

POSITION PAPER ON DRUG THERAPY OF CANCER

Issues related to the access of systemic therapy¹ for cancer, with recommendations

Few advances in medical treatment have been as dramatic as the development of drugs effective against cancer. In the 62 years following recognition of the anti-tumor effects of nitrogen mustard in Hodgkin's disease,² the discovery of drug therapies capable of curing or controlling malignant diseases includes such diverse entities as cytotoxic chemicals, hormones, anti-hormones and antibodies. Collectively, these drugs have reduced cancer mortality, contributed to the general increase in population longevity, and made the lives of patients with incurable cancer longer and more comfortable.³ An entirely new set of biologic agents is currently being developed and, as they are added to the list of effective drugs, will undoubtedly benefit many more cancer patients.

ISSUES ARISING FROM ADVANCES IN SYSTEMIC THERAPY OF CANCER

Advances in systemic therapy have come at a price: one of the major issues arising from the plethora of new cancer drugs is who will pay. This financial challenge to health care systems is occurring worldwide and is compounded by a relentlessly increasing number of cancer cases due to population growth, aging, and lifestyle. As a result, public demand is coming into conflict with payers who are ever more reluctant to accept the entire cost burden of cancer drugs.

Until the payment issue is satisfactorily resolved, cancer patients may be denied timely access to the new drugs. They must be made aware when that happens so they can act on their own behalf to obtain needed treatments.

In view of the likelihood that access will be increasingly delayed, the CACC describes the present system for providing oncology drugs to patients, indicates where problems have arisen, and recommends approaches to improve availability and access.

DRUG APPROVAL PROCESSES AT THE FEDERAL LEVEL

Safety and efficacy

Health Canada must first determine if there is sufficient evidence that a new drug is safe and effective. If such evidence is convincing, Health Canada then issues a Notice of Compliance (NOC), listing the approved indications for use of the drug. If any new indications are subsequently discovered a separate submission/review is required. Before the NOC is issued, physicians can apply to Health Canada's Special Access Program if the drug is deemed to possibly benefit a patient with a life-threatening condition and conventional therapies have failed, are unsuitable or unavailable.

Pricing

The drug price is established at the Federal level by the Patented Medicines Pricing Review Board (PMPRB). This Board attempts to maintain the cost of new therapy in the same range as the cost of therapy for other drugs that treat the same disease. Only a drug classified as a "clinical breakthrough" or one "providing a substantial improvement" can exceed the therapeutic class price. It can be expected that several of the new biologic agents will be classified as clinical breakthroughs even though this designation has historically been given to only a small fraction of new drugs.

Common Drug Review

After an NOC has been issued, new drug applications must be submitted to Common Drug Review (CDR) for a recommendation as to whether or not the provinces should list the drug as a benefit. CDR is a recent development at the national level, managed through the Canadian Council for Health Technology Assessment. It was intended to reduce the duplication of separate reviews by all provincial drug plans when deciding which products will be covered as benefits. Except for Quebec, all federal and provincial drug plans agreed to accept the CDR findings of a new drug's clinical value. Even so, the provinces reserve the right to make their own decisions about benefits, in some instances still maintaining their own separate review processes. Thus, while CDR was originally

introduced to decrease the time from NOC to clinical use, it has actually increased the average interval.

Elapsed time for approval

Health Canada has set targets for timely review of new drug submissions and has created a priority review process for breakthrough products, but none of the review targets are being met. Annual reports from Health Canada show that in 2003 average review times were 22 months, or 12 months for priority review. Within the biologics and radiopharmaceuticals category the average review time was 28 months, or 24 months for priority review. These approval times are substantially longer than those in Australia, Sweden, UK, and the USA.⁴ This, despite the fact that there are two-to-3.5 times the personnel devoted to the process in Canada compared to the other countries, except the USA.⁵ The median time for priority review in Canada since 1996 has been 304 days for 43 drugs approved; while in the United States, it took 184 days to review 70 drugs.⁶

DRUG APPROVAL PROCESSES AT THE PROVINCIAL LEVEL

Separate Guideline Process

Provincial cancer agencies may write their own guidelines about when and how to use a new product. The review process is by experts who may decide that the approved indication from Health Canada's NOC is too generous. Conversely, in unusual circumstances any provincial agency may recommend use of a drug even if it does not receive an NOC and has not gone through the CDR process. The combination of these differences has created inconsistencies from province to province in the interpretation of evidence about the best use of the drug.

Separate Funding Approval Process

After a new drug application has gone through the Federal processes, and after provincial guidelines have been set by expert medical committees, funding still has to be approved by the government in each province. Since all provincial health ministries are faced with increasing demands for health care dollars they may be in no hurry to allocate funds for a new drug even though it has received medical approval. Lobbying efforts may be required to expedite funding, particularly for life-saving drugs used for treating cancer patients.

