

Increase in Drug Spending in Canada Due to Extension of Data Protection for Biologics: A Descriptive Study

Accroissement des dépenses en médicaments au Canada en raison d'une prolongation de la protection des données pour les produits biologiques : une étude descriptive



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Abstract

Introduction: Biologics are currently protected from competition by eight years of data protection. The renegotiated North American Free Trade Agreement (NAFTA) increases data protection from 8 to 10 years. This study investigates the effect of such an extension on drug spending in Canada.

Methods: A list of currently available biologics eligible for data protection along with their 2017 sales was compiled. Two years were added to the current expiration date of data protection to see if it exceeded patent protection, and any theoretical change in spending due to delayed competition was calculated. The number of biologics approved after January 1, 1995, that have competition and the time until competition started was analyzed. Theoretical competition due to increased data protection for biologics where data protection has already expired was examined.

Results: Depending on how much of the market is captured by biologic competitors and how strong the patents are, lost savings from data protection extension could range from \$0 to \$305.8 million. One biologic competitor currently on the market could theoretically have been affected by an increase in data protection. Increased data protection would have had minor effects on products that have already lost data protection.

Discussion: The potential impact on drug expenditures of a two-year extension in data protection is highly variable. Possible increases in spending on biologics strengthen the rationale for a national pharmacare plan where monopsony buying power would help to control drug prices overall and offset increased spending on biologics.

Résumé

Introduction : Les produits biologiques bénéficient actuellement d'une protection des données de huit ans afin de les protéger de la concurrence. Cette protection passe de huit à dix ans dans le cadre du nouvel Accord de libre-échange nord-américain (ALENA). La présente étude s'intéresse aux effets d'une telle prolongation sur les dépenses en médicaments au Canada.

Méthode : Nous avons compilé une liste des produits biologiques actuellement admissibles en vertu de la protection des données, de paire avec leurs ventes en 2017. Deux années ont été ajoutées à la date d'expiration de la protection des données actuelle pour voir si elle dépassait la protection conférée par le brevet; et tout changement théorique de dépense dû au report de la concurrence a été calculé. Nous avons analysé le nombre de produits biologiques approuvés après le 1er janvier 1995 et qui sont soumis à la concurrence ainsi que le temps écoulé avant le début de la concurrence. Nous avons examiné la concurrence théorique due à l'accroissement de la protection des données des produits biologiques pour lesquels ladite protection est effectivement périmée.

Résultats : Dépendamment de la part du marché captée par les concurrents des produits biologiques et selon la solidité des brevets, la perte d'économie due à la prolongation de la protection des données se situe entre 0 et 305,8 millions de dollars. Un concurrent actuellement sur le marché pourrait théoriquement être affecté par un accroissement de la protection des données. Cet accroissement aurait des effets mineurs sur les produits qui ont déjà perdu la protection des données.

Discussion : L'impact potentiel d'une prolongation de deux ans de la protection des données sur les dépenses en médicaments est très variable. De possibles augmentations des dépenses pour les produits biologiques sont autant d'arguments en faveur d'un plan national d'assurance médicaments dans lequel le pouvoir d'achat d'un monopsonne aiderait à contrôler le coût général des médicaments et à compenser les dépenses accrues pour les produits biologiques.



Introduction

Originator drugs in Canada are protected by two types of intellectual property. Patents on both the product and the process used to make the product last for 20 years from the time that the patent is filed. Companies typically file multiple patents for a single drug, but not all patents are equal and some may not block generic entry. The second type of intellectual property is data protection. In this case, the data in question are the results of the pre-market clinical trials undertaken by the company to have the drug approved by Health Canada for marketing.

In order to qualify for data protection, drugs have to satisfy two conditions: they need to be new chemical entities, i.e., contain a medicinal ingredient never sold before in Canada, and the data supporting the approval of these drugs should have required considerable effort to generate, where considerable effort is defined as the use of clinical trials to produce the data (Health Products and Food Branch 2017). Data protection gives the originator company eight years of market exclusivity with the possibility of an additional six months if it has conducted pediatric clinical trials (Health Products and Food Branch 2017).

