. QALYs – Measuring the Value of Clinical Outcomes 	
Appendix 3	Prescription Drug Insurance	59
	<ol style="list-style-type: none"> 1. Insurance Status of Canadians 2. Eligibility Criteria for Federal Drug Plans 3. Cost-Sharing Requirements of Public Drug Plans 4. Private Insurance Cost-Sharing 5. Advantages of the Employer-Sponsored Insurance Model 	
Appendix 4	How Cancer Patients Cope With Financial Burdens	69
	<ol style="list-style-type: none"> 1. What Are the Financial Burdens Faced by Cancer Patients in Canada? 2. What Are the Trends? 3. What Are the Patients' Coping Strategies for Managing Unaffordable Drug Costs? 	
Appendix 5	Private payment options	74
	<ol style="list-style-type: none"> 1. Private Payment in Public Hospitals 2. Private Clinics 3. Private Payment Outside Canada 	
Appendix 6	Cancer Drug Pricing	76
	<ol style="list-style-type: none"> 1. The Costs of New Cancer Drugs 2. Price Controls in Canada 3. Price Setting in Canada 4. Forces Extending Patent Life 5. Forces Contracting Patent Life 6. Strategies for Minimizing Cancer Drug Costs 	

Executive Summary

Access to high quality cancer drugs is emerging as a crucial issue for Canadians. One in three of us is expected to develop cancer in our lifetimes¹ and, as our population ages, health is becoming a central concern for a growing proportion of citizens. Almost all cancer patients will receive drug therapies as part of their treatment. The introduction of new and effective targeted cancer medicines has opened up new options for many cancer patients. Decades of cellular research have led to highly targeted drugs which not only prolong survival but which also lack the severe toxicities of older chemotherapies.

But these advances have come at a high price. Cancer control budgets everywhere are being strained, both because these effective drug treatments are being used more often and because their prices are extraordinarily high. Although it currently comprises only four per cent of all pharmaceutical expenditures, spending on cancer drugs is escalating at six times the rate of growth of new cancer cases.² Part of the reason is that more drugs are being used – in combination regimens, added to other interventions such as surgery and radiation, and both earlier and later in the course of disease.

While increased utilization of cancer drugs accounts for some of the increase in spending, more than half of the growth is due to the higher prices paid for newer medications. Because of price controls, Canada and Europe pay from one-sixth to one-third less than prices in the U.S.³ However, cancer medicines introduced during the past decade still cost ten times as much as those introduced ten years before. Canadians spent \$868 million on 150 cancer drugs in 2006. Half of this amount was for only five drugs – all of which were introduced after 1990 – and the utilization of these products grew by over one-third in that year.⁴ Although these rising expenses are counterbalanced by the introduction of generic versions of drugs whose patents have expired, the trend towards increased overall costs is putting pressures on cancer drug budgets across Canada.

The risk to cancer patients is that cost containment efforts will restrict access to new cancer drugs. Arguments have been made that cancer treatment is under-funded in relation to other medical conditions and that the system should expand to cover the costs of all effective treatments. Questions also have been raised about the appropriateness of high prices that allow manufacturers to gain while the rest of the health system is forced to cut back. These cut-backs include restrictions by private and public insurers that limit access to cancer treatment medicines and to supportive care drugs used to manage the symptoms of cancer and the side-effects of its treatment. The means by which costs are contained can be controversial. Public drug plans will list only those drugs they deem to be cost-effective, however the methodology used to determine this value and the process by which these decisions are made, and by whom, are the subject of intense debate. In addition to limiting the number of funded drugs, both public and private insurance plans increasingly require patients to share the financial burden of coverage through deductibles,

¹ Canadian Cancer Society statistics, 2007.

² Canadian Cancer Society statistics, 2007.

³ Jönsson, B and Wilking, N; "A Global Comparison Regarding Patient Access to Cancer Drugs"; *Annals of Oncology*, June 2007.

⁴ Intercontinental Medical Statistics; Drugstore and Hospital Purchase 2006.

premiums, co-payments and caps. For some cancer patients, these costs can be unmanageable.

There are many reasons for high cancer drug prices, related both to the enormous costs of drug development and to market factors. Our present system of patent laws, price controls and reimbursement models has been the focus of calls for change. An ideal system would allow manufacturers to continue to develop new generations of effective medicines, while addressing the issue of affordability by publicly-funded healthcare systems.

Inequities in access to cancer drugs are a major concern for Canadians. Perhaps the most contentious disparity is that between provinces. For example, of 21 newer cancer drug programs funded by British Columbia, less than half were publicly funded in two other provinces.⁵ Some provinces take years to approve the same drugs that others take a few months to decide. Part of the reason for these disparities is that each province has been using a different system of evaluation — to assess the strength of the clinical and cost-effectiveness evidence, to determine the expected benefit for patients in that province, and to estimate the treatment's cost-effectiveness and affordability relative to other healthcare priorities.

The interprovincial Joint Oncology Drug Review process, initiated as a pilot project in March 2007, attempts to eliminate many of these disparities by improving the quality of decision making. Expertise is being expanded in the area of cost-effectiveness evaluation, a discipline still in an early stage of development but nonetheless crucial to cancer drug access. This new joint process is evolving from the starting point of the Ontario oncology drug review system and aims to incorporate a broader range of inputs, including those of ethicists and patients. Recommendations for drug funding based on clinical and cost-effectiveness evaluations are made to all provinces (except Quebec, which declined to participate). Each province will still make its own final decision, based largely on economic factors, however, so interprovincial inequities will continue to exist in the absence of centralized funding for cancer drugs.

Inequities also exist due to the insurance status of Canadians. Remarkably — because Canadians do not expect to pay for life-saving treatments under our public health system — prescription drug insurance is required to pay for cancer medicines administered at home. Today, half of all new cancer drugs are oral formulations that are not required to be publicly covered under the terms of the *Canada Health Act*. Yet, about one in six Canadians is currently not insured for routine costs of cancer drugs and 2% are not covered for catastrophic drug costs (defined as exceeding 4% of net household income), all of whom reside in Atlantic Canada. Many newer cancer treatment and supportive care drugs cost thousands of dollars, so not only is insurance required but the cost-sharing terms of many insurance plans mean that patients can be saddled with a significant financial burden even if they do have coverage.

First Nations and Inuit Canadians are insured by the Non-Insured Health Benefits program of Health Canada. This benefit plan insures aboriginal groups for expenses not covered by provincial health plans. The plan pays for prescription drug expenses and also subsidizes the costs of medical travel — an important aspect for patients in remote communities who must travel long distances to access treatment. Despite this coverage, however, aboriginal patients often experience financial hardship due

⁵ Reference: Table 1 in 'Issue 1' of this report.

to the lengthy stays required for treatment which are only partially reimbursed. Non-aboriginal patients living in remote areas of Canada are also faced with similar financial, practical and emotional concerns related to the necessity of receiving treatment far from home.

Patients without adequate insurance cope with unmanageable costs in several ways. Many are able to access alternative sources of funding, largely through manufacturers' compassionate use programs. Social workers and pharmacists are adept at sourcing funding and in helping patients to navigate the complexities of the system. However, some patients resort to measures such as cutting back on medications or other necessities and even go so far as to mortgage their homes or exhaust their retirement savings.

Inequities due to economic status are present in Canada today and are growing. Canadians of financial means are generally well insured for the costs of cancer drugs. If they require a medication that is not funded by the public system, they can obtain it through one of the private payment options available in this country or abroad. The poorest Canadians are, in general, well looked after by the public system because they are insured by their provincial drug program. It is the expanding group of the working poor and self-employed, many of whom have paid into the health system all of their lives, who are the most vulnerable. This group is not eligible for coverage under the public system in most provinces, and yet does not have access to affordable private drug insurance.

The area of cancer drug access is in a continual state of flux across Canada. In the past year alone, changes have been made at the levels of Health Canada, the Patented Medicines Prices Review Board, the Joint Oncology Drug Review, and the Canadian Partnership Against Cancer — all of which have a direct impact on cancer patients. Also, provincial drug plans continue to add new cancer drugs to their lists of benefits, and to expand public drug coverage to include more families. Therefore, this report must be seen as a reflection of the situation at one point in time and the information should be updated regularly to remain accurate.

Part 1

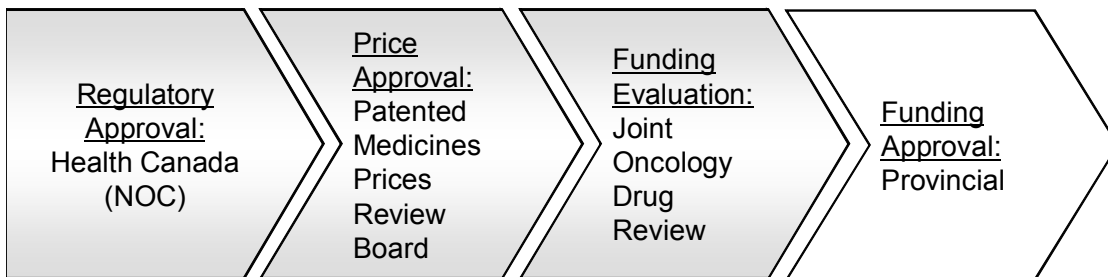
How Are Cancer Drugs Approved in Canada?

Introduction

The Canadian system of drug approvals follows a four-step process, outlined in Figure 1. The federal and interprovincial approval systems are the first gateway to access to cancer drugs in Canada. Factors such as the speed of the review, the rigidity of the process and the relevance of approval criteria to cancer all have an impact on whether and how quickly cancer drugs reach the Canadian market.

Section 1 describes the first three steps in this process; the provincial funding systems are covered in Section 2. Further details on the systems of approval are found in Appendices 1 and 2.

Figure 1 Federal and Inter-Provincial Approval Systems for Cancer Drugs in Canada



Canadians wait an average of 2.8 years from the time a drug submission is filed with Health Canada for access to a biological drug and 2.3 years for a pharmaceutical medicine.⁶ Approximately half of this time is taken up by Health Canada's approval time, and the remainder for provincial formularies to list the drug.

⁶ Fraser Institute Report "Access Delayed Access Denied – Waiting for Medicines in Canada", March 2007.

Section 1

National Cancer Drug Approval Systems

Contents

1. Regulatory Approval: Health Canada
2. Pricing Approval: Patented Medicines Prices Review Board
3. Cancer Drug Evaluation for Funding:
 - a. Joint Oncology Drug Review
 - b. Common Drug Review

1. Regulatory Approval: Health Canada

Health Canada is responsible for reviewing and approving all new prescription drug products based on their demonstrated safety and efficacy. Within Health Canada, the Therapeutic Products Directorate (TPD) reviews pharmaceutical products and the Biologics and Genetic Therapies Directorate (BGTD) handles products derived from biotechnology.

In regulatory terminology, “new drugs” refers not only to the first time a drug is licensed for marketing, but also the first time it is used in a different indication, or disease state.

Regulatory approval for cancer drugs follows the same process as for other prescription drugs in Canada. However, because they may be life-saving and are urgently needed, cancer drugs may experience faster approvals and require less exhaustive testing before approval.

The Drug Approval Process

Health Canada reviews applications from manufacturers against its standards of safety and efficacy. The review process can take from less than one year for priority or “fast-track” reviews to 2-3 years (or more) for non-life-saving drugs. Once approved, the company receives a Notice of Compliance (NOC) and a Drug Identification Number (DIN).

Before making a New Drug Submission to Health Canada for a new chemical entity, companies must do extensive preclinical and clinical testing. (This is described in more detail in Appendix 6.) For life-saving cancer drugs, however, Health Canada may agree to proceed with a review based on earlier clinical trial results.

Under certain circumstances, a conditional Notice of Compliance (NOC/c) may be granted. The approval to market the drug under a NOC/c requires a commitment by the manufacturer to conduct post-marketing safety studies. Fourteen cancer and supportive care drugs had received conditional approvals as of April 2008.⁷ To

⁷ http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/index_e.html

expedite access to new medications in the future, Health Canada is moving towards a progressive licensing system. This involves lifecycle regulation of drugs, and formalizes the Conditional Approval mechanism.⁸ Federal legislation was introduced in April 2008 to provide the legal framework for this initiative.

Health Canada is assisted in its regulation of cancer drugs by the Scientific Advisory Committee on Oncology Therapies. This Committee was established to provide the agency with scientific and medical advice related to the lifecycle regulation of oncology therapies and on related policy issues. Involvement of a broad cross-section of the scientific, medical and consumer communities is intended to improve the drug review process by enhancing transparency and by providing opportunities for proactive external guidance.⁹

Special Access Program

A manufacturer cannot market a drug until it receives a Notice of Compliance or NOC. However, for serious or life-threatening conditions, Health Canada may allow limited release under its Special Access Program while the drug is still under review. The cost of the drug may either be paid for by the manufacturer or by the patient (or their insurer).

The Special Access Program is an important mechanism by which cancer patients who have no other options can access promising new drugs quickly. However, most public drug plans do not cover drugs prior to approval and these are usually funded either by private insurers or by the manufacturers.

The Special Access Program may change in the future. In late 2007, a comprehensive review was initiated because it was felt that the Program had evolved beyond its original intentions. For example, several drugs had been available through the Program for several years, creating policy, legal and operational challenges for Health Canada. In addition, there was concern that this mechanism may act as a disincentive for manufacturers to seek market authorization for their drugs. Stakeholders had complained of a lack of timely follow-up and denials of requests, and there were concerns about the lack of insurance coverage for drugs made available through the Program.

Health Canada Drug Approval Concerns

Health Canada has historically had one of the slowest regulatory review times among OECD (Organization for Economic Cooperation and Development) countries. Approval delays have been a major reason why patients travel to the U.S. for treatments that are still under regulatory review in Canada.

According to the latest available figures, significant progress has been made in eliminating the review backlog and towards issuing review decisions within internationally comparable performance targets. A recent update from Health Canada in 2007 states that the agency has now met its goal of issuing 90% of decisions on new pharmaceutical and biological drugs within targets.¹⁰

⁸ "Blueprint for Renewal II: Modernizing Canada's Regulatory System for Health Products and Food"; Health Canada, 2007.

⁹ www.hc-sc.gc.ca/dhp-mps/prodpharma/activit/sci-com/onco/sacot_tor_ccso_att_e.html

¹⁰ Health Products and Food Branch; Report on the 2004-07 Strategic Plan.

For cancer drugs, Health Canada's record of approvals appears to be better, in general, than for other pharmaceutical and biological products. Of a list of 12 cancer drugs approved worldwide since 1994, the median lag was 0.8 years between approval in Canada and the first approval anywhere in the world.¹¹ This is a reasonable performance considering that part of this delay is because manufacturers usually submit for approval in other, larger markets first.

2. Pricing Approval: The Patented Medicines Prices Review Board (PMPRB)

Created in 1987 under the *Patent Act* as an independent, quasi-judicial tribunal, the Patented Medicines Prices Review Board limits the prices set by manufacturers for all patented medicines sold in Canada – new and existing, prescription or over-the-counter – to ensure they are not excessive.

Prices Review Criteria

To determine whether the price of a patented drug sold in Canada is excessive, the Patented Medicines Prices Review Board applies factors set out in the *Patent Act* and in its price guidelines.

Table 1 PMPRB Prices Review Criteria

<ul style="list-style-type: none">• Most new patented drug prices are limited so that the cost of therapy is in the range of the cost of therapy for existing drugs sold in Canada used to treat the same disease;• Breakthrough drug prices are limited to the median of the prices for the same drugs charged in other specified industrialized countries that are set out in the Patented Medicines Regulations (France, Germany, Italy, Sweden, Switzerland, U.K. and the U.S.).• Existing patented drug prices cannot increase by more than the Consumer Price Index (CPI);• In addition, the Canadian prices of patented medicines can never be the highest in the world.
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Because submissions to the Patented Medicines Prices Review Board are made by manufacturers within 60 days after the drug has been marketed, this review process does not add to the time taken for regulatory approval.

Implications of Price Controls for Cancer Drugs

Because newer generations of cancer drugs are much more expensive relative to older therapies, pricing has become a focus of attention.

In recent years, the disparity in prices between European markets and the U.S. has increased dramatically as many European countries have used their monopoly positions to force price cut-backs from manufacturers. Because of Canada's price control rules, this has effectively reduced the prices Canadian subsidiaries can charge for their products. Prices paid in Canada and Europe are reported to be 15-33% lower than those in the U.S.¹²

¹¹ Jönsson, B and Wilking, N; "A Global Comparison Regarding Patient Access to Cancer Drugs"; *Annals of Oncology*, June 2007.

¹² Jönsson, B and Wilking, N; "A Global Comparison Regarding Patient Access to Cancer Drugs";

As a result of the Patented Medicines Prices Review Board's rules, in June 2006 Bristol-Myers Squibb announced that it had decided not to market cetuximab (Erbix, to treat advanced colorectal cancer), despite its approval by Health Canada nine months prior, because the company could not agree with the PMPRB on an appropriate price for its product.¹³ Erbix is still available for sale under Health Canada's Special Access Program.

Another way that the Patented Medicines Prices Review Board's decisions affect cancer patients is demonstrated in a bulletin issued in April 2007. The Board stated that drugs provided at no cost to patients under clinical trials or compassionate release programs must be included in the calculation of the Average Transaction Price of that product in the Canadian market.¹⁴ This dramatically lowers the benchmark for the price of a new drug and for price increases. This strict interpretation of the regulations by the Patented Medicines Prices Review Board has caused at least one company to discontinue its compassionate use program and further actions by manufacturers are anticipated. The matter is now under discussion by the PMPRB and stakeholders.

3. Cancer Drug Evaluation for Funding

Once approved by Health Canada, each drug plan sponsor must decide whether to include a product on its formulary, or list of drugs. In addition to private insurance plans, each province and territory in Canada maintains its own publicly-funded drug insurance plan which covers certain eligible populations.

All provincial, territorial and federal drug plans, except Quebec, require a prior evaluation by one of the interprovincial drug review systems before considering whether to list a new drug. The new Joint Oncology Drug Review provides an assessment and recommendation for new cancer treatment products. The Common Drug Review evaluates supportive care drugs required for the management of cancer symptoms (such as pain) or for treatment side-effects (such as anemia or nausea).

After considering these recommendations, the public drug plan managers apply their own individual evaluation criteria. Province-specific factors such as budgets, priorities and political considerations affect final decisions and these can differ markedly across Canada.

a) Joint Oncology Drug Review

The interim Joint Oncology Drug Review came into being as a pilot project in March 2007. The goal of the Review is to help resolve interprovincial disparities by developing a common, high quality process for evaluating new cancer drugs.

During the interim period, CancerCare Ontario is accepting all new submissions on behalf of the provinces (except Quebec). These are reviewed by the Oncology Subcommittee – a collaboration between CancerCare Ontario and the Committee to

Annals of Oncology, June 2007.

¹³ PMPRB website <http://www.pmprb-cepmb.gc.ca/english/View.asp?x=669&mid=523> and interview with BMS's VP Corporate Affairs, 26 March 2007.

¹⁴ PMPRB Newsletter Vol. 11, Issue 2, April 2007: <http://www.pmprb-cepmb.gc.ca/english/View.asp?x=857&mid=688>

Evaluate Drugs (CED) of the province's publicly funded drug plan, the Ontario Drug Benefit Program. A Steering Committee oversees the project, and an Advisory Committee ensures that best practices from other provinces are incorporated into the Ontario system. All of the provinces participate with representatives and the territories participate *via* British Columbia and Alberta.

In October 2007, the Advisory Committee agreed to include two patient representatives and these were selected based on nominations by cancer patient groups. The patient representatives continue to involve the patient advocacy community in providing feedback to the Advisory Committee. One of the recommendations recently put forward is that patients should also be included on the drug evaluation committee. Transparency of the Joint Oncology Drug Review is another area of importance to patients, including timely and complete information on the Review's agenda and decisions.

It is anticipated that the Joint Review will become a permanent body within the next year. An evaluation will be conducted by an external consulting firm for a six-month period ending in October 2008. Based on the consultants' assessment of current and best practices, a recommendation will be developed for a permanent model and this will be presented to the participating Deputy Ministers of Health in January 2009.

b) Common Drug Review

The Common Drug Review evaluates supportive therapies, required for the management of symptoms of cancer and side effects its treatment. Similar to the Joint Oncology Drug Review, the Common Drug Review process was put in place to provide efficiencies in the evaluation processes on behalf of the 20 participating provincial and federal government drug plans (except Quebec).

The Common Drug Review was established in 2003 as a program of the Canadian Agency for Drugs and Technologies in Health. It conducts reviews of the clinical and cost effectiveness of new drugs and of new indications for existing drugs.

The Canadian Expert Drug Advisory Committee (CEDAC) is an independent advisory body to the Common Drug Review which makes recommendations to the participating drug plans regarding formulary listings of new drugs. Two members of the public were appointed to the Committee in October 2006.¹⁵

The Standing Committee on Health held reviews of the Common Drug Review's performance during May 2007, accepting input from all stakeholders. The pharmaceutical industry and many patient groups continue to disapprove of the low rate of positive decisions, need for greater transparency and the lack of an appropriate appeals process.¹⁶ In April 2008, the government responded to the Committee's recommendations put forward in December 2007, agreeing to all except the call for an independent appeals process.

