



MANAGING PHARMACEUTICAL EXPENDITURE: AN OVERVIEW AND OPTIONS FOR CANADA

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KEY MESSAGES

- ▼ Public drug plans in Canada continue to grapple with public sector pharmaceutical drug spending growth that exceeds revenue growth. Public drug spending is expected to account for 9% of public sector healthcare expenditures in 2010 (approximately 12.1 billion dollars) (CIHI, 2010).
- ▼ This issue persists despite the introduction over the last two decades of various drug reimbursement policies to control cost, including beneficiary cost sharing, mandatory generic drug substitution as well as prior authorization and other forms of utilization review. Other approaches are needed.
- ▼ Furthermore, some of these policies may have unintended consequences on patient health, access to drugs for those without comprehensive drug coverage, pharmaceutical innovation, the timely market entry of generic drugs, the provision of professional pharmacy services and spending on drugs.
- ▼ Promising policy options are available for consideration by governments to manage drug spending in Canada and at the same time provide incentives for innovation in appropriate areas.
- ▼ If governments elect to appropriately manage price and reward innovation using a mix of policy options other than the payment of high prices for new drugs as an isolated approach, then drug prices could be reduced and the development of valuable new drugs for Canadians would be rewarded.
 - ▼ Bulk purchasing and reference pricing policy have numerous advantages for all Canadians compared to the practice of best price policies by some provinces.
 - ▼ Innovation in important clinical areas can be encouraged and accelerated using approaches such as a pay-for-performance reward model, subsidizing the costs of pharmaceutical R&D (both basic research and clinical trials), and considering all sources of value in health technology assessment.
 - ▼ Reimbursement of generic drugs using a sliding scale and granting a royalty to the first generic firm would allow market forces to set the price of generic drugs and promote timely generic competition. The use of tendering can also effectively drive generic price down.
- ▼ The different mixes of policy options deserve fuller analysis. Provinces could experiment on a small scale. Further, governments in Canada should assess the level of financial support provided for pharmaceutical innovation and compare this to the country's financial capacity.

1 INTRODUCTION

Pharmaceuticals are becoming an increasingly important component of healthcare in Canada, both clinically and financially. Despite this sector's growing importance, drug reimbursement policy has been in a state of flux since 2006, with the provincial governments experimenting with their own approaches. Some of these policies may have unintended consequences on patient health, pharmaceutical innovation, and spending on drugs and other health services over the long term. This report, therefore, reviews these developments and presents policy options available to governments to manage drug spending in Canada, while at the same time recognizing the value of innovation. Some are new policy proposals and others are policies that have met with some success in other jurisdictions, both domestically and internationally. Given space constraints, there is not a comprehensive justification for each policy recommendation and each deserves fuller analysis. Moreover, the focus is on policies that have not yet been widely used in Canada. Therefore, important, but commonly used drug cost management policies, such as beneficiary cost sharing, prior authorization and other formulary management tools are not discussed in this paper.

2 BACKGROUND ON PRESCRIPTION DRUG COVERAGE IN CANADA

Most Canadians have some form of drug insurance, either through a public or private plan. Public coverage is dominated by provincial government plans for the elderly (those aged 65 and over), those with low income (social assistance recipients) and others with high drug costs relative to income. The federal government provides drug coverage primarily for Aboriginals, the Royal Canadian Mounted Police, and active and retired members of the military. Private coverage is typically an employment-related benefit.

The majority of drug plans in Canada require some form of beneficiary cost sharing. A variety of forms of cost sharing have emerged, including co-payment (a fixed fee per prescription), co-insurance (a proportion of ingredient cost and/or dispensing fee) and charges that vary with household income and total drug expenditures (such as income-based deductibles and limits on total payouts). Patient charges also vary by drug. For instance, some insurers (both public and private) refuse to cover so-called 'lifestyle' drugs, such as drugs for erectile dysfunction. This amounts to 100% co-insurance. Many public drug plans refuse to cover new drugs that do not offer sufficient therapeutic or cost advantages compared to existing therapies (Grootendorst 2002). There is considerable diversity in the provincial plans, in terms of which products are included on the formulary, which residents obtain coverage and the conditions of coverage. Public coverage of particularly expensive drugs often varies considerably by province (Menon, Stafinski and Stuart 2005; McLeod et al 2010).

According to the Canadian Institute for Health Information, spending on prescribed drugs used outside of hospitals was approximately \$25.4 billion in 2009. Public sector plans accounted for 45% of this total, followed by private sector plans (37%) and out-of-pocket payments by households (18%). Most of the \$25 billion spent on prescribed drugs accrues to manufacturers of innovative (brand) and generic drugs; the Patented Medicine Prices Review Board (PMPRB) reports that spending on patented (typically brand) drugs was \$13.3 billion in 2009 (PMPRB 2010), while the Canadian Generic Pharmaceutical Association estimates that spending on generic drugs was \$5.2 billion.¹ The remainder accrues to wholesalers and pharmacies, in the form of professional (i.e. dispensing) fees and markups on manufacturers' prices.

1 http://www.canadiangenerics.ca/en/resources/market_trends.asp

3 BACKGROUND ON INNOVATIVE DRUGS

Since drugs are an integral component of healthcare, pharmaceutical innovation generates enormous value for Canadians. Society rewards drug innovation using the patent system. Innovating firms receive a 20-year period of patent protection on novel, useful, non-obvious inventions during which other firms may not use the invention. However, since many of the patents are filed long before the innovative drug obtains marketing approval from Health Canada, the effective period of market exclusivity is typically in the range of 5 to 15 years.

