The New Wave of Cancer Drugs

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In the first Cancer Drug Access report,[1] we documented the marked inter-provincial variability in access to 24 new cancer drugs. It was clear, that as a cancer patient in Canada, where you live significantly impacts your ability to access new cancer drugs.

In Cancer Drug Access Part Two[2] we identified where improvements and deficiencies in cancer drug access were occurring in different parts of the country. We noted that an increasing number of treatments required self pay or private coverage. We documented the introduction of private chemotherapy infusion clinics, along with the advent and implementation of programs for charging patients for drugs not publicly funded but delivered within the public system.

In this report, Cancer Drug Access Part Three, we expand our study to include 18 additional new drugs (making a total of 42) representing a new wave of evolving treatment options for patients facing a variety of different cancers. We report on changes in access to the 24 drugs previously studied and the emergence of any trends in how patients are obtaining the 18 new drugs. We again note the increasing role of private payers and third-party insurance and we document once more that where you live in Canada makes a difference in your ability to access new cancer drugs.

Methodology

As previously reported, we surveyed medical oncology specialists and oncology pharmacy experts in each province as to the current funding status and availability of novel oncology drugs as of December 25, 2007. Data were compiled as previously described.[1,2]

In addition to prior categories describing drug access (see legend for Table 1), we also added an "O" category to highlight where a drug was being accessed out of country but paid for by a provincial health ministry.

We also added another category in pharmaceutical company sponsored assistance programs, P1, referring to expanded access programs which enabled patients to access drugs that may not yet have received Health Canada approval or provincial funding. This category is increasingly one of the limited ways to access new cancer drugs in this situation.

Key studies that reported the effectiveness of the selected cancer drugs and their dates of publication are listed including reports presented at major cancer meetings. Preliminary reports leading to regulatory approval, especially FDA approval, are increasingly being presented to the scientific community, and subsequently via various media to an increasingly informed public sector and cancer patients. The dates are included to illustrate the complex timelines of evolving new information.

The cost in Canadian dollars of a standard course of cancer drug therapy was calculated as previously described. US retail prices were used where drugs had not yet received approval by Health Canada, and/or were not yet commercially available in Canada.

Definition of Limited Access

Barriers and limitations to access were defined as follows:

L1 Only for specific disease indications (usually in the form of special authorization or case-by-case request and application)

L2 Only for specific patient groups (e.g., age over 65, or receiving social assistance)

L3 Only in some institutions within the same province

L4 Only available through private payment (e.g., self-pay, third party insurer) or manufacturer's compassionate access or assistance program but administered in a public institution

TABLE 1 **18 NEW CANCER DRUGS STUDIED SINCE DRUG ACCESS I AND II**
(STATUS AS OF DEC 25, 2007)

Cancer Drug (Trade Name)	**Cancer Indication**	**Level of Evidence**[3]	**Date of Approval in US** (FDA)	**Date of Approval in Canada** (Health Canada)	**Approval Timing Difference in Canada vs US**	**Drug Cost for Standard Course total duration** ($CDN unless otherwise stated)	**References for Key Studies**
Pemetrexed (Alimta)	Non-small cell lung cancer	1	Aug 19, 2004	Jan 11, 2007	28.7 mo	$23,000 (6 cycles)	(4)
Rituximab (Rituxan)	First line therapy of low grade NHL	1	Sept 29, 2006	Dec 20, 2005	-9,3 mo	$27,000 (8 cycles)	(5,6,7)
Rituximab (Rituxan)	Maintenance therapy of follicular NHL	1	Sept 29, 2006	July 28, 2006	-2 mo	$27,000 (8 doses over 2 years)	(8,9) (10,11) (12,13,14)
Cetuximab (Erbitux)	Locally advanced H&N cancer	1	Mar 1, 2006	Not approved; not commercially available in Canada	22+ mo	$16,000–$ 20,000 (7-8 weekly cycles)	(15)
Lenalidomide (Revlimid)	Relapsed multiple myeloma	1	June 29, 2006	Not approved; may be accessed through SAP	18+ mo	$74,000 US (1 year)	(16), (17)
Lenalidomide (Revlimid)	Myelodysplatic syndrome; 5q-	3	Dec 27, 2005	Not approved; May be accessed through SAP	24+ mo	$63,000 US (12 cycles; 1 year)	(18), (19)
Imatinib (Gleevec)	Adjuvant therapy for gastro-intestinal stromal tumour	1,3	Not approved; priority review pending	Not approved; Off label indication	N/A	$38,000 (1 year)	(20), (21), (22), (23)
Sunitinib (Sutent)	Advanced renal cell carcinoma	1	Jan 26, 2006	Aug 17, 2006	6.7 mo	$66,000–$75,000 (1 year)	(24,25,26)
Sunitinib (Sutent)	Relapsed GIST refractory or intolerant of imatinib	1	Jan 26, 2006	May 26, 2006	4 mo	$66,000–$75,000 (1 year)	(27,28)
Sorafenib (Nexavar)	Advanced renal cell carcinoma	1, 3	Oct 20, 2005	July 28, 2006	8.3 mo	$70,000 (1 year)	(29), (30,31)
Sorafenib (Nexavar)	Advanced hepato-cellular carcinoma	1	Nov 16, 2007	Not approved; off label use	1.3+ mo	$35,000 (6 months)	(32)
Pegylated liposomal doxorubicin (Caelyx)	Ovarian cancer	1	June 28, 1999	Jan 20, 2001	5.8 mo	$15,000–$16,000 (6 cycles)	(33), (34)
Azacytidine (Vidaza)	Myelodysplastic syndromes	1	May 19, 2004	Not approved; may be accessed through SAP	30+ mo	$56,000-$61,000 US (1 year; 12–13 cycles)	(35,36)
Dasatinib (Sprycel)	Ph+ ALL	3	June 28, 2006	July 7, 2007	12.3 mo	$55,000 (1 year)	(37,39), 38
Dasatinib (Sprycel)	Refractory CML	3	June 28, 2006	Mar 26, 2007	9 mo	$55,000 (1 year)	(37,40), 38, (41,42), (43,44)
Temsirolimus (Torisel)	Renal cell carcinoma	1	May 30, 2007	Dec 21, 2007	6.7 mo	$68,000 US (1 year)	(45)
Bexarotene (Targretin)	Cutaneous T-cell lymphoma	3	Dec 29, 1999	Not approved; may be accessed through SAP	96+ mo	$40,000–$45,000 US (8 months)	(46,47)
Lapatinib (Tykerb)	HER2/neu positive metastatic breast cancer	1	Mar 13, 2007	Not approved	9+ mo	$14,000–$18,000 US (6-8 cycles)	(48)