The recently concluded renegotiated NAFTA increases data protection for biologics to 10 years (Government of Canada 2018). Biologics include, among others, gene therapies, viral and bacterial vaccines and products produced through biotechnology (Health Canada 2018), and between 2008 and 2017, biologics went from accounting for 16% (\$1.9 billion) in sales of patented medicines in Canada to 42% (\$7.0 billion) (Patented Medicine Prices Review Board 2018). Competitors for biologics in Canada are referred to as subsequent entry biologics (SEBs).

Only drugs approved after the agreement comes into effect will be affected by the increase in data protection. The aim of this study is to examine currently marketed biologics to estimate the possible future changes in drug expenditures as a result of the increase in data protection.

Methods

Three methods were used to determine what effect extension in data protection might have on spending on biologics:

1. top-selling biologics that are on the market and currently subject to data protection were identified, and the impact of a two-year delay in the appearance of SEBs on sales was estimated;
2. biologics approved between January 1, 1995, and March 31, 2018, were examined to determine if any of them would have been affected by a change from 8 to 10 years of data protection; and
3. biologics with expired data protection were examined to determine if a two-year extension in data protection would have meant that data protection expired after the period of patent protection ended.

1. Impact of two-year extension of data protection on top-selling biologics that are currently subject to data protection

SELECTION OF BIOLOGICS

A list of the top-selling biologics in Canada was compiled from two sources. The names and 2017 annual sales for the top 10 selling biologics were taken from the 2017 annual report from the Patented Medicine Prices Review Board (PMPRB) (Patented Medicine Prices Review Board 2018). An additional seven biologics were listed in a slide presentation from the PMPRB (PMPRB nd). The 2017 sales of five of these additional drugs came from the annual report of the Canadian subsidiary of IQVIA, a human data science company (IQVIA 2018), whereas 2016 sales for the other two were available from the PMPRB slide presentation.

DETERMINATION OF DATA PROTECTION AND PATENT EXPIRATION

These 17 drugs were then searched in the Register of Innovative Drugs (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/register-innovative-drugs/register.html>) that lists which drugs have data protection and the expiry date of that protection. Patent expiration dates for drugs listed in the Register were obtained from the Patent Register Database (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/patent-register/database-download.html>). If a drug was covered by more than one patent, then the expiration dates of all of the patents were recorded. Searches of the Register of Innovative Drugs and the Patent Register Database were done on September 29, 2018. Patents that expired before September 29, 2018, were not included.

CALCULATION OF LOST SAVINGS DUE TO DATA PROTECTION EXTENSION

Two years (730 days) were added to the expiration date for data protection. Instances where patent expiration occurred before the extended data protection expired were recorded. The theoretical loss in savings from SEBs was calculated by taking the mean 26% price reduction from currently available SEBs (PMPRB nd) and then applying that percent to the 2017 sales of the biologics. Uptake of SEBs is highly variable depending on the country. In Canada, after one to two years, SEBs only capture 1%–3.5% of the market, whereas the median market share for all Organisation for Economic Co-operation and Development (OECD) countries is 50%, rising to 85% for the five OECD countries with the highest uptake (PMPRB nd). Calculations of lost savings from the two additional years of data protection were made assuming that the SEBs would capture 25%, 50%, 75% and 100% of the market.

2. Length of time before biologic is subject to competition

Starting in 1995, Health Canada began identifying newly approved biologics in annual reports (available by directly contacting Health Canada at publications@hc-sc.gc.ca). From

these reports, the generic names of biologics, excluding vaccines, immunization agents and diagnostic agents, approved from January 1, 1995, to March 31, 2018, and the date when these drugs were approved (received a Notice of Compliance) were recorded. The existence of an SEB for these biologics as of December 31, 2018, was determined by consulting the Drug Product Database (<https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>), and if there was an SEB, its date of marketing was recorded. The time between the approval of the biologic and the marketing of the SEB was computed in days.

