RESEARCH PAPER

Notice of Compliance with Conditions: A Policy in Limbo

Avis de conformité conditionnel : une politique incertaine

by JOEL LEXCHIN, MSC, MD
Professor, School of Health Policy and Management, York University
Emergency Physician, University Health Network
Associate Professor, Department of Family and Community Medicine, University of Toronto
Toronto, ON

Abstract

Since 1998, the Therapeutic Products Directorate (TPD) has had a policy termed the Notice of Compliance with conditions (NOC/c) in order to allow earlier marketing of promising drugs for serious conditions before the drugs have definitively demonstrated clinical efficacy. Drugs approved under the NOC/c must undergo post-marketing trials to show clinical benefits. The reasons that some drugs receive a NOC/c are not always apparent, and the TPD releases only general information regarding the conditions that need to be fulfilled. Some drugs have fulfilled their conditions in under 1.4 years, but others had unfulfilled conditions after seven years. Doctors may not be aware that drugs are marketed with a NOC/c nor that some drugs have had their NOC/c withdrawn, and as a consequence may be prescribing inappropriately for their patients. Other jurisdictions have similar policies but with stricter and more transparent requirements. Adopting these provisions, along with other reforms, could help ensure that the NOC/c policy meets it objectives.

Résumé

Les avis de conformité conditionnels (ACC) sont une politique en place à la Direction des produits thérapeutiques (DPT) depuis 1998 et visent à permettre une mise en marché anticipée de médicaments prometteurs conçus pour traiter des maladies graves avant que ces médicaments aient démontré leur efficacité clinique de façon certaine. Les médicaments faisant l'objet d'un ACC doivent être soumis à des essais après leur mise en marché afin d'en démontrer les avantages cliniques. Les raisons motivant l'assujettissement de certains médicaments à un ACC ne sont pas toujours apparentes et la DPT ne diffuse que des renseignements généraux sur les conditions qui doivent être remplies. Certains médicaments ont satisfait aux conditions qui leur étaient imposées en moins de 1,4 année, tandis que d'autres ne l'avaient toujours pas fait après sept ans. Les médecins peuvent ne pas savoir que des médicaments sur le marché sont assortis d'un ACC ou que l'ACC de certains médicaments a été retiré, et, par conséquent, peuvent donner des ordonnances inappropriées à leurs patients. D'autres secteurs de compétence ont des politiques semblables mais avec des exigences plus strictes et plus transparentes. L'adoption de ces dispositions, ainsi que d'autres réformes, pourrait aider à s'assurer que la politique des ACC atteigne ses objectifs.

Before a new medication can be marketed in Canada, it must go through the regulatory approval process overseen by either the Therapeutic Products Directorate (TPD), for drugs derived from chemical manufacturing, or the Biologics and Genetic Therapies Directorate (BGTD), for biological and radiopharmaceutical drugs, including blood and blood products and viral and bacterial vaccines. In either case, the company proposing to market the medication needs to present documentation from laboratory and animal studies, manufacturing processes and the results of clinical trials done in humans showing that the drug is efficacious (i.e., it works under conditions present in a clinical trial) and that its benefit-to-harm ratio is favourable (Health Products and Food Branch 2006a). (Since the procedure is the same for the TPD and the BGTD, for the purposes of this paper, both organizations will collectively be referred to as the TPD.)

The best proof that a drug is efficacious is that it alters the outcome of the illness in question; for example, it prolongs life, leads to faster healing or reduces the severity of symptoms. Before studies have definitively established efficacy, early human trials may indicate that drugs will be beneficial based on their effect on surrogate (or intermediate) outcomes. An example of a surrogate outcome is the lowering of high blood pressure. High blood pressure is not in and of itself a disease, but it is linked to cardiovascular and cerebrovascular disease. Therefore, a drug that has been shown only to reduce blood pressure might reasonably be expected to reduce the morbidity and mortality

from cardiovascular and cerebrovascular disease and would therefore be approved.