RESULTS

Access to Cancer Drugs

Of the 18 new drugs and indications studied, only two were for curative intent, while 16 were for palliative treatment. The two new drug indications for curative/adjuvant treatment were Erbitux combined with radiation for head and neck cancer, and Gleevec as adjuvant therapy for surgically resected GIST. The latter indication is undergoing phase III clinical trial testing with preliminary results showing disease free survival (DFS) benefit but not yet overall survival benefit. The trial was powered for DFS rather than overall survival - an increasingly popular trend in adjuvant treatment, enabling earlier detection of events.

There was Level 1 evidence (based on phase III clinical trials results) indicating a modest survival advantage in 11 of the 16 new drugs used for palliative treatment. The evidence for efficacy for the remaining five drugs was based on objective response rates and/or quality of life measures with lower level of evidence (Level 3 evidence from phase II clinical trials).

The cost of these 16 new drugs for palliative cancer indications ranged from $15,000–$75,000 for a full course of treatment. However it should be emphasized that when a new palliative treatment is not having the desired benefit, it is given for only a small fraction of the full course, typically two to three cycles or one to two months of treatment.

Of the 42 cancer drug indications studied, nine do not have approval in Canada including one from the initial 24 drugs studied (Thalomid for myeloma) and eight drugs from the 18 new drugs studied as of Dec 25, 2007 (Erbitux for head and neck cancer, Revlimid for relapsed myeloma, Revlimid for myelodysplastic syndromes, adjuvant Gleevec for resected GIST, Nexavar for liver cancer, Vidaza for myelodysplastic syndromes, Targretin for cutaneous T-cell lymphoma, and Tykerb for relapsed HER2 positive breast cancer). Eight of these nine non-approved drugs in Canada have been approved in the US by the FDA. Only Gleevec for adjuvant GIST is yet unapproved in both Canada and the US. Two of these nine drugs have Health Canada approval for other indications, confirming safety and efficacy in the form of Notice of Compliance (NOC) or NOC with conditions (NOC/c). In such instances the drug is commercially available in Canada for off label use: Gleevec approved for CML can be used off label for adjuvant GIST; Nexavar for advanced liver cancer.

Oxaliplatin finally received NOC for metastatic and adjuvant colon cancer in 2007. One drug, Erbitux, has been approved by Health Canada for metastatic colorectal cancer but the manufacturer and the Patented Medicine PriceS Review Board (PMPRB) could not agree upon a price and the drug has not yet been marketed in Canada despite its NOC. Access to this drug is only obtained on a case-by-case basis through Health Canada Special Access Program (SAP), and then purchased through US or European Union distributors.

Eleven of the 18 new drugs are given orally and seven intravenously. This distinction may influence whether or not they are funded within the public system for all patients with cancer, as many provinces only provide oral take home drugs through their separate provincial pharmacare plans for restricted populations (i.e., seniors or patients on social assistance).