3.1 The power of payers

The value of patent protection to an innovating firm depends on the willingness to pay of drug payers (i.e. public and private insurers and uninsured consumers). In many cases, drug payers wield and use significant bargaining power on account of their large size. For instance, the Ontario Drug Benefit (ODB) plan, the public plan in Ontario and largest plan in Canada, demands confidential rebates off some branded drug prices as a condition for formulary listing. The public drug plan in Quebec, la Régie de l'assurance maladie du Québec (RAMQ), requires that it receive the lowest drug price in Canada. The ODB and the public plan in British Columbia, Pharmacare, have experimented with competitive tenders for various drugs.

Drug plan managers cannot be faulted for attempting to get the best deal possible; they are under considerable pressure to control plan costs. However, one consequence of this is that if all drug plans constrain drug reimbursement, then there may not be sufficient incentives for drug companies to innovate (Scherer 2001). Given the small size of the Canadian market, actions by Canadian drug plans will likely not appreciably affect the R&D decisions of multinational drug companies (although they might affect the distribution of R&D spending across jurisdictions within and outside of Canada). But, if enough drug plans act this way then innovation may be adversely affected. Other countries consider international prices when negotiating their own pricing, so Canadian prices may affect innovation incentives outside our borders.

This dilemma over pricing and innovation is partly due to a misalignment of incentives. The federal government is responsible for setting patent policy, but does not bear the full burden of higher drug prices; these costs are borne by provincial government drug plans, private plans and households who lack comprehensive insurance (Anis 2000). Drug plan sponsors presumably care about innovation, but if there is any impact of price controls on innovation, this impact is likely very small, is at best indirect and occurs only after a considerable lag. Thus, there is a strong temptation to apply tough price controls, effectively shifting the burden of paying for innovation onto others. Other, more direct ways of supporting drug discovery may thus be preferred (Grootendorst et al 2010), some of which are reviewed later in this report.

3.2 Interprovincial price comparisons

The manner in which provincial drug plans have attempted to constrain drug prices has undesirable effects. Some provinces (Quebec, Manitoba and Newfoundland & Labrador) have “most-favoured nation” policies that require drug manufacturers to offer them the lowest price in the country. These policies effectively undermine the efforts of other provinces to negotiate lower prices, resulting ultimately in higher prices for everyone.

Such price comparison policies also encourage efforts to work around them. Ontario, for example, has attempted to avoid this problem by negotiating for secret rebates on sales insured by its public drug plans.² Thus, Ontario is setting a high nominal price, but is then being partially reimbursed by the

2 Ontario's ability to extract price concessions depends on the extent to which other payers are privy to the size of the price concessions.

manufacturer for all sales insured by the government. This high nominal price is becoming the price paid by other buyers with less bargaining power. Uninsured individuals who are likely to be relatively sensitive to price end up paying the highest prices. Across Canadian markets, it is likely that small provinces pay more than the largest provinces.³ Price discrimination on the basis of buyer market power is inequitable and leads to reduced access to drugs for some patients.

3.3 Research costs

One of the most challenging problems for innovative drug development is the increase in the average costs of developing new drugs. This is a global problem, but it is relevant for Canada. There are several reasons for increasing costs of pharmaceutical R&D, but an important reason is the high rate of failure of drugs in clinical trials (Mervis 2005). Candidates abandoned at Phase III clinical trials can be enormously costly. A recent high profile example was the failure of Pfizer's drug torcetrapib in Phase III trials in 2006, which reportedly cost the company \$1 billion (Berenson and Pollack 2006). The high attrition rate, in turn, reflects limitations of our understanding of disease mechanisms (Edwards 2008, 2009).

3.4 Direction of research

When a successful drug is introduced, there will often be a series of “me-too” or “follow-on” drugs that mimic the pioneer drug's action. For example, following the introduction of Viagra, other similar drugs were brought to market. Lichtenberg and Philipson (2002) show that competition from drugs in the same therapeutic class costs innovators more than the competition from generics after patent expiry. In many cases follow-on drugs are simply the natural outcome of simultaneous research programs (DiMasi and Paquette, 2005). In other cases, they are the result of an intentionally imitative research program (Garnier, 2008). Follow-on drug development is likely less risky than developing novel “first-in-class” therapies, so it may be an attractive business strategy. But the strategy may decrease the expected sales revenues and increase the costs of the pioneer. Costs increase because the pioneer firm typically spends on marketing and promotion to defend market share. A substantive, but unaddressed, research question is the extent to which the threat of follow-on competition reduces the incentive to conduct research into novel, first-in-class pharmaceutical drugs.

More generally, profit-maximizing firms are not necessarily health-maximizing firms. They invest in the products that will be profitable, not necessarily the products that will benefit society the most in terms of improvements to health. Follow-on drugs can be an example of this problem—it is likely that a greater allocation of resources to unmet medical needs would result in a better social outcome.

3.5 Reference pricing

It is often the case that therapeutically similar drugs vary in price. For instance, diuretics, angiotensin converting enzyme inhibitors (ACEIs) and calcium channel blockers (CCBs) all manage uncomplicated hypertension. Insurers would appear to favor diuretics—they are at least as effective as ACEIs and CCBs, but are a fraction of the cost.⁴ Yet diuretics are not commonly prescribed (Morgan et al 2005). This outcome is likely due to the fact that lower-priced, genericized drugs are typically not extensively promoted to physicians. Instead, pharmaceutical marketing is focused on those drugs that are high-priced.

3 Since Ontario's rebates are secret, we can't verify this conjecture.

4 For evidence on the efficacy of diuretics, ACEIs and CCBs, see: ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial⁹. The BC Therapeutics Initiative estimates the cost of 10 years' therapy (excluding dispensing fees) at maximum doses of a diuretic to be \$37 – substantially less than the cost of an ACEI (\$7139) or a CCB (\$7420). See: <http://www.ti.ubc.ca/node/53>

Some drug plans have used reference pricing (RP) to reduce spending on commonly prescribed drugs with close therapeutic substitutes. RP limits reimbursement of the higher priced drugs, but does not affect coverage of lower priced drugs. As such RP provides financial incentives to drug plan beneficiaries to use, at least initially, the lower priced drugs.