In the case of many serious and often fatal diseases, such as HIV/AIDS and many forms of cancer for which treatment is inadequate, waiting for definitive proof of efficacy may delay the availability of new and potentially beneficial drugs. In an attempt to make these treatments available in a timely manner, in 1998 the Therapeutic Products Program (now the Therapeutic Products Directorate) instituted a new policy, the Notice of Compliance with conditions (NOC/c) (Therapeutic Products Program 1998). (When the TPD has approved the marketing of a new drug, it issues a Notice of Compliance signalling that the product has fulfilled the requirements of the *Food and Drugs Act*.) The goal of this policy was to "provide patients suffering from serious, life threatening or severely debilitating diseases or conditions with earlier access to promising new drugs," where surrogate markers suggested that these new products offered "effective treatment, prevention or diagnosis of a disease or condition for which no drug is presently marketed in Canada or significantly improved efficacy or significantly diminished risk over existing therapies." (In the case of cancer, a surrogate outcome might be a shrinkage in tumour size or a longer time until the cancer recurs; for HIV/AIDS, it might be a reduction in viral load.) In return, companies would have to commit in writing to undertake confirmatory clinical studies, that is, studies that definitively establish efficacy, and submit the results of these to the TPD. Should these post-marketing trials not provide sufficient evidence of clinical benefit, the NOC/c can be revoked and the product removed from the market. A NOC/c might also be issued for a new indication for a drug that is already on the market.

This initial policy was subsequently revised effective February 2003 in response to complaints from industry and others that it was not being consistently applied and that there was a need for greater transparency and for the dissemination of educational materials to accompany products issued a NOC/c (Health Canada 2002).

It is important to note that the *Food and Drugs Act* does not provide for a NOC/c, and therefore, technically when a drug is approved under this policy it is in fact getting unrestricted marketing authorization. Thus, any limits that are set on what the company must do have no legislative basis. However, in order to receive a NOC/c, the company has to submit a Letter of Undertaking to the TPD outlining the steps it will take to provide further evidence of the drug's usefulness. In the absence of such a letter, the company would not be allowed to market the product (Health Products and Food Branch 2006b). Furthermore, the NOC/c cannot be issued on the grounds that there are unresolved safety concerns with the new product. While heightened post-marketing safety monitoring may be imposed as part of the NOC/c, this policy is designed to deal strictly with issues related to efficacy.

Although the NOC/c policy has been in existence for over eight years, it does not appear to have been subject to any published formal evaluation. The purpose of this commentary is to provide an overview of what has happened under this policy to the

end of December 2006 and to propose changes in the policy to enhance its ability to meet its objectives. The policy will be examined through three lenses: transparency of the reasons for a NOC/c and the conditions attached to it; monitoring and enforcement of the conditions to which companies have agreed; and effects on doctors' prescribing behaviour.

Transparency of the Reasons for a NOC/c and the Conditions Attached to It

The TPD website has a list of 19 drugs that have received a NOC/c for 22 different conditions (Health Canada 2006b). (Imatinib has three NOC/cs for three different indications, and bortezomib has NOC/cs for two different indications.) Three of the drugs on the list fulfilled their conditions (recombinant factor VII activated, alteplase and tenofovir), one had its NOC/c suspended (celecoxib) and the other 15 have yet to fulfill their conditions. However, this is not a comprehensive list, as it leaves out an additional six products identified through a search of the TPD Notice of Compliance Web page (Health Canada 2006a). Five of these drugs also fulfilled their conditions (abacavir, amprenavir, delavirdine, nevirapine and zanamivir) and one had its NOC/c revoked (bicalutamide). Information about these 25 products was gathered through material available on the TPD website (Health Canada 2006b) and by filing Access to Information (ATI) requests for drugs that received a NOC/c up to the end of 2005. See Table 1 (http://www.longwoods.com/product.php?productid=18862&cat=488) for the complete list of drugs, their indications and the dates on which they received a NOC/c.

The reasons for issuing a NOC/c, as opposed to a regular NOC, are usually not disclosed, and details of studies to be undertaken to confirm clinical efficacy are obscure for drugs granted a NOC/c prior to March 2003, even after examining the documents obtained through the ATI requests. For instance, NovoNordisk Canada agreed to undertake a trial to determine whether a lower dose of recombinant factor VIIa would provide a safety advantage. While this may have been a reasonable request, the concerns about safety problems with the approved dosage were not articulated, and so whatever advantage the TPD was seeking was unclear. The information received for riluzole, used for treating amyotrophic lateral sclerosis, was more forthright – there was an improvement in strength with riluzole compared to placebo – but only because the study in question had been published in the *New England Journal of Medicine* and thus the results were already publicly available (Bensimon et al. 1994).