- ✔ Approved and fully funded in that province
- **X** Not approved or funded in that province
- **L1** Limited access on a case to case basis (disease specific factors)
- **L2** Limited access based on coverage for only specific patient groups (patients factors such as over 65, or receiving social assistance)
- **L3** Limited access based on variable access in that province (institutional factors; only available in some centres but not others)
- **L4** Limited access based on private payment of the drug (self-pay, third party insurer or manufacturer's compassionate program) but administration of the drug provided by public cancer centre or hospital
- **R** Recommended for funding but not yet funded; approval still in process for decision
- **S** Self pay or third-party insurer, drug readily available through retail pharmacies
- **P** Pharmaceutical company sponsored reimbursement /assistance program
- **P1** Pharmaceutical company sponsored expanded access program
- **C** Compassionate release from pharmaceutical company
- **W** Funded through WCB (Workers' Compensation Board) or WSIB (Workplace Safety and Insurance Board in Ont.)
- **D** Funded partly by donated monies from charitable sources or foundations
- **T** Available by multi-centre Canadian clinical trial currently open
- **O** Out of country access through prior approval by the provincial ministry of health

TABLE 2 **CANCER DRUG ACCESS AND FUNDING BY DRUG AND PROVINCE FOR 24 PREVIOUSLY STUDIED DRUGS** (STATUS AS OF DEC. 25, 2007)

DRUG AND INDICATION	ACCESS	BC	AB	SK	MB	ON	QC	NB	PEI	NS	NL
Capecitabine (Xeloda) Adjuvant treatment of Duke C colon cancer	P S	✔	✔	✔	✔	L2 L4	✔	L2 L4 C	✔	L2 L4	L1 L2 L4 C
Oxaliplatin (Eloxatin) FOLFOX adjuvant treatment of colon cancer		✔ L1	✔	✔ L1	✔ L1	✔	✔	✔	✔	✔	✔
Oxaliplatin (Eloxatin) Metastatic colorectal cancer		✔ L1	✔	✔ L1	✔ L1	✔	✔	✔	✔	✔	✔
Pemetrexed (Alimta) With Cisplatin for mesothelioma	P W	✔	✔	✔ L1	✔ L1	X L3 L4	L1 L3	✔ L1	X	X	✔
Temozolomide (Temodal) With XRT and 6 months maintenance for GBM	P S	✔	✔	✔	✔	L1 L2 L4	✔	L2 L4 C	✔	L2 L4	L1 L2 L4 C
Trastuzumab (Herceptin) Adjuvant treatment of HER/neu positive breast cancer	P	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Rituximab (Rituxan) CHOP-Rituxan for DLC, B-cell non-Hodgkin's lymphoma	P	✔	✔	✔	✔ L1	✔	✔	✔	✔	✔	✔
Bevacizumab (Avastin) With chemotherapy for metastatic colorectal cancer	P	✔ L1	X L4	X L4	X R	X R L4 T	✔ L1	X L3 L4	X L4 T	X L3 L4	✔
Cetuximab (Erbitux) With chemotherapy for metastatic colorectal cancer		X	X L4	X	X	X L4 O	X L3	X L3 L4	X T	X	X
Alemtuzumab (MabCampath) Relapsed chronic lymphocytic leukemia		✔ L1	X L4	✔ L1	L1	X L4 T	L3	X L1 L3	X	✔	X
I-131 tositumomab (Bexxar) Relapsed NHL		✔ L3	X	X	X	X R	X L3	X	X	X	X
Yttrium-90 ibritumomab (Zevalin) Relapsed NHL		✔ L3	X L4	X	X	X R	L3	L1 L3	X	X	L1 L3
AI – Anastrazole (Arimidex) Adjuvant treatment of ER positive breast cancer	P C S	✔	✔	X R L4	✔	L2 L4	✔	L2 L4 C	✔	L2 L4 C	L1 L2 C
AI – Letrozole (Femara) Adjuvant treatment of ER positive breast cancer	P C S	✔	✔	X R L4	✔	L2 L4	✔	L2 L4 C	✔	L2 L4 C	L1 L2 C

Continued on following page

TABLE 2 CONTINUED **CANCER DRUG ACCESS AND FUNDING BY DRUG AND PROVINCE FOR 24 PREVIOUSLY STUDIED DRUGS** (STATUS AS OF DEC. 25, 2007)

DRUG AND INDICATION	ACCESS	BC	AB	SK	MB	ON	QC	NB	PEI	NS	NL
AI – Exemestane (Aromasin) Adjuvant treatment of ER positive breast cancer	PCS	✔	✔	X R L4	✔	L2 L4	✔	L2 L4 C	✔	L2 L4 C	L1 L2 C
Bisphophonate – Clodronate (Various/generic) Reduce bone complications from metastatic breast cancer	S	✔	L2 L4	✔	✔	L2 L4	✔	L2 L4 C	X L4	L2 L4	X
Bisphophonates – Pamidronate (Various/generic) Reduce bone complications from metastatic breast cancer		✔	L2 L4	✔	✔	✔	✔	✔	✔	✔	✔
Bisphophonate – Zoledronate (Zometa) Reduce bone complications from metastatic breast cancer	P	X	X L4	X L4	X	X	✔ L1	L3	✔	X	L1
Thalidomide (Thalomid) Relapsed multiple myeloma	C	X L2 L4 C	X L4 C	X C	L1 C	X C	L1 L3 C	X C	X C	X	L1 L2 C
Bortezomib (Velcade) Relapsed multiple myeloma		✔ L1	✔	✔	✔ L1	✔	✔	L1 L3	✔	✔	✔
Erlotinib (Tarceva) Non-small cell lung cancer	PCS	✔ L1	✔	✔	✔	L1 L2 L4	✔ L1	L2 L4 C	X	L2 L4	L2 L4 C
Gefitinib (Iressa) Non-small cell lung cancer		X	X	X	X	X	X	X	X	X	X
Imitanib(Gleevec) Chronic myelogenous leukemia	PCS	✔	✔	✔	✔	L2 L4	✔ L1	L2 L4 C	✔	L2 L4	L1 L2 C
Imatinib(Gleevec) Gastrointestinal stromal tumour	PCS	✔	✔	✔	✔	L1 L2 L4	✔ L1	L2 L4 C	✔	L2 L4	L1 L2 C