3. *Biologics with expired data protection*

Drugs with expired data protection are also listed in a section of the Register of Innovative Drugs. The names of all biologics in this section were recorded along with the date on which data protection ended. Two years were added to this date to account for the extension in the renegotiated trade agreement. The Patent Register Database was then consulted, and expiry dates for patents were recorded to see whether patent protection or the extended data protection would expire first. The Drug Product Database was used to determine if any of the drugs had competition from an SEB as of December 31, 2018.

STATISTICS

Descriptive data are reported, and all calculations were done using Excel (version 16.20 for Macintosh).

ETHICS

No patients were involved, and all data were publicly available. Therefore, ethics approval was not sought.

Results

Impact of two-year extension of data protection on top-selling biologics that are currently subject to data protection

Table 1 gives the names of the 17 biologics and their 2017 sales. Out of the 17 biologics only two were listed in the Register of Innovative Drugs – aflibercept and pertuzumab–trastuzumab with current data protection expiration dates of November 8, 2021, and April 12, 2021, respectively. Aflibercept was covered by two patents, one of which expires before the current end of data protection and one after. This situation would not change with the additional two years of data protection (Table 2 – available online at www.longwoods.com/content/25796). Pertuzumab–trastuzumab is covered by 10 patents that expire between December 10, 2018, and January 28, 2029. With the two-year extension of data protection, three of those patents would expire before data protection ends (Table 2).

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TABLE 1. List of biologics and 2017 annual sales

Generic name	Name of originator	Sales (\$ million) in 2017
Infliximab	Remicade	941
Adalimumab	Humira	706
Aflibercept	Eylea	403
Etanercept	Enbrel	319
Ranibizumab	Lucentis	319
Rituximab	Rituxan	252
Ustekinumab	Stelara	185
Pertuzumab–trastuzumab	Perjeta–Herceptin	185
Trastuzumab	Herceptin	185
Immune globulin (human)	Gamunex	168
Insulin glargine	Lantus	167
Omalizumab	Xolair	131
Bevacizumab	Avastin	116
Epoetin alfa	Eprex	104
Filgrastim	Neupogen	100
Natalizumab	Tysabri	50 (2016)
Follitropin alfa	Gonal-F	14 (2016)

Source: PMPRB (4, 5); IQVIA (6).

Depending on how much of the market is captured by SEBs, lost savings because of data protection extension for these two products theoretically could range from \$0 (patents necessary to keep SEBs off the market expire after extended data protection) to \$24.1 million (data protection for pertuzumab–trastuzumab only and only 25% of the market is captured) to \$305.8 million (both SEBs capture 100% of the market). Lost savings under this scenario would start on December 4, 2021, (current data expiration for pertuzumab–trastuzumab) and end on August 11, 2023, (extended data expiration for aflibercept), that is, a time span of 940 days.

Length of time before biologic is subject to competition

From January 1, 1995, to March 31, 2018, there were a total of 139 biologics approved by Health Canada. Out of these, nine had competitors (one product, infliximab, had two competitors), and the mean time to competition was 5,426 days (95% confidence interval 4441, 6411). One of these competitors (glucagon and ribosomal DNA origin) was marketed after eight years of data protection for the original biologic started but before 10 years

(Table 3 – available online at www.longwoods.com/content/25796). In this case, the extra two years of data protection could potentially have delayed the marketing of the SEB. Seventy-eight of the biologics were approved after January 1, 2009, and some of them may acquire competition after the current eight years of data protection but before a 10-year period.