For drugs with a NOC/c after March 2003, the situation is somewhat better. All these drugs are accompanied by three documents: a Fact Sheet directed at patients, a Health Care Professional Letter and a Qualifying Notice. The Health

Care Professional Letter summarizes the clinical evidence and explains the surrogate outcomes that form the basis for the NOC/c in most cases but not all. Letrozole was approved for treatment of breast cancer because it lengthened the time to recurrence of the cancer ("Approval with Conditions of PrFemara®" 2005), while memantine was shown to significantly lower the rate of decline in the global clinical condition in patients with moderate to severe Alzheimer's disease ("Approval of Ebixa® with Conditions" 2004). On the other hand, the letter for gefitinib merely says that it received a NOC/c "to reflect the promising nature of the clinical evidence in patients with this serious disease [lung cancer]" ("Dear Health Professional(s)" 2003).

Two specific examples, one before March 2003 and one after, raise further questions about the rationale for granting a NOC/c. In 1999, zanamivir was granted a NOC/c for the treatment of influenza. Influenza can be a significant cause of morbidity and mortality, but the difference in the mean symptomatic period with zanamivir compared to placebo is not large. Reductions ranged from 0.8 days in healthy adults to 1.0 day in children, with less conclusive results in high-risk populations such as the elderly and those in nursing homes, and there is limited evidence for all prevention strategies using zanamivir (Cooper et al. 2003). Celecoxib received a NOC/c for the prevention of bowel cancer. Although there was no drug licensed for this use and therefore celecoxib was technically eligible for a NOC/c, this is a disease that takes years to develop; it is not clear why the TPD believed that it was urgent to grant celecoxib a NOC/c for this indication.

"specific conditions associated with approval under the NOC/c policy are negotiated on a case-by-case basis and due to their proprietary nature, cannot be released by the department without prior consent by the drug sponsor"

The TPD's position about the availability of information regarding the conditions that need to be fulfilled, as articulated by a senior policy analyst, is that "specific conditions associated with approval under the NOC/c policy are negotiated on a case-by-case basis and due to their proprietary nature, cannot be released by the department without prior consent by the drug sponsor" (Tara Bower, personal communication with Alan Cassels, November 20, 2002). However, the Qualifying Notices do broadly outline some of the conditions that were agreed to by the TPD and the company in question. The notice to Janssen-Ortho, makers of bortezomib, committed the company to providing a complete study report on a trial comparing bortezomib with high-dose dexamethasone in patients with relapsed or refractory multiple myeloma (Therapeutic Products Directorate 2004b). The notice regarding memantine states

that Lundbeck will conduct a six to 12-month study in patients with moderate to severe Alzheimer's to confirm efficacy results of two previous six-month trials and the new study should employ clinically meaningful and validated efficacy outcomes (Therapeutic Products Directorate 2004a).

Monitoring and Enforcement of the Conditions to Which Companies Agree

Nothing that the TPD provides, either on its website or in the material it releases under ATI, establishes a timetable for the confirmatory studies, nor is there any hint as to how the TPD is monitoring the progress of the commitments. Riluzole has not fulfilled the conditions established in August 2000, and imatinib has been prescribed under a NOC/c since September 2001. Whether these drugs are still being evaluated, the nature of those evaluations and the estimated date to completion are all open questions.

Even for drugs that have fulfilled their conditions, Table 1 shows a significant variability in the time required: anastrozole took under 1.4 years, compared to over 7.25 years for recombinant factor VII. It may be that in some cases, conditions applied by the TPD are difficult to fulfill because a research protocol that will gain ethical approval is hard to design when sufficient doubt exists about efficacy. In other cases, trials may take a long time to be carried out because of small patient populations. But these possibilities are just speculations due to the lack of information provided by the TPD and the company.

Gefitinib was granted its NOC/c as a third-line treatment for non–small cell lung cancer based on two trials that showed tumour shrinkage. One of the conditions was that AstraZeneca conduct a larger trial to show a survival advantage; however, the subsequent study did not demonstrate this outcome. Since gefitinib was licensed only for this one indication, it might be assumed that the TPD would order the drug withdrawn from the market in accordance with its NOC/c policy. Rather than removing gefitinib from the market, in February 2005 the TPD elected to allow it to continue to be sold. The decision was to be revisited "following the provision of more detailed evidence by the manufacturer, if new safety concerns arise, or other therapeutic options arise" (Health Canada 2005). Three-quarters of a year later, Health Canada stopped the use of gefitinib in new patients and restricted its continued use to patients who were currently benefiting from the drug ("Health Canada Endorsed Important Safety and Efficacy Information" 2006).

