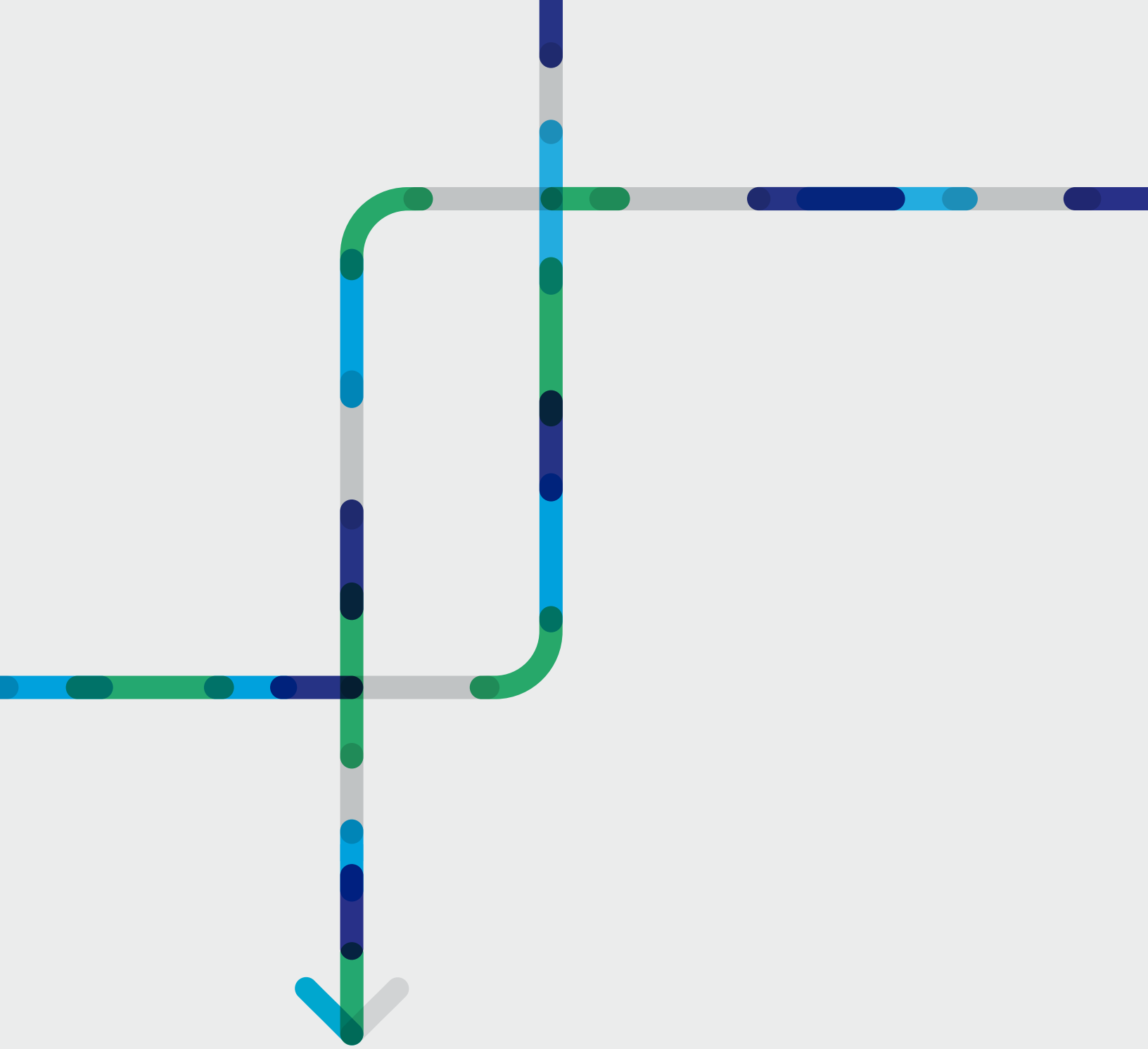
Patented Medicine Prices Review Board
Conseil d'examen du prix des médicaments brevetés
Canada

PMPRB GUIDELINES 2019



The Patented Medicine Prices Review Board
Standard Life Centre, Box L40
333 Laurier Avenue West, Suite 1400
Ottawa, ON K1P 1C1

Tel.: 1-877-861-2350
Fax: 613-288-9643
TTY: 613-288-9654

Email: PMPRB.Information-Renseignements.CEPMB@pmprb-cepmb.gc.ca
Web: www.pmprb-cepmb.gc.ca
Twitter: @PMPRB_CEPMB

