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Re: Patented Medicine Prices Review Board (PMPRB) Shaping the Future: A Discussion Guide for PMPRB Phase 2 Consultations on New Guidelines

Submitted via webportal

Boehringer Ingelheim (Canada) Ltd. is pleased to provide feedback on the discussion guide as published by the PMPRB on June 26, 2024.

List price guidelines have a significant impact on the pharmaceutical innovation landscape in Canada and on the timing of availability of innovative medicines for Canadian patients. Our experience is that the uncertainty associated with the guideline development process in recent years has created a negative impression of Canada and reduced its attractiveness for new product launches. While Boehringer Ingelheim understands that the PMPRB believes that is responding to the court rulings when identifying the items in the discussion guide, the reality is that the lack of certainty with respect to acceptable prices on an ongoing basis further increases the risk of Canada being deprioritized as an early launch country.

Prior to providing feedback on the seven topics identified in the discussion guide, we would like to take this opportunity to reiterate the following.

Effective Patent Duration in Canada versus the PMPRB11 Countries

When considering the appropriateness of comparing list prices in Canada to the basket of PMPRB-11 countries, we believe that such comparisons should represent an "*apples-to-apples*" approach and that significant differences in the period of market exclusivity (i.e., the *effective patent protection period)* allowed by Canada relative to each of the PMPRB-11 basket countries must be considered.

In addition to local market dynamics, the list price of medicines in a country is impacted by the time frame in which that medicine can be sold prior to the introduction of generic versions. When assessing this extremely important factor, significant differences exist between Canada and all the PMPRB-11 comparator countries. Whereas medicines in all PMPRB-11 comparator countries are eligible for a patent term extension of up to 5 years via the issuance of a Certificate of Supplementary Protection (CSP),[1] prior to the signing of the Comprehensive Economic and Trade Agreement (CETA) there were no such allowances in

[1] Supplementary Protection Certificates (SPCs) & Patent Term Extensions (PTEs) (mewburn.com)

Canada. The signing of the CETA agreement in September 2017 allowed for new chemical entities (drugs) that met specific criteria[2] and received first regulatory approval in Canada after September 2017 to potentially be eligible for up to a 2-year CSP patent term restoration period (Figure 1).

The CSP term begins the day after the expiration of the underlying patent, and then it ends on the date according to the calculation below, including both the "CSP Term Begins" date and the "CSP Term Ends" date. If the calculation below is greater than 2 years, the CSP Term is capped at 2 years. For example, if the NOC issued on December 31, 2017 and the patent was filed on January 1, 2012, the calculation would be as follows:

CSP Term = [NOC date – patent filing date] – 5 years
CSP Term = [December 31, 2017 – January 1, 2012] – 5 years = 6 years - 5 years = 1 year
The patent will expire 20 years from the patent filing date, which is January 1, 2032. Therefore, the CSP term would begin on January 2, 2032, and if it expired exactly one year later, the CSP would expire on January 1, 2033.