For example, Pharmacare, the provincial plan in British Columbia, limits reimbursement of each ACEI to about \$30/month. At this price, less costly ACEIs are reimbursed as per normal; higher priced ACEIs require additional patient contributions.⁵ A variant of RP is tiered cost sharing. Among private U.S. insurers, drugs in the top tier typically require a \$30 co-payment for a month's supply, whereas bottom tier generic drugs usually require a \$5 co-payment (Gleason, Gunderson and Gericke 2005).

Unlike conventional patient charges, RP fully subsidizes lower cost medicines and, for those who meet exemption criteria, higher cost medicines too. Reference pricing might therefore save money while avoiding the adverse patient health impacts associated with schemes that charge patients for all drugs. A recent review of the impact of RP applied in B.C. and internationally, suggests that the policy effectively reduced pharmaceutical drug spending (Aaserud et al 2006). No deleterious effects on patient health were observed, although the health indicators—which are based on hospital admissions and mortality data—are likely to be insensitive to subtler changes in patient health-related quality of life.

Reference pricing is a midpoint in the range of mechanisms relying on therapeutic substitution. At one end of the spectrum is a policy to not recognize the potential for therapeutic substitution. At the other end is a competitive tendering mechanism in which companies are required to compete to obtain exclusive or preferred access to the market.⁶ The approach of forcing companies to compete aggressively for all or nothing achieves lower prices, but at a cost of patient choice. Reference pricing directs patients, but still allows partial subsidization of higher priced therapies.

3.6 Pricing and procurement approaches and their relevance for Canada

The set of issues Canada needs to address with respect to innovative drugs may be framed as: (a) the extent (and quality) of innovation; (b) the degree of patient access to new medicines; and (c) financial support for pharmaceutical innovation. The design of insurance programs and policies directly affects these three issues, with the key choices for insurance programs being who is insured, which drugs are included on the formulary, the generosity of coverage for included drugs (i.e. the degree of cost sharing), and what prices are paid to suppliers.

The decision on price speaks to how drugs are procured. If an insurer wishes to get the lowest possible prices, the most effective approach will be to bargain with suppliers within specific molecules or therapeutic classes, and to cover only the lowest priced product. This kind of bargaining leads to a limited formulary, to be sure, but may allow for universal insurance and low premiums.

A different approach on pricing is to relate prices to value using a technical standard for value such as Quality-Adjusted Life-Years (QALYs) gained. The U.K.'s National Health Service uses such a cost-effectiveness analysis, and has explicitly stated a willingness to pay a threshold of £20,000 to £30,000 per QALY. Products with cost-effectiveness above this limit are typically not included in the formulary. Through this appraisal process, drug companies may be encouraged to set prices that satisfy the cost-effectiveness criteria.

5 Similar reimbursement limits have been applied to the CCBs, nitrates, H2-blockers and NSAIDs. See <http://www.health.gov.bc.ca/pharmacare/sa/criteria/rdpcategoriesindex.html#>.

6 Gagnon (2010) proposed that Canada consider employing this as part of a national pharmacare program.

A third approach on pricing is to enforce no limits at all, obviously creating problems of sustainability. This is usually solved by requiring drug plan beneficiaries to pay a fraction of drug costs. Cost sharing exerts downwards pressure on price, as buyers will simply fail to fill prescriptions for products that are too expensive. This may be seen as the traditional U.S. approach.

A fourth approach on pricing is to rely on the prices charged in other jurisdictions—price referencing—which allows an insurer to avoid any difficult analysis or negotiations. In this approach, the countries that are used as comparators are critically important. Canada has historically relied on price referencing to set the prices of breakthrough drugs (using the PMPRB's price comparison tests), and cost-effectiveness analysis (Common Drug Review) for determining formulary inclusion.

It is evident that the choices made will have an effect on the investment in innovation. Many argue that Canada should simply try to get the lowest prices since its effect on global innovation is small. Canada, in other words, should “free ride” on the R&D supported by other jurisdictions. This is not advisable for two reasons. First, Canada represents a small, but not insignificant, proportion of global pharmaceutical demand, but it also is part of an international community. Since innovation for new drugs creates global benefits, countries with financial capacity (such as Canada) should bear their fair share of the expenses required to make innovation feasible. Second, while free-riders pay proportionately less for pharmaceutical R&D, they benefit only in so far as their disease burden coincides with that in the jurisdictions that support R&D (Civan and Maloney 2006). In other words free-riding may come at a cost of a paucity of research on diseases that are most important to the free-rider. If Canada wishes to support R&D, the question is how should Canada make a contribution towards research? Presumably it should try to direct incentives for innovation into the most valuable uses, which means amply rewarding the innovations that deliver the most value to Canadians.

There is also an industrial policy angle to drug pricing, with each jurisdiction attempting to lure R&D investment away from other jurisdictions. To the extent that Canada engages in this, it should use the most direct policies available to attract investment, such as reductions in taxes, increases in funding to support research, or improved advanced education in cognate fields. Drug pricing is at best a very blunt tool for attracting R&D investment. The only attraction of using high drug prices to attract investment by pharmaceutical companies is that the funding does not flow directly through the government. Rather, high drug prices serve as a hidden tax. Hidden taxes, with all their inefficiencies, are generally not a good policy.

4 POLICY OPTIONS FOR INNOVATIVE DRUGS

Our policy recommendations attempt to meet the following principles for procurement of innovative drugs:

- ▶ Canada should adequately reward the development of valuable new drugs to sustain a continuing flow of investment into pharmaceutical R&D.
- ▶ Principle 1 above must be balanced by recognition of the need for financial sustainability for payers.
- ▶ Canada should attempt to ensure a stable, predictable policy regime to support investments into innovative drugs.