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- **L4** Limited access based on private payment of the drug (self-pay, third party insurer or manufacturer's compassionate program) but administration of the drug provided by public cancer centre or hospital
- **R** Recommended for funding but not yet funded; approval still in process for decision
- **S** Self pay or third-party insurer, drug readily available through retail pharmacies
- **P** Pharmaceutical company sponsored reimbursement /assistance program
- **P1** Pharmaceutical company sponsored expanded access program
- **C** Compassionate release from pharmaceutical company
- **W** Funded through WCB (Workers' Compensation Board) or WSIB (Workplace Safety and Insurance Board in Ont.)
- **D** Funded partly by donated monies from charitable sources or foundations
- **T** Available by multi-centre Canadian clinical trial currently open
- **O** Out of country access through prior approval by the provincial ministry of health

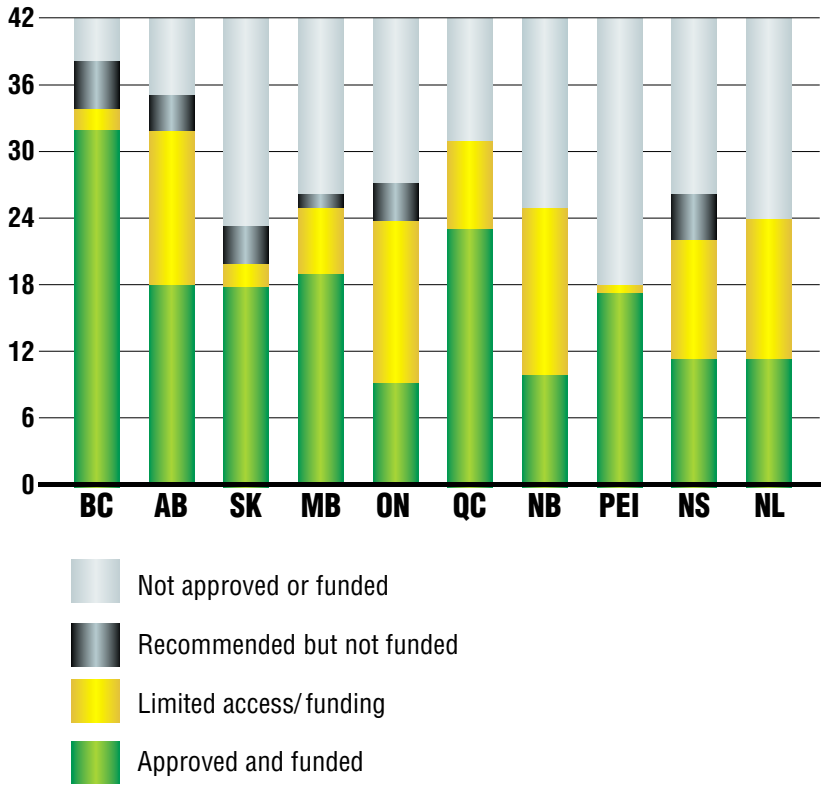
TABLE 2 **CANCER DRUG ACCESS AND FUNDING BY DRUG AND PROVINCE FOR 18 NEW DRUGS** (STATUS AS OF DEC. 25, 2007)