Effects on Doctors' Prescribing Behaviour

Whether doctors are aware that they are prescribing drugs that have been approved with a NOC/c is questionable. The TPD does not appear to have undertaken any

research to explore this question. Companies are required to send out a "Dear Health Care Professional" letter, all advertising material has to "contain boxed text with prominent disclosure of the nature of market authorization granted" and the product monograph has to contain a similar statement (Health Products and Food Branch 2006b). However, the most effective promotional vehicle is the company sales representative, and there is no TPD or industry directive requiring these people to mention that a drug has been approved under a NOC/c. Insertion of a statement about a NOC/c in the product monograph is probably of very limited benefit, since Canadian doctors' use of monographs is spotty. When physicians were last queried on this topic in 1992, only a third said that they used product monographs "frequently" (Decima Research 1992).

Physicians may also not know that a NOC/c has been revoked; aside from a message posted on the TPD website, there is no further publicity given to this decision. Bicalutamide and celecoxib both had their NOC/cs revoked, in the former case for therapy for prostate cancer in patients who were not suitable for radiotherapy or surgery, and in the latter case for the prevention of familial adenomatous polyposis, a precursor to bowel cancer. Since both drugs had other indications that were not subject to a NOC/c, they remained on the market. The statement about the NOC/c was simply removed from advertisements and from the product monographs. Physicians who were already prescribing these drugs might continue to prescribe them, unaware that clinical trials failed to confirm the preliminary data – in which case patients could be denied more effective treatment and be needlessly exposed to potential risks. Neither Health Canada nor the manufacturers seem to have conducted any studies to look into this situation.

It is beyond the scope of this paper to examine the individual products that have been issued NOC/cs to see how much benefit (or harm) may have resulted from their use. However, if doctors are prescribing them in ignorance of the fact that their approval is based on surrogate outcomes, then there is a strong possibility that they are being used inappropriately and could have a negative benefit-to-harm ratio.

Conclusion

At present, there is little oversight for drugs approved under the NOC/c policy, leaving many unanswered questions. How well is the TPD applying the criteria for awarding a NOC/c? What is the nature of the conditions that the TPD imposes? Why have some drugs not fulfilled their conditions five and six years after receiving a NOC/c? What happens to the drugs if the conditions are not fulfilled? Do doctors know when a drug has been approved under a NOC/c, and does such knowledge affect their prescribing?

The NOC/c policy is designed to improve care and outcomes for patients by allowing promising new drugs on the market faster. However, these drugs remain in

a state of uncertainty regarding clinical efficacy for prolonged periods of time, and the requirements to remove them from that state are a secret. Doctors, even if they are aware of the NOC/c status, have no way of knowing the benefit-to-risk ratio of the drugs, and if they are ignorant of the NOC/c status they may be prescribing these products inappropriately. In the absence of answers to the questions raised above, the actual benefits to patients from the NOC/c policy remain unknown. For manufacturers, the situation is different. Earlier market approval means a longer period of time to sell the drug before the patent expires and generic competition begins. Drug companies clearly benefit from receiving a NOC/c, especially since the requirement to provide follow-up studies in a timely manner to address the conditions does not appear to be rigorously enforced by the TPD.

The European Union has the equivalent of a NOC/c policy termed Conditional Marketing Authorisation (CHMP 2006). Under this policy, the European Medicines Agency (EMEA) is required to publish the list of obligations that recipients of conditional marketing authorization must fulfill, that is, the clinical studies that must be completed, together with the deadline for meeting each obligation. The equivalent of the product monograph, as well as all promotional literature, must mention the expiry date for the provisional licensing. In addition, conditional marketing is valid for only one year, and requests for renewal must be accompanied by an interim report on how the company has dealt with its commitments. Provisions of this type would serve as a useful starting point for reforming the NOC/c policy. The TPD also needs to undertake research to find out whether doctors are aware of the status of drugs approved under this policy. The TPD could require company sales representatives to inform doctors that a product has a NOC/c and then monitor compliance through periodic surveys of a random sample of physicians. The actual benefit-to-harm ratio to patients who receive these products could be explored through the use of observational studies employing databases that link receipt of the drugs with doctors' visits, hospitalizations and deaths.

At present, the NOC/c is a policy with good intentions but unknown consequences, a policy in limbo.

Correspondence may be directed to: Dr. Joel Lexchin, School of Health Policy and Management, York University, 4700 Keele St., Toronto, ON M3J 1P3. Tel.: 416-736-2100 x 22119. E-mail: jlexchin@yorku.ca.