¹⁵ CADTH Appoints New Chair and First Public Members to the Canadian Expert Drug Advisory Committee (CEDAC); 18 October 2006. (CADTH website)

¹⁶ International Comparison of Canadian Expert Drug Advisory Committee (CEDAC) Common Drug Review (CDR) Recommendations; Rx&D Report; November 2006.

Section 2 Provincial Cancer Drug Approval Systems

Content

1. Responsibility for Cancer Drugs by Province
2. Cancer Drug Evaluation Process

Cancer treatment drugs and supportive care medicines (used to manage the side effects of cancer and of chemotherapy) are funded either by private or public insurers. The system of coverage is different across Canada - some provinces automatically pay for all cancer treatments and in others a combination of public and private insurance (including individual payment) covers these costs.

Canada's patchwork system of coverage has led to interprovincial disparities in access to cancer treatment and supportive care drugs. The scope and implications of this situation are outlined in greater detail in Part 2 of this report. This Section describes how funding decisions for cancer drugs are made at the provincial level.

1. Responsibility for Cancer Drugs by Province

The funding body responsible for covering cancer treatment drugs in each province is listed in Table 1, below.

Table 1 Responsibility for Cancer Drugs by Province and Territory

	Individual Hospitals	Cancer Agency	Provincial or Territorial Drug Plan
BC		●	
AB		●	
SK		●	
MB		●	●
ON	●	●	●
QC	●		●
NB	●		●
PE	●		●
NS	●		●
NL	●		●
YK	●		●
NT	●		●
NU			●
NIHB			●

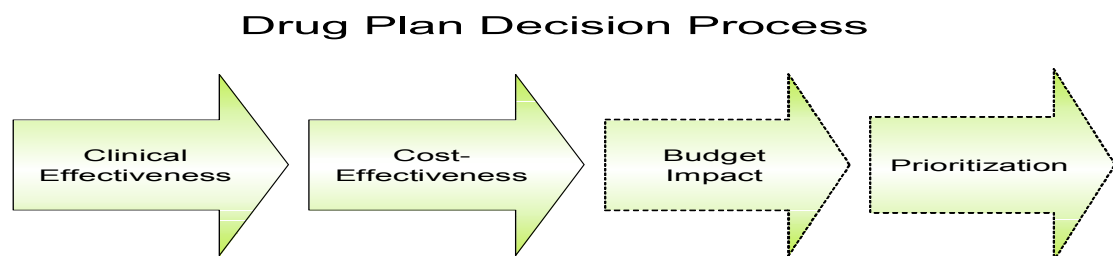
Note: Nunavut does not have chemotherapy centres. All infusions are done outside the territory and billed back.

Coverage for supportive care drugs is the responsibility of the provincial cancer agency in Saskatchewan only. In all other provinces and territories, hospitals cover supportive care drugs administered to inpatients and the responsibility for outpatient supportive care drugs lies with the patient. (The federal Non-Insured Health Benefits (NIHB) program covers First Nations and Inuit Canadians not covered under other plans and is included in this table because it insures half of all residents of the territories.)

2. Cancer Drug Evaluation Process

The evaluation and approval process followed by all drug plans is a variation on Figure 1.

Figure 1



Private drug plans conduct a simplified and streamlined evaluation based on information submitted by the manufacturer. Often, an independent third party organization conducts this review.

The public drug plans undertake a more exhaustive and lengthy review. As discussed in Section 1, all public plans (provincial, territorial and federal) except Quebec's require a prior evaluation by one of the federal/provincial Drug Reviews. For drugs that receive a positive recommendation, the individual drug plan manager will make a listing decision based on budget impact and resource prioritization.

The detailed stages of the process are as follows:

Clinical Effectiveness Evaluation

Drug plan managers need to know how a new drug will offer incremental improvements over the current standard of care. Clinical evidence provided by the manufacturer is first assessed for quality, according to the scientific rigour of the studies presented. Also, the comparators used and the endpoints examined in the study must be relevant. Because clinical studies are very costly, they are conducted globally and comparator drugs may not be the same as the standard of care in Canada or even within a province.

The quality and relevance of the evidence accounts for much of the disparity in how provinces interpret and assess the same information. Because, until recently, evaluations were not standardized, there was no general agreement as to what constituted strong or weak evidence; the importance of a comparator not being the exact regimen used in a particular province; or whether a non-clinical endpoint (such as biological tumour markers) was a reliable predictor of clinical response (such as time to tumour progression). These are the types of issues that the Joint Oncology Drug Review will address in developing its standards of evaluation.

Cost-Effectiveness Evaluation

Drug plans require manufacturers to submit cost-effectiveness (also called pharmacoeconomic) studies of their drugs as part of their submission for approval. There are two main concerns with this part of the evaluation.

The first is the threshold above which a drug is deemed to be cost-effective. The cost-effectiveness equation often boils down to one measurement: the cost per quality-adjusted life year (QALY) gained (discussed in more detail in Appendix 2). There is much speculation about the dollar value of this threshold, how it is employed and who decides that this is the right number. Transparency and public input are needed to ensure that societal values are incorporated into any determination of cost-effectiveness, however few formularies include public input in these decisions.

The second issue is that there is no validated and accepted methodology for conducting and analyzing cost-effectiveness studies. Manufacturers are given very little guidance and their analysis may or may not meet the requirements of the review committee. These studies are highly expensive and are done as part of global clinical drug development programs which may not address Canadian needs, much less those of a particular province.

Budget Impact Analysis

Based on the clinical and pricing information provided in the submission, the drug plan calculates the total number of patients that it expects will receive the new drug, and its aggregate incremental cost. As with other drugs, the impact of a new cancer drug's cost is considered only in terms of the drug budget and does not incorporate any measurements of savings elsewhere in the health system or in the economy at large.

Drug Plan Prioritization

Drug plan managers must balance the priorities of all health areas for the short- and long-term impacts. Prioritization of cancer drug recommendations is a formal process in some, but not all, provinces.

Formulary Listing Status

Part of the recommendation for funding is the listing status of a new drug. Limitations may be placed on its use for safety reasons or as a means of controlling costs. Most cancer drugs have some form of limitation, and these have different terminologies in different provinces.

Appeals

The Non-Insured Health Benefits (NIHB) program has an independent appeals process for claims made under the plan.¹⁷ This is one area that the Joint Oncology Drug Review is being encouraged by patient advocacy groups to pursue.

¹⁷ http://www.hc-sc.gc.ca/fnih-spni/nihb-ssna/benefit-prestation/appe/index_e.html

Part 2

Issues of Cancer Drug Access in Canada

Issue 1

Why are some cancer drugs available in some provinces and not others?

Contents

1. Where Do Examples of Inequities Exist?
2. Responsibility for Funding Cancer Drugs
3. Differences in Provincial Drug Evaluation Processes
4. Implications of Geographic Inequities for Cancer Patients

Access to cancer treatment drugs and to drugs used in the supportive care of cancer patients (to manage symptoms of cancer and side effects of treatment) differs by province and territory. This is due to several factors. Responsibility for providing access to cancer drugs is a patchwork of public and private coverage. Also, within the systems of public coverage, each province makes an independent decision on whether to fund new treatments. This section of the report explores the scope of the issue, how each factor contributes to interprovincial disparities, and what the implications are for cancer patients in Canada.

1. Where Do Examples of Inequities Exist?

Access to many of the new cancer drugs through the publicly funded health system depends to a large extent on which province a patient resides in.

Drug treatments are not included in the *Canada Health Act* definition of 'medically necessary' health care services and it is therefore the province or territory's decision which drugs will be funded by the public system. Each province makes its decision independently based on its own evaluation criteria and on the priority that cancer holds in the health budget. As well, each province also takes a different length of time to make a decision.

A few recent examples of interprovincial inequities are:

1. Avastin (bevacizumab) was approved by Health Canada for the treatment of advanced colorectal cancer in 2005. It is publicly funded in British Columbia, Newfoundland & Labrador, Quebec and Saskatchewan. The remaining provinces have denied funding because of lack of cost-effectiveness.
2. Tarceva (erlotinib) was marketed for the treatment of lung cancer in July 2005. Two provinces (Prince Edward Island and Manitoba) have not yet completed their review of the product nearly three years later.
3. The drug class of aromatase inhibitors is used as adjuvant treatment for breast cancer. All provinces except Saskatchewan provide coverage for these drugs which are considered standard of care in all other jurisdictions.

Interprovincial Comparison of Cancer Drug Coverage

The interprovincial disparities are evident in Table 1, which compares coverage for a selection of newer cancer drugs by public drug plans.

Table 1 Funding Status of Selected Newer Cancer Treatment Drugs (as at 9 April 2008)

Legend: ● Covered for at least some patients ● Denied listing on formulary x Denied listing on formulary R Under review

Brand Name	Generic Name	Cancer Type	Form	NOC	BC	AB	SK	MB	ON	QC	NB	PE	NS	NL	YK	NIHB
Abraxane	NAB-paclitaxel	Breast	IV	06/06	R	R	R	R	●	R	R	R	R	R	R	R
Alimta	pemetrexed	Mesothelioma	IV	07/04	●	●	●	●	●x	●	●	x	x	●	●	●
Alimta	pemetrexed	Lung	IV	01/07	R	R	R	R	R	x	R	R	R	R	R	R
Arimidex	anastrozole	Breast	oral	08/96	●	●	x	●	●	●	●	●	●	●	●	●
Aromasin	exemestane	Breast	oral	08/00	●	●	x	●	●	●	●	●	●	●	●	●
Avastin	bevacizumab	Colorectal	IV	11/05	●	x	●	x	x	●	x	x	x	●	●	●
Bexxar	¹³¹ I-tositumomab	Lymphoma	IV	04/06	●	x	x	x	x	x	x	x	x	x	x	x
Erbix	cetuximab	Colorectal	IV	09/06	x	x	x	x	x	x	x	x	x	x	x	x
Erbix	cetuximab	Head and neck	IV	n/a	●	x	x	x	x	x	x	x	x	x	x	x
Femara	letrozole	Breast	oral	09/97	●	●	x	●	●	●	●	●	●	●	●	●
Gleevec	imatinib	Leukemia, GI	oral	10/01	●	●	●	●	●	●	●	●	●	●	●	●
Herceptin	trastuzumab	Breast	IV	08/99	●	●	●	●	●	●	●	●	●	●	●	●
MabCampath	alemtuzumab	Leukemia	IV	11/05	●	x	●	●	x	x	x	x	x	●	x	x
Nexavar	sorafenib	Kidney	oral	08/06	●	●	R	R	●	x	●	x	●	x	●	x
Nexavar	sorafenib	Liver	oral	01/08	●	R	R	R	R	R	R	R	R	R	R	R
Revlimid	lenalidomide	Multiple myeloma	oral	01/08	R	R	R	R	R	R	R	R	R	R	R	R
Rituxan	rituximab	Lymphoma	IV	04/00	●	●	●	●	●	●	●	●	●	●	●	●
Sprycel	dasatinib	Leukemia	oral	03/07	●	R	R	R	●	●	●	●	R	R	●	R
Sutent	sunitinib	Kidney	oral	06/06	●	R	R	R	●	●	●	●	R	●	R	x
Sutent	sunitinib	Gastrointestinal	oral	05/06	●	●	R	R	●	●	●	●	R	●	R	●
Tarceva	erlotinib	Lung	oral	07/05	●	●	●	R	●	●	●	●	R	●	R	●
Temodal	temozolomide	Brain	oral	10/99	●	●	●	●	●	●	●	x	●	●	●	●
Torisel	temsirolimus	Kidney	oral	12/07	R	R	R	R	R	R	R	R	R	R	R	R
Velcade	bortezomib	Multiple myeloma	IV	02/05	●	●	●	●	●	●	●	●	●	●	●	●
Xeloda	capecitabine	Colorectal, breast	oral	10/98	●	●	●	●	●	●	●	●	●	●	●	●
Zevalin	⁹⁰ Y-ibritumomab	Lymphoma	IV	06/06	●	x	x	●	x	●	●	●	x	●	x	●

Notes to Table:

- In Ontario, Alimta is covered only by the Workers' Safety and Insurance Board (to treat mesothelioma from occupational exposure to asbestos).
- Nova Scotia does not fund Gleevec for gastrointestinal stromal tumours (GIST); all other provinces fund Gleevec for both leukemia and GIST.
- Saskatchewan does not publish information on its formulary. Listings are from the Cancer Advocacy Coalition's 2007 Report Card and news reports.
- NWT and Nunavut use the Non-Insured Health Benefit (NIHB) drug benefit list; NIHB is a federal plan covering First Nations and Inuit.

Caution must be used in drawing conclusions about specific drugs from this summary. Where drugs are noted as funded (•), no distinction is made between those that are widely available and those funded under highly restricted criteria. Also, because published sources were used to document funding status, informal arrangements that provide access to drugs to individual patients are not captured.

2. Responsibility for Funding Cancer Drugs

Responsibility for cancer treatment drugs and drugs used for supportive care (to manage the symptoms of cancer and the side effects of treatment) differs in each province, as shown in Table 2.

Table 2 Payers for Cancer Treatment and Supportive Care Drugs by Province and Territory

	Cancer Treatment Drugs						Supportive Care Drugs			
	Intravenous Drugs			Oral Drugs			I.V. Drugs		Oral Drugs	
	Hospital	Cancer Agency	Private Pmt.	Cancer Agency	Public Drug Plan	Private Pmt.	Hospital	Cancer Agency	Public Drug Plan	Private Pmt.
BC		•	•	•		•	•		•	•
AB		•	•	•		•	•		•	•
SK		•	•	•		•		•		•
MB		•	•		•	•	•		•	•
ON	•	•	•		•	•	•		•	•
QC	•		•		•	•	•		•	•
NB	•		•		•	•	•		•	•
PE	•				•	•	•		•	•
NS	•		•		•	•	•		•	•
NL	•		•		•	•	•		•	•
YK	•				•	•	•		•	•
NT	•				•	•	•		•	•
NU	•				•	•	•		•	•

Cancer and supportive care drugs administered in hospitals and hospital-based cancer clinics are paid for by the public health system. Intravenous drugs that are not funded by the public system may be purchased privately either through a private clinic or at a public hospital, depending on the province.

Oral drugs are the responsibility of the patient. Patients may be covered for these costs by a public plan or through private insurance. (The insurance status of Canadians is discussed in Appendix 3.)

Each of the drug plans noted in Table 2 makes its own decision about which drugs to fund. This complex situation creates inequities between provinces and also within provinces where oral therapies are covered by a combination of public and private plans.

3. Differences in Provincial Drug Evaluation Processes

The responsible funding body in each province makes a decision to list a new drug based on a similar process, as outlined in Part 1. However, different approaches result in disparate decisions. Some of these differences in process are:

- Prioritization of drugs may or may not be part of the evaluation
- Cost-effectiveness evaluation may be done quantitatively or qualitatively; quantitative thresholds differ among provinces
- Total budget impact may or may not be considered
- Cancer drugs are usually approved for use in defined clinical conditions, and treatment practices differ from province to province
- Exceptional Access mechanisms exist in all provinces to allow for flexibility, however different rules apply in each province
- In some provinces, the agency responsible for the drug budget makes the final decision (e.g., the BC Cancer Agency). In other provinces, a higher level decision is required (e.g., in Ontario, the CED-CCO Oncology Subcommittee makes a recommendation to the CED which makes a recommendation to the Executive Officer for Drug Programs who makes the final decision)

In future, the Joint Oncology Drug Review will eliminate some of these disparities, as described in Part 1. However, even if a drug receives a positive recommendation, it may still be turned down by a province for economic or other reasons.

4. Implications of Geographic Inequities for Cancer Patients

There are three main impacts for cancer patients of the geographic disparities described above.

First, these inequities are contrary to the tenets of the *Canada Health Act*, which promises access to medically necessary services “without financial or other barriers” through a system that is universal, accessible, portable, comprehensive and publicly-administered. There are few other areas of medicine that Canadians would deem more “medically necessary” than access to life-saving cancer drugs, and yet because each province makes decisions independently, based on different priorities and economic circumstances, access may be denied simply because of where a patient lives.

Second, the geographic inequity is linked to socioeconomic inequity because of the variations in public and private payment systems for cancer drugs. In provinces where oral cancer drugs are not included in a universal system of coverage, access is determined not by medical need but by an individual’s ability to afford good quality private insurance.

The third impact is the lack of portability of drug coverage. For patients who require expensive oral cancer drugs, access can be interrupted simply because they move from one jurisdiction to another. As more cancer drugs are developed in formulations that are given at home, this will become an increasingly important issue.

Additional mention should be made about the situation for aboriginal groups covered under the federal Non-Insured Health Benefits (NIHB) program. Both the NIHB and

the provincial / territorial drug plans state that they are payers of last resort. While aboriginal cancer patients are eligible to be included under P/T plans, jurisdictional responsibility for aboriginal groups is very unclear. Hospital expenses, including cancer drugs, are the province's or territory's responsibility and reciprocal billing systems allow for patients in the territories to receive their initial treatments at a cancer centre in one of the southern provinces. For oral cancer drugs, the situation is more complex. For example, the three territories' Pharmacare programs cover all residents with cancer. Aboriginal cancer patients are residents of the territory and therefore eligible for coverage by the territorial plan, however in practice oral cancer therapies are covered by NIHB. Fortunately, these interjurisdictional disputes are usually invisible to patients. However, if a drug is required that is listed on the Pharmacare formulary but not on the NIHB, bureaucratic red tape can interfere with patients getting access in a timely manner.¹⁸

¹⁸ Jennifer Forsyth, Health Technical Advisor, Inuit Tapairiit Kanatami; 11 October 2007.

Issue 2

How much does access depend on what a patient can afford to pay?

Content

1. Why Do Canadians Need Prescription Drug Insurance?
2. Which Canadians Need Insurance for Cancer Drug Costs?
3. What Insurance Plans Are Available?
4. How Many Canadians Are Covered by Public and Private Plans?
5. How Good is Insurance Coverage?
6. Options for Private Payment of Unfunded Intravenous Cancer Drugs
7. Implications of Socioeconomic Inequities for Cancer Patients

Perhaps surprisingly, access to cancer drugs in Canada is dependent to a significant extent on socioeconomic status. This has arisen because of the fundamental division of responsibility between those areas of medicine that are funded by the state and those that are the responsibility of the individual.

Table 2 in the previous section outlines where the responsibility for cancer drugs lies by province and territory. This section reviews the sources of payment for cancer drugs and who is eligible for which type of coverage.

1. Why Do Canadians Need Prescription Drug Insurance?

The public health system is not required to pay for drugs administered outside of hospitals (or hospital-based cancer treatment centres) – this is the patient’s responsibility. The magnitude of this liability is significant.

In 2006, 45% of expenditures for cancer drugs were for those taken outside hospitals.¹⁹ And these costs are escalating rapidly. Purchases of cancer drugs taken at home have grown at more than 14% a year for the past five years.

The new generation of cancer drugs is also much more expensive – roughly ten times what cancer drugs cost ten years ago – as Table 1 on the next page illustrates.

¹⁹ Intercontinental Medical Statistics (IMS); Drugstore and Hospital Purchases; 2006.

Table 1 Costs of Selected Oral Cancer Drugs

Cancer Drug	Cancer Site	Drug Cost for Standard Course of Therapy
Aromatase Inhibitors (Arimidex, Femara, Aromasin)	Breast (hormone-responsive patients)	\$1800 per year
Xeloda	Colon cancer	\$6,000
Tarceva	Lung cancer	\$14,000
Gleevec	Leukemia	\$35-70,000 per year
Nexavar	Kidney	\$7350/6 weeks
Sutent	Kidney and Gastrointestinal	\$7330/6 weeks
Temodal	Brain	\$20,000

Source: Cancer Advocacy Coalition of Canada Report 2005-6.

In addition to cancer treatment drugs, community-based therapies used to treat the symptoms of cancer or the management of treatment side effects must also be considered. Zofran, for example, used to reduce nausea and vomiting following radiation or chemotherapy, costs \$25 per pill and generic versions at half the cost are still expensive. Eprex (EPO), used to treat anemia due to chemotherapy, costs thousands of dollars per course of treatment.

2. Which Canadians Need Insurance for Cancer Drug Costs?

Seventy-three per cent of Canadians require insurance for oral cancer drugs. These citizens reside outside the three provinces and three territories that cover the cost of cancer drugs for all residents. All Canadians living outside Saskatchewan (97%) need insurance coverage for supportive care drugs administered at home.

Table 2 on the next page shows the provinces and territories in which cancer patients need either public or private insurance to cover the cost of drugs received outside hospitals.

Table 2 Public Drug Plan Coverage of Cancer Treatment and Supportive Care Drugs Taken at Home, by Province

	Cancer Treatment Drugs	Supportive Care Drugs
BC	All residents covered by cancer agency	Insurance required
AB	All residents covered by cancer agency	Insurance required
SK	All residents covered by cancer agency	All residents covered by cancer agency
MB	Insurance required	Insurance required
ON	Insurance required	Insurance required
QC	Insurance required	Insurance required
NB	Insurance required	Insurance required
PE	Insurance required	Insurance required
NS	Insurance required	Insurance required
NL	Insurance required	Insurance required
YK	All residents with cancer covered by territorial drug benefit plan	Insurance required
NT	All residents with cancer covered by territorial drug benefit plan	Insurance required
NU	All residents with cancer covered by territorial drug benefit plan	Insurance required

3. What Insurance Plans Are Available?

The following public and private insurance plans are available to Canadians to cover the cost of cancer treatment and supportive care drugs.

