Top 10 Updates on Canadian Market Access, Exclusivity, and Pricing Issues

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In the last year, several changes were instituted that will impact pharmaceutical companies, healthcare providers, consumers, and other stakeholders operating in the Canadian pharmaceutical industry. The following provides an overview of some of the more important issues.

1. *Implementation of the Comprehensive Economic and Trade Agreement (CETA) and the Right to Supplementary Protection for Patents for Pharmaceutical Drugs*

Canadian and European Union leaders signed the Comprehensive Economic and Trade Agreement (CETA) in October 2016 and it was implemented in September 2017 with resulting reforms to Canadian laws including changes to the *Patent Act*.[1] These reforms introduce a single-track pharmaceutical patent litigation system under the *Patented Medicines (Notice of Compliance) Regulations* (PMNOC Regulations) and extended patent-like protection for pharmaceuticals under the *Certificate of Supplementary Protection Regulations*.[2]

Previously, parties could choose to litigate a patent by way of a summary prohibition proceeding under the PMNOC Regulations, similar to proceedings under the *Hatch-Waxman Act* in the United States. This often resulted in dual litigation with subsequent infringement actions between the same parties. The new single-track litigation system replaces the summary prohibition proceedings with full actions that determine the infringement and validity of the patent. Actions must be completed within two years and allow for full oral and documentary discovery as well as *viva voce* trial evidence. Under the previous scheme, innovator companies were often unable to appeal the outcome, however under the new regulations either party may appeal.

Additionally, the legislation provides for Certificates of Supplementary Protection (CSPs). CSPs extend the patent term of eligible pharmaceutical products by up to two years to partially compensate for the additional time required to develop pharmaceuticals in research and the regulatory approval process. A CSP provides "patent-like rights" that take effect after patent expiry and is subject to the "same limitations and exceptions" as the patent.

2. *Updates to the Canadian Drug Pricing Regime for Patented Medicines*

In December 2017, the Canadian government revealed proposed amendments to the *Patented Medicines Regulations*. These proposed amendments confer new powers on the PMPRB, the Canadian body responsible for monitoring the prices of patented medicines and set the stage for revised guidelines from the PMPRB.

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The proposed amendments aim to empower the PMPRB to: (a) consider new factors in assessing prices; (b) require broader disclosure of price adjustments, such as third-party rebates under formulary listing agreements with the provinces; (c) provide reduced reporting obligations for patented medicines perceived to be at low risk of excessive pricing; and (d) address a new and expanded schedule of international comparator countries.[3]

New Factors for Assessing Excessive Pricing

In reviewing drug prices for patented medicines, the PMPRB currently considers: (i) the degree of therapeutic benefit of the drug relative to existing drugs on the market, (ii) price of the drug in comparator countries, and (iii) the highest priced drug in Canada in the same therapeutic class.

The proposed amendments would also allow the PMPRB to consider: (i) the pharmacoeconomic value of the drug, (ii) the market size for the drug in Canada; and (iii) the gross domestic product and per capita gross domestic product for Canada.

The amendments contain specific guidance regarding the triggers and timing for reporting cost-utility analyses and market size information.

New Obligations to Report Price Adjustments

The proposed amendments expand the information that must be reported to include any price adjustments made by the patentee or any party that directly or indirectly purchases the medication or reimburses the cost of the medicine. This includes confidential third-party rebates paid to insurers under formulary listing agreements.

More Medicines to Benefit from Reduced Risk-Based Reporting

Some medications have reduced reporting requirements. The proposed amendments would extend this benefit to drugs considered to be low risk for excessive pricing, including all non-prescription and over-the-counter drugs, veterinary medicines, and generic drugs.

Revised International Comparators

The list of international comparator countries (known as the PMPRB 7) will be modified to remove the United States and Switzerland and to add Australia, Belgium, Japan, the Netherlands, Norway, the Republic of Korea, and Spain. France, Germany, Italy, Sweden, and the United Kingdom remain on the list (to be referred to as the PMPRB12).

3. *Updated Guidelines for the Pharmacoeconomic Evaluations of Drugs*

The Canadian Agency for Drugs and Technology in Health (CADTH) is an independent organization that provides health

care decision-makers with an objective evaluation of the pharmacoeconomic value of a drug and provides reimbursement recommendations to most of Canada's public drug plans.

In March 2017, CADTH published its fourth edition of the economic guidelines that help standardize the pharmacoeconomic evaluation of drugs in Canada.[4]

Further, in February 2018, CADTH, provided new guidelines for a streamlined approach to pharmacoeconomic assessments of biosimilars.[5] Biosimilar submissions will benefit from:

- Shorter timelines (reduced to three months from six months).
- Fewer submission requirements (templates have been modified to reduce submission requirements and duplication).
- A new fee structure (subject to lower review fees).

CADTH will not issue reimbursement recommendations for biosimilars. CADTH reviewers will, however, review manufacturer-completed templates, provide a summary of stakeholder inputs and comment on the manufacturer's cost-comparison table. CADTH may also consider evidence for switching between biosimilars.

4. Recent Decreases in Generic Drug Price Reimbursement

In Canada, a significant portion of prescription drugs are paid for by public payors. The pan-Canadian Pharmaceutical Alliance, an organization representing public payors, and the Canadian Generic Pharmaceutical Association recently issued a joint statement regarding a five-year initiative that seeks to provide savings on generic drugs.[6] Generally, generics are reimbursed at 25 to 85% of the innovative product's price, however certain enumerated products are currently reimbursed at 18%. Effective April 1, 2018, the list of generic drugs reimbursed at 18% will be expanded, and the price of 20 generic products will be further reduced to 10% of the innovative product's price.