REFERENCES

Approval of Ebixa® with Conditions. 2004. Retrieved April 13, 2007. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/conditions/ebixa_dhcpl_lapds_085203_e.html>.

Approval with Conditions of Femara®-2.5 mg for Use in the Extended Adjuvant Treatment of Hormone Receptor-Positive Early Breast Cancer in Postmenopausal Women Who Have Received Approximately 5 Years of Prior Standard Adjuvant Tamoxifen Therapy. 2005. Retrieved April 13,

2007. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/conditions/femara_dhcpl_lapds_091486_e.html>.

Bensimon, G., L. Lacomblez and V. Meininger. 1994. "A Controlled Trial of Riluzole in Amyotrophic Lateral Sclerosis. ALS/Riluzole Study Group." *New England Journal of Medicine* 330: 585–91.

Committee for Medicinal Products for Human Use (CHMP). 2006. "Guideline on the Scientific Application and the Practical Arrangements Necessary to Implement Commission Regulation (EC) No. 507/2006 on the Conditional Marketing Authorisation for Medicinal Products for Human Use Falling within the Scope of Regulation (EC) No. 726/2004." Retrieved April 13, 2007. <http://www.emea.eu.int/htms/general/direct/legislation/legislationhuman.htm>.

Cooper, N.J., A.J. Sutton, K.R. Abrams, A. Wailoo, D. Turner and K.G. Nicholson. 2003. "Effectiveness of Neuraminidase Inhibitors in Treatment and Prevention of Influenza A and B: Systematic Review and Meta-analyses of Randomised Controlled Trials." *British Medical Journal* 326: 1235–40.

"Dear Health Professional(s)." 2003. Retrieved April 13, 2007. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/conditions/iressa_dhcpl_lapds_081219_e.html>.

Decima Research. 1992. *A Report to Health and Welfare Canada, Drug Regulatory Affairs Division: Health Professional Attitudinal Survey on the Use of Medicines and Drug Information Needs*. Toronto: Author.

Health Canada. 2002. *Notice of Compliance with Conditions (NOC/c)*. Ottawa: Author.

Health Canada. 2005. "Clarification from Health Canada Regarding the Status of Iressa® (Gefitinib) in Canada." Retrieved April 13, 2007. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/activit/fs-fi/fact_iressa_e.html>.

Health Canada. 2006a. *Notice of Compliance Listings*. Retrieved April 13, 2007. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/list/index_e.html>.

Health Canada. 2006b. *Notice of Compliance with Conditions (NOC/c)*. Retrieved April 13, 2007. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/conditions/index_e.html>.

"Health Canada Endorsed Important Safety and Efficacy Information on Iressa® (Gefitinib) 250 mg Tablets." 2006. Retrieved April 13, 2007. <http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/iressa_3_hpc-cps_e.html>.

Health Products and Food Branch. 2006a. *Access to Therapeutic Products: The Regulatory Process in Canada*. Ottawa: Health Canada.

Health Products and Food Branch. 2006b. *Guidance for Industry – Notice of Compliance with Conditions (NOC/c)*. Ottawa: Health Canada.

Therapeutic Products Directorate. 2004a. "Ebixa®: Notice of Compliance with Conditions – Qualifying Notice." April 13, 2007. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/conditions/ebixa_qn_aa_085203_e.html>.

Therapeutic Products Directorate. 2004b. "Velcade®: Notice of Compliance with Conditions – Qualifying Notice." Retrieved April 13, 2007. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/conditions/velcade_qn_aa_090084_e.html>.

Therapeutic Products Program. 1998. *Notice of Compliance with Conditions (NOC/c) Policy*. Ottawa: Author.