4.1 Improve health technology assessment

We recommend that health technology assessment (HTA) agencies in Canada reconsider how pharmaceutical innovation is valued. HTA agencies typically focus on the clinical value of new pharmaceuticals (measured by QALYs gained when used for approved indications), but fail to

systematically incorporate other sources of value such as patient convenience (Goldman et al 2010). Our view is that a key limitation of HTA, as typically practiced, is that it fails to reflect the dynamic benefits of new technology. A drug may be deemed unattractive based on a static net benefit (cost-per-QALY) threshold, but could be attractive if the flow over time of the net benefits produced by the drug is tallied. Future QALYs can exceed the present QALY as new therapeutic uses are discovered. Thus, for instance, the ACEI ramipril was shown to have additional clinical uses after it was initially approved as a treatment for hypertension. Future costs can be below present costs as generic versions of the drug become available. The problem is that drug companies are discouraged from developing products whose static net benefit is below the threshold set by the HTA agency (Vernon, Goldberg and Golec 2009), even if the drug delivers net benefits over time in excess of the threshold.

The Common Drug Review evaluation process should be reviewed to consider all sources of value provided by new pharmaceutical drugs.

Governments in Canada should assess the level of financial support provided for pharmaceutical innovation (via drug plan willingness to pay for innovative drugs, direct and indirect subsidies for R&D costs and other means) and compare this to the level of support commensurate with financial capacity. Further, governments should adjust the level of support upwards (or downwards, as the case may be) and consider the best mix of supports (e.g. supra-competitive prices, subsidies of R&D costs and other means). Should governments wish to use mechanisms other than high prices to support innovation, then the following price control mechanisms are recommended:

4.2 Bulk purchasing

Since bulk-purchasing is an effective mechanism for exercising buyer market power, it can be used to drive prices down. However, this creates a risk that the creators of innovative drugs will not be appropriately compensated. As discussed above, bulk-buying should be used in concert with other supports for pharmaceutical innovation if governments in Canada are willing to pay for innovation that delivers real value.

We recommend experimentation with coordinated bulk-purchasing for some patented drugs. This would solve price discrimination problems through buyer market power. Bulk-purchasing arrangements could include a combination of provinces and private insurers willing to align with the provinces.

4.3 Avoid best-price policies

Best price policies effectively create a floor price that may ultimately lead to higher prices for all provinces. They lead to higher prices in the provinces that are used as comparators; they inhibit innovation in pricing strategies; and they encourage provinces to use costly schemes to get around the price comparisons.

We recommend that the RAMQ (Quebec), Manitoba, and Newfoundland & Labrador policies requiring manufacturers to grant them the lowest price in Canada be reconsidered.

4.4 Reference pricing

Reference pricing, as described above, offers a useful way of applying pricing pressure on products that offer little or no therapeutic benefit over others in the class.

We recommend that provinces investigate the use of reference pricing in therapeutic categories with multiple similar products.

4.5 Subsidize the cost of pharmaceutical R&D

In addition to paying supra-competitive prices for innovative drugs, governments can support pharmaceutical innovation by subsidizing the costs of pharmaceutical R&D, both basic research and clinical trials. Such subsidies will encourage companies to shift R&D to Canada, and will enable research to be undertaken that cannot be commercially justified on a risk-adjusted basis.

4.5.1 Publicly-funded basic research

Public subsidies for basic research are not new—indeed, much of the budget of the U.S. National Institutes of Health and the Canadian Institutes for Health Research sponsors basic research germane to pharmaceutical R&D. Public funding is the dominant source of finance for most basic R&D. What is new are proposals that target the high failure rate of drugs in clinical trials. One option is public subsidy of large-scale, not-for-profit consortia that conduct the basic research necessary to identify and validate drug targets in humans (Edwards 2008, 2009; Maurer 2009). The idea is to declare proof-of-concept trials as the boundary between pre-competitive and competitive drug discovery, and to fund this collectively. Specific aspects of this proposal include: 1. having costs of this research shared by all stakeholders (industry, non-profit research institutions and governments) to spread risk; (ii) placing the research findings in the public domain to: disseminate findings rapidly and widely so as to avoid duplication of effort; conserve the time and energy required to define patent rights over future scientific discoveries; and negotiate legal agreements to share existing knowledge or reagents; and (iii) conducting research in partnership between academic and industrial scientists to capitalize on their respective skills and promote collective learning and technology transfer. The Structural Genomics Consortium⁷ provides an example of the potential of such collaborations.

We recommend that governments consider how they can partner with for-profit pharmaceutical research companies to accelerate drug innovation inside Canada.

4.5.2 Publicly-funded clinical trials

Another proposal to encourage drug innovation that is currently attracting attention is public funding of Phase III clinical trials (Lewis, Reichman and So 2007; Baker 2008, Boldrin and Levine 2008; Jayadev and Stiglitz 2009). Government-organized clinical trials could offer some benefits owing to potential reductions in the cost of capital and a focus on clinically important therapies. Publicly-funded safety

⁷ <http://www.thesgc.org/>

and efficacy trials might also produce information that is more credible and clinically useful than industry-funded trials. At the same time, since clinical trials are extremely expensive, one could expect that decisions over which clinical trials should be financed would become a political issue. Some governments, such as Saskatchewan's, have already committed to sponsor clinical trials of MS therapies, perhaps because they have a relatively high burden of MS.

If governments are to engage in such sponsorship, we recommend that a process be established for determining which clinical trials should be run, free of political interference. The process would also have to carefully consider how government funding would interact with private funding, and control of intellectual property.