According to strict interpretation of the Canada Health Act, drugs given intravenously represent an insured service when administered in a hospital

setting: the hospital is required to pay for the drug and third-party payment is prohibited. Under these circumstances, only the ministry of health in each province can reimburse hospitals for the costs of such drugs. Oral cancer drugs are also covered by provincial government drug plans, but only for eligible patients. In 2001, the number of Canadians covered by provincial plans was estimated to be between 10.5 and 11.5 million.⁷

Historically, the private sector has paid for the majority of prescription drugs in Canada, however most oncology drugs are paid by publicly funded programs and institutions. The share of prescribed drug expenditure financed by the public sector is forecast to have risen to 46.9% in 2002, and 47.2% in 2003.⁸

The combination of differing provincial guidelines, dates of availability, and patterns of practice leads to considerable inter-provincial variation in patient access to cancer drugs. This could partially explain why cancer mortality is so different from province to province.⁹

Guidelines Used to Regulate Medical Practice

The original purpose of clinical guidelines for use of cancer drugs was to inform physicians regarding best practice. Guidelines can never cover all situations, but the exceptional circumstances that do arise can be recognized by trained oncologists. However, in some circumstances guidelines can also become the rules by which the provincial governments control the cost of their drug plans and the drug budgets of their cancer agencies. Where exceptions arise, instead of being allowed to exercise best judgment, oncologists must submit documentation requesting special approval for the patient to have coverage for the drug. Not only does this delay needed cancer treatment, experienced oncologists report that as much as 10-20 percent of their time is spent on the documentation required for these special approvals. Furthermore, a fundamental conflict of interest exists if those people responsible for writing guidelines or adjudicating the doctors' requests for exceptions are also responsible for the organization's budget.

Patient Options for Access to Unfunded Drugs

Given the variations in coverage and access to cancer drugs among provinces, the possibility arises that patients will not be informed about systemic therapy that is not covered by their government. In addition, oncologists stretched to the limit coping with the increasing volume of cancer patients might not be taking all the extra steps necessary to get the special approvals necessary for use of a new drug. For

whatever reason, it seems apparent that patients do not receive full information about cancer drugs.

If patients search for information independently of their providers they often learn of the existence of effective drugs covered in provinces other than their own. As a rule, patients cannot get the drug covered by traveling to another province, or personally pay for an infusion therapy. They must therefore pursue compassionate use programs established by the drug company, or travel to a foreign country to personally pay for the treatment.

COST-EFFECTIVENESS vs. COST CONTAINMENT

The advent of breakthrough medicines represents a major structural shift: from provision of traditional medical services to the consumption of medical products.⁵ More effective drugs can replace surgery, reduce visits to doctors' offices and emergency rooms, decrease length of hospital stay, delay or delete terminal palliative care, reduce family financial burdens and abolish use of drugs that are less effective but still costly.^{10 11 12} The new class of biologic agents coming on stream will accelerate this structural shift.

Healthier, more productive citizens contribute to the economy after their recovery, in a sense paying back the cost of their own treatment. From that perspective, the cost of cancer drugs is an investment in citizen productivity analogous to expenditures for education, transportation and public safety.

The fact remains, however, that the new drugs are expensive, and most would agree cost-effectiveness should factor into their deployment. The current methods for making financial decisions about provincial drug listings are based on inadequate data and lack of consistency.¹³ Up until now, cost-effectiveness is usually modeled on the basis of the available data and, if possible, expressed in terms of the incremental cost per quality-adjusted life-year gained (QALY). It would be preferable if judgments were made in a larger context, attempting to resolve the tensions among efficiency, equity, and opportunity costs.¹⁴

While cancer drugs represent a large cost increase to one part of the health system, the increase may be more apparent than real when viewed in the overall context of economic gains from increased productivity and cost-avoidance of protracted, less effective treatments. Unfortunately, the economic benefit of investing in cancer survival is not as visible

when health care budgets are silos. Cost savings realized in one agency, department or institution are not readily transferred to the others to pay for the new drug. As a consequence, all budgets simply grow. This is a deceptive growth, leading to the faulty conclusion that "we cannot spend any more money on health."

Cost Reduction Measures

Provinces have experimented with various measures to control the cost of drug plans, including listing agreements, restricted listing, co-payments, generic substitution, and reference-based pricing. In most cases these measures are largely inapplicable to oncology agents, leading to use of a last resort measure: the simple unavailability of new cancer drugs.

CACC RECOMMENDATIONS

1. Streamline the system

To produce optimum outcomes in cancer management the various segments of the system need to function seamlessly together. Disease-specific management algorithms should be constructed through involvement of multiple stakeholders. Then regularly scheduled disease-specific multidisciplinary conferences should be held, applying the algorithm to each newly-diagnosed patient, in order to collectively plan an integrated approach to that patient's disease *at the time of diagnosis*. If coupled with an information-gathering system based on modern technology, this would allow:

- (a) continuity of care and coordination among providers,
- (b) reductions in waiting times,
- (c) monitoring of the different components contributing to clinical outcomes,
- (d) recognition of opportunities for system-wide efficiencies and cost savings,
- (e) assessment of cost-effectiveness of new drugs in a broad societal context.