Federal Drug Plan Coverage

The federal government assumes the full cost of providing prescription drugs for First Nations and Inuit, inmates of federal jails, refugees, members of the military, and certain armed forces and RCMP veterans.

Provincial Drug Plan Coverage

Eligibility for coverage under the provincial drug plan varies by province. Table 3 shows which groups are eligible for coverage under specific provincial plans.

Table 3 Eligibility for Provincial Drug Plan Coverage

	BC	AB	SK	MB	ON	QC	NB	PE	NS	NL	YK	NT	NU
Universal Coverage	●	●	●	●		●			●				
Seniors		●	n/a		●	●	Low income	●	●	GIS	●	●	●
Income Support	●	●	n/a		●	●	●	●	●	●		●	●
Under 65		●	n/a			●			●				
Low Income			n/a					●	Cancer	●			
High Drug Costs			n/a		●			*		●			

Notes to table:

- In B.C. the same universal plan is available to all residents, however income support clients do not pay cost-sharing amounts.
- In Alberta and Quebec, coverage is universal but there are different plans for different groups.
- Saskatchewan covers the costs of all cancer treatment and supportive care drugs through the Saskatchewan Cancer Agency.
- Prince Edward Island has a Cancer Drug Cost Program that covers part of the costs of Gleevec (imatinib) and Xeloda (capecitabine) for patients with annual incomes of less than \$150,000.
- Nova Scotia has a special plan for cancer patients with low incomes. As of November 2007, coverage with income-based cost-sharing is now available to all families.
- Newfoundland & Labrador's drug plan covers only those seniors receiving the Guaranteed Income Supplement.

Private Drug Plan Coverage

Most private insurance (95%) is through employer-sponsored plans and 60% of workers are covered under these extended health benefits.²⁰ Private drug insurance can be purchased by individuals although at a higher cost than for group plans.

4. How Many Canadians Are Covered By Public and Private Insurance Plans?

The Canadian Life and Health Insurance Association calculates that 61.5% of the population was covered for extended health benefits from private plans in 2005.²¹ Two per cent of the population are covered under one of the federal health benefit programs. From the perspective of coverage for cancer and supportive care drugs, 28% of Canadians are covered by a provincial plan (either the provincial drug benefit plan, the cancer agency or both). The remainder, approximately 8% of the population, is not enrolled in any insurance plan and is not automatically covered for the costs of both cancer treatment and supportive care drugs by the province in which they reside.²²

This analysis, however, does not take into account coverage for catastrophic costs for which an individual would be eligible if their drug costs reached a high enough

²⁰ Applied Management; "Canadians' Access to Insurance for Prescription Medicines – Volume 2"; March, 2000.

²¹ Canadian Life and Health Insurance Association; "Facts and Figures" 2005.

²² Author's calculations from figures supplied by Applied Management, 15 June 2007.

proportion of their family income. The generally accepted threshold of catastrophic drug expenses is 4% of net household income. From this perspective, 42% of Canadians are covered by their provincial plan and 2% are without coverage, all of whom reside in the Atlantic Provinces.²³

5. How Good Is Insurance Coverage?

Having prescription drug insurance cannot be assumed to mean that patients will have no financial burden in accessing the drugs they need for their treatment. The quality of coverage can be assessed against the following four criteria:

- Coverage of high drug expenses (catastrophic coverage)
- Reasonable cost-sharing requirements
- Drug plan formulary includes all clinically recommended cancer treatments
- Plan flexibility

Catastrophic Coverage

Although most private insurance plans do not place limits or caps on claims, some insurers do impose financial limitations that are below the costs of many of the newer cancer drugs.

The public drug plans do not provide a cap on coverage (except Alberta's Non-Group Plan, which has a \$25,000 annual cap, although this can be waived). All provinces except Prince Edward Island and New Brunswick have some form of catastrophic coverage for cancer drugs available to their residents. For those provinces offering this type of coverage, prescription drug costs must exceed a certain percentage of net household income. This ranges from 3% to over 10% depending on the province and income bracket.

Cost-Sharing

Most beneficiaries are required to contribute to the cost of their prescriptions through deductibles and co-payments (in addition to the annual premiums that some beneficiaries pay). Almost one-fifth of expenditures on prescription drugs in Canada are paid by individuals.²⁴ A typical private drug benefits plan has an annual deductible of \$100 and co-payment of 20% of cost of each prescription once the deductible is met.²⁵ These requirements can result in financial hardship for patients who require very expensive drugs. At a cost of \$35,000 - \$70,000 per year for Gleevec, for example, the 20% co-payment would be \$7,000 - \$14,000 a year for life – a lot to pay for a family earning the median household income of \$60,600.²⁶

Details of cost-sharing requirements of provincial drug plans are in Appendix 3.

Formulary Quality

Public drug plans' formularies, or lists of covered drugs, vary widely as shown in Issue 1 above. Even if a drug is covered, limitations may be placed on how it can be

²³ Applied Management; "Canadians' Access to Insurance for Prescription Medicines – Volume 2"; March, 2000. NL and NS recently introduced coverage for all families, however the cost-sharing requirements are high and coverage does not apply until drug expenses exceed the 4% threshold for catastrophic expenses.

²⁴ Canadian Institutes for Health Information, 2006.

²⁵ Kapur, V and Basu, K; "Drug coverage in Canada: Who is at risk?"; Health Policy Vol. 71, p. 181, 2005.

²⁶ Statistics Canada, 2005 data (latest available).

used. Also, delays due to funding decisions may create barriers to access if the drug is not reimbursed by the plan during the review period.

Plan Flexibility

Another important consideration for cancer patients is the flexibility of the public or private insurance plan. The ability to make premiums and deductible payments by installments, for example, benefits patients whose income has been interrupted by their illness. Also, an exceptional review or appeals process is important for patients with unusual cancers or with co-existing medical conditions that require special treatment with drugs that are normally not covered.

6. Options for Private Payment of Unfunded Intravenous Cancer Drugs

Most hospital-administered cancer therapies are covered by the public health system. A drug may not be covered because it has been evaluated and denied funding, because it has not yet been approved by Health Canada, because the manufacturer has not marketed the drug, or because it is still under review.

For patients who require drugs that have been recommended by their oncologists but that are not funded by the public system, there are three payment options:

- Private insurance coverage
- Free drug from the manufacturer
- Out-of-pocket payment

Manufacturers' Compassionate Use Programs

Many pharmaceutical companies set up Compassionate Use programs to provide specific drugs free of charge to patients who have no other means of payment. These programs usually apply to drugs for which regulatory approvals or funding decisions have not yet been made, but some also extend to cover marketed drugs.

Companies may also provide financial subsidies to cover partial costs. These are designed to cover high co-payment costs and are usually means-tested or require a deductible to be paid before financial assistance is provided.

Out-of-Country Treatments

Patients with private means can elect to be treated at cancer centres outside Canada. Ontario is the only province that has a published policy of funding drug treatments received outside of Canada, however this system has been applied inconsistently and is currently under review.

Private Payment at Public Hospitals

Provinces such as New Brunswick, Saskatchewan, Alberta and British Columbia have specific policies allowing patients to pay privately to receive infusions of unfunded cancer drugs in public hospitals. In Ontario, several cancer centres are infusing privately-paid cancer drugs, but in the absence of a clear policy directive from the government. Other provinces may allow the practice but do not have published policies.

Private Clinics

Private infusion clinics are in operation in many major cities across the country. The most widespread are the Bayshore Clinics which operate in most major centres across Canada. Toronto's Provis Clinic, opened in 2005, was the first private clinic offering infusions of cancer drugs. The False Creek Surgical Centre in Vancouver provides the same services.

7. Implications of Socioeconomic Inequities for Cancer Patients

The relatively sudden appearance on the market of expensive cancer treatments and supportive care drugs over the last decade has challenged both the private and the public insurance systems to continue to provide adequate coverage to Canadians. The division of responsibility for cancer drug coverage between public and private systems and the inability of the public system to pay for all cancer drugs has created barriers to access based on socioeconomic factors.

Having high quality insurance or personal financial means translates into higher quality of life and, in some cases, improved clinical outcomes for cancer patients who are able to access the latest drugs for treatment and supportive care.

Another implication of these socioeconomic disparities is the financial burden of cost-sharing provisions of public and private insurance plans. Coupled with other financial strains experienced by cancer patients – interrupted income, costs of household care, travel and medical supplies – patients with fewer financial resources will experience greater hardship and may need to forgo necessities in order to cope. This is discussed in greater detail in the next section.

For Canadians who are not eligible for public plan coverage, private insurance is difficult to obtain at a reasonable premium. Older persons, those with pre-existing illnesses, low wage earners and the self-employed are particularly disadvantaged. In this context, Quebec's 1997 policy requiring that all residents have prescription drug insurance is an example of a far-sighted approach to the issue.

Issue 3

The impact on patients - what happens when people can't afford cancer drugs?

Contents:

1. Which Cancer Patients Are Vulnerable to High Drug Costs?
2. How Do Patients Cope when They Can't Afford Drugs?

1. Which Cancer Patients Are Vulnerable to High Drug Costs?

Canadians without adequate prescription drug insurance for expensive oral therapies are vulnerable to financial hardship in most provinces and territories.

Financial Risk of Catastrophic Drug Costs

Table 1 shows, for each province and territory, what an average income earner without access to private insurance would pay out-of-pocket for a \$20,000 course of treatment with an oral cancer drug (assuming that the drug is listed on the provincial drug plan formulary). For comparison, the out-of-pocket costs for a patient with a typical private drug plan are also calculated.

Results are shown for:

- Senior couples earning the Canadian median net income of \$46,300²⁷
- Non-senior couples with a median net income \$62,700

As the table shows, there is significant variation in the amount the patient would have to pay, depending on his or her province of residence and whether he or she has private or public insurance coverage. Residents of New Brunswick and Prince Edward Island are especially vulnerable to these expenditures.

²⁷ Statistics Canada 2005 (latest available data).

Table 1 Out-of-Pocket Costs for a Couple Earning the National Average Income and Spending \$20,000 for an Oral Cancer Drug

	Public Drug Plan	Age	Deductible or Premium	Co-payment	Out-of-Pocket
BC	BC Cancer Agency	Senior	None	None	\$0
		Non-senior			
AB	Alberta Cancer Board	Senior	None	None	\$0
		Non-senior			
SK	Saskatchewan Cancer Agency	Senior	None	None	\$0
		Non-senior			
MB	Pharmacare	Senior	4.41% of adjusted family income	None	\$1,910
		Non-senior			\$2,633
ON	Ontario Drug Benefit Program	Senior	\$100	\$6.11	\$106
	Trillium Program	Non-senior	4% net income	\$2	\$2,510
QC	RAMQ	Senior	Combination	Combination	\$904
		Non-senior			
NB	Not eligible	Senior			\$20,000
		Non-senior			
PE	Seniors' Drug Cost Assistance Program	Senior		\$11.00 plus pharmacy fee	~\$20
	High Cost Drugs Program (if Xeloda or Gleeevec)	Non-senior		\$7 + some % of drug cost*	<\$20,000
	Not eligible (if not Xeloda or Gleeevec)	Non-senior			\$20,000
NS	Seniors' Pharmacare	Senior	\$848	\$764 (max)	\$1,612
	Family Pharmacare	Non-senior	1% adjusted income	20%	\$8,776
NL	NL Prescription Drug Program	Senior	7.5%		\$3,473
		Non-senior			\$4,703
YK	Pharmacare	All (cancer patients)	\$250	None	\$250
NT	Extended Health Benefits	All (cancer patients)	None	None	\$0
NU	Extended Health Benefits	All (cancer patients)	None	None	\$0
NIHB	Non-Insured Health Benefits	Senior	None	None	\$0
		Non-senior			
CAN	Private Insurance	All	\$100	20%	\$4,100

* The High Cost Drugs Program covers a portion of drug cost for these two drugs for families with net incomes under \$150,000. Figures are unavailable from the government of PEI on what percentage would apply to specific income levels.

Financial Risk of Routine Drug Costs

For patients with low incomes who are not receiving social assistance, the costs of even routine drug expenditures can present significant financial hardship.

Table 2 shows the out-of-pocket expenses that the average-income patients described above would pay in each province for a 30-day prescription for generic ondansetron (Zofran) costing \$400.00.

Table 2 Out-of-Pocket Costs for a Couple Earning the National Average Income and Spending \$400 for an Oral Cancer Drug

	Public Drug Plan	Age	Deductible or Premium	Co-payment	Out-of-Pocket
BC	Pharmacare	Senior*	1% net income	25%	\$400
		Non-senior	3% net income	30%	\$400
AB	Alberta Health & Wellness Prescription Drug Plan	Senior	None	30% to max \$25 per Rx	\$25
		Non-senior (Non-Group Plan)	\$492	30% to max \$25 per Rx	\$492 + \$25 co-pay**
SK	Saskatchewan Cancer Agency	Senior	None	None	\$0
		Non-senior			
MB	Pharmacare	Senior	4.41% of adjusted income	None	\$400
		Non-senior			
ON	Ontario Drug Benefit Program	Senior	\$100	\$6.11	\$106
	Not eligible	Non-senior			\$400
QC	RAMQ	Senior	\$557	30%	\$557 + \$120 co-pay**
		Non-senior			
NB	Not eligible	Senior			\$400
		Non-senior			
PE	Seniors' Drug Cost Assistance Program	Senior		\$11 + \$10 pharmacy fee	\$21
NS	Seniors' Pharmacare	Senior	\$848	33%	\$848 + \$132 co-pay**
	Family Pharmacare	Non-senior	1% adjusted income	20%	\$400

NL	Not eligible	Senior			\$400
		Non-senior			
YK	Pharmacare	Senior	\$250	None	\$250
	Not eligible	Non-senior			\$400
NT	Extended Health Benefits	Senior	None	None	\$0
	Not eligible	Non-senior			\$400
NU	Extended Health Benefits	Senior	None	None	\$0
	Not eligible	Non-senior			\$400
NIHB	Non-Insured Health Benefits	Aboriginal groups	None	None	\$0
CAN	Private Insurance	All	\$100	20%	\$180

* If born before 1939.

** The family would pay the annual premium whether or not they made any drug claims. The co-pay for this prescription is in addition to the premium.

2. How do patients cope when they can't afford drugs?

When patients cannot afford the high costs for cancer treatments, there are a few ways they can find varying degrees of financial relief.

- Manufacturers' compassionate use or patient assistance programs (as discussed in the previous section)
- Charitable programs (some divisions of the Canadian Cancer Society, religious organizations and certain health foundations)
- CancerCare Ontario maintains a Free Drug Service
- Community fundraising

Social workers in the Psychosocial Oncology units of major cancer centres have become quite adept at locating alternative sources of funding for patients and in persuading the system to help. Not all patients, however, have access to these resources and many are reluctant to ask for help.

When the above sources of help do not work, patients cope with financial burdens in different ways.

- Reduce essential prescription drug use^{28,29}
- Cut back on necessities and increase debt³⁰

²⁸ Tamblin, R. et al. "Adverse events associated with prescription drug cost-sharing among poor and elderly persons." JAMA. 2001 Jan 24-31;285(4):421-9.

²⁹ Anis, AH et al. "When patients have to pay a share of drug costs: effects on frequency of physician visits, hospital admissions and filling of prescriptions"; Canadian Medical Association Journal, vol. 173 no. 11, p. 1335, November 2005.

- Patients without access were more likely to be: uninsured, having a low income, in a poorer state of health, experiencing debilitating pain and seeing a doctor more frequently³¹

The results of several Canadian and U.S. studies are similar to the reports from social workers in Canadian cancer centres. Details of these studies are found in Appendix 4.

³⁰ Heisler, M et al. "Patient strategies to cope with high prescription medication costs: who is cutting back on necessities, increasing debt, or underusing medications?"; J Behav Med. Vol. 28 no. 1 p. 43, Feb 2005.

³¹ Kennedy and Morgan; "A Cross-National Study of Prescription Non-Adherence Due to Cost: Data from the Joint Canada-United States Survey of Health"; Clin. Ther., vol. 28 #8 p. 1217, Aug. 2006.

Issue 4

How patient-centred are Canada's cancer drug access systems?

Content

1. How Easy Is It for Patients to Access the Drugs They Need?
2. How Responsive Is the System to Patients' Needs?
3. Appeals Processes and Transparency

1. How Easy Is It for Patients to Access the Drugs They Need?

Patients' ease in obtaining cancer drugs depends on several factors, including the number of plans an individual patient must access, whether the drug is listed on the drug plan formulary, the availability of patient navigation resources and the overall bureaucracy of the system in the province.

A comparison of the system in each province was prepared using a scorecard format, shown in Table 1, according to the following criteria:

Number of Plans Per Patient

The higher the number of drug plans that an individual patient must deal with, the more complex the system will be for them. Plans cover IV and oral drugs; routine and catastrophic costs; and manufacturer's programs for unfunded drugs.

Number of Drugs Covered

A basket of 20 newer cancer treatment and supportive care drugs was used to compare provinces.³² Only those drugs that had been approved by Health Canada for more than one year were included. Radioimmunotherapies were excluded because not all provinces have facilities to administer these drugs.

Patient Navigation

Provinces that take a very systematic and proactive approach to addressing patients' needs were rated highest. A lower rating was given if assistance is available only on request, or is inconsistent across the province.

Gap-Filling Programs

Programs to help patients who cannot afford the out-of-pocket costs for approved treatments were rated according to whether they are in place and how well they operate.

'Agony' Factor

This refers to how much bureaucracy, time and frustration is involved in accessing cancer drugs. This includes exceptional access mechanisms, requirements for

³² Abraxane, Alimta (2 indications), Arimidex, Aromasin, Avastin, Femara, Gleevec (2 indications), Herceptin, MabCampath, Nexavar (kidney), Rituxan, Sprycel, Sutent (2 indications), Tarceva, Temodal, Velcade, Xeloda

income-based documentation, and limitations to drug access. The ratings are based on feedback from health professionals and cancer patients.

Table 1 Cancer Drug 'Ease of Access' Scorecard

	Plans per Patient	New Drugs (List of 20)	Navigation Resources	Programs to Fill Gaps	"Agony" Factor
BC	3	18	Yellow	Green	Green
AB	3	14	Green	Green	Green
SK	2	11	Yellow	Red	Green
MB	3	12	Yellow	Red	Yellow
ON	7	16	Yellow	Yellow	Red
QC	3	16	Yellow	Yellow	Yellow
NB*	3	15	Green	Green	Red
PE	4	10	Yellow	Green	Red
NS	5	12	Yellow	Red	Red
NL	4	15	Yellow	Red	Red
YK**	4	7/12	Green	Red	Green
NT**	4	9/12	Green	Red	Green
NU**	4	9/12	Green	Red	Green
NIHB	2	9/12	Green	Red	Green

* New Brunswick added 8 patient navigators for adults and 2 for children with cancer in April 2008, however their impact has not yet been assessed.

** The territorial systems are rated only for non-NIHB residents. (The NIHB (Non-Insured Health Benefits) program covers all Status Indians and Inuit for treatments received outside hospitals.) The territories are rated on the number of oral drugs available, since patients from the north receive intravenous infusions outside of the territory.

In interpreting this scorecard, an individual province or territory's system should be viewed as a whole. For example, a program or resource may not in place because it is not needed, therefore a "Red" rating may be misleading if taken on its own.

2. How Responsive Is the System to Patients' Needs?

A high quality system of access to cancer drugs would respond to the needs of individual patients by providing:

- Rapid access to new drugs
- Flexibility to make unapproved or unfunded drugs available for patients with unusual cancers or clinical conditions

How Quickly Are Cancer Drugs Approved in Canada?

As discussed in Part 1, Canadians have historically waited just under one year longer, on average, than the first approval anywhere in the world for a new cancer drug. During the period of review, Health Canada's Special Access Program may allow limited release of drugs for serious or life-threatening conditions, however these are almost never funded by the public health system.

Access to Drugs for Patients in Exceptional Circumstances

Many private drug plans will consider a special request for coverage of a drug that is not yet approved by Health Canada. For patients insured by their provincial drug

plan who require approved drugs that are not listed on the formulary, all provinces have Exceptional Access mechanisms that consider these requests. Provinces vary considerably, however, in the amount of latitude they offer within the Exceptional Access procedure.

How Financially Flexible are Drug Plans?

Cancer patients covered by plans with a deductible will meet this amount very quickly – perhaps with their first prescription – and have to find hundreds of dollars of unexpected expenses at once. Fortunately, installment plans are now available for almost all coverage requiring deductibles. Some provincial plans will waive cost-sharing amounts in special circumstances, although usually this requires paperwork.

3. Appeals Processes and Transparency

A high quality system of cancer drug access includes an independent appeals process and transparency of the reasons for drug plan decisions.

When coverage is denied to patients by provincial drug plans, there is rarely an opportunity to appeal to an independent body. The Non-Insured Health Benefits program (which insures First Nations and Inuit) provides recourse to an independent committee for patients whose claims are denied.

Provincial drug plan managers are gradually becoming more open to making public their decisions and explaining the rationale behind those decisions. The Common Drug Review was the first agency to adopt this practice and regularly posts its recommendations on its website. As of July 2007, Ontario (and, hence, the Joint Oncology Drug Review) now posts its decisions, although the website is not kept up to date. Quebec and Nova Scotia are also committed to similar systems.