DRUG AND INDICATION	ACCESS	BC	AB	SK	MB	ON	QC	NB	PEI	NS	NL
Pemetrexed (Alimta) Non-small cell lung cancer	P	✔	X R L4	X	X	X	X	L1	X	✔	X
Rituximab (Rituxan) With CVP for advanced stage, low grade follicular NHL	P	✔	✔	✔	✔ L1	✔	✔	✔	✔	✔	✔
Rituximab (Rituxan) Maintenance Rituxan for follicular lymphoma after induction therapy	P	✔ L1	✔	✔	✔ L1	✔	✔	✔	✔	✔	✔
Cetuximab (Erbitux) With radiation for locally advanced H&N cancer		X L1 R	X	X	X	X	X	X	X	X	X
Lenalidomide (Revlimid) Relapsed multiple myeloma	T	X R T	X T	X T	X	X T	X T	X	X T	X	X
Lenalidomide (Revlimid) Myelodysplasia (5q- syndrome)		X R	X	X	X	X	X	L4	X	X	X
Imatinib (Gleevec) Adjuvant GIST	PCS	✔ L1	X L4	X	L1	X L4	L1 L4	X	X	R X L4	X L4
Sunitinib (Sutent) Advanced renal cell carcinoma	PS	✔ L1	X L4 R	X	X	L1 L2 L4	✔ L1	X L4	X	L2 L4	X L4
Sunitinib (Sutent) 2nd line GIST	PS	✔ L1	✔ L1	✔ L1	X	L1 L2 L4	✔ L1	X L4	X	X R L4	L2 L4
Sorafenib (Nexavar) Advanced renal cell carcinoma	PS	✔ L1	X L4	X	X	X L4	X L4	X L4	X	L2 L4	X
Sorafenib (Nexavar) Advanced hepato cellular carcinoma	PS	X L4 R	X L4	X	X	X L4	X L4	X L4	X	X L4	X
Pegylated liposomal doxorubicin (Caelyx) Ovarian cancer refractory to Platinum	P	✔	✔	✔	✔	✔	✔	✔ L3	✔	✔	✔
Azacytidine (Vidaza) Myelodysplastic syndrome		X R	X L4	X	L1	X	X L3	L1	X	X	X
Dasatinib (Sprycel) Refractory Ph+ ALL	PS	✔ L1	X L4	X	X	L1 L2 L4	X	X L4	X	X R L4	X
Dasatinib (Sprycel) Refractory CML	PS	✔ L1	X L4 R	X	X	L1 L2 L4	✔ L1	X L4	X	X R L4	L2 L4
Temsirolimus (Torisel) Advanced renal cell carcinoma	C	✔ L1	X	X C	X	X C	X C	X	X	X C	X C
Bexarotene (Targretin) Cutaneous T-cell lymphoma		✔ L1	X L4	X	X	X	X	X	X	X	X
Lapatinib (Tykerb) HER2/neu positive metastatic breast cancer	P1	X T	X	X P1	X	X P1 T	X T	X	X	X	X

TABLE 3 **SUMMARY OF CANCER DRUG ACCESS AND PUBLIC FUNDING STATUS COMPARING PAST 24 DRUGS STUDIED AND 18 NEW DRUG INDICATIONS**
(Status as of Dec. 25, 2007)

	PAST 24 DRUG INDICATIONS				18 NEW DRUG INDICATIONS			
PROVINCE	APPROVED AND FUNDED	LIMITED ACCESS FUNDING	RECOMMENDED BUT NOT FUNDED	NOT APPROVED OR FUNDED	APPROVED AND FUNDED	LIMITED ACCESS FUNDING	RECOMMENDED BUT NOT FUNDED	NOT APPROVED OR FUNDED
BC	20	1	0	3	12	1	4	1
AB	14	7	0	3	4	7	3	4
SK	14	2	3	5	4	0	0	14
MB	16	2	1	5	3	4	0	11
ON	6	11	3	4	3	4	0	11
QC	16	6	0	2	7	2	0	9
NB	6	13	0	5	4	2	0	12
PEI	14	1	0	9	3	0	0	15
NS	7	9	0	8	4	2	4	8
NL	8	11	0	5	3	2	0	13

FIGURE 1 **ACCESS TO 42 CANCER DRUGS, BY PROVINCE, 2007**



In Table 3 and Figure 1 the column heading "Approved and Funded" refers to a ✔or a ✔plus L1. In both instances, a decision has been taken that any patient who needs the drug for a specific indication will receive it.

TABLE 4 **SUMMARY OF LIMITED ACCESS VARIABLES FOR 42 CANCER DRUGS**
(STATUS AS OF DEC 25, 2007)

PROVINCE	CASE BY CASE REVIEW	SPECIFIC GROUPS ONLY	VARIABLE ACROSS THE PROVINCE	PRIVATE PAY	TOTAL NUMBER OF LIMITATIONS	NUMBER OF DRUGS WITH LIMITATIONS
BC	16	1	2	2	21	2
AB	1	2	0	17	20	14
SK	5	0	0	5	10	2
MB	11	0	0	0	11	6
ON	7	13	1	20	41	15
QC	11	0	7	3	21	8
NB	6	9	7	18	40	15
PEI	0	0	0	2	2	1
NS	0	11	1	17	29	11
NL	10	11	1	7	29	13

Table 4 is a summary of all the limitations in play, derived from Table 2. There are 224 limitations on 42 drugs. For example, Nova Scotia has 29 limitations but there are only 11 drugs involved. The final column on the far right is the number used to summarize these limitations, per drug, on the opposite page (Table 3 and Figure 1).

CANCER DRUG ACCESS BY PROVINCE

British Columbia

BC provides and funds 13 of the 18 new drugs studied but with increasing limitations through the BC Cancer Agency (BCCA) Compassionate Access Program (CAP). Each request for use of each drug is processed electronically through the Provincial Systemic Therapy Program to ensure the request fits the increasingly tight eligibility criteria defined by Provincial Tumour Groups. Each new drug submission undergoes evaluation by the BCCA Priorities and Evaluation Committee (PEC) that defines its provincial treatment policies and treatments. These treatment protocols with accompanying preprinted orders, and patient information handouts are continually refined in real time for cancer care teams throughout the province, and disseminated on-line throughout the province through the BCCA website.