4.6 Pay-for-performance reward model: licensing

The licensing model, in which drug companies agree to sell new drugs close to variable cost in exchange for a licensing fee, forms the basis for several recent proposals for rewarding innovation without the distortions caused by patents. One of these proposals is the Health Impact Fund (Hollis and Pogge 2008). The Health Impact Fund (HIF) would set the licensing fee based on the measured health impact of the drug in each of the 10 years following market launch. The HIF therefore pays the licensing fee in a series of 10 installments. Each payment represents a share of a reward fund; the reward fund share for drug x in a given year is equal to drug x's share of the global health produced by all participating drugs in that year. Health impacts would be measured using many of the same methods of health technology assessment currently used by drug plans when deciding whether or not to reimburse a new drug (Claxton et al 2008; Brazier et al 2007). For example, if all participating drugs were estimated to have saved twenty million QALYs in a given year, and if drug x had saved two million of these QALYs, then it would receive 10% of the fund. This proposal therefore rewards drugs to the extent that they improve health.

The HIF creates another significant advantage as a supplement to the patent system. Because the patent system is market-driven, firms have little incentive to conduct R&D into important diseases that primarily afflict the poor. The HIF, in contrast, could be used to reward the development of drugs with large health impacts, even if the beneficiaries are themselves not funding the reward payments. The HIF could similarly provide incentives to develop new uses of older drugs for which there would otherwise be no significant reward.

We recommend that provinces explore systems of prizes or licensing to stimulate drug discovery that are compliant with the World Trade Organization's Trade-related Intellectual Property Rights agreement.

5 BACKGROUND ON MULTI-SOURCE DRUGS AND PHARMACY SERVICES

In this paper, generic drugs and pharmacy services are considered together since, for historical reasons, the funding of pharmacy services in Canada has been intimately linked to generic sales.

Multi-source drugs are typically those with both a branded product and bio-equivalent generic products. Because they offer no quality advantages over their branded counterparts, generic drugs compete for market share by offering low prices. Most provinces have exploited this by mandating that if a generic

version of a drug is available, reimbursement be limited to the price of the cheapest bioequivalent version. This policy has encouraged generic drug use. In 2009, more than half—54%—of the 483 million prescriptions in Canada were filled using generic drugs (IMS Health 2010).⁸

5.1 The system of rebates

While the provinces have successfully created incentives for generic drug use, they have been less successful in procuring these drugs at low prices. Until recently, the ODB program, the largest drug plan in Canada, effectively determined generic drug reimbursement prices. Since 1993, the ODB has set its generic drug reimbursement at some fraction of the price of the reference branded drug. Initially this was 75% (Anis, Guh and Woolcott 2003). In October 2006, it was lowered to 50% and now it is 25%. Prior to October 2006, public and private plans across Canada used the ODB generic reimbursement rate to set their own prices.⁹ Thus, the ODB set a kind of national standard generic drug reimbursement rate. But, this rate was quite generous. Generic manufacturers were willing to sell for less and did so to earn pharmacy business. Pharmacies captured the difference between the reimbursement price and the pharmacy's actual acquisition price of the generic drug. This difference is known variously as the "rebate" or "professional allowance". Although there are no official statistics, the average rebate was said to be in the order of 50% of the ODB generic reimbursement price. Rebate revenue accruing to retail pharmacies in Canada was likely in the order of \$2 billion (Grootendorst, Rocchi and Segal 2008). The recent reductions in prices paid for generic drugs by the ODB and other drug plans have thus affected the economics of the retail pharmacy sector in Canada.

The ODB generic drug reimbursement policy also affected the market entry of generic drugs. Rebates are generally greatest when many generic drug firms compete to sell the same drug. However, if only one generic firm is selling a drug, then the balance of power shifts. The pharmacy is obliged to stock that generic drug and this means that the pharmacy is less able to demand a rebate. Therefore, the first generic firm on the market enjoys temporary market power and can earn substantial profits if the drug in question is commonly prescribed and the reimbursement price is high. For most major products, there are multiple generic firms launching within a month of the first generic—often within days—so that the exercise of market power is usually very short-lived. But even these temporary windfall profits can provide strong incentives for a generic firm to be first to enter the market.

5.2 Generic drug litigation

Generic firms typically must spend a lot on litigation in order to be first to enter the market. There is a common misperception that generic competition arises following expiry of the patent. In reality, most branded products are protected by several patents that expire at different points in time. The patents relate to different aspects of the drug including its formulation and manufacture. Typically only some of those patents are effective barriers to generic entry. Generic producers can work around other patents, and can show in court that yet other patents are invalid. However, this process is time-consuming and costly. A generic firm would contemplate incurring these costs only if the profits from being the first generic on the market are sufficiently high. But, as noted earlier, the profits from being first in the market depend on the generic reimbursement price less the rebate, and the time until competitive entry. The higher the price, and the slower expected competitive entry, the more likely a generic firm will find it profitable to attempt to challenge the branded firm's patents in court.

8 IMS Health also estimates that in 2009, branded drug prescriptions were \$45 more expensive, on average, than generic prescriptions. Had all generic prescriptions instead been filled with a branded drug (and assuming that these branded drugs cost \$45 more) drug spending would have been about \$12 billion higher.

9 Since the 2006 price decreases in Ontario, there has been much more divergence across provinces and between private and public plans. There is some evidence that the reimbursed prices for private plans actually increased in 2006.

The reason that litigating a branded drug's patents is so costly has to do with the rules governing pharmaceutical patents in Canada, known as the Patented Medicine (Notice of Compliance) Regulations, or NOC Regulations. Under these rules, a firm that wishes to launch a generic version of a patented drug must serve the patentee (the brand firm) a Notice of Allegation (NOA) that demonstrates either: (i) its generic will not infringe on any of the brand firm's patents or, (ii) the patents are invalid. The patents in question are those listed by the Minister of Health on the Patent Register.¹⁰ For a drug to be sold in Canada, it must receive a Notice of Compliance (NOC) from Health Canada. The brand firm, should it disagree with the claims in the NOA, can ask a court to prevent the Minister of Health from issuing an NOC for the generic product until after the matter is adjudicated, or after 24 months elapse, whichever comes first.¹¹

The NOC Regulations are intended to lead to a summary judicial review of the claims contained in the NOA. Instead of quickly resolving cases of patent infringement, however, the procedure has dramatically extended litigation in some cases.