Issue 5

Why are cancer drugs so expensive?

Content

1. Scope of the Issue of High Cancer Drug Prices
2. The High-Cost, High-Risk Drug Development Process
3. Recouping Investments
4. What Can Canada Do about High Cancer Drug Prices?

1. Scope of the Issue of High Cancer Drug Prices

High prices for cancer drugs have an enormous impact on cancer drug access. If not for the ten-fold increases in prices over the past decade, many of the issues related to equity and sustainability would not be of concern today.

Of the 15 cancer drugs approved in Canada over the past decade, three-quarters are reported to cost more than \$20,000 for a normal course of treatment.³³ Cancer drug budgets now consume one-quarter of the total cost of cancer control in some jurisdictions³⁴ and are forecast to quadruple over the next 10 years.³⁵ Of the 150 different cancer drugs purchased in Canada in 2006, the top five accounted for half of all expenditures.³⁶

At issue is whether drug companies are charging too much for their products. The system that we as a society have created must benefit both commercial and public interests to be sustainable. To judge whether prices for drugs are reasonable and to offer potential solutions, it is necessary to understand the costs and risks of bringing new products to market.

2. The High-Cost, High-Risk Drug Development Process

The pharmaceutical drug industry is not always understood as a high-stakes business, and yet the risks and costs at every stage of the drug development process contribute to the high prices of medicines. A recent study from the Canadian pharmaceutical industry association revealed that only three out of 10 new medicines on the market recover their research and development (R&D) investment.³⁷

Each step along the product lifecycle from discovery to approval, to funding, to patent expiry, and finally to the introduction of generic copies, contains significant risks and, sometimes, great rewards. Companies who develop new drugs for markets where medications already exist must overcome escalating hurdles of safety and efficacy as each new entry into the market must prove that it is better than the

³³ CBC News report; 25 Feb 2007

³⁴ Interview with Dr. Tony Fields, Vice-President Alberta Cancer Board; 15 August 2007.

³⁵ Authors calculations, based on a projection of current growth rates.

³⁶ Intercontinental Medical Statistics (IMS); Drug Store and Hospital Purchases; 2006.

³⁷ Rx&D; The Pharmaceutical Industry In Canada; July 2007.

current standard of care. Proving superiority to existing treatments requires large and expensive studies. Also, because each company operates independently, decisions to develop a new drug are taken in isolation and with little concrete knowledge of what patients will need when the drug is approved 12 or 14 years later.

From Discovery to Approval: The Investment and Risk to Develop a New Drug

The average cost of shepherding a drug from development through approval is now estimated at US\$980 million and the process takes 14.2 years on average, according to a study from the Tufts Centre for the Study of Drug Development.³⁸ Many of the new cancer therapies are biologicals, that is they are produced by living cells rather than by conventional chemical synthesis, and their development costs average about \$1.2 billion per new medicine.

A company’s R&D costs include drugs that fail during the development process. According to the process illustrated below, of the 5,000 drugs initially screened, only one is approved. Another study puts the ratio at one in 10,000.³⁹

Chart 1 Drug Development Process

Clinical Trials										
	Discovery / Preclinical Testing	File IND with Health Canada	Phase I	Phase II	Phase III	File NDS with Health Canada	Health Canada	Phase IV		
Years	6.5			1.5	2		3.5		2-3	
Test Population	Laboratory and animal studies			20 to 100 healthy volunteers	100 to 500 patient volunteers		1,000 – 5,000 patient volunteers		Review process / approval	Additional post-marketing testing required by Health Canada
Purpose	Assess safety, biological activity and formulations			Determine safety and dosage	Evaluate effectiveness, look for side effects		Confirm effectiveness, monitor adverse reactions from long-term use			
Success Rate	5,000 compounds evaluated			5 enter trials					1 approved	

Adapted from 2005 PhRMA Survey “Medicines to Treat Older Americans”, 2005.
Abbreviations: IND = Investigational New Drug submission (required before a new drug can be administered to humans); NDS = New Drug Submission (request for marketing approval)

From Product Approval to Patent Expiry: The Investment and Risk to Market a New Drug

Once a drug is approved, the company continues to invest in its development in a number of ways. Most cancer drugs in Canada receive a conditional approval, known as a NOC/c or Notice of Compliance with Conditions⁴⁰ which requires the company to

³⁸ Associated Press; “Cautious FDA pinches drug pipeline”; August 18, 2007.

³⁹ Rx&D December 2005.

⁴⁰ Conditional NOCs are granted for drugs that treat life-threatening illness for which there are no alternatives. This is done to bring an important new therapy to market as quickly as possible.

conduct specific clinical studies, at their expense, to increase knowledge about the drug's safety profile. Companies also continue to invest in clinical trials to develop new indications, or uses, which may or may not receive approval.

Drugs may also be withdrawn from the market if their use in large populations brings uncommon side effects to light. Iressa (gefitinib) is an example of a once-promising lung cancer drug whose use has been severely curtailed following the appearance of side effects following its introduction. The manufacturer now bears these "sunk" costs.

In addition to these clinical risks, delays in funding for new drugs create financial risks for companies. Public drug plans, which pay for the majority of cancer drugs in Canada, take from six months to several years and require the manufacturer to conduct costly health economic studies.

Lastly, companies incur expenses by providing their drugs free of charge or by subsidizing patients' drug expenses until a decision is made by drug plans (and sometimes beyond, for patients without financial means).

The Intellectual Property Value Chain

Over the past decade or more, companies have filled up their dwindling pipelines with drug candidates from biotechnology companies. Because of these business relationships, the companies marketing the product do not have total control over the price charged and the intellectual property is divided among many players, all of whom expect a return on their investment. Also, costs have been added to the system because of the higher expectations of venture capitalists who fund the early stages of drug development.

Accounting Rules: Reinvesting Today's Profits to Discover Tomorrow's Drugs

For high-risk industries like pharmaceuticals, where increased revenues from R&D investments are not assured, research costs cannot be capitalized and written off against future income. Rather, the taxation system requires that these costs are expensed in the year in which they were made. This means that companies must maintain a steady revenue stream, year after year, in order to fund R&D machinery to develop new drugs.

3. Recouping Investments

Companies recoup their R&D investment through profits obtained once a drug is marketed. The patent system allows a defined period of market exclusivity to assist in this process. The company maximizes this opportunity using the levers of price and promotion.

The Patent System

The patent system provides a company with a period of exclusivity in the market and, in return, the company must disclose proprietary information about the product and its manufacturing processes which benefits other inventors.

Patent applications are made early in the process, so that by the time the drug is approved and funded, usually only six or seven years remain on a 20-year patent. (Changes to Canada's patent laws in 2006 mean that new drugs now have eight

years of protection after approval, however formulary listing decisions effectively subtract a year from this period.)

Price Setting

Companies are motivated to obtain the highest price that will meet the requirements of both the global market and price regulators, and that local markets will accept.

Global pricing is the largest consideration for prices in Canada. Companies set a global price corridor to avoid price differentials between countries that can be exploited by systems of arbitrage. The U.S. remains the largest and most price-tolerant market and global prices tend to be set according to what Americans will pay.

Prices in Canada are regulated by the Patented Medicines Prices Review Board, discussed in Part 1. Its rules limit prices to ensure they are not excessive.

The Canadian market's willingness to pay a certain price depends on the value offered by the new entity. This is evaluated by private and public drug plans independently, as discussed in Part 1.

For cancer drug pricing, additional complexities can arise because drugs are usually developed in stages for different indications. Because of the risk that each successive indication may or may not be approved, companies can reap windfalls or suffer financial disasters by setting the wrong initial price.

4. What Can Canada Do about High Cancer Drug Prices?

Strategies gleaned from other jurisdictions and areas of healthcare could potentially be employed to seek a more workable approach which allows companies to continue bringing needed medications to the market, yet is affordable to the people who have, indirectly through their tax dollars, supported the research that has made these discoveries possible.

The following approaches are discussed in greater detail in Appendix 6.

- Take from the pharmaceutical companies:
 - Dismantle the patent system
 - Limit profits
- Take from patients:
 - Limit drug budgets and ration care
 - Increase private payment options
- Take from the health system:
 - Increase public funding for cancer
- Share the burden:
 - Pay for performance
 - Allow differential pricing based on volume
 - Price limitations on generics
- Long-term solutions:
 - Invest in screening systems to better target therapies
 - Take costs out of the development process
 - Increase the flexibility of the patent system
 - Gated pricing aligned with new indications

Issue 6

Where is the voice of the patient heard in the system?

Content

1. The Context of Public Involvement in Health Care Policy
2. Where Are Patients Currently Heard in the Canadian Cancer Drug Access System?

1. The Context of Public Involvement in Health Care Policy

The voice of the public needs has been heard at critical junctures in the development of health policy in Canada. Canadians' perspectives were sought during the establishment of Medicare, the *Canada Health Act* and subsequent reform initiatives earlier in this decade. There is an increasing expectation for public organizations to include public input before making decisions that have a fundamental impact on them. (The "Conversation on Health" in British Columbia is a recent example.)

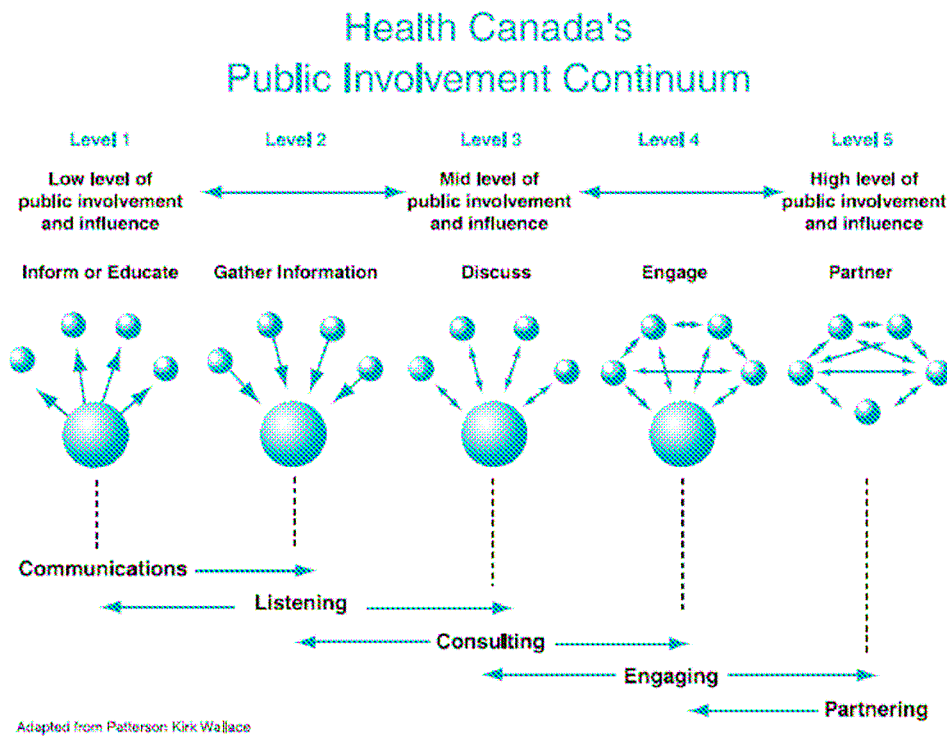
The World Health Organization endorsed the idea of public participation in health care planning as early as 1978. They report that the payback of this approach includes an alignment of goals; enhanced effectiveness through strong partnerships; a focus on patients' needs, rather than those of the system; and decision-making based on clinical and economic evidence, but also on social values. Public involvement has the potential of producing not only better decisions but, perhaps more importantly, building public confidence in the system.

The Health Canada Policy Toolkit for Public Involvement in Decision Making, shown in Figure 1, provides a model of public involvement.⁴¹ The choice of whether to inform, consult or engage depends on the implications of the decision in terms of its complexity, the expected impact on patients and the political ramifications. It also depends on practical concerns about timing, budget and the accessibility of appropriate public representatives.

Other jurisdictions, such as National Institute for Health and Clinical Excellence (NICE) the UK and the FDA in the US have implemented structured processes for patient involvement in policy and regulatory decision-making.

⁴¹ The Health Canada Policy Toolkit for Public Involvement in Decision Making; 2000.
http://www.hc-sc.gc.ca/ahc-asc/pubs/public-consult/2000decision/pol-continuum_e.html

Figure 1



2. Where Are Patients Currently Heard in the Canadian Cancer Drug Access System?

Patients' voices are heard increasingly throughout the system of access to cancer drugs in Canada.

Health Canada

In its vision statement, Health Canada commits to public involvement which is integral to decision making and providing quality service. The Health Products and Food Branch of Health Canada has a Public Advisory Committee which provides advice on consumer/public involvement activities.⁴² Also, as mentioned in Part 1, the Scientific Advisory Committee on Oncology Therapies includes consumer representation.

Health Canada's recent Blueprint for Renewal included a series of seven regional consultation sessions in November 2006 to seek stakeholders' views on the initiative. The Health Products and Food Branch 2007 Progress Report on the 2004-07 Strategic Plan provided summaries of its activities in promoting the inclusion of the public in decision making.

⁴² The University of Toronto Priority Setting in Health Care Research Group; "Recommendations for Establishing a Citizens' Council to Guide Drug Policy in Ontario"; November 2006.

Joint Oncology Drug Review

As part of the evolution of its processes and structures, the Joint Oncology Drug Review included two patient representatives on its Advisory Committee in October 2007. The Ontario process being used by the Review intends to incorporate two patients in the evaluation committee.

Common Drug Review

Two representatives of the public were added to the Canadian Expert Drug Advisory Committee in October 2006 to provide a societal perspective on recommendations for drug listings.

Provinces and Territories

Four provinces having formal roles for participation of patients or members of the public in health policy and/or drug funding decisions.

In Ontario, a commitment was made in June 2006 for a Citizens' Council to advise on issues where a societal perspective is required. (The Council has not yet been formed.) The Ontario Drug Benefit's Committee to Evaluate Drugs recently included two patients with voting powers. As mentioned above, two patients are also planned to be included in the joint CancerCare Ontario – Ontario Drug Benefit Oncology Subcommittee.

In Quebec, the *Act Respecting Prescription Drug Insurance* stipulates that members of the public will be included in two committees. The Conseil du médicament, which makes drug listing decisions, consists of 15 members, four of whom are not linked to the health system. In addition, a medication advisory panel – the "Table de concertation du médicament" – which advises the council on priorities and actions includes two public representatives.

Nova Scotia's Cancer Systemic Therapy Policy Committee provides the Department of Health with advice on what cancer drugs should qualify for public funding. The committee is made up of 23 people, including cancer specialists, a cancer survivor, a member of the public, a pharmacist, ethicist other health care providers and members from the Department of Health.⁴³

In its Provincial Health Plan, released in April 2008, New Brunswick announced the formation of a Health Council to engage citizens in monitoring health system performance and providing recommendations to the Minister of Health. Of the Council's up to 16 members, half would be from the community and stakeholder groups.

⁴³ http://www.gov.ns.ca/health/cancer_drugs/Terms_of_Reference_Oct_2006.pdf

Appendices

Appendix 1

National Cancer Drug Approval Systems

Contents

1. Regulatory Approval: Health Canada
2. Pricing Approval: Patented Medicines Prices Review Board
3. Cancer Drug Evaluation for Funding:
 - a. Joint Oncology Drug Review
 - b. Common Drug Review

1. Regulatory Approval: Health Canada

Regulatory approval for cancer drugs follows the same process as other prescription drugs in Canada, although because some of these drugs may be life-saving and are urgently needed, they may experience faster approvals and require less exhaustive testing before approval.

Health Canada is responsible for reviewing and approving all new prescription drug products, based on their demonstrated safety and efficacy. Within Health Canada, the Therapeutic Products Directorate (TPD) reviews pharmaceutical products and the Biologics and Genetic Therapies Directorate (BGTD) handles products derived from biotechnology. Monoclonal antibodies, including many of the newer cancer drugs, are approved through the latter body. (The suffix “mab” found in, for example, rituximab stands for “monoclonal antibody”. Drugs whose generic names end in “mib” or “nib” are also biological therapies.) For the purposes of this report, Health Canada is referred to as the body responsible for regulatory approval.

In regulatory terminology, “new drugs” refers not only to the first time a drug is licensed for marketing, but also the first time it is used in a different indication, or disease state. The following table defines the classifications and uses of drugs that require regulatory approval.

The Drug Approval Process

Health Canada reviews applications from manufacturers against its standards of safety and efficacy, which are aligned with, but not identical to, those in other countries. The review process can take from less than one year for priority or “fast-track” reviews to two or three years (or more) for non-life-saving drugs. Once approved, the company receives a Notice of Compliance (NOC) and a Drug Identification Number (DIN).

Before making a New Drug Submission to Health Canada for a new chemical entity, companies must do extensive preclinical and clinical testing. This is described in more detail in Appendix 6.

Table 1 New Drug Products as Defined Under the *Food and Drugs Act*

Approval Required	Definition
New chemical entities (NCEs)	Chemical structures that have never been administered to humans.
New indications	The use of an approved drug for a disease not previously treated with this product. e.g., Gleevec was already approved for leukemia and received additional approval for the treatment of gastrointestinal stromal tumours.
	The use of an approved drug in a new treatment regimen. e.g., Rituxan initially was approved in combination with CHOP chemotherapy to treat diffuse large-cell, B-cell non-Hodkgin's lymphoma. It later received an additional approval for use with the CHOP-R regimen.
New formulations	A new means of delivery of an approved drug. e.g., an extended-release tablet
Generics	A copy of an original, approved drug that meets certain pharmacological standards.
Biological products	Drugs derived from biological sources, either by extraction and purification or by recombinant technology.
Radio-pharmaceuticals	Combination drugs containing a chemical element and a radioisotope (e.g., Bexxar, Zevalin).

To prove the safety and efficacy of the drug, the manufacturer must conduct preclinical testing in at least two animal species. An Investigational New Drug (IND) submission is made before the drug can be tested in humans. Clinical trials in human subjects include three progressive phases of testing. At least two pivotal clinical trials including large populations of patients are usually required for a submission. For life-saving cancer drugs, however, Health Canada may agree to proceed with a review based on just the Phase I and Phase II clinical trial results. These include fewer patients and may also have less rigorous study endpoints (for example, surrogate markers such as laboratory values instead of clinical outcomes such as disease-free survival or time to progression of a tumour). In addition, manufacturing facilities and processes are examined and certified.

A Supplemental New Drug Submission is made for any subsequent new formulation and indication. This is a shorter document and review times are typically 18-24 months.

Under certain circumstances, a conditional Notice of Compliance (NOC/c) may be granted. Usually, this decision is reserved for drugs that are thought to provide a

clear (and sometimes urgently needed) benefit to patients, but around which there remain questions about safety. The approval to market the drug is predicated on a commitment by the manufacturer to conduct post-marketing safety studies to monitor for adverse events and/or collect further data on the drug's safety in specific patient populations. The following fourteen cancer and supportive care drugs had received conditional approvals as of July 2007.

Table 2 Cancer and Supportive Care Drugs With Conditional Approvals

Brand Name	Active Ingredient
Gleevec	imatinib mesylate
Sprycel	dasatinib
Taxotere	docetaxel
Femara	letrozole
Sutent	sunitinib maleate
Nexavar	sorafenib tablets
Aromasin	exemestane
Velcade	bortezomib mannitol boronic ester
Xeloda	capecitabine
Sativex	delta-9-tetrahydrocannabinol / cannabidiol
Femara	letrozole
Velcade	bortezomib
Arimidex	anastrozole
Iressa	gefitinib
Revlimid	lenalidomide

To expedite access to new medications, Health Canada is moving towards a progressive licensing system. In 2007, the ministry published its Blueprint for

Renewal II process which entails a comprehensive review of all aspects of the regulatory system. Much of the focus of the renewal process will be on lifecycle regulation of drugs, which formalizes the conditional approval mechanism described above.⁴⁴ Legislation was introduced in Parliament in April 2008 to provide the legal framework for this strategy and has provoked a range of opinions from healthcare providers, academics and patient groups.

Cancer Drug Approvals

Cancer drugs are generally developed and approved faster than other prescription drugs, for the following reasons.

1. Phase I and Phase II testing are combined. (Traditional Phase I studies that test drugs in healthy volunteers are not done for cancer drugs because of their toxicity).
2. Development is often done in collaboration with cancer research and clinical trials groups, making the process more efficient.
3. The regulatory review process can be expedited if the drug is very effective in treating serious or life-threatening illness.

Special Access Program

A manufacturer cannot market a drug until it receives a Notice of Compliance. However, for serious or life-threatening conditions, Health Canada may allow limited release under its Special Access Program while the drug is still under review. Health Canada will authorize the manufacturer to sell the drug prior to approval, provided that no alternative is available on the Canadian market. The cost of the drug may either be paid for by the manufacturer or by the patient (or their insurer).

Also, a patient who receives an experimental (i.e. unapproved) drug while he / she is a participant in a clinical trial may continue to receive the drug after the trial is completed under the Special Access Program.

The Special Access Program is widely used. In 2005, approximately 30,000 requests were processed and about 23,000 authorizations issued.⁴⁵ The Special Access Program is an important mechanism by which cancer patients who have no other options can access promising new drugs quickly. Commonly-used cancer drugs such as thalidomide (Thalomid) and cetuximab (Erbix) are only available through this Program (as of time of writing). However, public drug plans almost never cover drugs prior to approval and these are usually funded either by private insurers or by manufacturers.