The BCAA through its provincial oncology drug budget is the payer and provider for all oral, take home cancer drugs and intravenous cancer drugs for every resident of the province. The provincial pharmacare plan is responsible for most supportive care drugs for cancer but does not cover cancer drugs. Through its central management of all cancer drugs, BC is able to negotiate volume drug pricing, standardize treatments, obtain timely evidence based and consensus driven guidelines, provide common resources for patients and care providers, and evaluate utilization and outcomes for cancer drugs.

Alberta

Alberta fully funds four of the 18 new drugs and provides an additional seven through "Directors Privileges" where patients can access these drugs through private payer options. A medication incident in Alberta (and another in Manitoba) stimulated a detailed review of cancer drug safety. The resulting recommendations were implemented in Alberta and many other provinces. The incidents also led to the creation of the Systemic Therapy Working Group at the Canadian Association of Provincial Cancer Agencies which has helped increase cancer drug safety and standards nation wide.

British Columbia and Alberta reached an agreement to look at common sourcing of drugs for the two provinces, but cancer drugs are not included.

Saskatchewan

Saskatchewan approved four of the new drugs/indications. The Self Pay Drug Program (SPDP) contains only

two parenteral (intravenous) drugs: Avastin and Zometa. Maintenance Rituxan for follicular lymphoma, formerly available only through the SPDP, is now on formulary and fully funded. Most of the expensive new oral drugs studied are included in the SPDP for private pay. The recently elected Saskatchewan (Conservative) Party fulfilled a campaign pledge to fund Avastin for metastic colorectal cancer. Billing for Avastin for the first line treatment of colorectal cancer patients was stopped January 30, 2008 and patients who paid for Avastin are being reimbursed retroactive to November 7, 2007.

Saskatchewan has incorporated the Varian Medical Oncology (VMO) electronic cancer system making it the third province after Manitoba and Alberta to use this platform. The system will be an important tool for evaluating utilization and outcomes analysis of cancer treatments.

Manitoba

Manitoba provided access to seven of the 18 new drugs/indications. The provincial intravenous cancer drug budget has been consolidated under Cancer Care Manitoba (CCM). An inter-provincial purchasing agreement with Saskatchewan will allow for volume pricing and purchasing for the two provinces.

The VMO electronic cancer system (designed in Manitoba initially as the OpTx system) has been implemented province-wide across all 23 locations providing chemotherapy in Manitoba including the 14 Community Oncology Network sites and four community hospitals. Chemotherapy dispensing services in Winnipeg have been consolidated to the main CCM clinic sites. Oral cancer drugs now provided through Manitoba Pharmacare will eventually be included in the CCM budget.

Ontario

Ontario has approved seven of the 18 new drugs/indications.

Newer oral cancer drugs are increasingly funded on an exceptional access basis only. Exceptional access is not available for drugs administered in a hospital/clinic setting. Streamlining of the exceptional access process (formerly known as Section 8) will mean creating a list of specific drugs that would be available via this mechanism, as opposed to the previous practice of physicians applying for any drug that their patients might need.

The Trillium Drug Plan, for citizens under age 65, is an income-based, formulary-based plan, in place since 1995 to assist with high cost prescription drugs.

The Ministry of Health has yet to make any public comment on the Cancer Care Ontario (CCO) proposal for providing self pay parenteral cancer drug treatments within the 14 CCO regional cancer centres, but the practice has quietly taken root across the province.

Ontario is the home jurisdiction for Joint Oncology Drug Review (JODR), evaluating new drug submissions on behalf of eight other provinces (all but Quebec) and replacing the Common Drug Review in that role. JODR will soon complete its one year trial period and is due for evaluation. A multi-province Advisory Committee has been created to provide oversight to JODR. Many provinces continue their own pre-existing processes for evaluating new cancer drugs and deciding their funding priorities.

Quebec

Quebec has approved nine of the 18 new drugs studied, in whole or in part. Avastin is now funded for both first line and second line treatment of metastatic colorectal cancer. Thus Quebec is the third province to fund this indication, after BC and Newfoundland.

As noted in previous Report Cards, approval of new drugs in Quebec, unlike other provinces, does not automatically result in funding in each hospital or centre. On the other hand, individual hospitals in Quebec have the mandate and ability to approve individual cancer drugs more flexibly in their individual institutions than in many other provinces. For example, Zevalin is provided within the McGill system but not in the rest of Quebec and prior to its provincial funding approval, Avastin was provided for individual cases in some academic institutions provided a third party payer covered the cost.

Quebec remains independent of JODR. In 2005 a provincial cancer committee was established to coordinate approaches in oncology within Quebec attempting to emulate centralized oncology initiatives in other provinces. At the same time, a pharmacy body has been advising on oncology treatment guidelines. However, the Registry system, the data collection capability, and therapy consensus and approval mechanisms, are not yet uniform.

New Brunswick

New Brunswick funded six of the new drugs studied, in whole or in part. The New Brunswick Cancer Network initiated in October 2005 continues to develop a provincial systemic therapy review process. New Brunswick follows JODR recommendations for funding new cancer drugs. The prior process remains in place for self pay or case-by-case provision of expensive cancer drugs through individual hospitals within regional health authorities.