Notice of Compliance with Conditions: A Policy in Limbo

JOEL LEXCHIN

Appendix

TABLE 1. List of drugs granted NOC/c, 1998–2006

Year	Date of NOC/c	Drug	Manufacturer	Generic name	Therapeutic class	Disorder for which granted NOC/c	Status of NOC/c	Time between NOC/c and fulfillment of conditions or suspension
1998	July 22	Rescriptor**	Pharmacia & Upjohn	delavirdine	antiretroviral	HIV/AIDS	Conditions fulfilled July 22, 2003	5 years
	Sept. 4	Viramune**	Boehinger Ingelheim	nevirapine	antiretroviral	HIV/AIDS	Conditions fulfilled Sept. 13, 2004	6 years
1999	Feb. 12	Niastase*	NovoNordisk Canada Inc.	recombinant factor VIIa	coagulation factor	clotting disorders	Conditions fulfilled May 19, 2006	7.26 years
	Feb. 16	Activase*	Hoffman-LaRoche	alteplase	fibrinolytic	stroke	Conditions fulfilled Jan. 26, 2005	5.9 years
	June 4	Ziagen**	Glaxo Wellcome	abacavir	antiretroviral agent	HIV/AIDS	Conditions fulfilled Sept. 10, 2001	2.25 years
	Nov. 2	Relenza**	Glaxo Wellcome	zanamivir	antiretroviral agent	influenza	Conditions fulfilled Aug. 26, 2003	3.25 years
	Aug. 30	Rilutek*	Aventis Pharma Inc.	riluzole	antiglutamate	amyotrophic lateral sclerosis		

TABLE 1. Continued

2001	Mar. 1	Agenerase**	Glaxo Wellcome	amprenavir	antiretroviral	HIV/AIDS	Conditions fulfilled July 5, 2004	3.25 years
	Sept. 20	Gleevec*	Novartis	imatinib	protein kinase inhibitor	gastrointestinal stromal tumour		
2002	Aug. 7	Gleevec*	Novartis	imatinib	protein kinase inhibitor	chronic myelogenous leukemia – blast crisis		
	Nov. 25	Casodex**	AstraZeneca	bicalutamide	non-steroidal antiandrogen	prostate cancer	NOC/c revoked for this indication Aug. 18, 2003	0.75 years
2003	Mar. 18	Viread*	Gilead Sciences	tenofovir	antiretroviral	HIV/AIDS	Conditions fulfilled July 20, 2005	2.34 years
	Oct. 8	Gleevec*	Novartis	imatinib	protein kinase inhibitor	chronic myelogenous leukemia – newly diagnosed		

TABLE 1. Continued

	Dec. 17	Iressa*	AstraZeneca	gefitinib	tyrosine kinase inhibitor	lung cancer	NOC/c not fulfilled but drug left on market (Feb. 14, 2005); subsequently restricted to only patients who continue to benefit from drug (June 5, 2006)	
2004	Feb. 6	Replagal*	Transkaryotic Therapies	agalsidase alfa	enzyme replacement therapy	Fabry disease		
	May 20	Celebrex*	Pfizer	celecoxib	anti-inflammatory analgesic agent	prevention of bowel cancer	NOC/c for this indication suspended Dec. 17, 2004	0.58 years
	June 30	Arimidex*	AstraZeneca	anastrozole	non-steroidal aromatase inhibitor	breast cancer	Conditions fulfilled Nov. 1, 2005	1.34 years
	Dec. 8	Ebixa*	Lundbeck	memantine	NMDA receptor antagonist	Alzheimer's disease		

TABLE 1. Continued

2005	Jan. 27	Velcade*	Janssen-Ortho	bort-ezomib	antineoplastic agent	multiple myeloma (bone marrow cancer) – relapsed following first-line therapy and refractory to most recent therapy		
	April 1	Femara*	Novartis	letrozole	non-steroidal aromatase inhibitor	breast cancer		
	April 15	Sativex*	GW Pharma	delta-9-tetrahydrocannabinol/cannabidiol	cannabinoid analgesic	neuropathic pain in multiple sclerosis		
	Dec. 7	Xeloda*	Hoffmann-LaRoche	capecitabine	antineoplastic agent	bowel cancer		
2006	April 24	Velcade*	Janssen-Ortho	bort-ezomib	antineoplasic agent	multiple myeloma (bone marrow cancer) – progressive; patient must have received previous therapy and have undergone or be unsuitable for stem cell transplantation		

TABLE 1. Continued

	May 12	Aromasin*	Pfizer	exemestane	anti-tumour agent	breast cancer		
	July 28	Nexavar*	Bayer	sorafenib	antineoplastic agent	kidney cancer		
	July 28	Prezista*	Janssen-Ortho	darunavir	antiretroviral	HIV/AIDS		
	Aug. 17	Sutent*	Pfizer	sunitnib	tyrosine kinase inhibitor	kidney cancer		
	Oct. 19	Exjabe*	Novartis	deferasirox	iron chelating agent	thalassemia (red blood cell disorder)		

*Listed on Health Canada NOC/c website
**Not listed on Health Canada NOC/c website