Health Canada Drug Approval Concerns

Health Canada has historically had one of the slowest regulatory review times among OECD (Organization for Economic Cooperation and Development) countries. While the U.S. and other countries have taken measures to speed up their review processes since the 1990's, until recently Health Canada had not kept pace. Health Canada delays are often a major reason why patients travel to the U.S. for treatments that are still unapproved in Canada.

⁴⁴ "Blueprint for Renewal II: Modernizing Canada's Regulatory System for Health Products and Food"; Health Canada, 2007.

⁴⁵ OECD Health Working Paper "Pharmaceutical Pricing and Reimbursement Policies in Canada"; December 2006.

In 2003, Health Canada initiated its five-year Therapeutics Access Strategy to improve performance on regulatory timelines. According to the 2005 Annual Summary of Performance (latest available figures), significant progress has been made in eliminating the review backlog and towards issuing review decisions within performance targets. However, as Table 3 shows, a significant gap persists between the target and actual median review times, especially for biological products (including many cancer drugs).

Table 3 Performance Targets for First Review Cycle Concerning Market Authorization

Submission for New Brand Name Drug Target Times (calendar days)

Category	Target*	Median Actual (2005)
Priority Pharmaceutical	180 or 200	252
Standard Pharmaceutical	180 or 300	480
Priority Biological	180 or 200	603
Standard Biological	180 or 300	1149

* depending on submission class

A more recent update from Health Canada in 2007 stated that the backlog for submissions had been eliminated in September 2005 for pharmaceutical drugs and in September 2006 for biologicals. The same report also stated that Health Canada has now met its goal of issuing 90% of decisions on new pharmaceutical and biological drugs within internationally comparable targets (compared with just 13% and 16%, respectively, in 2003).⁴⁶

For cancer drugs, the gap may be less. Table 4 shows a list of 12 cancer drugs approved in Canada since 1994 for which dates of first approval elsewhere in the world could be found. According to these data, the delay in approval was a median of 0.8 years following a first introduction. This is a reasonable performance considering that part of this delay is because manufacturers usually submit for approval in larger markets first. Only the U.S., the UK and Germany had shorter timelines.⁴⁷ By this measure, Canada is within an acceptable range of international performance for approving cancer drugs.

Table 4 Delay in Approval of Cancer Drugs in Canada After First Global Introduction

Brand Name	Generic Name	Date of First Introduction	Date Canadian Approval	Delay (years)
Gemzar	gemcitabine	Jun 95	Feb 97	1.7
Rituxan	rituximab	Nov 97	Apr 00	2.4
Xeloda	capecitabine	May 98	Oct 98	0.4
Thalomid	thalidomide	Oct 98	Not yet approved	8.6+
Herceptin	trastuzumab	Oct 98	Aug 99	0.8
Temodal	temozolomide	Feb 99	Oct 99	0.7

⁴⁶ Health Products and Food Branch; Report on the 2004-07 Strategic Plan.

⁴⁷ Jönsson, B and Wilking, N; "A Global Comparison Regarding Patient Access to Cancer Drugs"; Annals of Oncology, June 2007.

Gleevec	imatinib	May 01	Oct 01	0.4
Iressa	gefitinib	Jul 02	Dec 03	1.4
Velcade	bortezomib	May 03	Feb 05	1.8
Avastin	bevacizumab	Feb 04	Nov 05	1.8
Alimta	pemetrexed	Feb 04	Jul 04	0.4
Tarceva	erlotinib	Nov 04	Jul 05	0.7

2. Pricing Approval: The Patented Medicines Prices Review Board (PMPRB)

Created in 1987 under the *Patent Act* as an independent quasi-judicial tribunal, the Patented Medicines Prices Review Board limits the prices set by manufacturers for all patented medicines sold in Canada – new and existing, prescription or over-the-counter – to ensure they are not excessive.

Prices Review Criteria

To determine whether the price of a patented drug sold in Canada is excessive, the Patented Medicines Prices Review Board applies factors set out in the *Patent Act* and in its price guidelines.

Table 5 PMPRB Prices Review Criteria

<ul style="list-style-type: none"> • Most new patented drug prices are limited so that the cost of therapy is in the range of the cost of therapy for existing drugs sold in Canada used to treat the same disease; • Breakthrough drug prices are limited to the median of the prices charged for the same drugs in other specified industrialized countries that are set out in the Patented Medicines Regulations (France, Germany, Italy, Sweden, Switzerland, U.K. and the U.S.). • Existing patented drug prices cannot increase by more than the Consumer Price Index (CPI); • In addition, the Canadian prices of patented medicines can never be the highest in the world.

Submissions to the Patented Medicines Prices Review Board are made by manufacturers within 60 days after the drug has been marketed, so this process does not add delays to the regulatory approval.

Implications Of Price Controls For Cancer Drugs

Because newer generations of cancer drugs are more expensive relative to older therapies, price controls have become a focus of attention.

For example, in June 2006, Bristol-Myers Squibb announced that it had decided not to market cetuximab (Erbix), despite its approval by Health Canada nine months prior, because the company could not agree with the Patented Medicines Prices Review Board on an appropriate price for its product. The Patented Medicines Prices Review Board would have approved a price at the median of the seven reference countries listed above, however the company argued that the price should be closer to that in the U.S. (and almost double that in Europe) because this price better reflected the value of the research and development that had gone into the

product⁴⁸. Erbitux is still available for sale at the European price under Health Canada's Special Access Program (described in the last section).

In recent years, the disparity in prices between European markets and the U.S. has increased dramatically as many European countries have used their monopoly positions to force price cut-backs from manufacturers. Because of Canada's price control rules, this has effectively reduced the prices Canadian subsidiaries can charge for their products. There is concern among manufacturers that these rules do not take into account the high costs of research and development (see Appendix 6 for a full discussion of these costs). Also, six of the seven comparator countries do not have comparable systems because their health systems are national. The Patented Medicines Prices Review Board is in the process of reviewing its Excessive Price Guidelines.⁴⁹

Another way that the Patented Medicines Prices Review Board's decisions affect cancer patients is demonstrated by a recent change in the way that free drugs provided by pharmaceutical companies affect their allowable pricing. As of a Federal Court ruling in March 2007, drugs provided free under a compassionate release program or trial prescription program are no longer exempt from the Patented Medicines Prices Review Board's calculation of the Average Transaction Price of that product in the Canadian market.⁵⁰ The reduced Average Transaction Price becomes the benchmark against which a price is set and against which price increases are allowed. This strict interpretation of the regulations by the Patented Medicines Prices Review Board has caused at least one company to discontinue its compassionate use program and further actions by manufacturers are anticipated. The Board is continuing to consult with stakeholders regarding this action, however the issue has not been resolved.

3. Cancer Drug Evaluation for Funding

Once approved by Health Canada, drug plan sponsors decide whether to include a product on their formulary, or list of drugs. The public drug plans, except for Quebec, have combined forces to achieve efficiencies in these reviews, and also to improve the process by which decisions are made.

The interim interprovincial Joint Oncology Drug Review provides an assessment and recommendation for new cancer treatment products. The Common Drug Review evaluates supportive care drugs required for the management of cancer symptoms such as pain, or for treatment side-effects such as anemia or nausea.

Once either the Joint Oncology Drug Review or the Common Drug Review evaluation is completed, the provincial drug plan managers consider their recommendations and apply their own individual evaluation criteria.

⁴⁸ PMPRB website <http://www.pmprb-cepmb.gc.ca/english/View.asp?x=669&mid=523> and interview with BMS's VP Corporate Affairs, 26 March 2007.

⁴⁹ Minutes of PMPRB meeting September 27, 2006. <http://www.pmprb-cepmb.gc.ca/english/View.asp?x=801&mp=125>

⁵⁰ PMPRB Newsletter Vol. 11, Issue 2, April 2007: <http://www.pmprb-cepmb.gc.ca/english/View.asp?x=857&mid=688>

Joint Oncology Drug Review

In March 2007 the Joint Oncology Drug Review was launched as a one-year pilot initiative. This came about from agreement between the premiers of Saskatchewan and Manitoba that national standards should be developed for evaluation of new cancer drugs as a means to help resolve interprovincial disparities. Other provinces soon joined and presently all provinces except Quebec participate.

Ontario was chosen and the starting point for developing a nationwide evaluation process and CancerCare Ontario accepts all new submissions on behalf of the participating provinces. These are reviewed by the Oncology Subcommittee, which is a collaboration between CancerCare Ontario and the Committee to Evaluate Drugs of the province's publicly funded drug plan, the Ontario Drug Benefit Program. A Steering Committee oversees the project, and an Advisory Committee ensures that best practices from other provinces are incorporated. The provinces are members of the Steering Committee and representatives of participating drug plans act as observers to the Ontario process. The territories participate *via* British Columbia and Alberta.

Implementation of the Joint Oncology Drug Review process is occurring as an emergent process. The Ontario system is considered as a "straw dog" to be continuously improved over time with the inputs of the provinces and other organizations (e.g., the Common Drug Review, the Canadian Partnership Against Cancer's Clinical Practice Guideline Group, the National Cancer Institute of Canada's Working Group on Economic Analysis).

In October 2007, two patient representatives were included as members of the Advisory Committee, nominated by cancer advocacy groups. A process of input and feedback is currently being developed that will allow patient groups to comment on the Review's activities and make recommendations for improvements.

The Joint Oncology Drug Review process will be evaluated between April and October 2008 and a formal recommendation for a permanent structure will be made to the Deputy Ministers of Health in January 2009. The recommendation will be based on a model incorporating best practices from across Canada and it has been proposed that patient groups are consulted as part of the evaluation process. Issues of concern to patient advocates include transparency, timeliness, flexibility, a holistic approach to cost-effectiveness analyses and an independent appeals process.

Common Drug Review

The Common Drug Review evaluates supportive therapies required for the management of symptoms of cancer and side effects and its treatment. Similar to the Joint Oncology Drug Review, the Common Drug Review process was put in place to provide efficiencies in the evaluation processes on behalf of the 20 provincial and federal government drug plans (Quebec does not participate).

The Common Drug Review was established in 2003 as a program of the Canadian Agency for Drugs and Technologies in Health. It conducts reviews of the clinical and cost effectiveness of new drugs and, as of April 2007, new indications for existing drugs.

Expert advice is provided to the Common Drug Review by the following committees:

- The Advisory Committee on Pharmaceuticals comprises representatives from the participating federal, provincial, and territorial publicly funded drug plans and other related health organizations. This committee provides advice on the Common Drug Review process, and pharmaceutical issues and assessments; and facilitates the effective sharing of pharmaceutical information.
- The Canadian Expert Drug Advisory Committee (CEDAC) is an independent advisory body composed of individuals with expertise in drug therapy and drug evaluation. This Committee makes recommendations to each of the participating federal, provincial, and territorial publicly funded drug plans regarding the listings on their formularies. Two members of the public were appointed to the Committee in October 2006.⁵¹

Concerns have been expressed that the addition of a Common Drug Review process would slow down drug approvals and that the motivation for recommendations would be cost-containment and not access to the best drugs. A recent review of the Common Drug Review conducted for Rx&D (the brand-name pharmaceutical industry association) concluded that the average review time falls within the target timelines of 20-26 weeks.

However, the study showed that from its inception in 2003 to May 2007, 53% of the 75 recommendations made by the Common Drug Review have been negative. Many fewer drugs were recommended than were approved by the four European countries for which data were available (Sweden, Switzerland, UK and France) but more than Australia or New Zealand.⁵²

The Standing Committee on Health held reviews of the Common Drug Review's performance during May 2007 and accepted input from all stakeholders. The pharmaceutical industry and many patient groups continue to disapprove of the low rate of positive decisions, and the lack of an appropriate appeals process. (Currently, decisions can only be appealed by manufacturers within a short timeframe following communication of the Canadian Expert Drug Advisory Committee recommendation. The Canadian Expert Drug Advisory Committee, and not an independent body, reviews the appeal.) Disease associations recommended improvements to the Common Drug Review's transparency processes and recommended inclusion of consumer-friendly explanations of its decisions.

In its report to the House of Commons in December 2007, the Standing Committee recommended that independent external performance evaluations of the Common Drug Review are conducted. Enhanced transparency was also identified as an area for improvement, as was increasing the level of public involvement. A clear and timely independent appeals process was also recommended.⁵³ The government responded in April 2008, agreeing to implement all of the recommendations except the independent appeals process, which it indicated would be discussed further with the participating provinces and territories.⁵⁴

⁵¹ CADTH Appoints New Chair and First Public Members to the Canadian Expert Drug Advisory Committee (CEDAC); 18 October 2006. (CADTH website)

⁵² International Comparison of Canadian Expert Drug Advisory Committee (CEDAC) Common Drug Review (CDR) Recommendations; Rx&D Report; November 2006.

⁵³ <http://cmte.parl.gc.ca/cmte/CommitteePublication.aspx?COM=13189&Lang=1&SourceId=228685>

⁵⁴ <http://cmte.parl.gc.ca/cmte/CommitteePublication.aspx?COM=13189&Lang=1&SourceId=233945>

Appendix 2

Provincial Cancer Drug Approval Systems

Content

1. Comparison of Provincial Coverage for Supportive Care Drugs
2. Cancer Treatment Drug Approval Processes by Province
3. QALYs – Measuring the Value of Clinical Outcomes

The systems of coverage for cancer treatment drugs were described in Part 1 of the report. This Appendix reviews the elements of provincial drug coverage not included in Part 1.

1. Comparison of Provincial Coverage for Supportive Care Drugs

Supportive care drugs are integral to cancer treatment regimens. Effective control of cancer symptoms and treatment of side effects allows patients to withstand more intensive treatment and to experience an improved quality of life.

What Are Supportive Care Drugs?

Supportive care drugs include treatments for the following:

- Nausea and vomiting
- Diarrhea
- Constipation
- Mouth Care / Stomatitis / Mucositis
- Anemia
- Extravasation (leakage of fluid outside blood vessels)
- Hypercalcemia (elevated calcium ion levels in the blood causing a range of debilitating symptoms)
- Hyperuricemia (elevated uric acid levels in the blood causing kidney and joint problems)
- Hypokalemia (elevated potassium ions in the blood causing cardiovascular and muscle abnormalities)
- Neutropenia (low white blood cell count causing increased susceptibility to infection)
- Infection
- Skin Care – Alopecia (loss of hair)
- Pain management
- Anorexia / Cachexia (loss of appetite, wasting)

Who Is Responsible for Covering Supportive Care Drugs?

Coverage for supportive care drugs is the responsibility of the provincial cancer agency in Saskatchewan only. In all other provinces and territories, hospitals cover

supportive care drugs administered to inpatients and the responsibility for outpatient supportive care drugs lies with the patient.

In most provinces, about one-fifth of the population is covered under the provincial drug plan and most of the remainder have private coverage (see Appendix 3 for details of insurance coverage by province). For patients dependent on the provincial or territorial plan, such as many seniors and low-income families, coverage of supportive drugs on the public drug plan formulary, or list of drugs, is very important.

Which Supportive Care Drugs Are Covered By Provincial and Territorial Formularies?

Generally, older cheaper medications are listed as full benefits on public formularies. The distinctions between provinces become apparent with the more expensive newer drugs. For example, the anti-nauseant Gravol (dimenhydrinate) is either covered by the drug plan for cancer patients or is available for a few dollars over-the-counter. However, Zofran (ondansetron) and other newer agents cost \$25 or more per pill and are not covered by many formularies. (The patent for Zofran recently expired allowing cheaper generics to come onto the market, but even at half the price this is still an expensive drug for many patients.)

Biological drugs used to treat anemia include Eprex (epoetin alfa, also known as erythropoietin or EPO) and its newer version Aranesp (darbepoetin alfa). Neupogen (filgrastim) and its advanced version, Neulasta (pegfilgrastim), treat neutropenia or reduction in white blood cell (neutrophil) counts. This group of drugs costs several thousand dollars per course of treatment. While both anemia and neutropenia are serious side effects of chemotherapy, both conditions will improve in time as the patient's own blood system recovers from the assault of chemotherapy. Treatment with one of these agents allows faster recovery so patients can receive chemotherapy for a longer duration or more frequently. The risk of infection may be reduced with Neupogen or Neulasta. Eprex and Aranesp reduce fatigue and potential cardiovascular complications.

Coverage for supportive care drugs on provincial formularies is variable, as shown in Table 1. For the sake of simplicity, Zofran and Kytril (granisetron) are chosen as examples of funding for expensive anti-nauseants, and Eprex and Neupogen are representative of the class of blood cell restorers, or haematopoietic agents.

The same cautions apply to this Table as to the interprovincial comparison shown in Part 1. The criteria for funding differ by province and a detailed explanation of coverage is not provided here. If the drug appears on the provincial formulary, it is indicated as covered (●) regardless of restrictions to its use. Likewise, it is indicated as not covered (×) if it is not listed, however it may be available to patients in exceptional circumstances.

Table 1 Funding Status of Selected Supportive Care Drugs by Province

	Zofran	Kytril	Eprex	Neupogen
BC	●	●	×	×
AB	●	●	●	●
SK	?	?	×	×
MB	●	●	●	●
ON	●	●	●	●
QC	●	●	●	●
NB	●×	●	●	●×
PE	●	×	×	×
NS	●	●	●	×
NL	●	●	●	●
YK	●	●	●	●
NT	●	●	×	●
NU	●	●	×	●
NIHB	●	●	×	●

Notes:

New Brunswick covers Zofran and Neupogen only for patients discharged from hospital and receiving treatment at home.

The Saskatchewan Cancer Agency, which is responsible for providing supportive care drugs, does not publish a formulary so it cannot be determined whether Zofran or Kytril are covered.

2. Cancer Treatment Drug Approval Processes by Province

The general process of evaluation for cancer drugs is as follows:

Assessment of Data Quality

The evidence presented by manufacturers is assessed for quality according to the scientific rigour and relevance of the studies. Large, double-blind, randomized, controlled clinical trials are the highest level of evidence; single cases are the lowest level and there are many gradations in between. The choice of comparator is important, because if this is not the same as the treatment regimen used in the evaluating jurisdiction, conclusions about the incremental benefit provided by the new treatment will be difficult to quantify. For example, gemcitabine (Gemzar) was denied funding in Ontario for the treatment of metastatic breast cancer because the comparator used in the studies was paclitaxel (Taxol) and not docetaxel (Taxotere).

How each province weighs the quality of evidence accounts for some of the disparity in funding decisions. Significant delays and denials can result if the submission is based on weak evidence. In Ontario, the manufacturer of bortezomib (Velcade) resubmitted additional studies over a period of almost two years before its request was finally accepted in 2006. Imatinib (Gleevec) received exceptional listing status in Ontario for use in gastrointestinal stromal tumours because the evidence was judged to be too weak to allow for unrestricted utilization.

Clinical Effectiveness Evaluation

Although Health Canada approves new drugs based on their demonstrated safety and efficacy, drug plan managers are interested in knowing how a new drug will offer incremental improvements over the current standard of care in their province.

The clinical evidence provided by the manufacturer consists of both published studies and proprietary information from the drug's clinical development program. In cancer, the treatment arms of the study usually compare the standard care with the combination of standard care plus the new drug. Because of this incremental approach, as each new drug in a category is marketed, the "bar" or standard against which its clinical benefit is measured is raised. While early chemotherapies were measured according to their effectiveness in prolonging survival or time-to-progression of disease, later agents had either to exceed these important parameters or to meet them and provide additional benefits such as increased tolerability (allowing higher, more effective dosing regimens), symptomatic benefits (e.g., tumour debulking), or convenience of administration (e.g., oral vs IV forms).

Another important consideration for drug access is that many new drugs are approved by Health Canada based on earlier, and therefore lower quality, data through its conditional approval process. While this approach is designed to speed up access, if formulary managers are not prepared to give an equally conditional form of approval to their funding decisions and instead continue to insist on higher quality data, these time savings will be lost as the process waits for the results of later, larger studies.

The importance of "real world" efficacy is also emerging as an important measure of effectiveness. Clinical studies are conducted with patients having minimal comorbidities and other risk factors such as advanced age, pregnancy, etc. Predicting how these results might translate to the patient population covered by the drug plan (i.e. the "real world") is essential to determining a new drug's expected efficacy and yet can be extremely difficult to evaluate from the data presented.

In cancer, it can be especially problematic to assess real-world efficacy because of the high levels of interpatient variability in the disease itself. Systems for collecting and analyzing data are required to maintain the detailed databases that enable these analyses and currently few jurisdictions have these in place.

Cost-Effectiveness Evaluation

Evaluation of cost-effectiveness is perhaps the area in which there is the least agreement and most controversy.

Drug plans require manufacturers to submit cost-effectiveness (also called pharmacoeconomic) studies of their drugs as part of their submission for approval. There are two main issues with this part of the evaluation.

The first issue is the threshold above which a drug is deemed to be cost-effective. The cost-effectiveness equation often boils down to one measurement: the assessment of cost per quality-adjusted life year (QALY) gained (discussed in more detail at the end of this Appendix). There is much speculation about the dollar value of this threshold, how it is employed and who decides that this is the right number. Transparency and public input are needed to ensure that societal values are incorporated into any determination of cost-effectiveness, however few formularies include public input in these decisions.