Table of Contents

1 Preface

1. The Patented Medicine Prices Review Board (PMPRB) was created in 1987 as the consumer protection "pillar" of a major set of reforms to the *Patent Act* ("Act"), The PMPRB is a quasi-judicial body with a regulatory mandate to prevent pharmaceutical patentees from charging consumers excessive prices during the statutory monopoly period. Its creation arose out of concern that stronger patent protection for medicines might cause their prices to rise unacceptably and become unaffordable to consumers. As a member of the Health Portfolio, the PMPRB contributes to a modern and sustainable health system by ensuring that Canadians continue to have access to patented medicines at reasonable prices.
2. These Guidelines, which are issued pursuant to subsection 96(4) of the Act, are intended to provide transparency and predictability to patentees regarding the process typically engaged in by public servant employees of the PMPRB ("Staff") in seeking to determine whether a patented medicine appears to be priced excessively in any market in Canada. The Guidelines also provide an overview of the processes patentees should be aware of regarding their filing obligations under the *Patented Medicines Regulations* ("Regulations").
3. If a patented medicine appears to be priced excessively based on these Guidelines and an acceptable Voluntary Compliance Undertaking ("VCU") has not been submitted by the patentee, the Chairperson may receive a recommendation from Staff that a hearing be held on the matter. If such a hearing is deemed to be in the public interest by the Chairperson, and it is confirmed by a hearing panel composed of Board members ("Hearing Panel") that the patented medicine was priced excessively in any market, an order may be issued to the patentee that the price be reduced and that measures be taken to offset any excess revenues that may have been earned through sales of the patented medicine at an excessive price.

II Interpretation

4. The Guidelines provide information on the PMPRB's general approach to the price review process and investigations. They supersede all previous guidance documents, policy communiqués and written or verbal statements of any kind by the PMPRB regarding the administration of the price review process and investigations, including all previous versions of the PMPRB's *Compendium of Guidelines, Policies and Procedures*. The Guidelines should be read in conjunction with the Act, the Regulations, the appendices to these Guidelines and other related guidance documents published by the PMPRB from time to time, including the *Patentee's Guide to Reporting*.
5. In accordance with subsection 96(4) of the Act, these Guidelines are not binding on Staff, the Chairperson, Hearing Panels or patentees, and are not intended to create any legal rights or presumptions, to restate the law or to constitute a definitive statement on the interpretation of the legislation related to the PMPRB. The enforcement decisions of Staff and the ultimate resolution of issues will depend on the particular circumstances of the matter in question. Final interpretation of the law is the responsibility of the Board (sitting as a Hearing Panel) and the courts.
6. Certain aspects of these Guidelines may be revisited by the PMPRB in light of experience and changing circumstances. Guidelines and policies issued by the PMPRB are developed in an open manner with opportunities for full consultation with interested parties. When any changes to the Guidelines are considered, stakeholders will be consulted by the PMPRB in accordance with the commentary process established under subsection 96(5) of the Act.
7. Every reasonable effort will be made by the PMPRB to assist patentees in understanding the Guidelines and their application. For example, upon request, patentees will be advised by Staff on the appropriate methodologies to be applied in the price review of a new patented medicine sold in Canada. In addition, upon request and if there is sufficient information satisfying the Board that the price at which a patentee is selling or proposes to sell a patented medicine would not be found to be excessive, a non-binding certificate to that effect may be issued under subsection 98(4) of the Act.

8. The Guidelines do not provide an exhaustive description of all steps that may be taken or all issues that may arise in the context of a price review. In exceptional circumstances or in the event of a hearing, any methods or tests deemed appropriate and consistent with the Act and Regulations may be used by the PMPRB, regardless of whether they are addressed in the Guidelines or otherwise differ from the approach set out therein. In no case will Staff or Board members be bound or limited by these Guidelines.

9. For additional information on the application of the relevant provisions of the Act, the Regulations, these Guidelines or Staff's general approach to price reviews and investigations, please see the PMPRB's website or contact Staff at the following:

Patented Medicine Prices Review Board
Box L40
Standard Life Centre
333 Laurier Avenue West
Suite 1400
Ottawa, Ontario
K1P 1C1
Attention: Secretary of the Board