Consider, for instance, litigation between AstraZeneca and the generic firm Apotex over the patents on the blockbuster drug Losec (omeprazole). To date this litigation has lasted 17 years. Apotex has served 12 different NOAs on AstraZeneca in respect of Losec; the Federal Court has returned 55 decisions in this litigation, the Federal Court of Appeal has returned 15 decisions and the Supreme Court has returned 1 decision. Many of these trials are complicated and expensive. As an example, the dispute over the validity of the 751 patent on the omeprazole tablet involved over 11 experts in the area of pharmaceutical chemistry.¹² Five experts testified in the litigation over the 668 and 762 patents¹³; with one expert alone billing \$92,900 plus expenses.¹⁴ Apotex was able to launch a generic version of Losec capsules in January 2004; litigation over the tablets is ongoing. While regulatory changes enacted in 2006 now prevent the issuance of multiple, consecutive stays, the NOC Regulations continue to allow brand firms to extend monopolies based on patents that are ultimately found invalid or not infringed.

Losec is just one of numerous drugs that Apotex has challenged. Apotex has been a party in 432 different cases considered by the Federal Court and the Federal Court of Appeal since 1997. Apotex has also been a party to seven Supreme Court cases. Apotex recently claimed that in the last 10 years, it has spent \$800 million on litigation. Extrapolating from this to the other generic and brand firms, it appears that annual litigation costs relating to pharmaceuticals in Canada are in the hundreds of millions of dollars, chiefly for litigation between generic and brand name firms. Indeed, there are in the order of 100 Federal Court cases each year involving pharmaceutical patents.

As mentioned in the previous section, the ODB has reduced the generic reimbursement price to 25%. Other provinces have followed suit. For instance, B.C. has dropped its rate to 35% and Alberta has dropped its rate to 45%.¹⁵ This will no doubt reduce public spending on generic drugs already on the market. However, these policies may somewhat reduce the temporary windfall profits earned by the first generic, and may therefore reduce the financial incentive for generic firms to challenge patents on branded drugs. Thus, drug plans will pay more for branded drugs whose patents, if challenged in court, would be found to be invalid or not infringed by a generic product.

10 <http://www.patentregister.ca/>

11 The 24-month period is prescribed by paragraph 7(1)(e) of the Regulations. Prior to amendments in 1998, the stay period was 36 months.

12 <http://decisions.fct-cf.gc.ca/en/2003/2003fct771/2003fct771.html>

13 <http://decisions.fct-cf.gc.ca/en/2007/2007fc688/2007fc688.html>

14 <http://decisions.fct-cf.gc.ca/en/2009/2009fc822/2009fc822.html>

15 Private insurers may pay considerably more.

Lower generic drug reimbursement prices will render litigation less profitable for another reason. The NOC Regulations do not resolve issues of patent validity or infringement; a generic that prevails in the NOC litigation can still be sued for patent infringement under Section 57 of the Patent Act. This feature of our pharmaceutical patent rules resembles “double jeopardy”. Should the generic firm prevail in the NOC litigation but lose in a patent infringement suit, then it is responsible for compensating the brand firm its lost profits. Of course, the generic firm can use the profits that it earned to compensate the brand firm. But the generic firm’s profits are typically lower than the profits that the brand would have earned from the same unit sales. (Recall that the generic drug reimbursement price is regulated to be a fraction of the branded drug price.) Thus, double jeopardy exposes a generic firm that prevails in the NOC litigation to potentially large losses. A reduction in generic drug reimbursement will reduce the generic firm’s profits and thereby increase these potential losses. This aspect of our regulatory system may discourage generic firms from challenging branded drug patents.

Litigation by generics is critically important to drug plans, and yet drug plans don’t explicitly reward such litigation.¹⁶ For example, Pfizer’s blockbuster product amlodipine recently became available as a generic after litigation led to impeachment of the remaining patent. In the absence of the litigation, the patent declared invalid would have extended Pfizer’s exclusivity for years. Generic litigation saved Canadians hundreds of millions of dollars. Pfizer had fought vigorously to maintain its patent. Yet, when Ratiopharm, the generic litigant, prevailed, Saskatchewan rewarded Pfizer by granting its subsidiary the exclusive contract to sell generic amlodipine in the province, at a generic price enabled by Ratiopharm’s litigation.

The ODB recently introduced a special rule to compensate generic firms for enabling competition by litigating weak patents. Starting in 2014, the ODB will allow for a higher generic price if it finds that generic entry was enabled by litigation. In particular, it will reimburse generic drugs at 50% (rather than 25%) of the brand name drug price for a three-month period after the first generic drug becomes listed on the ODB formulary. Whether the ODB policy will appreciably alter the incentives to challenge weak patents is doubtful, in that all generic firms benefit from the higher price, not just the successful litigant. Ontario is the first province to create such a reward and it is a positive step.

5.3 Retail pharmacy

The sharp reductions in generic drug reimbursement prices chiefly reduce the rebate income accruing to pharmacies. And these reductions in rebates are radically altering the economics of the retail pharmacy sector.

The expansion of generic drug rebates over the last four decades has affected both the density of pharmacies and the range of services they offer (Grootendorst, Rocchi and Segal 2008). In particular, rebates increased the average revenue earned per prescription dispensed and this increase in gross margins has likely attracted additional pharmacies into the industry or sustained marginal pharmacies. These marginal pharmacies have sufficiently high average dispensing costs such that they would not be viable—and hence would not have entered or remained in the market—without the rebate income.

A reduction in rebate income will, in turn, induce these same pharmacies to exit the industry. The reduction in the number of pharmacies will have various secondary effects. First, surviving pharmacies will absorb the dispensing volumes of pharmacies that close. Surviving pharmacies will exploit scale economies; that is, their average dispensing costs will decline as their dispensing volume grows. Second, pharmacy closures might increase patient travel time and reduce access to community care, especially in some rural areas where pharmacy density is relatively low.