The second issue is that there is not a validated and accepted methodology for conducting and analyzing cost-effectiveness studies. Manufacturers are given little guidance and their analysis may or may not meet the requirements of the review committee. These studies are very expensive and are done as part of global clinical drug development programs which may not address Canadian needs, much less those of a particular province.

Also, in drug plans that cover all prescription drugs, cancer-specific considerations may not be taken into account. The impact of the new treatment on the overall cost of illness, including economic and social impacts measured over a lifetime, is rarely included in the analysis.

Provincial drug review structures vary widely in their capabilities in this area. Provinces such as Ontario and Quebec have developed teams of pharmacoeconomists to analyze the cost-effectiveness information provided by manufacturers. Health economists, ethicists and patients (in Quebec) sit on their review committees and have a vote on the decision.

British Columbia has similar pharmacoeconomic capabilities but does not include direct inputs from ethicists or patients. B.C. also uses a different cost-effectiveness measure than do other provinces – life-years gained, instead of quality-adjusted life years gained (QALYs). Uniquely, the B.C. Cancer Agency also retrospectively measures the health and cost outcomes of decisions through analysis of data in their cancer registry.

Although Alberta has both pharmacoeconomists and health economists on the drug review committee, they conduct only a descriptive, qualitative analysis and do not calculate a cost-effectiveness ratio. Saskatchewan does not have any pharmacoeconomists on staff but pharmacists on the review committee interpret the data provided by manufacturers and determine a QALY value. Manitoba deconstructs and rebuilds the evaluation provided by the manufacturer according to its own models.

The provinces in Atlantic Canada have smaller staffs and are not able to conduct such robust analyses. New Brunswick, Prince Edward Island and Newfoundland & Labrador do not conduct formal pharmacoeconomic reviews. Nova Scotia recently undertook a re-evaluation of its drug review methodologies and is including ethical and societal impacts in making funding decisions. Patients are also included as voting members on the review committee.

The territories rely on their provincial counterparts' formularies as a basis for their drug benefits lists. The Federal Pharmacy and Therapeutics Committee makes decisions for the NIHB (Non-Insured Health Benefits program covering First Nations and Inuit) and other federal drug plans, and requires a prior review by either the Joint Oncology Drug Review or the Common Drug Review.

Budget Impact Analysis

Based on the clinical and pricing information provided in the submission, the drug plan calculates the total number of patients expected to receive the new drug, and its aggregate incremental cost. As with other drugs, the impact of a new cancer drug's cost is considered only in terms of the drug budget, and does not incorporate measures of savings elsewhere in the health system or in the economy.

For most provinces, the total anticipated expense of adopting a new drug is a key element in the prioritization process. Ontario is the exception – only the cost-effectiveness ratio of the individual drug is considered in the funding decision. If this is a reasonable amount, the drug will be recommended to government for funding.

Drug Plan Prioritization

Drug plan managers must balance the priorities of all health areas for the short- and long-term impacts. Prioritization of cancer drug recommendations is a formal process in some provinces and not in others.

In British Columbia, a new drug review must include a recommendation for priority: highly recommend, recommend, recommend as a low priority and do not fund. In Saskatchewan, drug priorities are ranked according to the potential for curative benefit and to how many other drugs must be tried first (i.e. whether the new drug is used first, second or third-line). Once these new drug programs are prioritized, they are matched with the incremental budgets allocated by government. Drug programs that exceed the new funding provided are deferred until the next budget cycle. In Manitoba, cancer drug prioritization is recognized as a gap to be addressed.

In Quebec, incremental budgets may be made available for costly new programs for cancer drugs administered in hospitals, even though it is the individual hospital's responsibility to cover the cost of the drug. (The recent approval of bevacizumab (Avastin) in that province is an example of this process.) The Atlantic provinces do not have formal prioritization processes in place but recommend major incremental funding both during the annual budget cycle and, if needed, outside of these timelines.

The political realities of public pressure over cancer drugs can override managers' decisions, and the generosity of a particular government can influence the degree of rationing in the system. This was seen in relation to Herceptin funding when results of a new study showing significant improvement in survival in the adjuvant setting (i.e. after surgery, in earlier-stage HER2 receptor-positive breast cancer) were presented in June 2005 at an oncology meeting. Although not approved by Health Canada for this additional indication until 2006, breast cancer advocacy groups across the country successfully lobbied parliamentarians to fund this new program. Herceptin is now the highest-selling cancer drug in Canada.

Formulary Listing Status

The recommendation for funding includes the listing status of a new drug. Limitations may be placed on its use for safety reasons or as a means of controlling costs. Most cancer drugs have some form of limitation, and the terminologies are different in each province. 'Limited Use' criteria are usually fairly broad and there is rarely a strict mechanism in place to closely monitor use. 'Exceptional Drug Status' or 'Special Authorization' categories are much more narrowly defined and usually require prior documentation to be filed. Monitoring of use is done either formally or informally. In Alberta, the formulary includes a list of oncologists who must authorize the prescription.

Appeals

All provinces will allow an appeal to their funding decision based on new data. Companies continue to invest in clinical trials and as new results appear these are considered. This was the case for bortezomib (Velcade) in Ontario, where a decision

not to fund the drug was made based on the weakness of the clinical and cost-effectiveness data provided by the manufacturer. Further studies providing a more robust set of information allowed the review committee to come to a positive decision.

The Non-Insured Health Benefits (NIHB) program has an independent appeals process for claims that are denied. This is one area that the Joint Oncology Drug Review is being encouraged to pursue by patient advocacy groups.

3. QALYs – Measuring the Value of Clinical Outcomes

Pharmacoeconomic models are used to assess the cost-effectiveness of individual health technologies. Also, cost-utility analyses employing a calculation of cost-effectiveness can be used to compare different medical interventions and enable allocation of healthcare resources across the system to benefit the most people. Both of these applications are discussed below.

Pharmacoeconomic Ratios

Two models are most commonly used in evaluation of new drugs: 'life-years gained' and 'quality-adjusted life years gained' (QALYs). Most, but not all, drug formularies use QALYs, some preferring the 'cleaner' calculation of life-years gained to the cruder and potentially misleading calculation of a QALY.

There is great controversy about the use of QALYs, since this is an inexact science, subject to interpretation and difficult to validate. The attractiveness and simplicity of a number makes QALYs potentially dangerous in decision-making. Such analyses should be viewed with caution and in a comparative context wherever possible.

QALYs in Evaluating New Drugs

A cost-effectiveness ratio such as a \$-per-QALY is used to determine the value of a drug. The calculation includes both clinical endpoints such as increased survival or cure and also quality-of-life measures linked to a change in health status. In cancer, the incremental benefit is measured against the standard treatment.

Cost-effectiveness data is usually collected during the clinical studies conducted for registration of the drug. These involve relatively large populations of patients designed to prove the clinical efficacy and safety. Quality of life measurements are incorporated into the study design.

Calculation of QALYs

QALYs are calculated as follows:

- A year in perfect health is assigned a value of 1.0, and death is valued at 0. If the years gained through the treatment would not be lived in full health then the extra life-years are given a value between 0 and 1.

- The values between 0 and 1 are usually determined by methods such as:
 - Time-trade-off (TTO). Patients are asked to choose between remaining in a state of ill health for a period of time, or being restored to perfect health but having a shorter life expectancy.
 - Standard gamble (SG) - Patients are asked to choose between remaining in a state of ill health for a period of time, or choosing a

- o medical intervention which has a chance of either restoring them to perfect health, or killing them.
- o Visual analogue scale (VAS) - Patients are asked to rate a state of ill health on a scale from 0 to 100, with 0 representing death and 100 representing perfect health.
- o Other methods include specific questionnaires such as the "EQ-5D", a descriptive system consisting of 5 dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression.

QALY Thresholds – How Much Is Too Much?

Drug plan managers do not use a defined threshold but rather a range of values below which a drug will be considered cost-effective and above which it will be considered to provide too little value. For drugs falling in between these two extremes, other qualitative factors are brought to bear in making a final determination.

An example of this approach comes from the UK:

Evidence quality	Cost per QALY gained (£)			
	<£3K	£3–20K	>£20K	Negative
I. At least one randomised controlled trial	Strongly recommended	Strongly recommended	Limited support	Not supported
II. Well designed controlled trial	Strongly recommended	Supported	Limited support	Not supported
III. Expert consensus or opinion	Supported	Limited support	Limited support	Not supported
IV. Conflicting or inadequate evidence	Not proven	Not proven	Not proven	Not supported

Source: Bandolier (UK)

This methodology incorporates the quality of evidence on which the calculation is based, to guard against making hard decisions from soft facts.

The threshold of \$50,000 per QALY is widely discussed. This reported figure came from a study of renal dialysis patients conducted in the U.S. in the 1970s. It has also been noted by several authors that \$50,000 is widely used in Europe as a benchmark. Critics of QALYs argue that there is no empirical basis for this figure and that in practice healthcare managers will pay much more for effective treatments.

A recent international comparison of cancer drug access noted that the UK is the only country that acknowledges a threshold cost per QALY at £20-30,000 (\$45-65,000 CDN). The WHO meanwhile has recommended that interventions costing less than 3 times GDP per capita for each Disability-Adjusted Life Year (DALY) saved should be funded.⁵⁵ Europe is in the process of establishing a formal network of health

⁵⁵ Jönsson, B and Wilking, N; "A Global Comparison Regarding Patient Access to Cancer Drugs"; Annals of Oncology, June 2007.

technology assessment agencies to achieve economies of scale and more international cooperation on this topic is expected in future.

Application to Healthcare Resource Allocation

One of the advantages of a \$-per-QALY approach is that different healthcare interventions can be compared, provided that the methods to collect the cost and quality of life data are consistent.

An example of how interventions that are funded within the same health system can vary in cost-effectiveness is provided by the following study from the UK:

Intervention	£/QALY at 1990 prices
Cholesterol testing and diet therapy (all adults aged 40–69)	220
Neurosurgical intervention for head injury	240
GP advice to stop smoking	270
Neurosurgical intervention for subarachnoid haemorrhage	490
Antihypertensive treatment to prevent stroke (ages 45–64)	940
Pacemaker implantation	1,100
Hip replacement	1,180
Valve replacement for aortic stenosis	1,410
Cholesterol testing and treatment (all adults aged 40–69)	1,480
Docetaxel (as opposed to paclitaxel) in treatment of recurrent metastatic breast cancer	1,890*
CABG (left main-vessel disease, severe angina)	2,090
Kidney transplantation	4,710
Breast cancer screening	5,780
Heart transplantation	7,840
Cholesterol testing and treatment incrementally (all adults aged 25–39)	14,150
Home haemodialysis	17,260
CABG (one-vessel disease, moderate angina)	18,830
Hospital haemodialysis	21,970
Erythropoietin treatment for anaemia in dialysis patients (assuming 10% reduction in mortality)	54,380
Addition of interferon-α2b to conventional treatment in newly diagnosed multiple myeloma	55,060 [§]
Neurosurgical intervention for malignant intracranial tumours	107,780
Erythropoietin treatment for anaemia in dialysis patients (assuming no increase in survival)	126,290

* Adjusted to 1990 prices using *Hospital and Community Health Service Pay and Prices Index, Unit Costs of Health and Social Care*. PPSSRU, 1996. (2,431 ÷ 200.7 × 155.6 = 1,890. [§] Translated into 1990 prices, as above

Source: Bandolier (UK)

Appendix 3

Prescription Drug Insurance

Content

1. Insurance Status of Canadians
2. Eligibility Criteria for Federal Drug Plans
3. Cost-Sharing Requirements of Public Drug Plans
4. Private Insurance Cost-Sharing
5. Advantages of the Employer-Sponsored Insurance Model

Issue 2 in Part 2 of this report summarized by province where insurance coverage was needed by cancer patients and discussed the types of drug insurance plans available and the eligibility criteria for the provincial drug plans.

This Appendix provides additional detail on the insurance status of Canadians, and outlines the eligibility criteria for federal drug plans. Cost-sharing requirements for both provincial and private drug plans are also presented.

1. Insurance Status of Canadians

Canadians require insurance to cover the costs of drugs administered outside hospitals. Insurance can be provided by the provincial cancer agency, by the provincial drug plan or by private insurance, depending on the province and on whether the person is eligible for coverage.

How Is 'Coverage' Defined?

The question of who is covered by insurance for prescription drugs is surprisingly difficult to answer. 'Coverage' can be defined in different ways and, just because an individual is a beneficiary of an insurance plan, their coverage cannot be assumed to be adequate.

There is a gradient of coverage which makes clean comparisons difficult. Insurance plans can pay for:

- All costs of prescriptions
- Costs above a deductible amount, either:
 - Fixed annual deductible
 - Deductible based on a percentage of income
- Partial costs of prescriptions
 - Pharmacy dispensing fee
 - Fixed payment per prescription
 - Percentage of the cost of a prescription

Some insurance plans will also require an annual premium to be paid, regardless of whether any claims are made for prescription drug costs.

Another complicating factor is that individuals may have several sources of coverage. Drug plans handle this by declaring themselves to be payers of first or last resort.

Retirees covered by an employer’s plan, for example, would be required to use this first and the provincial plan may top up coverage to 100% of the cost. (Some plans will even coordinate benefits between plans so that the process is seamless for beneficiaries.) In a statistical analysis, individuals with multiple sources of coverage would show as being insured both by their private insurance and the provincial plan.

In an attempt to present an accurate picture of how many Canadians are covered by the different types of plans available, two sets of data are shown below.

Who Is Registered with an Insurance Plan?

Table 2 shows the percentages of Canadians covered by different categories of insurance for the costs of both cancer treatment and supportive care drugs.

Data for this table was taken from a mix of sources, so caution should be used in its interpretation.

- Information on coverage by private and federal plans was provided courtesy of Applied Management (from the updated database used to calculate Canada’s catastrophic drug coverage requirements for the Kirby Commission).
- Coverage by provincial formularies was taken from published government sources. Some provinces may interpret ‘coverage’ by the provincial plan to mean the percentage of eligible residents, while others may report only the number of beneficiaries who have actually applied for coverage. Since Saskatchewan is the only province that covers the cost of all cancer treatment and supportive care drugs, 100% of residents are covered by the provincial plan.

By this categorization, 15% of Canadians have no coverage – a higher figure than other published estimates. The difference is due to the perspective taken for this summary. ‘No Coverage’ in this context means that these individuals have not applied for coverage by an insurance plan. If, however, their income levels dropped and/or if they incurred catastrophic drug expenses, those residents of a province with an income-based provincial plan (i.e., outside of New Brunswick or Prince Edward Island) would be covered.

Table 2 Coverage of Canadians for Cancer Treatment and Supportive Care Drug Expenses

Province	Private	Federal		Provincial Plan	Not Covered	Total
		NIHB	Veterans			
NL	48%	3%	1%	40%	8%	100%
PEI	52%	1%	0%	20%	27%	100%
NS	58%	1%	2%	20%	19%	100%
NB	52%	1%	1%	18%	28%	100%
QC	59%	1%	0%	40%	0%	100%
ON	56%	1%	0%	23%	20%	100%
MB	63%	10%	1%	26%	0%	100%
SK	0%	0%	0%	100%	0%	100%
AB	52%	3%	0%	16%	29%	100%
BC	54%	3%	1%	19%	23%	100%
Terr.	17%	53%	0%	20%	10%	100%
Canada	54%	2%	0%	28%	15%	100%

Sources: Applied Management; Personal Communication, 15 June 2007 and provincial drug plan estimates (from website documents).

Who Is Covered for Catastrophic Drug Expenses?

Of particular concern to cancer patients is whether coverage extends to include catastrophic drug expenses.

As mentioned above, residents of most provinces would be covered by an income-assessed or universal provincial plan for catastrophic drug expenses. The threshold defining 'catastrophic', however, varies by province. In Ontario and British Columbia, drug expenses over 4% of net household income are covered, whereas in Manitoba it is 5.5% and in Newfoundland & Labrador 10%. Nova Scotia applies a combination of income-based deductible and co-payment that can exceed 10% of family income.

Nationally, 8.5% of Canadian households reported spending 4% or more of after-tax income on prescription drugs in 2004, a figure that has been rising steadily from 6.5% in 1997⁵⁶.

Looking at catastrophic coverage from the perspective of ability to pay reveals some surprises. A 2004 study from the University of British Columbia⁵⁷ applied the cost-sharing rules from provincial drug plans to a nationally representative set of 4,860 household types differing in size, age composition, income and drug expense levels. They then analyzed what percentage of household income Canadians would have to pay out-of-pocket under each of these rules.

The patterns from this study are clear, as shown in Table 3. Western Canada has the lowest percentages of residents who would have to pay more than 4% of their net income on prescription drug costs (the widely accepted threshold defining 'catastrophic'), mainly due to their universal drug plans. The lack of public insurance coverage in the Atlantic provinces means that many families would be faced with paying these costs privately. (The extended coverage recently offered by Newfoundland & Labrador and by Nova Scotia are not included in these calculations since they came into effect after this study was completed.) Ontario's catastrophic drug plan, the Trillium Drug Program, means that no family pays over 4% of their income on prescription drug expenses. The results for Quebec are surprising. Twenty-six per cent of seniors and 11% of non-senior households would have to pay more than 4% of their income on drug costs. This is despite the policy in Quebec of universal mandatory drug insurance and demonstrates the financial burden of the provincial plan's premiums and co-payment structures. None of the three territories has a catastrophic drug program, although all cancer patients are covered by the territorial plans.

⁵⁶ Healthy Canadians. A federal report on comparable health indicators 2006, p. 21.

⁵⁷ Coombes, et al.; "Who's the Fairest of Them All? Which Provincial Pharmacare Model Would Best Protect Canadians Against Catastrophic Drug Costs?"; Longwoods Review Vol. 2 No. 3, 2004.

Table 3 Provincial Comparison of Senior and Non-Senior Households' Out-of-Pocket Expenditures on Prescription Drugs as a Percentage of Household Income

Table 3. Percentage of senior households by out-of-pocket expenditure on prescription drugs as a percentage of annual household income, by province										
	BC	AB	SK	MB	ON	QC	NB	NS	PE	NF
<1%	44.1%	65.7%	22.9%	22.9%	81.1%	2.1%	6.5%	12.5%	38.6%	32.5%
1-1.9%	46.6%	18.8%	14.6%	14.6%	18.8%	13.0%	15.9%	23.5%	33.7%	17.6%
2-2.9%	8.8%	6.0%	25.1%	26.0%	0.1%	23.1%	16.5%	15.0%	16.1%	24.7%
3-3.9%	0.4%	1.7%	37.3%	36.5%	0.0%	26.0%	19.1%	7.8%	7.3%	6.0%
4-4.9%	0.0%	5.2%	0.0%	0.0%	0.0%	21.2%	25.9%	12.2%	3.0%	0.4%
5-5.9%	0.0%	2.5%	0.0%	0.0%	0.0%	14.7%	16.1%	28.9%	1.1%	13.7%
10-14.9%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.1%	0.1%	0.8%
15-19.9%	0.0%	0.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.1%	4.2%
>=20%	0.0%	0.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

Table 4. Percentage of non-senior households by out-of-pocket expenditure on prescription drugs as a percentage of annual household income, by province										
	BC	AB	SK	MB	ON	QC	NB	NS	PE	NF
<1%	54.1%	43.3%	54.1%	54.1%	52.4%	17.5%	50.0%	50.0%	57.2%	54.1%
1-1.9%	19.1%	38.7%	17.2%	17.2%	26.1%	36.1%	21.4%	21.4%	20.7%	19.1%
2-2.9%	11.7%	10.6%	7.3%	13.1%	12.5%	24.5%	9.1%	9.1%	8.2%	8.3%
3-3.9%	11.6%	4.3%	21.4%	15.5%	9.1%	11.0%	6.3%	5.8%	4.3%	5.6%
4-4.9%	3.6%	0.9%	0.0%	0.0%	0.0%	6.7%	1.8%	2.1%	1.5%	1.6%
5-5.9%	0.0%	2.1%	0.0%	0.0%	0.0%	4.2%	8.4%	8.6%	6.5%	8.3%
10-14.9%	0.0%	0.1%	0.0%	0.0%	0.0%	0.0%	0.7%	0.7%	0.6%	0.7%
15-19.9%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	1.9%	1.9%	0.9%	1.9%
>=20%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.4%	0.4%	0.0%	0.4%

2. Eligibility for Federal Drug Plans

The federal government assumes the full cost of providing prescription drugs for some aboriginal populations and certain armed forces veterans. Special groups such as refugees are also covered on a temporary basis.

Table 4 Federally-Funded Drug Plans

Federal Plan	Eligible Groups
National Defence Health Services	Members of the Regular Force and members of the Reserve Force may be eligible for prescription drug benefits.
Correctional Services of Canada (CSC)	CSC provides essential health services for all Federal inmates. These services include the provision of prescription drugs.
Non-Insured Health Benefits Program	The Non-Insured Health Benefits (NIHB) Program of the First Nations and Inuit Health Branch (FNIHB) of Health Canada provides a range of medically necessary goods and services to eligible First Nations (including registered Indians under the terms of The Indian Act) and recognized Inuit clients in Canada. These goods and services, which include prescription medications, supplement benefits provided through other private, federal, provincial and territorial healthcare programs.