III Legal Framework

10. The PMPRB was established in 1987 as part of a sweeping set of amendments to the *Patent Act* brought into effect by Bill C-22[1]. These amendments strengthened patent protection for medicines, both in terms of the scope of patentable subject matter and length of the patent-derived exclusivity period, thereby creating what policy makers believed to be a more favourable investment climate in Canada for pharmaceutical research and development (R&D). As a concession to opponents of these changes who were concerned that stronger patent protection for pharmaceuticals might cause prices to rise to unacceptable levels and become unaffordable to Canadians, Bill C-22 also created the PMPRB. The PMPRB is a consumer protection agency with a regulatory mandate to ensure that prices of patented medicines are not excessive. In essence, Bill C-22 sought to strike a balance between the need to recognize and reward pharmaceutical innovation by providing patentees with a period of market exclusivity, and ensuring that prices charged during that exclusivity period remain reasonable. The PMPRB's existence as the only sector-specific price regulator under the Act reflects a recognition by policy makers that the unfettered ability to set prices for patented medicines is not in the public interest given the unique harm that can ensue if consumers are denied access to them.

11. The PMPRB has a dual mandate: in its regulatory role, it protects consumers by ensuring that the prices of patented medicines are not excessive; in its reporting role, it provides information on pricing trends in the pharmaceutical industry via its Annual Reports. Further to a directive from the Minister of Health under section 90 of the Act, the PMPRB also supports informed and evidence-based health policy by reporting on medicine price, utilization and cost trends under the National Prescription Drug Utilization Information System (NPDUIS) initiative.

12. The PMPRB Board consists of five members appointed by the Governor–in-Council under section 91 of the Act for terms of up to five (5) years, renewable once. The Chairperson of the Board acts as the Chief Executive Officer (CEO) of the PMPRB and has supervision over and direction of its work. The PMPRB employs public servants (i.e., Staff) pursuant to section 94 of the Act to carry out its day-to-day work. The PMPRB's Executive Director is its senior public servant, Chief Operating Officer (COO) and Chief Financial Officer (CFO), and is responsible for the management of Staff.

1 *An Act to Amend the Patent Act* (R.S., 1985, c. 33 (3rd Supp.)).

13. The PMPRB is established under the Act as an independent, quasi-judicial body. To ensure this independence and autonomy, no express or implicit power is provided under the Act to Health Canada or any other government entity to direct the PMPRB in the exercise of its regulatory function. The PMPRB maintains an arm's length relationship from the Minister of Health (who is responsible for the sections of the Act pertaining to the PMPRB), the Minister of Innovation, Science and Economic Development (who is responsible for the Act as a whole) and its various stakeholders. Similarly, the PMPRB is structured in a manner that separates the work and functions of Staff, the Chairperson and Board members. Investigation, litigation and reporting functions reside with Staff and are separate from the adjudication functions that are reserved for Board members only.

14. The monitoring of patentees' compliance with regulatory filing requirements and the administrative price reviews of patented medicines are the responsibility of Staff. When a patented medicine appears to be priced excessively and the issue cannot be resolved through voluntary price reduction and/or measures to offset revenues from sales at that price by the patentee, the matter may be brought by Staff to the Chairperson who will determine whether a hearing is in the public interest. If the decision to hold a hearing is made, a Notice of Hearing is issued and a Hearing Panel is appointed by the Chairperson to adjudicate the matter. The Chairperson's decision to issue a Notice of Hearing is a purely administrative act and does not express his or her view of the merits of the underlying matter.

15. The PMPRB reviews the prices of patented medicines sold at arm's-length by patentees (i.e., the "ex-factory" price or **List Price**). Sales in Canada may include, but are not limited to, medicines subject to a Notice of Compliance (NOC), the Special Access Programme, the List of Drugs for an Urgent Public Health Need, Clinical Trial Applications, or Investigational New Drugs. The PMPRB has no authority over prices charged by parties other than patentees, such as prices charged by wholesalers or retailers, or over pharmacists' professional fees.

16. Under the Act, the PMPRB is given jurisdiction to determine whether a patented medicine is or has been sold by a rights holder (a patentee, former patentee or the person for the time being entitled to the benefit of a certificate of supplementary protection for an invention pertaining to a medicine) at an excessive price in any market in Canada.[2] The term "patentee" is defined in the Act as a person who is entitled to the benefit of a patent for an invention for a period, including any other person entitled to exercise rights in relation to the patent, such as a holder of an express or implied license.[3]

17. An invention pertains to a medicine if the invention is intended or capable of being used for medicine or for the preparation or production of medicine. The phrase "pertain to a medicine" has a broad meaning. The Federal Court of Appeal has determined that the nature of that connection may be "tenuous"[4]. It is satisfied, for example, where there may "only be a slender thread of a connection between a patented invention and the medicine sold in Canada"[5].[6]

---

2 Pursuant to subsection 81(3) of the *Patent Act*, the PMPRB may make remedial orders against former patentees for up to three (3) years from the day on which the former patentee ceased to be entitled to the benefit of the patent or to exercise any rights in relation to the patent or certificate of supplementary protection.