¹⁶ In New Zealand, where the government is the sole insurer, it has in some cases litigated to have patents delisted, as generic companies are unwilling to invest in this activity there.

A reduction in gross margins may also reduce the incentive among surviving pharmacies to compete for market share by offering counseling and other ancillary patient services, store improvements and other dimensions of quality. For uninsured consumers, pharmacies offering lower levels of quality, but also lower prescription drug prices may be welcome. The policy may be less welcomed by those who rely on pharmacist counseling to help manage their medication use.

6 POLICY OPTIONS FOR MULTI-SOURCE DRUGS AND PHARMACY SERVICES

Our policy recommendations attempt to meet the following principles for procurement of multi-source drugs and pharmacy services:

- ▶ The prices of generic drugs paid by consumers should be as low as possible to benefit consumers, especially those who lack comprehensive insurance.
- ▶ Adequate financial incentives should be provided to generic firms to engage in costly litigation in the absence of any other mechanism for enabling competitive entry into the market. Such incentives should be conditional on the success of the litigant.
- ▶ Pharmacies should be adequately compensated for providing professional services to patients, and in particular to those patients whose medication regimens require extra professional oversight.
- ▶ Pharmacies should be adequately compensated for the cost of dispensing. That being said, there is no single dispensing cost; instead the average dispensing cost depends on the volume of prescriptions dispensed by the pharmacy (“pharmacy size”).¹⁷ There could be a few very large pharmacies operating at very low average cost or many small pharmacies operating at high average cost. Policy-makers need to select an acceptable pharmacy size (and, by implication, the regional density of pharmacies) and pay dispensing fees commensurate with this choice of size.

6.1 An effective system of driving price down

The ODB’s goal of lowering generic drug prices is commendable, although there could be a different mechanism for achieving this. This mechanism, first proposed by Hollis (2009), is a sliding scale in which the generic reimbursement price (expressed as a fraction of the brand price) decreases as more generic firms supply the market. This mechanism affords two advantages relative to the across-the-board 25% reimbursement rate now used by the ODB. First, reimbursement for the first generic could be quite generous, so that generic firms would have an incentive to enter markets in a timely manner. Second, under the proposed mechanism, the reimbursement price will decline until it is approximately equal to the generic’s average total production cost, which is the lowest feasible price that the ODB can pay. This result arises naturally because generic firms will keep entering the market until it is no longer profitable to do so. Profits are positive as long as the firm’s revenues exceed its total costs, or equivalently, so long as the price received per unit exceeds its average cost. The zero profit condition is satisfied when the reimbursement price is just equal to average cost. Thus, under the proposed mechanism, the generic reimbursement rate would be related to production costs. The ODB’s fixed 25% rule, by contrast, will lead to excessive prices for some generic products and to prices below cost for others.

We propose that provinces experiment with a declining price scheme using one or two products.

¹⁷ For empirical evidence on dispensing costs, see: Mentorx. Costs of Ontario Community Pharmacy Services – 2008. Final Report, 2008. <http://workbench.cacds.asitechinc.com/lib/db2file.asp?file=127>; and AT Kearney. Activity Based Costing Study. Final Report: Study Findings and Analysis January 2007. <http://www.health.gov.bc.ca/pharmacare/publications.html#>

6.2 Tendering

Tendering is a strategy that can effectively work to reduce drug prices. The typical implementation of a tender requires an insurer to choose an exclusive generic supplier for some period. Saskatchewan has used a tender mechanism for a number of drugs, using its “standing offer contract” that makes the chosen generic the only one available in the province. Saskatchewan offers a number of advantages including reduced administration and speedy payment terms. Unfortunately, as Hollis (2009) describes, this mechanism has had limited success in reducing prices because of Quebec’s best price requirement. Ontario recently attempted to use a tender mechanism within a complex mechanism allowing for two generic suppliers, but this effort was frustrated by a lack of cooperation from generic manufacturers. B.C. has used a tender for olanzapine. Tenders are also used extensively in other countries, effectively driving prices down.

There are complications involved in tenders, particularly when the provincial insurer is only one of many insurers. Cooperation between insurers in a province would make tenders generally more successful. In both Ontario and B.C., brand manufacturers dominated the tender: it seems that provinces should be careful about using tenders when a drug is first genericized.

We recommend continued experimentation with tenders for generic drugs, starting no earlier than one year after generic entry.

6.3 Bulk purchasing

It is likely possible to motivate generic firms to offer lower prices if the buyers exercise market power more effectively through combined efforts. For example, the sliding scale reimbursement mechanism described in section 7.1 would be more effective if adopted by multiple provinces.

We recommend that the provinces explore bulk purchasing of generic drugs, with or without private insurers.

6.4 Price uniformity within provinces

The recent Ontario regulations have made it clear that all payers in Ontario are to benefit from the low prices negotiated by the Ontario public drug plans. Since the taxpayers who benefit from reduced pricing for the Ontario Public Drug Program are generally the same individuals who benefit from reduced pricing for their employment-based insurance plan, this seems appropriate. In addition, it is likely inefficient to allow very high pricing for uninsured individuals. Price uniformity implies price transparency, if even uninsured consumers obtain the same price, and this means that provinces would not be able to obtain secret rebates as part of a price negotiation. This creates an additional incentive for bulk buying by several provinces. If the buyer is small relative to the overall market in Canada, the supplier will not be willing to offer a low price that leads to decreased prices in other provinces. However, if the buying group represents most of Canada, then there is less concern about reduced prices in other provinces.

We recommend that the provinces ensure that all payers in the province obtain the same price as the provincial drug insurance plan.