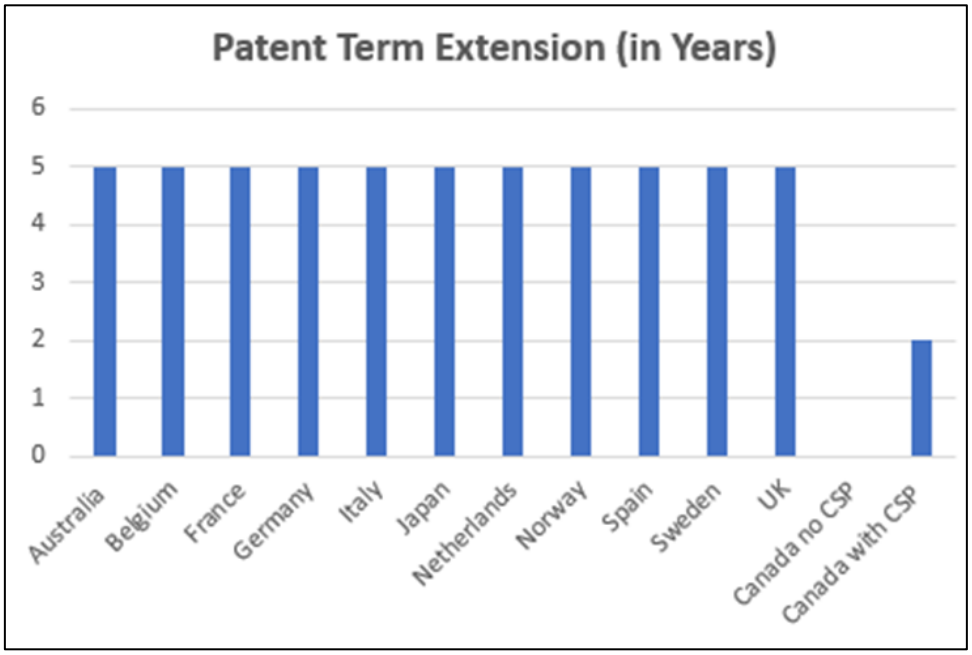


Figure 1. Patent term extension (in years) for the PMPRB 11 countries versus Canada

Operationally, this means that drugs in Canada issued a NOC prior to September 2017 may face generic competition up to 5 years earlier than the same drug in another PMPRB-11 country.[3,4] Even when one considers the potential for the granting of a 2-year CSP (post CETA) in Canada, the market and generic competition dynamics remain different between Canada and the PMPRB-11 countries. The importance of this additional 3 to 5 years of market exclusivity (from generics) in the PMPRB-11 countries versus Canada cannot be overstated as it has a significant impact on the pricing of a medicine, allowing PMPRB-11

[2] **(1)**When it filed its application for the authorization for sale in Canada (i.e. an NDS), no application for a marketing approval equivalent to an authorization for sale, with respect to the medicinal ingredient or combination of medicinal ingredients, as the case may be, had been submitted in a country prescribed by paragraph 6(1)(a) of the CSP Regulations (the European Union and any country that is a member of the European Union, the United States of America, Australia, Switzerland, Japan, and the United Kingdom); or **(2)** if one or more of those applications for a marketing approval had been submitted in one or more of those countries, the NDS was filed before the end of the i) 24-month period, if the application for a CSP was filed no later than the first anniversary of the day on which section 59 of the CETA Implementation Act comes into force, or ii) 12-month period, in any other case, prescribed in paragraph 6(1)(b) of the CSP Regulations that begins on the date of submission of the first of those marketing approval applications.
[3] Can I request an extension of the patent term in Japan? | Epo.org
[4] Patent Term Extension In Different Countries | IIPRD

countries to lower list prices over time while maintaining the ability to generate revenue required to fund future research and development of innovative new medicines. These differences are highly relevant when considering some of the topics included in the Scoping Paper, including (but not limited to): The approach that the Board should take with respect to Existing Medicines with prices above the HIP of the PMPRB11; Distinguishing between medicines that existed as of July 2022 (Existing Medicines) and medicines introduced afterwards (new medicines), and; the frequency and type of price reviews that occur during a product life cycle.

As an example, in the case of Pradaxa (dabigatran), the first generic dabigatran was approved by Health Canada on **February 19, 2018**. This is in contrast with the first generic dabigatran that was approved by the European Medicines Agency on **May 31, 2023**, over 5 years later.

Notice of Compliance Search Results

From Health Canada

Click on the link to get more details of an individual Notice of Compliance.