3 *Canada (Attorney General) v. Sandoz Canada Inc.*, 2015 FCA 249.

4 Canada (Attorney General) v. Galderma Canada Inc. et al., 2019 FCA 196.

5 *ICN Pharmaceuticals, Inc. v. Canada (Staff of the Patented Medicine Prices Review Board) et al.*, [1997] 1 FC 32.

6 Patentees are reminded that patents that are not eligible for listing on the Patent Register under the Patented Medicines (Notice of Compliance) Regulations may nonetheless "pertain to" medicines sold in Canada and trigger PMPRB jurisdiction.

18. The term "medicine" is defined in the Act as including a drug (i.e., a substance or a mixture of substances manufactured, sold or represented for use in (i) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms, in human beings or animals; or (ii) restoring, correcting or modifying organic functions in human beings or animals) and a medicinal ingredient.[7] Unless otherwise specified, in these *Guidelines*, a reference to a "medicine" includes all dosage forms and strengths (i.e., all DINs) of the medicine.

19. The PMPRB recognizes that the term "medicinal ingredient" is generally understood to mean the "active pharmaceutical ingredient" (API) used as raw materials during the manufacture of the finished dosage form. Patented medicines under the PMPRB's jurisdiction include vaccines, topical preparations, anaesthetics and diagnostic products used *in vivo*, regardless of delivery mechanism (i.e., trans-dermal patch, capsule, injectable, inhaler). However, the PMPRB does not consider medical devices, *in vitro* diagnostic products and disinfectants that are not used *in vivo* to be patented medicines for the purpose of price review provisions in the Act.

20. The PMPRB has jurisdiction during the life of an eligible and issued patent including the pre-grant period. The PMPRB also has jurisdiction for the extended period of protection granted via a certificate of supplementary protection.[8]

21. The PMPRB's jurisdiction over the price at which a patented medicine is sold in any market in Canada persists after the patent has been dedicated and until the cancellation or surrender of the patent pursuant to the express provisions of the Act or the expiry of the term of the patent. Patent dedication is not expressly recognized in the Act as a mechanism by which patent rights may be terminated before the normal expiry of the patent term.

22. Orders issued by the Board are enforceable in the same manner as orders of the Federal Court or any superior court in Canada and may be enforced by the PMPRB or by the Federal Court. Decisions embodied in orders issued by the PMPRB may be subject to judicial review by the Federal Court in accordance with administrative law principles and the *Federal Courts Act*.

---

7 *Canada-European Union Comprehensive Economic and Trade Agreement Implementation Act* (S.C. 2017, c.6) C-30 (Royal Assent dated May 16, 2017), Part 2 [Related Amendments -Patent Act] s. 46(2); *Patent Act*. s. 104.

8 *Canada-European Union Comprehensive Economic and Trade Agreement Implementation Act* (S.C. 2017, c.6) C-30 (Royal Assent dated May 16, 2017), Part 2 [Related Amendments -Patent Act].

IV Filing Requirements Pertaining to Price Reviews

23. Access to timely and accurate information regarding the sale of patented medicines is necessary for the PMPRB to fulfil its regulatory mandate. Therefore, patentees and former patentees are required to submit this information to the PMPRB.

24. The information that must be supplied is set out in section 82 of the Act and in the Regulations. Further information to assist patentees in identifying the content and form of information to be supplied and the strict deadlines set out in the legislation may be found in the *Patentee's Guide to Reporting*, a reference document issued by Staff. Compliance with filing obligations is the sole responsibility of patentees. These statutory obligations cannot be waived or amended by Staff.

25. Information that patentees or former patentees may be required to file under the Regulations includes, but is not limited to:

- A notification describing a patentee's intention to offer a patented medicine for sale in a market in Canada in which such patented medicine has not previously been sold (i.e., the first sale of the patented medicine), along with related information (Notification of Intention to Sell a Patented Medicine);
- Prescribed information relating to the identity and characteristics of a patented medicine, such as the product monograph for the patented medicine or equivalent information, and the DINs assigned for each dosage form and strength of the patented medicine;
- Prescribed information relating to the price of a patented medicine, such as information concerning the price at which each dosage form and strength of the patented medicine is or has been sold in any market in Canada or in any of the eleven countries set out in the Regulations (the "**PMPRB11**"); or
- Prescribed information relating to cost-utility analyses prepared by publicly funded Canadian health technology assessment (HTA) agencies, for which the outcomes are expressed as the cost per quality-adjusted life year (QALY) for each indication that is the subject of the analysis; and
- Prescribed information relating to the estimated maximum use of the patented medicine in Canada for a given time period, by quantity of the patented medicine in final dosage form.