Veterans Affairs Canada	Veterans Affairs Canada (VAC) provides a wide range of benefits and services, including prescription drugs, to qualified veterans, still-serving Canadian Forces members, RCMP members, and certain civilians as well as their dependants and survivors.
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Eligibility for provincial plans is summarized in Issue 2.

3. Cost-Sharing Requirements of Public Drug Plans

All provinces require cost-sharing payments by at least some of its beneficiaries. These are summarized in Table 5.

Table 5 Cost-Sharing Requirements of Provincial Drug Plans

Prov.	Plan Name	Beneficiaries	Premium	Deductible	Co-payment	Maximum Payments
BC	Pharmacare	Less than \$15,000	n/a	2% net income	30%	2% net income
		\$15,000 - \$30,000	n/a	2% net income	30%	3% net income
		over \$30,000	n/a	3% net income	30%	4% net income
	Enhanced Assistance (Born before 1939)	Less than \$33,000	n/a	None	25%	1.25% net income
		\$33,000 - \$50,000	n/a	1% net income	25%	3% net income
Pharmacare	Social assistance recipients	n/a	None	None	None	
AB	Non-Group Plan	All residents of Alberta	Regular: \$246 single \$492 family Subsidized: \$172.20 single \$344.40 family	n/a	30% to max. \$25 per Rx	Max. \$25,000 claims per year
	Coverage for Seniors	Seniors	None	n/a	30% to max. \$25 per Rx	Max. \$25,000 claims per year*
	Health Benefits Card	Income Support recipients	None	n/a	None	None

Prov.	Plan Name	Beneficiaries	Premium	Deductible	Co-payment	Maximum Payments
MB	Pharmacare	Net income of \$15,000 or less	n/a	2.56% of adjusted total family income*	None	Deductible amount
		\$15,000 to \$40,000	n/a	3.83%	None	Deductible amount
		\$40,000 to \$75,000	n/a	4.41%	None	Deductible amount
		over \$75,000	n/a	5.51%	None	Deductible amount
ON	Ontario Drug Benefit	<u>Seniors:</u> Net income of \$16,017 (single) or \$24,174 (couple)	n/a	None	None	\$0
		<u>Seniors:</u> Net income over \$16,017 (single) or \$24,174 (couple)	n/a	\$100	\$6.11 per Rx	None
		Social assistance	n/a	None	\$2 per Rx	None
	Trillium Drug Program	Non ODB-eligible residents	n/a	Up to 4% of net income**	\$2 per Rx	Deductible amount
QC	RAMQ	Adults not eligible for a private plan, including seniors not receiving GIS	\$0-\$557 <i>per</i> adult depending on income	n/a	30%	\$904 max payment
		Seniors receiving partial GIS (<94%)	\$0-\$557 <i>per</i> adult depending on income	n/a	30%	\$579 max payment
		Seniors receiving 94-100% GIS	None	n/a	None	\$0
		Employment assistance recipients	None	n/a	None	\$0

Prov.	Plan Name	Beneficiaries	Premium	Deductible	Co-payment	Maximum Payments
NB	NB Prescription Drug Benefit Plan	Seniors receiving GIS or income <\$17,198 (single) or <\$26,955 (couple)	n/a	n/a	\$9.05	\$250
		Social assistance	n/a	n/a	\$4 adult \$2 child	\$250
PEI	Family Health Benefit Program	Net family (at least one child) income <\$22,000, plus \$2,000 for each additional child	n/a	n/a	Pharmacy fee	None
	Seniors' Drug Cost Assistance Program	Age 65 and over	n/a	n/a	\$11.00 plus pharmacy fee	None
	Financial Assistance Program	Social assistance recipients	n/a	n/a	None	\$0
	High Cost Drugs Program	Gleevec and Xeloda and net household income of less than \$150,000	n/a	n/a	From \$7 to 100% of Rx cost	None
NS	Drug Assistance for Cancer Patients	Gross family income <\$15,720. Covers cancer-related medications only.	None	n/a	Up to \$5	None
	Pharmacare	Seniors	\$424	n/a	33%	\$382 max copayment. \$806 total payment maximum
		Seniors receiving GIS	None	n/a		\$0

Prov.	Plan Name	Beneficiaries	Premium	Deductible	Co-payment	Maximum Payments
		Seniors with incomes <\$24,000 (single) or <\$28,000 (couple)	Reduced premium	n/a	33%	\$382 max copayment
		Employment Support and Income Assistance	None	n/a	\$5	None
		Family	n/a	Income-based percentage	20%	Income-based deductible + co-pay maximum
NL	NL Prescription Drug Benefit Plan	Seniors receiving GIS	n/a	n/a	Pharmacy fee	None
		Income assistance recipients	n/a	n/a	Pharmacy fee	None
		All residents	n/a	n/a	100%	5% - 10% net family income
	Low Income Drug Program		n/a	n/a	20% to 70% of costs depending on income	5% - 10% net family income
YK	Pharmacare	Seniors Cancer patients	n/a	single: \$250 family:\$500	None	None
NT	Extended Benefits	Seniors Cancer patients	n/a	None	None	None
NU	Extended Benefits	Seniors Cancer patients	n/a	None	None	None
NIHB		First Nations and Inuit	None	None	None	None

* Subtract \$3,000 from income of one spouse

** Information on how to calculate the deductible is available on the website of the Ontario Ministry of Health and Long-Term Care.

Cancer-Related Provisions of Provincial and Territorial Drug Plans

Various provinces and territories have put the following measures in place that are important to cancer patients:

- Coverage of all cancer treatment drugs, whether administered in hospital or at home, is provided to all residents free of charge in British Columbia, Alberta, Saskatchewan (Saskatchewan also covers supportive care drugs) and in the three territories (Yukon, Northwest Territories and Nunavut).
- Deductible payments and premiums can be made by installments in some provinces; Quebec has maximum monthly payments, over which 100% of drug costs are covered.
- Reductions in deductible amounts following a sudden drop in income may be available in some plans.

4. Private Insurance Cost-Sharing

Information about cost-sharing provisions of individual private insurance plans is not available since each plan is individually structured, however this is an increasingly used method of maintaining rapidly increasing drug costs at levels that sponsoring employers find reasonable.

A 2004 study by global benefits consulting firm Watson Wyatt reported that, in the U.S., plans with co-payments became more common in the period 2000-2003, increasing from 48% to 55%. Plans including both a co-payment and a deductible accounted for about 30% of plans. An average of 20% of costs were paid by beneficiaries. The same report noted that annual deductibles averaged US\$261 and annual out-of-pocket maximums averaged US\$1,433 in 2003.⁵⁸ Comparable Canadian figures are not available.

Private health plans can be regulated by the provinces and territories, resulting in different policies across Canada. For instance, while risk selection is allowed in most provinces, it is prohibited in Quebec. Since 1997, prescription drug insurance coverage has been compulsory for all Quebecers, either through private plans or the public drug plan; as well, termination of coverage is regulated and insurers have the obligation to pool risks in the private system. Private plans are further required to maintain minimum coverage standards (they must be at least as generous as the provincial public plan in terms of coverage and they have no latitude to deny claims). Quebec also requires private plans to undertake education and prevention activities in order to optimize drug coverage.⁵⁹

5. Advantages of the Employer-Sponsored Insurance Model

One of the interesting aspects of the employer-sponsored model is the holistic perspective taken. Because employers also foot the bill for disability insurance, which is enormously expensive, they are concerned not only with the costs of drugs but also with the productivity costs of illness. Companies who invest in new cancer

⁵⁸ Roland McDevitt; Medical Benefits and Cost Sharing Trends, 2000-2003; Watson Wyatt Worldwide; September 2004.

⁵⁹ Valérie Paris and Elizabeth Docteur; "Pharmaceutical Pricing And Reimbursement Policies In Canada"; OECD Working Paper; 22-Dec-2006.

drugs than enable patients to recover more quickly and attain a higher quality of life (decreased fatigue, better mental functioning, etc.) can return to productivity sooner, thus avoiding longer-term disability payments.

Appendix 4

How Cancer Patients Cope With Financial Burdens

Content

1. What Are the Financial Burdens Faced by Cancer Patients in Canada?
2. What Are the Trends?
3. What Are Patients' Coping Strategies for Managing Unaffordable Drug Costs?

1. What Are the Financial Burdens Faced by Cancer Patients in Canada?

For many cancer patients, the added out-of-pocket costs for prescription drugs are part of a greater financial burden related to their illness. A study in Alberta reported that some 25% of cancer patients will require the services of social workers to deal with financial and practical issues.⁶⁰

In a survey of patients in five Ontario cancer centres, the mean monthly out-of-pocket cost (including medications, medical supplies and care-giver services) was \$213, with an additional \$372 related to imputed travel costs. For those patients who reported their financial burden to be 'significant' (16.5%), their out-of-pocket cost was \$452. In the case of patients responding that their burden was 'unmanageable' (3.9%), their out-of-pocket cost was \$544. (These statistics reflect the observations of volunteers and social workers who estimate that a small minority of patients currently have trouble accessing medications but for these individuals the problem is enormous.) The survey also showed that 35.6% of patients required others to take time from work and this was higher in the under-65 category. The mean number of days lost from work in the previous 30 days for these caregivers was 7 days.⁶¹

A similar study (co-sponsored by the Canadian Cancer Society) showed the following patterns in Newfoundland & Labrador

"One in three (34%) rural cancer patients pay more than \$200 out-of-pocket for travel and lodging for a single visit to an oncologist, one in 11 cancer patients (9%) pay more than \$1,000, and some pay over \$5,000. More rural than urban patients cite travel time, and the costs of travel, childcare, and drugs as key factors influencing decisions about their care....To reduce out-of-pocket costs, some cancer patients ration their medications, extend the time between follow-up visits, or choose to go into hospital rather than die at home. Although most patients do not spend any money on drugs, 10 per cent spend more than \$100 each month."⁶²

Patients in remote communities have to face additional costs of travel to receive treatment. While attempts are being made to provide treatment closer to home, this

⁶⁰ Carlson, LE and Bultz, BD; "Benefits of psychosocial oncology care: Improved quality of life and medical cost offset"; Health and Quality of Life Outcomes, 2003.

⁶¹ Longo, CJ et al.; "Financial and family burden associated with cancer treatment in Ontario, Canada"; Supportive Care in Cancer; Volume 14, Number 11 / November, 2006

⁶² Mattews, M and Basky, G "Closer to home: The burden of out-of-pocket expenses on cancer patients in Newfoundland & Labrador" (book); Memorial University, Newfoundland, 2001.

will remain a reality for many regions of Canada. The three territorial health plans and the Non-Insured Health Benefits (NIHB) program covering First Nations and Inuit will subsidize medical travel costs, however the patient must bear part of the costs themselves. This results in financial hardship for many families in the north.

2. What Are the Trends?

The major trend in prescription drug expenditures is its continuing double-digit annual growth. Drug costs have grown by an average of 10.5% during the past ten years – more than triple the rate of inflation.⁶³ Drug plan managers in both the public and private sectors are struggling to control these outlays.

Cost Shifting from Public to Private Sector

Over the past two decades, private insurers have picked up a greater percentage of prescription drug costs, as seen in Table 1. The total growth in private insurers' costs has escalated much more than that of either the public plans or individuals.

Table 1 Sources of Finance for Prescription Drugs 1988 and 2006 (\$ millions)

	Public	Private Insurers	Out-of-Pocket	Total
1988	\$1,703	\$1,130	\$904	\$3,736
2006	\$9,618	\$7,558	\$3,913	\$21,090
Total Growth	465%	569%	333%	465%

Source: Canadian Institutes for Health Information

While both public and private drug plans are facing escalating costs, they have responded in different ways. Public plans have contained costs by limiting access to drugs and, in some provinces, by imposing cost-sharing requirements. Private plans have sought greater funding from the employer sponsors and from beneficiaries. Very few private plans have limited access to drugs and most have increased the cost-sharing requirements.

Limiting Access to New Drugs

One way the public sector has contained costs is through limiting access to newer, more expensive medications. Patients are increasingly restricted in the number of drugs to which they have access through publicly-sponsored drug plans. Limitations on the use of new drugs through prior authorization, limited use or exceptional access criteria are increasingly common for newer drugs. Some formularies refuse to list drugs beyond a certain threshold of cost-effectiveness despite their clinical benefit and this has sparked controversy. For patients requiring a drug that has been recommended as the clinical standard of care, but is unfunded, private payment is the only route of access.

Although until now most private insurers have automatically listed all new drugs, the industry is closely examining the impact of expensive new drugs for cancer, multiple sclerosis, psoriasis and rheumatoid arthritis. The vast majority of private insurance plans will pay for all cancer drugs, however anecdotal reports suggest that a significant minority of private insurers have inconsistent policies that can change during the course of a patient's treatment.

⁶³ CIHI; Drug Expenditure in Canada, 1985 to 2006.

Shifting Costs onto Individuals

Although out-of-pocket expenses have grown at a slower rate than those of the drug plans, they have still risen at more than six times the rate of inflation. A small part of this increase is driven by patients paying out of pocket for drugs that are not covered by their insurance plan. The majority of the increase comes from cost-shifting from drug plans onto individuals.

This includes cost-sharing requirements such as co-payments, premiums and deductibles. In addition, annual and lifetime caps transfer some of the responsibility for payment to the individual. For cancer patients, this is a serious concern. As was seen in Part 2, the out-of-pocket expenses for cancer treatment and supportive care drugs can be very high, even for patients with insurance.

3. What Are Patients' Coping Strategies for Managing Unaffordable Drug Costs?

The impact of cost-shifting onto patients has unintended health consequences that are well documented in the Canadian health literature.

Increased Use of the Health System

Researchers in several provinces have tracked the impact on patients of cost-sharing measures adopted over the last ten years or so.

Following Quebec's introduction of user fees, researchers from McGill University documented reductions in essential prescription drug use which resulted in increased rates of adverse events and use of emergency departments among drug plan beneficiaries.⁶⁴

Similarly, a study from the University of British Columbia examined the impact of co-payments on health services utilization by patients with rheumatoid arthritis. Increased use of the health system (physician visits, hospital admissions) correlated with a decreased number and frequency of prescriptions filled among patients who had to pay for part of their prescription cost compared to those for whom the prescriptions were free.⁶⁵

Underuse of Prescription Drugs and Cutting Back on Other Necessities

A recent study from the U.S. Veterans Administration system which identified surveyed 4,055 adults taking prescription medications for one of five chronic diseases concluded:

"Overall, 31% of respondents reported pursuing at least one of the [following] strategies over the prior 12 months. Twenty-two percent had cut back on necessities, 16% had increased their debt burden, and 18% had underused prescription drugs. Among patients who underused their medication, 67% also had cut necessities or

⁶⁴ Tamblin, R. et al. "Adverse events associated with prescription drug cost-sharing among poor and elderly persons." JAMA. 2001 Jan 24-31;285(4):421-9.

⁶⁵ Anis, AH et al. "When patients have to pay a share of drug costs: effects on frequency of physician visits, hospital admissions and filling of prescriptions"; Canadian Medical Association Journal, vol. 173 no. 11, p. 1335, November 2005.

increased debt. ... [The] use of all these strategies was especially common among patients who were low-income, in poor health, and taking multiple medications.⁶⁶

In a large health survey, of 13,587 Canadian patients who were prescribed medications, 9.0% said they did not take them as prescribed because of cost concerns.⁶⁷

Who Is Most Vulnerable to Increased Costs for Prescription Drugs?

To help answer the question of who is most vulnerable to cost-shifting measures, a joint Canada-U.S. study analyzed predisposing socioeconomic factors in patients for whom cost was a reason for not to adhere to their prescriptions. Table 2 shows the percentage of patients and the relative odds ratio of 123,977 U.S. and Canadian patients who were non-adherent. These individuals were more likely to be: uninsured, having a low income, in a poorer state of health, experiencing debilitating pain and seeing a doctor more frequently.⁶⁸

Table 2 Population Predisposing Factors of Cost-Associated Nonadherence Among Adults ≥18 Years in the United States and Canada

Comparison Group	Nonadherence Due to Drug Cost (%)	Odds Ratio (Multivariate Model)
<i>Country of Residence</i>		
U.S.	16.5	2.0
Canada	9.0	Referent
<i>Household Income</i>		
Lowest quintile	34.2	3.4
Second-lowest quintile	19.1	2.2
3 rd , 4 th or 5 th quintile	7.6	Referent
<i>Self-Assessed Health Status</i>		
Good, very good or excellent	12.4	Referent
Fair or poor	29.4	2.0
<i>Pain Limitations</i>		
No limiting pain or discomfort	12.4	Referent
Chronic pain or discomfort limits activity	29.9	2.1
<i>No. of visits to any physician</i>		
≥ 10 in prior year	23.9	0.9
< 10 in prior year	14.2	Referent
<i>Insurance Status</i>		
Uninsured	63.4	7.3
Insurance without prescription-drug coverage	27.1	4.3
Insurance with prescription-drug coverage	10.0	Referent

Adapted from: Kennedy and Morgan, 2006 (reference in footnote)

⁶⁶ Heisler, M et al. "Patient strategies to cope with high prescription medication costs: who is cutting back on necessities, increasing debt, or underusing medications?"; J Behav Med. Vol. 28 no. 1 p. 43, Feb 2005.

⁶⁷ Kennedy and Morgan; "A Cross-National Study of Prescription Non-Adherence Due to Cost: Data from the Joint Canada-United States Survey of Health"; Clin. Ther., vol. 28 #8 p. 1217, Aug. 2006.

⁶⁸ Kennedy and Morgan; "A Cross-National Study of Prescription Non-Adherence Due to Cost: Data from the Joint Canada-United States Survey of Health"; Clin. Ther., vol. 28 #8 p. 1217, Aug. 2006.

Perspectives from Canadian Social Workers, Volunteers and Patients

The coping strategies described in the studies cited above were borne out by social workers interviewed in each province and territory across Canada, by focus groups of Canadian Cancer Society support group volunteer leaders in Ontario and by interviews with cancer patients in Ontario and British Columbia.

The following consistent patterns were noted:

- Patients are often reluctant to discuss their financial circumstances and many go without other necessities because they are embarrassed to discuss financial matters with strangers.
- There are relatively few of patients for whom high drug costs are a problem (estimated by social workers to be less than 10% or up to 20%, depending on the province), however for those patients this is their major concern over all other factors in their treatment.
- Financial distress is caused by a number of factors, of which drug costs may be only one. Costs for travel to cancer treatment centres are burdensome, as are costs for medical supplies (ostomy bags, nutritional supplements, etc.) and home care. Patients will deplete their retirement savings and sometimes even mortgage their homes to pay these expenses.
- For patients with low incomes in some provinces, the cost of gas and meals for a one-hour trip to a cancer centre is more than they can financially manage, and yet their income is too high to qualify for social assistance, through which their drug expenses would be covered.
- In the north, patients must travel to southern centres for their initial treatment. This can take several weeks and the patient often requires an escort either because of their poor health or for language reasons. Although the system provides for travel subsidies and some jurisdictions operate lodging facilities for patients, the costs of transportation, meals and the deductible amounts (also child care expenses for some patients) can mount up to thousands of dollars and result in financial hardship for many families.
- Another issue related to Canadians living in remote communities is access to programs for prevention and screening. Because of the lack of healthcare resources, the vast distances and sparse populations across much of Canada's geography, cancer is often not diagnosed until very advanced stages in the north. For these patients, unfortunately, treatment is often palliative. Many patients refuse to travel to receive end-stage treatments because of the considerable financial and emotional strains of travel. There is therefore an immediate need for high quality drug treatments for late-stage cancers and for palliation in the north, as well as a longer-term need for more aggressive strategies to improve efforts aimed at prevention and earlier detection.⁶⁹

⁶⁹ Jennifer Forsyth, Health Technical Advisor, Inuit Tapiriit Kanatami; 11 October 2007.

Appendix 5

Private payment options

Content

1. Private Payment in Public Hospitals
2. Private Clinics
3. Private Payment for Treatments Received Outside Canada

For patients who are willing to pay for treatments not funded in their province, there are several private options available.

1. Private Payment in Public Hospitals

Some public hospitals will allow private payment of unfunded intravenous drugs. Provinces such as New Brunswick, Saskatchewan, Alberta and B.C. have specific policies. Ontario has received from CancerCare Ontario a recommendation on how such a policy could be implemented, however the government has yet to make an announcement and, in the absence of a clear direction, several cancer centres have gone ahead and implemented their own policies.

2. Private Clinics

Private infusion clinics are in operation in almost all major cities in Canada.

The most widespread are the Bayshore Clinics, the first of which opened in late 2006 and others continue to open across the country. These are operated by a consortium of Bayshore Home Health, Roche Canada and McKesson Canada. The clinics will infuse any of Roche's intravenous products (Avastin, Herceptin, Rituxan) provided that an oncologist has written a prescription for the drug. An on-site physician administers the infusion, however this is not necessarily an oncologist.

Toronto's Provis Clinic was the first private clinic that infused cancer drugs and has been in operation since 2005. Provis infuses only drugs that have received Health Canada approval but are not covered by the public system for the treatment of cancer, arthritis and neurological conditions such as multiple sclerosis. (A list of oncology and radioimmunotherapy drugs is available on their website www.provis.ca.) An oncologist or haematologist must have written the prescription and the oncology team in the public system remains the primary caregiver – Provis assumes responsibility only while the patient is receiving treatment in their clinic.