5. Health Canada Consults on Changes to Broaden Access to Generic Drug Equivalence

In July 2017, Health Canada began the consultation process on amendments to the *Food and Drug Regulations* that will expand which drug products may be approved by way of an ANDS (the equivalent of a US ANDA).

In Canada, generic drug products can be approved via the ANDS pathway by making reference to a Canadian Reference Product (CRP), provided the manufacturer can demonstrate that its product is pharmaceutically equivalent and bioequivalent to the CRP, it has the same route of administration, and the conditions of use fall within those of the CRP. Approval through the ANDS pathway constitutes a declaration of "therapeutic equivalence."[7]

Products with the same medicinal ingredient in the same dosage form are currently considered "pharmaceutical equivalents." The proposed changes would allow drug products with different salts, esters, or complexes of the medicinal ingredient, and/or generic drug products with different but comparable dosage forms to the CRP to be considered "pharmaceutical alternatives." Both pharmaceutical equivalents and pharmaceutical alternatives would be approvable by way of an ANDS and be viewed as therapeutically equivalent, provided bioequivalence with the CRP has been demonstrated and the product has the same route of administration and the same safety and effectiveness.

6. Health Canada Updates Guidance on the Use of Foreign Reference Products in Drug Submissions

In November 2017, Health Canada published an updated guidance document on the use of a foreign-sourced reference product as a CRP for the purpose of an ANDS. The guidance provides clarity on the acceptability of foreign reference products for establishing bioequivalence and states that to use a drug product purchased in another country as a CRP, parties should:

- demonstrate that the drug product is authorised for marketing by a regulatory authority of a country or region with drug assessment criteria comparable to those in Canada;
- provide evidence that the foreign-sourced reference product is marketed in the country or region of origin by the same innovator company or corporate entity which currently markets the identical amount(s) of the identical medicinal ingredient(s) in the identical dosage form in Canada;
- provide the product labeling, certificates of analysis, proof of purchase, and sample products of the reference product marketed in Canada and the foreign-sourced reference product; and
- for all comparative in-vitro testing, analyze the foreign-sourced reference product and the innovator product marketed in Canada and provide the results of these analyses.[8]

Furthermore, the guidance document prohibits the use of a foreign-sourced reference product when it contains high risk medicinal ingredients, or for drugs that require patient monitoring in order to avoid the consequences of under or over-treatment.[9]

7. The Establishment of a New Risk-Based Framework for Self-Care Products in Canada

Health Canada is proposing to change the way that it regulates non-prescription drugs, natural health products, and cosmetics in Canada (collectively Self-Care Products). While all self-care products are regulated under the *Food and Drugs Act*, there are currently three separate sets of regulations and the requirements for bringing these products to market varies.[10]

It has been proposed that three new regulatory pathways will be created and the appropriate approval pathway will depend on the level of risk posed to consumers. The level of risk identified will determine (a) the amount and type of information Health Canada will need to review, (b) the degree of scrutiny necessary before the product can be made available in Canada, and (c) the level of monitoring required for safety and compliance once the product is available on the market. The proposed categories are:

- *Lower-Risk Products*. Health Canada will not review claims or license lower-risk products, such as vitamins, minerals, and cosmetics.
- *Moderate-Risk Products*. Health Canada will perform some review of claims and license medium-risk products such as pain relievers, cough and cold medicines, laxatives, and allergy relief products. Health Canada will perform its review on scientific evidence of safety and efficacy, which would be published in a monograph.
- *Higher-Risk Products*. Higher-risk products, such as products containing new medicinal ingredients and products related to cardiovascular health, will undergo a full review and approval by Health Canada before being sold. Companies will be required to provide evidence to support the safety, quality and efficacy of these products, and claims will be approved based on scientific evidence.

8. Amendments to the Food and Drug Regulations Require Further Disclosure of Clinical Information

In December 2017, the Government of Canada released a White Paper discussing its intention to amend the *Food and Drug Regulations* and the *Medical Devices Regulations* to make certain clinical information in drug submissions and medical device applications publicly available after a final regulatory decision. If the amendments are brought into force, clinical summaries, reports and supporting data from clinical trials would no longer be considered confidential business information. Manufacturers can request redaction of any information not used to support the proposed indication or that describes tests, methods or assays exclusively used by the manufacturer.[11]

9. The Potential for a National Pharmacare Program

The Federal government tabled the 2018-2019 budget in February 2018, which included an announcement of steps toward the creation of a national pharmacare program to cover the reimbursement of certain prescription medications.[12]

The government will create an Advisory Council on the Implementation of National Pharmacare, with the goal of starting a national dialogue on pricing and reimbursement of prescription medications. The Advisory Council will undertake a social and economic assessment of domestic and international pricing and reimbursement models and provide recommendations to the Federal government on how to move forward on this subject.

The Advisory Council is scheduled to provide a report in the spring of 2019. The government has indicated that this timing will allow national pharmacare to become a focus for the 2019 Federal election.

10. New Healthcare Transparency Legislation

Although not strictly related to market access, exclusivity, or pricing, Ontario has recently enacted legislation that will require the disclosure of financial relationships in the healthcare system. Similar to the US Sunshine Act, Ontario's *Health Sector Payment Transparency Act* will require manufacturers and other enumerated payors to report payments made to physicians and other enumerated payees on an annual basis. [13]

The first reporting year will begin in January 2020.[14]

Other provinces have not enacted similar legislation at this time.

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14. "Ontario Open Payments: Proposed Rule for the Health Sector Payment Transparency Act," http://www.policymed.com/2018/03/ontario-open-payments-proposed-rule-for-the-health-sector-payment-transparency-act.html (Mar. 1, 2018).