26. As per s. 7 of the Regulations, patentees shall submit required filings by email using the electronic forms on the PMPRB's website. The forms should bear the electronic signature of an authorized individual who certifies that the information is true and complete.

27. It is the responsibility of each patentee to independently ensure that the information filed with the PMPRB (including domestic and foreign prices) is accurate. Ad hoc audits of patentee filings, including pricing, revenue and patent information, may be conducted by Staff. In the event of such an audit, patentees may be asked to provide additional supporting materials and/or corrections or confirmation of the information filed.

28. The failure to file required information within the specified period or the filing of erroneous or false information may have significant consequences for patentees or former patentees. In appropriate circumstances, an order granting certain remedies may be issued by the Board, including an *ex parte* order requiring that the missing information be submitted. Alternatively, the matter may lead to summary conviction proceedings under subsection 76.1(1) of the Act. Further, the filing of false information is an indictable offence under section 76 of the Act that, on conviction, can lead to monetary fines or terms of imprisonment.

29. The Act provides for the confidentiality of information supplied to the PMPRB in certain circumstances. Specifically, information or documents provided to the PMPRB in accordance with the provisions dealing with pricing information in sections 80, 81 and 82 of the Act, or in any proceeding relating to excessive prices under section 83, is privileged and cannot be disclosed to the public without authorization of the disclosing party, unless such information has been disclosed at a public hearing under section 83 of the Act or is subject to the exceptions outlined in section 87(2) of the Act.

30. Information provided to the PMPRB may be subject to certain provisions in the *Access to Information Act* and the *Privacy Act*.

V Price Review Process

31. The price review process consists of a series of steps whereby (i) medicines are divided into categories depending on their date of introduction and on criteria related to their market characteristics and (ii) ceiling prices are identified and used to assess the medicines' prices. Price reviews are normally conducted by Staff using the methods and tests set out in these Guidelines based on the information filed by the patentees or obtained by Staff from relevant outside sources such as public formularies.

32. As an initial review step, patented medicines are divided into: (i) the dosage strengths and forms for patented medicines which received a Drug Information Number (DIN) prior to August 21, 2019 ("grandfathered" products); and (ii) all other dosage strengths and forms of patented medicines which had not received a DIN as of August 21, 2019.

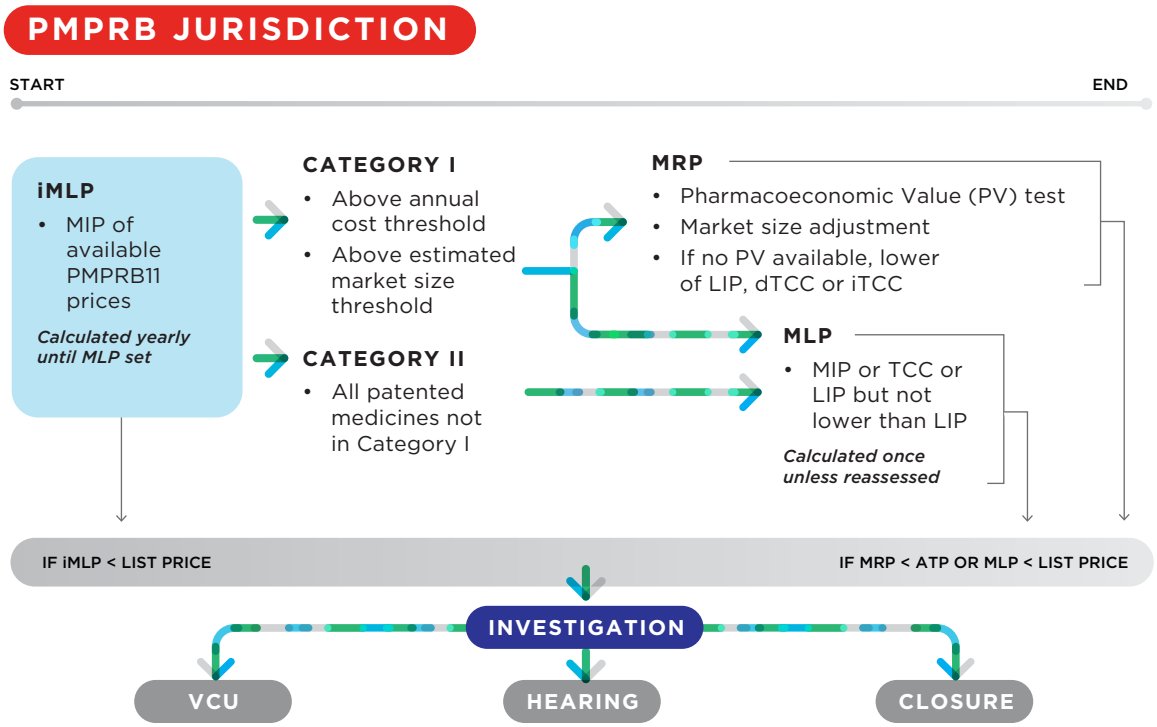
33. The price review factors for grandfathered patented medicines (previous section 85(1) factors) and for all other patented medicines (both previous and new section 85(1) factors) are as follows:

- Grandfathered patented medicines:
  - The prices at which the medicine has been sold in the relevant market
  - The prices at which other medicines in the same therapeutic class have been sold in the relevant market
  - The prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada
  - Changes in the Consumer Price Index (CPI)
- All other patented medicines:
  - The prices at which the medicine has been sold in the relevant market
  - The prices at which other medicines in the same therapeutic class have been sold in the relevant market
  - The prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada
  - Changes in the Consumer Price Index (CPI)
  - The pharmacoeconomic value in Canada of the medicine
  - The size of the market for the medicine in Canada
  - The gross domestic product in Canada and the gross domestic product per capita in Canada

34. The specific review processes and tests applicable to patented medicines and grandfathered patented medicines are detailed hereafter.

A. Price Review Process for Non-Grandfathered Patented Medicines

35. Information filed by patentees and information obtained from other sources is reviewed by the PMPRB to assess whether any patented medicine introduced in Canada appears to be priced excessively. The following diagram illustrates the review process for new patented medicines:



36. Each of the above steps is detailed hereafter.

1. STEP 1: iMLP (ALL PATENTED MEDICINES)

37. At introduction, an **interim maximum List Price** ceiling is set (the "**iMLP**") for the sale of the patented medicine. The iMLP is set at the median international list price ("**MIP**") for the PMPRB11 countries for which the patentee has provided information during the interim period. Patentees must ensure that the patented medicine's gross[9] publicly available Canadian ex-factory price ("**List Price**") is no higher than the iMLP for the period during which it is applicable, failing which the price may be subject to additional review or investigation by Staff.

38. The iMLP will be recalculated annually and will apply until the ***earlier of***: (i) three (3) years from the date of the introduction of the patented medicine in Canada; or (ii) the date when the patentee has filed international price information for at least five (5) of the PMPRB11 countries. At the end of the interim period, the MLP will be set (see Step 2) and the iMLP will cease to apply.

9 This is the "publicly available ex-factory price" referred to in s. 4(1)(f)(ii) of the *Patented Medicines Regulations*. These Guidelines utilize the terms "publicly available ex-factory price", "Gross Price" and "List Price" interchangeably.

2. STEP 2: MLP (ALL PATENTED MEDICINES)

39. Subject to the procedure described above, the iMLP will be replaced by a **Maximum List Price** ("**MLP**"). The MLP will be set by the lower of the MIP or the median domestic Therapeutic Class Comparison ("**dTCC**") but is subject to a price floor set by the lowest international price ("**LIP**") for the PMPRB11 countries for which the patentee has provided information at the end of the interim period.

40. The MLP is set as follows:

- The MIP and the LIP are identified.
- The dTCC price is identified (see Appendix A, "dTCC and iTCC").
- If the dTCC price is higher than the MIP, the MLP is set by the MIP.
- If the dTCC price is lower than the MIP but higher than the LIP, the MLP is set by the dTCC.
- If the dTCC price is lower than the LIP, the MLP is set by the LIP.

41. There may be circumstances where the MLP is lower than the iMLP set during the interim period. In these circumstances, patentees will be granted until the subsequent reporting period after the MLP is set to ensure the List Price of the patented medicine is lowered to a level that is no higher than the MLP.

42. If the MLP was set by the MIP and, in subsequent periods, the prevailing MIP exceeds the MLP by more than 10%, the MLP may be adjusted based on actual lagged CPI[10], as long as the MLP does not exceed the MIP[11]. The MLP may also be subject to the possible reassessment of the patented medicine at a later point in time if the MLP was set by the MIP and, in subsequent periods, the prevailing MIP is lower than MLP by more than 10% (see section VI).