New search

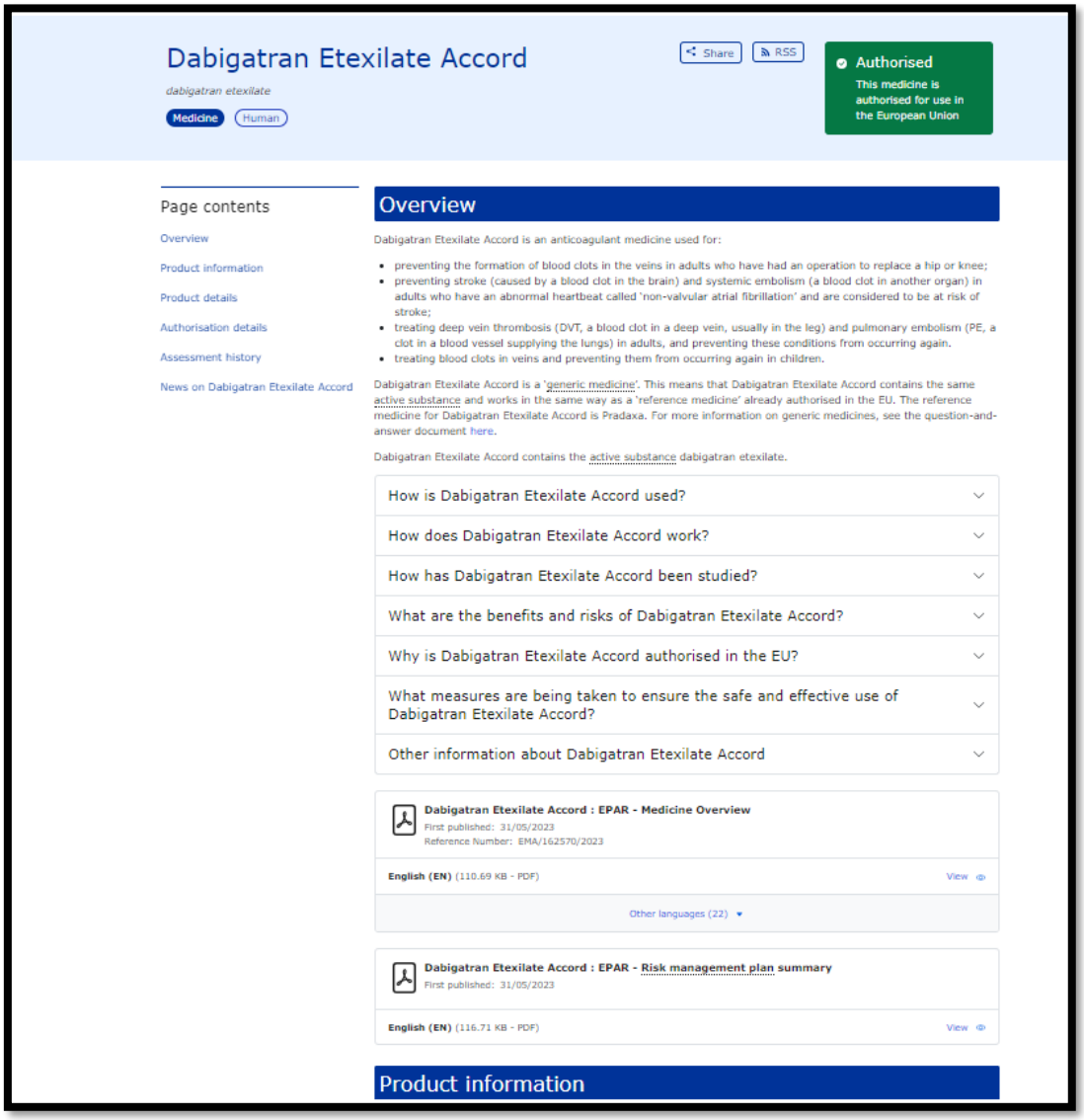
Filter items | Showing 1 to 10 of 12 entries | Show 10 entries

List of searched Notices of Compliance (NOC)