Prince Edward Island

PEI funded three of the 18 new drugs/indications. Moreover, PEI now approximates the inter-provincial average, having increased the number of fully funded drugs from five (second lowest in Canada in 2006) to 14

in 2007. This was made possible by a one time allocation of an additional $1 million for cancer drugs in 2007. This is a huge sum for a province of 140,000 people and one hopes ongoing funding will be provided for future patients requiring these treatments. A provincial process for evaluating cancer drugs remains to be developed.

Nova Scotia

Nova Scotia funded six of the new drugs/indications. Sutent for renal cell carcinoma and refractory GIST was added the Pharmacare formulary. The Provincial Systemic Therapy Program continues to evolve, incorporating an ethical framework for vetting new drug treatments in addition to clinical and pharmacoeconomic review.

A universal drug plan for the province as second payer after private insurance will come into effect March 1, 2008, covering drugs that are listed as formulary benefits in the existing Seniors' Pharmacare program. Family income determines the deductible and annual caps for deductible and copayment. A separate program, Drug Assistance for Cancer Patients, helps pay the cost of approved cancer-related drugs where the family income is $15,720 or less. Standard benefits include chemotherapeutic agents, pain medications, antiemetic agents and laxatives for use with chronic opioid therapy.

Newfoundland and Labrador

Newfoundland has funded five of the new drugs studied. Xeloda and Temodol are the only two oral drugs funded through the Oncology Drug Budget, which usually includes only IV chemotherapy drugs). Other oral take home cancer drugs are provided mainly through the provincial pharmacare plan (i.e., Provincial Drug Program).

The Cancer Care Program became the insurer of last resort after third party insurers for a select few expensive oral cancer drugs. The provincial cancer program will cover the costs of these drugs when patients do not have private insurance, and will financially assist those patients not able to cover their co-pays for these cancer drugs. Lack of human resources, particularly oncology pharmacists, prevents tracking of utilization and appropriate special authority use of cancer drugs. Special authority access in NL is based on a list of drugs that are available through this mechanism.

After expanding the prescription drug plan in January 2007 to cover lower-income families, NL further expanded drug coverage in October 2007 for all citizens facing high prescription drug costs. The sliding scale of financial support is available to families with a total family income of $150,000 or less. Drugs covered are those listed on the provincial formulary and those approved by special authorization.

DISCUSSION

Inter-provincial Drug Approval Timelines

The variable and delayed access to effective cancer drugs has been compounded in 2007 by the appearance of still more new drugs and new treatment indications for existing drugs, a trend that will undoubtedly continue. This has been aggravated by the ongoing variability in provincial treatment guidelines and provincial drug funding processes.

Many provinces, particularly the western provinces and some of the Atlantic provinces, are moving toward integrated single plans for cancer drugs encompassing oral, take home and intravenous cancer drugs. Moreover, the western provinces have province-wide electronic systems to improve access to electronic patient cancer records and chemotherapy ordering systems. Alberta, Saskatchewan, and Manitoba have deployed the comprehensive Varian Medical Oncology (VMO) cancer system and electronic cancer chart, with an electronic drug order entry component. British Columbia provides an electronic cancer chart available at the four regional cancer centres and five of the satellite clinics staffed by BCCA physicians.

Overall, across the provinces, there remain variable timelines for approval, funding, and listing on provincial formularies despite the new JODR process. There is increasing use of special authority access within provincial cancer organizations and Special Access Programs and expanded access programs to gain access to drugs not yet approved or marketed in Canada. The complexity of the process for doctors and patients accessing new drugs, although better in some areas, has not improved substantially.

Approval Timelines in Canada and the US

The time difference between Canada and the US to approve new cancer drugs is now a median of seven months, for the 10 (of 18) new drugs that received NOC from Health Canada. This compares favourably with the median delay of 15 months noted for the 24 previous drugs studied in the 2005 Report Card.

It should be noted that application for NOC for a new cancer drug or indication through Health Canada's Therapeutic Products Directorate is an entirely voluntary process for manufacturers. Most new drugs are submitted for approval to the US FDA first, as the United States is the world's largest market. A decision to submit for approval in Canada (representing only two per cent of the world market for drugs) is influenced mostly by fiscal parameters, based on a business model.

Many patients with rare or less common cancers may face difficulty accessing drugs for which there is only a small market and no incentive for approval in Canada (in addition to variable access within the publicly funded system). Consequently, the differences in approval times

between Canada and the US reflect several factors including Health Canada timeliness of review, and whether or not the drug manufacturer has submitted an application.

A manufacturer's decision about whether (or when) to market a drug in Canada is influenced by the relative ease of entry, or difficulty, compared to other countries. The multiple regulatory steps in Canada are more cumbersome than in the US, where FDA approval opens a vast market immediately. In Canada, federal approval to market the drug is followed by: federal drug pricing approval at PMPRB, (which is now expressing an interest in conducting cost-effectiveness reviews); JODR reviews of clinical evidence and cost-effectiveness (with a subset of clinical and pharmacoeconomic reviews by others); province by province funding approvals with related reviews and price negotiations (often duplicating work already done by other Canadian agencies and jurisdictions); and guideline writing by each province to ensure different notions of appropriate use fit the payment model.