43. As with the iMLP, patentees must ensure that the patented medicine's List Price is no higher than the MLP for the period during which it is applicable, failing which the price may be subject to additional review or investigation by Staff.

a) List Price of the patented medicine in Canada

44. As per the Regulations, patentees must file information about the List Price for each dosage form, strength and package size (i.e., for each DIN) of the patented medicine in each province and territory.

45. List Prices may vary within Canadian markets (i.e., between provinces or territories). Where there are multiple List Prices in different markets, the highest List Price will be used for the purpose of the iMLP and MLP comparison.

---

10 The CPI factor used will be the actual CPI published by Statistics Canada in January of that year for the previous year-over-year period ending in December.

11 For patented medicines with multiple DINs, comparison of the MLP against the MIP is only conducted for the DIN whose MLP was initially set by the MIP, and not for DINs whose MLPs were set by the Reasonable Relationship (RR) test (see Appendix B). However, if a DIN's MLP is adjusted for CPI, additional MLPs set by the RR test in reference to this MLP will be adjusted accordingly.

b) List Prices of the patented medicine in the PMPRB11

46. The MIP and the LIP are based on the information filed by the patentee. Where there are multiple List Prices in the same country, the lowest price will be used. The prices for all countries in the PMPRB11 provided by the patentee will be used.

47. When comparing prices in the PMPRB11, the local currency is converted into Canadian dollars using exchange rates calculated as the simple average of the thirty-six (36) monthly average noon spot exchange rates for each country (taken to eight (8) decimal places) as published by the Bank of Canada. For a patented medicine's introductory period, the thirty-six (36) months ending in the second month of the previous reporting period (i.e., February or August) will be used. Subsequently, the thirty-six (36) months ending in the second month of the reporting period under review will be used.

3. STEP 3: MRP (CATEGORY I PATENTED MEDICINES ONLY)

48. Patented medicines will be classified as either **Category I** or **Category II** based on certain market characteristics. In addition to the iMLP/MLP, Category I patented medicines are also subject to a "**Maximum Rebated Price**" ceiling ("**MRP**"). The MRP takes into account therapeutic value and affordability measures (i.e., the pharmacoeconomic value and market size for the patented medicine). Patentees must ensure that the patented medicine's **Net Price**[12] in Canada, (i.e., its average transaction price or "**ATP**") is no higher than the MRP, failing which the price may be subject to additional review or investigation by Staff.

a) Classifying a patented medicine as Category I

49. A patented medicine will be classified as Category I if it meets either of the following criteria:

- ***12-month treatment cost greater than 50% of GDP per capita:*** following the filing of introductory period pricing information, the medicine's 12-month treatment cost will be calculated by Staff based on the maximum dosage per course of treatment listed in the product monograph; the maximum number of courses of treatment per 12 months, based on the nature of the condition, clinical practices, and other relevant criteria; and the highest Canadian List Price. If a List Price is not available, the national Net Price will be used.
- ***Estimated or actual market size (revenue) exceeds annual Market Size Threshold:*** the annual Market Size Threshold will initially be set at $25 million.[13]

50. All other patented medicines will be classified as Category II. This includes line extensions of grandfathered patented medicines to which a DIN was assigned on or after August 21, 2019, where the DIN does not relate to a new indication.

---

12 This is the "average price per package" or "net revenue from sales of each dosage form" referred to in s. 4(1)(f)(i) and 4(4) of the *Patented Medicines Regulations*. These Guidelines use the terms "Net Price", "ATP", and "average price per package" interchangeably.

13 See Appendix D "Market Size Adjustment Methodology". This threshold may be adjusted from time to time, and at least every five years, to reflect changes in CPI and GDP.

a) MRP calculation

51. The **MRP** is calculated as follows:

- The Incremental Cost-Effectiveness Ratio ("**ICER**") measured in cost per quality-adjusted life years ("**QALYs**") for each indication of the patented medicine will be identified from the cost-utility analyses filed by the patentee.
- The ICER will be compared against the applicable Pharmacoeconomic Value Threshold ("**PVT**") of $60,000 per QALY (see Appendix C, "Pharmacoeconomic Value Assessment").
- The price at which the patented medicine's ICER would be equivalent to the PVT will be identified (the "Pharmacoeconomic Price" or "**PEP**").
- The PEP may be further adjusted for market size if the patented medicine realizes annual quantities such that, if priced at the MRP set by the PEP, revenues would be in excess of $25 million (see Appendix D, "Market Size Adjustment Methodology").
- For patented medicines with an estimated total prevalence no greater than 1 in 2,000 across all approved indications, the MRP will be set at 50% above the PEP, but will be further adjusted for market size if the patented medicine realizes annual revenues in excess of $12.5 million (see Appendix D, "Market Size Adjustment Methodology").