2. Establish principles for patient access to new cancer drugs

(a) Expedite approval processes by governments

The federal process for cancer drug approval is unreasonably protracted and complex. It could be shortened by willingness to achieve review targets. As well, provincial drug plans and cancer agencies have ample notice that new drugs will become available, and are able to plan well in advance for the release of the drug: there should be no delays to patient access at the provincial level.

(b) Develop national clinical practice guidelines

Developing multiple sets of provincial guidelines wastes professional time and leads to delay and obstruction. National clinical practice guidelines should be established regarding the use of new drugs. The guidelines should be based on carefully planned clinical trials and adopted by funders. This would ensure patients should have fair and equitable access to cancer drugs across the country. Availability of a drug in this sense includes ensuring facilities for its safe delivery and for patient support, care and follow-up.

(c) Disclose all treatment options and share decision-making with the patient

The patient must be provided with all the information regarding treatment. Specifically, the patient has the right to know the range of treatments available whether or not they are available in their political jurisdiction. Furthermore, the choice of treatment is a shared decision between the physician and patient and must be based on full disclosure of the risks and benefits associated with treatment options. Patient preferences about quality of life should be incorporated into the treatment plan.

(d) Disclose inability to deliver specific treatments

Whatever the reason, when a provincial government is unable to deliver the new treatments, it should publish the rationale, relative to other spending decisions. This level of disclosure would alert physicians to variations from best practice and enable patients to recognize differences and investigate other options available to them.

(e) Refer patients to other centres

Physicians should remember to exercise their option to refer their patients to other centres able to deliver best practice.

(f) Financial issues must be separated from treatment recommendations

Medical advice regarding best treatment should not be influenced by drug pricing, the policies of individual cancer centres or provincial governments about coverage, or the patient's ability to pay or his/her insurance status.

(g) Health care providers' advocacy role must be exercised and protected

Part of the commitment of all professional health care providers is to advocate on behalf of their patient. This should be exercised. Further, the oncologist should be explicitly protected from administrative retribution if he or she fully informs the patient of treatment options, and where and how to access them. Finally, the professional Colleges have an obligation to ensure that the advocacy role is both exercised and protected.

¹ The difference between focal treatment intervention provided by a surgical excision or ionizing radiation and an intervention that potentially reaches all the cells of the body. Cytotoxic drugs, hormones and immunologic interventions are systemic and are the only effective strategy to target cancer cells that have spread or escaped from the primary site of origin of the cancer.

² Gilman A. The original clinical trial of nitrogen mustard. *Am. J. of Surgery* 1963, 105:574-8

³ Lichtenberg F. *The Economic Value of Medical Research*. University of Chicago Press 2002

⁴ Rawson NS. Timeliness of review and approval of new drugs in Canada from 1999 through 2001: is progress being made? *Clin. Ther.* 2003, 25:1230-47

⁵ Rawson NS. Human resources for the approval of new drugs in Canada, Australia, Sweden, the United Kingdom, and the United States. *Can. J. Clin. Pharm.* 2002 :73-8.

⁶ Rawson NS, Kaitin KI. Canadian and US drug approval times and safety considerations. *Annals of Pharmacotherapy* 2003, 37: 1403

⁷ Bryan Ferguson, .A Presentation to the Senate Hearings on the State of Health Care in Canada,. (FCMC Partner Applied Management: Toronto, June 13, 2002) (with reference to *Canadians' Access to Insurance for Prescribed Medicines*, submitted to Health Canada in March 2000 by Applied Management in association with Fraser Group, and Tristat Resources)

⁸ Canadian Institute for Health Information, Drug Expenditures in Canada 1985-2003. www.cihi.ca

⁹ Cancer Advocacy Coalition of Canada. *Cancer Care in Canada* 2003, 6:7-9

¹⁰ Thomas M, Mann J. Increased thrombotic events after change in statins. *Lancet* 1998, 352:1830

¹¹ Maroun J, Asche C, Romeyer F, et al. A cost comparison of oral tegafur plus uracil/folinic acid and parenteral fluorouracil for colorectal cancer in Canada. *Pharmacoeconomics* 2003, 21:1039-51

¹² Jansman FG, Postma MJ, van Hartkamp D, et al. Cost-benefit analysis of capecitabine versus 5-FU/Leucovorin in the treatment of colorectal cancer in the Netherlands. *Clin. Ther.* 2004, 26:579-89

¹³ West R, Borden EK, Collet JP, et al. "Cost-effectiveness" estimates result in flawed decision-making listing drugs for reimbursement. *Can. J. Public Health* 2002, 93:421-5

¹⁴ Rawlins, MD. NICE Work--Providing guidance to the British National Health Service. *New Engl. J. Med.* 2004, 351:1383-4