Unlike the FDA system, Health Canada does not disclose ongoing reviews of new drugs nor whether they are undergoing priority reviews. The Health Canada website could be redesigned for better organization, clarity and transparency along the lines of the FDA website to more accurately relay the current status, submitted documentation and evidence (including negative studies), and updates of its drug reviews.

The JODR process will require better coordination and integration with approval processes at Health Canada, as well as more efficient utilization of provincial cancer agency expertise and input. JODR is in discussions with the Canadian Partnership Against Cancer (CPAC) about what roles CPAC may play in cancer drug evaluation and access, especially through its Cancer Control Guidelines Action Group.

The Rising Prices and Costs of Cancer Drugs

The emerging new cancer drugs offer modest incremental benefits at very high cost that are challenging for most public and private payers to bear. Emerging efforts to control these costs include volume purchasing as developed between Manitoba and Saskatchewan. The western provinces with more developed provincial cancer information systems and infrastructure are able to better gate expensive new drugs through special authority type access. These systems permit utilization monitoring and outcomes analysis when new drugs are delivered to the general population.

New tools are emerging that incorporate and prioritize the complex issues, values and competing interests or principles inherent in making difficult decisions around expensive cancer drugs.[49] In fact, we suspect many of the cancer agencies in Canada that are successful at vetting and providing new cancer drugs are to some extent incorporating the components of these tools. Further research to correlate the success rate and timeliness of approving new drugs inter-provincially with the degree of comprehensiveness and sophistication of analytical tools might validate them.

As other countries and their national public health systems struggle to evaluate new expensive cancer drugs, novel access and payment processes have emerged. In Britain, the National Institute for Clinical Excellence (NICE), which is responsible for evaluating cost effectiveness of new drugs, recommended against Velcade as a benefit under the National Health Service. Rather than drop the price, the manufacturer offered to pay for the drug for those patients who do not respond to it.[50] A situation like this happened in Canada many years ago with Taxotere for metastatic breast cancer for a brief period of time where the manufacturer, Rhone-Poulenc Rorer at that time, offered to pay for two cycles and if patients were responding, the public system would pay the subsequent cost. This "pay for results" could be applied to the more expensive new drugs for public funding, as a mechanism to help identify patients who benefit. Governments should fund post-market research to corroborate the results of new cancer drugs and find more cost effective ways to use them. Increased research needs to be done to identify the subsets of patients who benefit the most from new cancer drugs, so that patients who do not benefit are not subjected to ineffective treatments.[51]

Patient Needs and Challenges

Evidence of effectiveness and median survival rates (i.e., who benefits for how long) do not always adequately address the realistic possibility of long-term survival for some patients, who are disadvantaged when caught in aggregates, medians and averages. Such generalized analysis is driven by the absence of precise information about the type of patient who will benefit from an expensive new drug. Without biomarkers to identify the patient, or phase 4 trials to report on real-world effectiveness of new drugs, funders retreat, to the detriment of current and future cancer patients. Exceptional access is increasingly limited to narrow indications, further decreasing the likelihood of great successes for some patients. Exceptional access could be more readily available if designed on a two-month trial basis, followed by the routine restaging tests that accompany any new treatment, to quickly demonstrate whether a new drug is effective for a patient. This concept could be applied in cases where previous treatments have failed, adding much-needed data about real-world effectiveness of new drugs. Trial prescriptions are commonly used in other diseases to determine patient response before continuing with a new treatment and have helped to optimize the appropriate use of drugs. The same structure could be developed for cancer patients.

In the meantime, physicians involved with treating cancer increasingly struggle with access to new cancer drugs for their patients and have to make bedside rationing decisions to balance the competing needs of individuals, public payers and society when prescribing expensive new cancer drugs.[52]

As further discussed in The Cost of Cancer Drugs, page 51, private payers, employers and individuals will either bear more of the brunt of the cost of cancer drugs not paid by the public system, or not be able to access them at all. It may be time to explore a national comprehensive public or public-private insurance program such as the one recently implemented in the Netherlands.[53]

Recommendations

The complex issues around access to cancer drugs remain unresolved and require:

1. Establishment of a national catastrophic drug strategy and drug plan;
2. Development and implementation of Canada-wide guidelines in a timely and consistent manner to speed access and provide national consistency;
3. Introduction of an ongoing evaluation process for new drugs which includes a robust pharmacoeconomic model;
4. Establishment of a single oncology drug budget and formulary in each province integrating parenteral and take-home cancer drugs;
5. Increased translational research to identify the subsets of patients who benefit from the new drugs;
6. Phase 4 (post-approval) trials to confirm treatment results in the cancer population at large;
7. Incorporation of substantial patient involvement into decision-making;
8. Transparency about decision-making;
9. A repository of accurate information regarding applicable funding sources for each drug whether government ministries, third party insurers, research agencies, or compassionate assistance programs of pharmaceutical companies;
10. Redesign the Health Canada website for better organization and clarity along the lines of the FDA website to more transparently and accurately relay the current status and submitted documentation of its drug reviews.

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