In Vancouver, the False Creek Surgical Centre provides infusions of cancer drugs as well as conducting surgical and emergency procedures for private payment.

Doctors in the public system dislike these arrangements because of the discontinuity of care - many side-effects are delayed and care of the patient reverts back to them. Discontinuity of care was one of the reasons that private payment for drugs infused in public hospitals was considered in Ontario.

3. Private Payment for Treatments Received Outside Canada

Outside Canada, patients can elect to be treated at cancer centres anywhere in the world, provided of course that they (or their insurers) are willing to pay the cost.

Some patients will travel to the U.S. (or other countries) to receive speedier care and at a higher standard than they believe is available in Canada. Access to advanced technologies, including new drugs, is a major reason for this decision. American centres are very willing to take on Canadian patients. The MD Anderson Cancer Centre, for example, has an office in Toronto through which patients can make bookings. MedExtra of Montreal offers a service to locate treatment centres in the U.S.

To access drugs not yet available in Canada, patients living close to the U.S. border frequently travel to clinics in bordering cities such as Buffalo, N.Y. In the past in Ontario, when drugs such as Avastin and Erbitux were unavailable in the public system and there was no option for private payment in Canada, treatments were reimbursed by the provincial health insurance plan (OHIP) under certain conditions. Reimbursement, however, was inconsistent and left some patients with bills in the tens of thousands of dollars. A review of the system was announced in January 2007. No other province has a policy to reimburse drug treatments received outside the country.

Doctors in Canada, however, warn patients that the U.S. system has several downsides and recommend that they exercise caution when considering this option. U.S. physicians receive incentives to continue treating patients, through fee-for-service billings and/or by bonuses paid based on the health of their patients. Also, they can make a profit on the drugs they infuse. In addition to draining their financial resources, patients may build up false hopes when successions of new treatments are offered.

Appendix 6

Cancer Drug Pricing

Content

1. The Costs of New Cancer Drugs
2. Price Controls in Canada
3. Forces Extending Patent Life
4. Forces Contracting Patent Life
5. Strategies for Minimizing Cancer Drug Costs

1. The Costs of New Cancer Drugs

Cancer is one of a few areas in medicine, along with immune diseases such as multiple sclerosis and arthritis, that has seen enormous increases in the cost of therapy in the recent past, largely due to the advent of targeted biological medications. Of the 15 cancer drugs approved in Canada over the past decade, three-quarters are reported to cost more than \$20,000 for a normal course of treatment.⁷⁰

Table 1 shows the cost per standard course of therapy for a selection of newer cancer drugs. (These costs are not precise because a course of therapy will differ by patient – most of these drugs are given until no further response is demonstrated and can vary from a few weeks to several months.) In a few instances, such as Gleevec, the drug will be given for the remainder of a patient's life.

Viewing cancer as a chronic condition to be managed over years, not months, is a relatively new phenomenon. Also, the expectation of curing cancer "two months at a time" has now become common among researchers who achieve incremental gains with new cancer drug 'cocktails' in which each drug attacks the tumour via a different mechanism of action. Both of these trends foretell the escalation in costs that can be expected in the near future, due not only to the advent of more very expensive drugs but also to increased utilization.

2. Price Controls in Canada

As discussed in Part 1, the Patented Medicines Prices Review Board ensures that prices of patented drugs in Canada are not excessive. Manufacturers are effectively restricted to charging prices equivalent to those in European countries many of which, unlike Canada, have socialized health systems and central purchasing of prescription drugs. It is estimated that prices paid in Canada and Europe are 15-33% lower than those in the U.S.⁷¹

⁷⁰ CBC News report; 25 Feb 2007

⁷¹ Jönsson, B and Wilking, N; "A Global Comparison Regarding Patient Access to Cancer Drugs"; *Annals of Oncology*, June 2007.

Table 5.6 Cost of Selected New Cancer Drugs

Drug Name Generic Name	Form	Cancer Site	Drug Cost for Standard Course
MabCampath <i>alemtuzumab</i>	<i>IV</i>	Leukemia	\$22,000
<u>Aromatase inhibitors:</u> Arimidex <i>anastrozole</i> Femara <i>letrozole</i> Aromasin <i>exemestane</i>	<i>oral</i>	Adjuvant treatment of estrogen receptor-positive breast cancer	\$1800 per year
Avastin <i>bevacizumab</i>	<i>IV</i>	Advanced colorectal cancer	\$30 - 60,000
Velcade <i>bortezomib</i>	<i>IV</i>	Multiple myeloma	\$30-57,000
Xeloda <i>capecitabine</i>	<i>oral</i>	Adjuvant treatment of colorectal cancer	\$6,000
Erbix <i>cetuximab</i>	<i>IV</i>	Advanced colorectal cancer	\$56,000
Tarceva <i>erlotinib</i>	<i>oral</i>	Lung cancer	\$14,000
Gleevec <i>imatinib</i>	<i>oral</i>	Leukemia and GI cancer	\$35-70,000 per year
Eloxatin <i>oxaliplatin</i>	<i>IV</i>	Advanced colorectal cancer	\$20-25,000
Alimta <i>pemetrexed</i>	<i>IV</i>	Mesothelioma	\$20-25,000
Rituxan <i>rituximab</i>	<i>IV</i>	Lymphoma	\$20-34,000
Nexavar <i>sorafenib</i>	<i>oral</i>	Kidney cancer	\$7350/6 weeks
Sutent <i>sunitinib</i>	<i>oral</i>	Kidney and GI cancers	\$7330/6 weeks
Temodal <i>temozolomide</i>	<i>oral</i>	Brain cancer	\$20,000
Thalidomid <i>thalidomide</i>	<i>oral</i>	Relapsed multiple myeloma	\$44,000
Herceptin <i>trastuzumab</i>	<i>IV</i>	Hormone receptor-positive breast cancer	\$45-50,000

Source: Cancer Advocacy Coalition of Canada Report 2005-6 and trade media reports

3. Price Setting in Canada

Canadian subsidiaries of pharmaceutical companies are constrained by several factors in the prices they can set for new cancer drugs. Global pricing is the most important of these factors. Global companies generally price within a range, or price corridor, to prevent cross-border sales of their products eroding profit margins. The target price range for a new drug is usually set in accordance with the U.S. market, since this is the largest pharmaceutical market in the world and one of the least price-sensitive.

A second constraint is the price ceiling established by the Patented Medicines Prices Review Board, and the restrictions placed on future price increases.

Within these limitations, companies are motivated to obtain the highest price that the local market will accept. Products have a finite patent life, and there is a short period of time in which revenues can be generated. Prices must be calculated against the number of potential patients that will be treated with the new drug, taking into account the duration of treatment and the number of competitors. A specific type of cancer will have a relatively small population and a shorter duration of treatment compared to more common conditions such as cardiovascular disease, for example. Yet, the cost of development for cancer drugs is as high and this must be recouped over a much smaller population.

It has been suggested that cancer patients may be willing to pay more for a treatment because it provides hope for a cure or respite from an imminent, life-threatening episode. Faced with such a sudden and emotional decision, patients may opt to pay for a new treatment with little regard for its cost. While this may be a factor that influences prices charged in private markets such as the U.S., in Canada it is not the patient but the public health system that makes the purchasing decision. The company must prove the value of the new cancer drug through a systematic and rational process which, ideally, distributes resources equitably across all therapeutic categories. The cost of a course of therapy for a new cancer drug is comparable to the lifetime cost of treating a cardiovascular patient, so a case can be made that the prices of new cancer drugs are not out of proportion to their benefit.

High prices also help to offset the risks inherent in bringing a new product to market. Unpredictable events can quickly and dramatically reduce sales, such as a clinical study showing superiority of a competitor's drug, or side effects of the new drug that become apparent only after it has been marketed for a period of time. Patent challenges are also common and the more successful a product is the more likely it will be a target for such actions.

4. Forces Extending Patent Life

The patent life of a marketed drug is the sole opportunity for a company to recoup its years of investment in research and development and to reward its financial risk-taking. The revenue stream generated by patented medicines is needed for ongoing investment in the research and development of new drugs and companies are strongly motivated to extend the patent life for as long as possible. Although patents are valid for a period of 20 years, because they are issued early in the drug's

development, only about one-third of the term remains after regulatory approval (and even less after the additional time taken for funding approval).

Extending patent life benefits primarily the pharmaceutical company and its shareholders, however it also indirectly benefits research institutions, specialists and hospitals because the company is able to continue to fund research from its revenues. There are several factors in play today that effectively expand a drug's patent life.

Canada's New Patent Laws Guarantee Eight Years of Market Exclusivity

Canada recently joined other countries in applying the World Trade Organization's TRIPS agreement (Agreement on Trade-Related Aspects of Intellectual Property Rights), signed in 1994. The TRIPS agreement was an attempt to narrow the gaps in the way intellectual property rights are protected around the world, and to bring them under common international rules.

In October 2006, the Government of Canada put in place new regulations creating an intellectual property framework for pharmaceuticals and bio-pharmaceuticals. New and innovative drugs now receive an internationally competitive, guaranteed minimum period of market exclusivity of eight years — up from the previous five years. This was done in part because biologic drugs often have little patent protection left by the time they are approved for sale due to lengthy development and regulatory review times.⁷²

Evergreening Patents

A controversial trend that has helped to extend patent life for many drugs in recent years is the so-called 'evergreening' strategies employed by manufacturers. Throughout the course of the drug's lifecycle patents are filed that offer minimal actual improvements on the product but that are legally considered new inventions and so are patentable. The laddering of patents in this way can extend the period of protection for years beyond the expiry of the original patent.

This practice has increasingly been frowned upon by regulators because it distorts the intent of the patent system, which is to balance public and private interests. It is now much more difficult for these kinds of patents to receive approval.

Faster Clinical Trials in Overseas Markets

Clinical studies are increasingly being conducted in overseas markets because they can be done more quickly and in large numbers of patients at vastly reduced costs. Although the numbers of such studies are still relatively small, this trend is expected to accelerate. A recent news article reported that China has just surpassed India as one of the fastest-growing locations for drug trials.⁷³

Health Canada's Progressive Licensing Strategy

Quicker regulatory approvals effectively expand the period of exclusivity for a product while it is still under patent. In 2007, Health Canada published its Blueprint for Renewal II process which advocates for lifecycle regulation of drugs, allowing for potentially earlier approvals of life-saving drugs and in exchange for enhanced post-

72 Industry Canada

<http://www.ic.gc.ca/cmb/welcomeic.nsf/558d636590992942852564880052155b/85256a5d006b97208525720b004a7124!OpenDocument>

73 Andrew Jack and Amy Yee; "China overtakes India in drug testing"; The Financial Times; August 27 2007.

marketing regulatory control.⁷⁴ This would mean quicker approvals and hence extend the period of marketing exclusivity for the originator. Legislation allowing for progressive licensing was introduced in Parliament in April 2008.

Expedited Funding Approval Processes

Some provincial drug plans have taken steps to mirror Health Canada's efforts to make life-saving drugs available more quickly. British Columbia is usually the first province to approve new cancer drugs. A goal of Ontario's *Transparent Drug System for Patients Act* was to expedite reviews of breakthrough drugs by implementing a Conditional Listing process and an Exceptional Review mechanism.

4. Forces Contracting Patent Life

At the same time as these factors are stretching out the period of market exclusivity, forces that effectively shorten this window are acting in opposition.

Biosimilar Generic Copies

Perhaps the most important emerging trend limiting market exclusivity is the development of generic copies to biological products. A large proportion of the new and expensive cancer drugs are of biological origins – that is, they are manufactured using living cells rather than by chemical synthesis. (A rule of thumb is that any drug whose generic name ends in –mab, –mib or –nib is a biological molecule.) Until recently, these manufacturing techniques were beyond the scope of most generic companies' capabilities since they require very large investments in dedicated facilities and highly expert manufacturing experience.

There were also a legal obstacles to be overcome. Biological products, unlike their chemically synthesized counterparts, do not have identical structures because they are manufactured by different cell lines using different processes. It is therefore very difficult for a generic manufacturer to claim that its product is identical to the original. Not being identical, the generic company cannot use the data submitted by the originator to gain approval. This means that the generic manufacturer must conduct the same clinical trials as the original manufacturer in order to prove the safety and efficacy of this new and different product. Having to jump through these enormously costly regulatory hoops is prohibitive for generic companies which are not set up to conduct extensive clinical trials, and also has the effect of increasing the price they must charge.

However, both the regulatory environment and the manufacturing capabilities of generic firms are changing. The European Union issued guidelines on *Similar Biological Medicinal Products* in October 2005 and approved the first 'biosimilar' drug, a growth hormone, in 2006. The U.S. Food and Drug Administration also approved the same growth hormone, but stopped short of opening the floodgates for new biosimilar products by allowing abbreviated submissions that do not require the manufacturer to replicate the clinical program of the original drug. As of time of writing, legislation is proceeding through the U.S. Congress that, if passed, will allow the FDA to develop such guidelines. In February 2008, Health Canada issued its draft guidelines on Subsequent Entry Biologics and indicated that the Food and Drug

⁷⁴ "Blueprint for Renewal II: Modernizing Canada's Regulatory System for Health Products and Food"; Health Canada, 2007.

Regulations will be amended to provide a legal and regulatory basis for approving biosimilars.

At the same time, companies have emerged that have the capability of manufacturing biological products. As an example, Dr. Reddy's, a large generic pharmaceutical manufacturer based in India, announced in 2007 that it could produce rituximab (Rituxan) in its facilities.

Compulsory Licensing

The TRIPS agreement on intellectual property rights described previously has provisions that offer countries a way around the patent rules. By stating that a drug is needed for public health emergencies such as pandemics, the country can force the manufacturer to issue a compulsory licence allowing a generic manufacturer to use their processes. Countries such as Thailand have recently announced that they are issuing compulsory licences for HIV/AIDS and cancer drugs. In July 2007, India's high court upheld a patent challenge which negated the validity of the patent for Gleevec in that country.

Increased Requirements for Funding Submissions

Another factor reducing the effective window of opportunity is the delay in funding approval caused by weak clinical or health economic data. As described in Appendix 2, manufacturers must submit a package of information on clinical and economic studies for the drug evaluation committee to review.

The first step in the review process is to categorize the quality of the evidence presented. As evidence becomes more important in decision-making, the bar for the level of evidence required is raised. Consequently, funding decisions are often deferred until better evidence can be produced. While Health Canada has its foot on the gas trying to speed up regulatory approvals and accepting lower quality data in the process, it appears that the provinces have their foot on the brake in requiring higher standards of studies. Velcade (bortezomib) is a case in point. Data submitted to the Ontario review process in 2004 was deemed inadequate to make a recommendation (although other provinces decided to approve the drug based on the same evidence). Once a major study was completed some months later, the company resubmitted the new data and gained approval. The process took over two years, during which time the patent clock for Velcade was ticking.

5. Strategies for Minimizing Cancer Drug Costs

The negative impacts of high cancer drug costs may be minimized both through clinical and financial strategies. The overall aim is to establish an appropriate balance of responsibility and financial burden between the private and public sectors. It is felt by many health professionals, patient groups and industry observers that the balance has been tipped too far in favour of the drug industry, to the disadvantage of patients and Canadians as funders of the public health system.

Many argue that the answer is not increased funding – we do not need more money in the health system because this would only sap our ability as a country to generate wealth. Rather, we need to ensure that available resources are allocated to the areas where they will do the most good, and that the net benefits are fairly distributed within the system.

The following options for reducing drug costs have been proposed by individuals interviewed for this report and by authors of health policy studies.

a) Reduce Unnecessary Utilization

Clinical guidelines promote the use of cancer drugs in specific populations and these are becoming more widely used. This is one of the main reasons cited by the B.C. Cancer Agency for its ability to afford new cancer drugs while maintaining its budget at a level proportional to new cancer cases in the province.

Wastage of drugs is another potential route for savings. Intravenous drugs in non-reusable containers are wasted by discarding the remaining contents after use in a single patient. At the cost of thousands of dollars per treatment, salvaging this excess product can potentially trim millions of dollars from Canada's cancer drug bill. Companies are beginning to respond to this opportunity by introducing multiple formats of their products.

b) Take from the Pharmaceutical Companies

There have been calls to strip patent protection from companies that have developed valuable but costly new drugs. This is not unknown in Canada. Until 1987, Canada overruled patent rights by forcing companies to issue licences to generic firms to copy their drugs for a tiny royalty. As mentioned above, both Thailand and India (which wanted to support its burgeoning drug manufacturing industry) broke patents for cancer drugs under the TRIPS rules.

This short-term solution allows specific jurisdictions to benefit from the availability of cheap copies of innovative drugs. Once a critical mass of countries takes this approach, there will be no further incentive for companies to invest in the research and development that makes these new drugs possible.

Price controls are another way to shift the burden of costs onto pharmaceutical companies. Some countries, such as the UK, limit the profit that companies are allowed to make. Certain European countries impose price controls, as does Canada. Others, Canada included, require companies to invest a certain level of sales in that country. (The Canadian pharmaceutical industry is required to invest 10% of its total revenues in research and development in this country.)

c) Take from Patients

This is essentially the situation we are in today. The 'Avastin wall', as it has been called, has shown us the limits to the public purse. Although it has been recommended by clinicians as a valuable option for patients with advanced colorectal cancer, Avastin was denied funding in several provinces because its cost exceeded the threshold of clinical and quality of life benefit that was considered acceptable by these public drug plans. The Avastin example is a warning of greater inequities in future as patients with private means pay for drugs that ordinary citizens cannot access through the public health system.

Cost containment practices such as rationing of drug treatments, delays in regulatory and funding approvals, and increasing cost-sharing requirements all contribute to the burden placed on patients.

d) Take from the Public System

Authors from the Karolinska Institute in Stockholm argued in a recent paper that the burden of illness for cancer compared to other diseases is far greater than the proportion of health dollars it consumes. The improved quality of life obtained by using expensive new drugs would return the cost of treating cancer patients through increased taxes and reduced utilization of the health system.

This broad approach to evaluating cancer drugs provides an interesting possibility of how all health treatments might be prioritized so that our finite health resources could be optimally spent. It does not, however, establish an appropriate equilibrium between the private and public sectors but rather asks the public sector to continue to pump more funds into the system.

e) Share the Burden

Pay-for-performance has been proposed by at least two pharmaceutical companies as a way to share costs. In the UK, Janssen Ortho recently announced a scheme for Velcade (bortezomib, for multiple myeloma) whereby the company would refund the cost of the drug for patients who did not respond to therapy.⁷⁵ Pfizer is also reported to have a price-reduction deal for Sutent (sunitinib, for kidney cancer) for at least one health region in the UK.⁷⁶

Other approaches link price and volume. The B.C. Cancer Agency negotiates better financial terms with manufacturers through its centralized purchasing authority, as do Alberta and Saskatchewan. Part of Ontario's recent drug system reform included negotiating pricing deals with individual manufacturers.

On an individual patient basis, some firms in the U.S. have agreed to cap total payments for a specific drug. After much criticism about price, Genentech moved to cap the total cost of Avastin at \$55,000 a year for patients below a certain income level.⁷⁷ And Amgen has said that for its new colon-cancer drug, Vectibix, patients won't be required to pay more than 5% of their annual income in out-of-pocket costs.

The introduction of generic cancer drugs has been shown to reduce costs by half. Given that the development costs for generic drugs are a small fraction of those of the originator, there may be further price elasticity that has not yet been captured. A centralized purchasing authority or regulations limiting generic prices (as there is in Ontario for generics sold in retail pharmacies) may offer a way to capitalize on future patent expirations.

f) Long-Term Solutions

Targeting cancer drugs to those patients who will most likely benefit will mean enormous cost-savings. Diagnostic tests designed to predict which patients will respond to certain types of therapy hold great promise for reducing drug costs and improving therapy. As with trastuzumab (Herceptin), where patients are now routinely tested for HER2 receptor levels, screening tests for targets such as epidermal growth factor receptor (EGFR) may help to identify patients with a high expected rate of response. Investing in screening tools that will identify markers of

⁷⁵ Nicole Martin; "U-turn on cancer drug offers hope to victims"; Daily Telegraph (UK); 4 June 2007.

⁷⁶ Barry Nelson; "Firm vows to cut cancer drug cost"; The Northern Echo(UK); 5 June 2007.

⁷⁷ Penni Crabtree; "Biotechs criticized for rising treatment costs"; Union-Tribune, November 10, 2006.

responders before treatment is a potential way of reducing downstream drug costs, and also of avoiding unnecessary chemotherapy for patients.

Another interesting approach has been suggested which focuses on one of the root causes of high drug prices. Costs can be taken out of the system by reducing research and development expenditures. Cancer networks could reduce their charges for conducting clinical trials in return for better prices. Similarly, negotiating with regulatory authorities to keep requirements for clinical trials to a reasonable level would help maintain a balance between safety, rapid access and cost.

Along similar lines, the patent system could be made more flexible. Patent extensions could be granted for investments in developing new indications for older, cheaper drugs in much the same way as companies receive an additional six months of exclusivity for investing in paediatric indications.

Gated pricing could also be employed so that, as the number of potential patients increased with every new indication approved, the price per patient would drop. This would remove much of the pricing risk on introduction of the drug. A system of rebates could be established so that the price reduction would not be apparent to other jurisdictions that use Canada as a benchmark for prices.