Product(s)	Manufacturer	Published Notes	Notice of Compliance date	Medicinal ingredient(s)	DIN(s)
APO-DABIGATRAN	APOTEX INC		2022-07-20	DABIGATRAN ETEXILATE MESILATE	00000N/A
APO-DABIGATRAN	APOTEX INC		2020-08-27	DABIGATRAN ETEXILATE MESILATE	00000N/A
APO-DABIGATRAN	APOTEX INC		2019-09-04	DABIGATRAN ETEXILATE MESILATE	00000N/A
PRADAXA	BOEHRINGER INGELHEIM (CANADA) LTD LTEE		2019-02-07	DABIGATRAN ETEXILATE MESILATE	00000N/A
APO-DABIGATRAN	APOTEX INC		2018-02-19	DABIGATRAN ETEXILATE MESILATE	02468913, 02468905, 02468891
TEVA-DABIGATRAN	TEVA CANADA LIMITED		2018-02-19	DABIGATRAN ETEXILATE	02463458, 02463466
PRADAXA	BOEHRINGER INGELHEIM (CANADA) LTD LTEE		2015-06-09	DABIGATRAN ETEXILATE MESILATE	00000N/A
PRADAXA	BOEHRINGER INGELHEIM (CANADA) LTD LTEE		2014-08-12	DABIGATRAN ETEXILATE	00000N/A
PRADAXA	BOEHRINGER INGELHEIM (CANADA) LTD LTEE		2014-06-26	DABIGATRAN ETEXILATE MESILATE	00000N/A
PRADAXA	BOEHRINGER INGELHEIM CANADA LTD LTEE		2012-09-07	DABIGATRAN ETEXILATE	02312433, 02358808, 02312441

1 2 Next

Notice of Compliance Search Results (canada.ca)



Dabigatran Etexilate Accord | European Medicines Agency (europa.eu)

International Price Referencing (IPR)

When launching new drugs and/or new indications, it is common for corporate head offices of pharmaceutical companies to use IPR tools such as the NAVLIN Database by Eversana (NAVLIN | Global Pricing & Market Access Database) to determine launch sequencing.

Below are the countries that NAVLIN cites that directly (primary) or indirectly (secondary) use Canada as a price reference country. The list is inclusive of price referencing at launch and during the life cycle of the drug. It is our experience that international companies set pricing with mandatory minimums, reflecting these IPR considerations, and countries which cannot address corporate requirements are de-prioritized.

COUNTRY	REFERS TO	PRIMARY/SECONDARY
AUSTRALIA	CANADA	P
BAHRAIN	CANADA	S
BRAZIL	CANADA	P
CHINA	CANADA	P
COLOMBIA	CANADA	P
CHILE	CANADA	P
EGYPT	CANADA	P
INDIA	CANADA	P
KUWAIT	CANADA	P
LEBANON	CANADA	S
MALAYSIA	CANADA	P
MEXICO	CANADA	P
NEW ZEALAND	CANADA	P
OMAN	CANADA	P
PHILIPPINES	CANADA	P
QATAR	CANADA	S
SAUDI ARABIA	CANADA	P
SOUTH AFRICA	CANADA	P
SOUTH KOREA	CANADA	P
TAIWAN	CANADA	P
THAILAND	CANADA	P
UNITED ARAB EMIRATES	CANADA	P
VIETNAM	CANADA	P

Source: NAVLIN 2023, P = primary referencing, S = secondary referencing

Existing Medicines

As the PMPRB appears to be mindful of their mandate with respect to not acting as a price regulator, it should be clear that medicines launched before July 1st 2022 should be "grandfathered" and considered compliant as per the Guidelines that were in effect at the time. These medicines should only be assessed if their list price is increased greater than CPI. These medicines were assessed per the PMPRB-7 and the change to the basket of countries should not be applied to medicines which were compliant per the previous guidelines. In addition, whereas the majority of drugs that were launched in Canada prior to July 1, 2022 would not be eligible for any additional patent protection (the potential eligibility for a CSP up to 2 years came into effect in 2017 for select medicines), those same drugs launched in the PMPRB-11 countries are eligible for up to 5 years additional protection. Rights holders need certainty through the duration of patent life of new medicines as not having a price certainty would impact decisions to launch innovative and life saving therapies in Canada.

Boehringer Ingelheim's Response to topics in the Discussion Guide

Topic 1. Price level within the PMPRB11 to be used in the initial and post-initial price review

- Option 1: MIP
- Option 2: HIP, or
- Option 3: midpoint between the MIP and HIP

RESPONSE: Option 2: HIP

A **one time** assessment should be conducted at the time of product launch (assuming that there are several PMPRB11 comparator country prices available) or at such time when the price in several countries is available, with the price level of assessment being the Highest International Price (HIP). Ongoing assessments of these medicines should only occur if their list price is increase is greater than allowable CPI. As ongoing (semi-annual) price international price assessments are affected by factors outside of rights holders control, such as changes in (currency) exchange rates and the previously discussed differences in patent term restoration period (CSP), there should be no routine/ongoing assessments following the initial review.