Biologics with expired data protection

There were 17 biologics with expired data protection, but one product was not listed in the Patent Register Database leaving 16 for analysis. In three cases, data protection already exceeded patent protection, and the additional two years could have theoretically further delayed competition. In seven cases, patent protection would have exceeded 10 years of data protection. In five cases, where drugs had multiple patents, even without the additional two years of data protection, it was unclear whether data or patent protection would have expired first, and the situation was not changed with extended data protection. In one case, again where the drug had multiple patents, if data protection were eight years, it would have expired before patent protection, but with the additional two years, it was unclear which would have expired first (Table 4 – available online at www.longwoods.com/content/25796). There was no competition for any of the 17 drugs as of December 31, 2018.

Discussion

Even with 10 years of data protection, patent protection might continue to be the most important factor in delaying competition for biologics. The potential impact on overall Canadian drug expenditures of a two-year extension in data protection is highly variable, ranging from no increase to a high of \$305.8 million over slightly more than two and a half years depending on the strength of patent protection and whether those patents are challenged in court. These amounts are based on drugs currently available in the market and cannot predict spending on new biologics that will appear and be subject to extended data protection. However, the cost of some of these future biologics could be considerable. In 2006, only one of the top 10 patent medicines by sales was a biologic, whereas by 2017, seven were biologics (PMPRB 2018). In addition, depending on how the new agreement is eventually interpreted, the criteria for eligibility for data protection may be expanded, thereby increasing the number of drugs that qualify for it. Finally, as previously mentioned, patents can be challenged in court whereas data protection cannot be. Therefore, in cases where it appears that data protection will expire before patents, successful challenges may mean that data protection will actually last longer than patents.

The possibility that there will be any substantial increase in expenditures also needs to take into account findings about existing competition for biologics and theoretical

competition for biologics where data protection has already expired. Both of these results indicate a minimal effect of an additional two years of data protection. Out of nine biologics (of 139 approved) that had competition as of December 31, 2018, only one SEB might have been delayed if data protection was 10 years instead of 8. In the other eight cases, competitors appeared after the expiration of 10 years of data protection, indicating that patent protection was potentially the more important of the two. However, 78 biologics were approved after January 1, 2009, that is, before the expiration of a 10-year period for data protection, and if the extended period were already in effect, it is possible that competition for some of these might theoretically be delayed.

For 16 drugs where data protection had already expired, the additional two years would have changed the status for one product, going from a situation where data protection expired before patent protection to a situation where it was unclear which would have expired first because of the existence of multiple patents. In five other cases, also where drugs had multiple patents, with eight years of data protection, it was unclear which was more important, and two more years of data protection might have further delayed competition, again depending on which patent was the strongest. There were three drugs where data protection already exceeded patent protection, and in these three instances, competition could have theoretically been further delayed by two more years of data protection.

Finally, at present, the market share of SEBs in Canada is quite small (PMPRB nd), so even if extra data protection delays the introduction of competition for most biologics, the impact on spending might be quite small because there are currently few savings from SEBs.

Limitations

The assumption was made that competition among SEBs would not affect savings, that is, that SEBs do not compete on price. It was also assumed that sales of the originator biologics would remain stable during the extra two years of data protection. For the products where data protection had already expired, there were no publicly available data to use to estimate theoretical changes in spending in the cases where the additional two years of data protection might have made a difference in the marketing of a competitor.

Conclusion

Any changes in spending on biologics because of the additional two years of data protection will only affect biologics approved after the renegotiated NAFTA takes effect. At this point, a definitive answer about increases in expenditures is unknown, and the range could be from trivial to substantial. However, the possibility of a large increase, even if this possibility is small, should prompt the federal government to take a precautionary principle approach and take action to guard against increases through the creation of a national pharmacare program. Such a program would create a situation where monopsony buying power can be used to control the prices of drugs in general. The Parliamentary Budget Office report on

the cost of a pharmacare plan estimated that prices could be reduced by 25% (Office of the Parliamentary Budget Officer 2017). Reductions in overall prices would help to offset any increases in spending on biologics due to the two-year delay in the introduction of SEBs.

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