6.5 Review of pharmacy professional fees

A reduction in generic reimbursement rates will necessarily reduce rebates and this may have some deleterious effects on consumers. In particular, there may be pharmacy closures and reductions in the provision of counseling and other professional services. The ODB introduced policies to mitigate these effects. In particular, pharmacies will receive a \$60 payment for reviewing the medication use of those taking three or more medications.¹⁸ Also, rural pharmacies are provided with professional (dispensing) fees of up to \$12 to help them remain commercially viable. All other pharmacies in the province now receive a slightly larger professional fee (\$8 up from the \$6.50 fee paid before October 2006). The \$8 fee might be below the cost of dispensing for even high volume pharmacies, but it is a move in the right direction.

We recommend further exploration of how the remuneration for pharmacy professional services should be structured.

6.6 Review of the NOC Regulations

The NOC Regulations that govern generic drug entry are extremely costly, and appear to offer considerable scope for improvements in efficiency in terms of reduced litigation and earlier entry.

The provinces should engage with the federal government to undertake a review of the performance of the NOC Regulations, in combination with the other measures that are intended to provide innovators with market exclusivity (patents and data exclusivity).

6.7 A royalty for successful generic litigants

Ideally, the regulations governing generic entry would be reformed. If they are not reformed, then there needs to be a financial incentive for the first generic firm that demonstrates in litigation that the patents on a branded drug are invalid or not infringed. Hollis (2009) proposes that this incentive consist of a pre-specified, time-limited royalty paid to the litigating generic by all sellers of bio-equivalent products for each unit they sell. Such a mechanism explicitly rewards the generic firm that prevails in patent litigation for the benefit that it creates by enabling competition. One may question why a separate special reward is necessary, given that the sliding scale generic reimbursement mechanism described above provides the most generous reimbursement to the first generic firm on the market. The reason is that this mechanism does not necessarily reward the successful generic litigant. In some cases, other generic firms are able to have their drug listed on the drug plan formularies prior to the successful litigant.

The royalty approach requires that the drug plan (or some regulatory body) set the royalty rate and if this rate is set too high, the royalty may discourage subsequent generic entry. If it is set too low, too little litigation will ensue. However, at present the royalty rate is set at zero, and this is likely to lead to extended exclusivity periods based on patents that would be found invalid or not infringed if challenged in court.

We recommend experimentation with such a scheme on one or two drugs.

¹⁸ <http://www.health.gov.on.ca/cs/medscheck/index.html>

7 BACKGROUND ON SUBSEQUENT ENTRY BIOLOGIC DRUGS

One of the most important developments in pharmaceutical markets in recent years is the growth in the share of sales accruing to “biologic” products. These are generally complex proteins manufactured through biological, rather than chemical, processes. The percentage of sales from biotechnology products within the world’s top 100 drugs is expected to reach 48% globally by 2016 (Van Arnum 2010). (Generic and over the counter drugs will continue to be dominated by conventional small-molecule drugs.) Pharmaceutical policies should obviously be crafted giving due consideration to this class of products, given the cost implications.

The first observation to be made about biologic products is that many (though not all) such products are chiefly dispensed inside hospitals, rather than through retail pharmacies. Hospitals, as informed buyers, can aggressively negotiate on price, since the prices achieved may be confidential. In such relationships, there are no problems caused by the market power exercised by pharmacists. However, hospitals may have incentives to functionally restrict their own formularies in order to reduce costs.

The second key distinction between biologics and small-molecule drugs is that there are no “generic” biologic products, and no standard of demonstrating bio-equivalence that would allow a prescription to be filled with any bio-equivalent product. If a firm develops a product that is very similar to an existing brand name biologic, it is called a “subsequent entry biologic” (SEB) in Canada. A SEB application is treated by Health Canada as a new drug application, although it may to some extent (and subject to data exclusivity regulations) rely on the data files submitted for the brand name reference product to help demonstrate effectiveness and safety.

Unless a SEB is able to demonstrate clinical superiority to the reference small-molecule product, SEB needs to compete on the basis of price (as for ordinary generic drugs). But, price competition is not easy for SEBs since there is no substitution at the pharmacy. It is difficult to use price to change what prescriptions are written as prescribing physicians are not directly affected by price and have historically been relatively insensitive to price differences in their prescribing patterns. At the same time, given the costs of detailing doctors and the difficulty of obtaining a high volume of sales, costs of SEBs are likely to be relatively high, and given entry barriers, prices will be high too, with relatively small discounts off the reference product price. The competitive tools available to SEB manufacturers are therefore limited. One approach is for the manufacturer to seek formulary listing for a wider range of indications for the SEB, given its lower price.

8 POLICY OPTIONS FOR SUBSEQUENT ENTRY BIOLOGIC DRUGS

8.1 Reference pricing

Since SEBs are therapeutically similar, but not interchangeable with each other or the reference product, reference pricing may be an appropriate tool for encouraging price competition. Reference pricing would encourage physicians to consider price in their prescribing decisions for those patients for whom the SEB would be a good therapeutic substitute for the reference product. Applications for exceptional coverage of a more expensive product could be made when the prescriber documents medical need. For some types of biologics taken by a patient over the course of years (such as for therapies for multiple sclerosis), such a strategy could create effective price competition.

We recommend that provinces consider whether reference pricing strategies would be effective for Subsequent Entry Biologic drug markets.

9 CONCLUSION

Public drug plans in Canada are increasingly leveraging their buying power to reduce prices paid for brand and generic drugs. Drug plan managers cannot be faulted for constraining program expenditures. However, there may be unintended consequences for pharmaceutical innovation, the timely market entry of generic drugs, the provision of professional pharmacy services, and access to drugs for those without comprehensive drug coverage. This report highlights some of these consequences, which are of concern to Canadians, and presents policy options that attempt to manage drug spending through price control mechanisms while stimulating innovation through reward mechanisms. We have presented a number of options that can be explored on a drug-by-drug basis to test their feasibility and effectiveness.

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