Proposed pricing reviews using the median (MIP) or the midpoint between the MIP and HIP means that the PMPRB will be assuming a role beyond its mandate regarding patent abuse and excessive price ceilings. It is also concerning that the PMPRB now proposes to determine allowable price through annual reviews using factors (i.e., international price points and therapeutic comparators) that may be different than those which existed when a rights holder made its investment decision.

In addition, there should be a minimum number of PMPRB11 countries that have launched prior to a pricing review being undertaken (e.g., 6 of the 11 countries) and under no circumstances should a pricing assessment be performed if there is only one comparator country. We would be pleased to follow-up with the Board with recent learnings and challenges we faced, at your convenience.

Topic 2. The length of time Staff should wait, following the implementation of the Guidelines, to determine whether the IPC identification criterion for an Existing medicine is met:

- Option 1: one year
- Option 2: two years
- Option 3: three years

RESPONSE: Option 3: three years

It is our belief that all drugs that were launched before July 1st 2022 and deemed non-excessive under the guidelines that were in place at that time should grandfathered and not subject to assessment versus the PMPRB11.

Topic 3. In-depth review based on CPI increase criteria

- Option 1: if the list price increase is above one-year CPI
- Option 2: if the cumulative increase in list price over the last two years is above the combined CPI for the past two years and the increase only took place within the last year (i.e. no

increase in price in the first of the two years, followed by an increase on the second year)

RESPONSE: Boehringer Ingelheim has no preference

Topic 4. The individuals/groups permitted to submit a complaint:

- Option 1: limit complaints to the Federal Minister of Health or any of his/her Provincial or Territorial counterparts
- Option 2A: limit complaints to option 1 above plus public payors only; or
- Option 2B: limit complaints to option 1 above plus private and public payors
- Option 3: limit complaints to everyone except for Rights Holders.
- Option 4: no limits/restrictions.

RESPONSE: Option 2A: limit complaints to option 1 above plus public payors only

Topic 5. Expanding the list of products that would only be subject to an in-depth review following a complaint to include biosimilars and/or vaccines:

- Option 1: The PMPRB will treat patented biosimilars and/or vaccines the same as other medicines.
- Option 2: The PMPRB will only open an in-depth review for biosimilars and/or vaccines when a complaint is received.

RESPONSE: Option 1: The PMPRB will treat patented biosimilars and/or vaccines the same as other medicines

Topic 6. Use of clinical evidence to contextualize the degree of similarity of comparators identified for the TCC.

- Option 1: one level of similarity is identified for the comparators as a whole.
- Option 2: each comparator will be assigned a level of similarity.

There is insufficient information to provide meaningful input. Notwithstanding this, Boehringer Ingelheim is concerned with the level of discretionary powers afforded to the staff without any assurance that the level of innovation of new medicines will be acknowledged.

Topic 7. Future role of HDAP

- Option 1: HDAP will be used only on an ad hoc basis when deemed necessary by Staff.
- Option 2: No HDAP – the scientific process will be conducted by Staff.

It is our belief that The Board needs to maintain the services of HDAP and not just on ad-hoc basis.

In summary, Boehringer Ingelheim urges the PMPRB to take a forward-looking approach to the guideline development that is supportive of innovation and which facilitates early access to new and innovative medicines in Canada by providing pricing certainty. In addition, we recommend the following:

- All patented medicines launched in Canada prior to July 1, 2022 be "grandfathered" and future investigations of those medicines are restricted to those that have taken price increases in excess of CPI;
- The list price of medicines launched after July 1 2022 be assessed against the Highest International Price (HIP) when there are prices available for six (6) or more of the PMPRB11 comparator countries;
- Subsequent (post initial) assessment of the price of medicines launched after July 1 2022 is restricted to those medicines that have increased their price in excess of CPI.

Boehringer Ingelheim (Canada) Ltd.

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