52. If the procedure above results in an MRP that exceeds the MLP, the MRP will be set at the same level as the MLP.

b) Exceptional circumstances

53. If a patentee does not file a cost-utility analysis prepared by a publicly funded Canadian organization for a Category I patented medicine, or if the analysis submitted does not allow for the determination of the MRP as described above, the MRP may be set by using alternative methods. Such methods may include, but are not limited to:

- The MRP being set by the lower of the LIP, the dTCC or the international Therapeutic Class Comparison ("**iTCC**"), with further adjustments based on the Market Size Adjustment Methodology.

54. Because these scenarios are expected to be rare and fact-dependent, they will be dealt with on a case-by-case basis.

55. Once set, the MRP will be only reassessed at a later point in time if it meets the criteria set out in section VI.

4. STEP 4: IDENTIFICATION OF RELEVANT INDICATION

56. For patented medicines with more than one approved indication, the Relevant Indication for which the MLP (and MRP, if applicable) will be assessed will be determined by Staff. This could occur at introduction, or as part of a reassessment if additional indications are approved during the life cycle of the patented medicine (see section VI).

57. For Category I medicines, the Relevant Indication will be the indication triggering the Category I classification criteria for annual treatment cost in these Guidelines. For Category I medicines where more than one, or no, indications meet this threshold, and for Category II medicines, the Relevant Indication will be the indication treating the condition with the highest prevalence (i.e., the largest patient population).

B. Price Review Process for Grandfathered Patented Medicines

58. Grandfathered patented medicines will be subject to an MLP but not to an MRP.

59. The MLP for all grandfathered patented medicines will be set at the lower of (i) the MIP for the PMPRB11 countries for which the patentee has provided information, or (ii) the patented medicine's ceiling under the Guidelines applicable prior to the issuance of these Guidelines.[14] If the MLP is set by the MIP and, in subsequent periods, the prevailing MIP exceeds the MLP by more than 10%, the MLP may be adjusted based on actual lagged CPI[15], as long as the MLP does not exceed the MIP. The MLP may also be subject to reassessment if it is set by the MIP and, in subsequent periods, the prevailing MIP is lower than the MLP by more than 10% (see section VI). Patentees must ensure that the patented medicine's List Price is no higher than the MLP for the period during which it is applicable, failing which the price may be subject to additional review or investigation by Staff.

60. The MIP and List Prices for grandfathered patented medicines will be calculated in the same manner as for new patented medicines under these Guidelines (see section V(A), "Price Review Process for Non-Grandfathered Patented Medicines").

61. Patentees will be granted until the subsequent reporting period after the MLP is set to ensure the List Price of the grandfathered patented medicine is lowered to a level that is no higher than the MLP or may be subject to additional review or investigation by Staff.

---

14 For example, the Maximum Average Potential Price (MAPP) for the introductory period or the Non-Excessive Average Price (NEAP) for all subsequent periods set as per the PMPRB's *Compendium of Policies, Guidelines and Procedures – Updated February 2017*.

15 The CPI factor used will be the actual CPI published by Statistics Canada in January of that year for the previous year-over-year period ending in December.

VI Reassessment

62. The categories or price ceilings of patented medicines may be reassessed to ensure that they remain relevant in light of material changes in market conditions or the medicine's usage.

63. For non-grandfathered patented medicines, a reassessment may be conducted if any of the following situations arise:

- A patented medicine (Category I or Category II) is approved for a new indication;
- A Category II patented medicine has sales exceeding the Market Size Threshold (see Appendix D), contrary to the initial estimate filed by the patentee; or
- A Category I patented medicine's total prevalence across all approved indications, as estimated by Staff, increases above 1 in 2,000; or
- A Category I patented medicine's cost-utility analysis is updated; or

64. A patented medicine receiving a new indication may have its Relevant Indication changed in accordance with the procedures described in section V. A new indication may alter the patented medicine's market size, therapeutic class comparators, and cost-effectiveness. As a result, there may be an increase or decrease in the MLP and/or the MRP.

65. A Category II patented medicine receiving a new indication may be recategorized to Category I if it meets the Category I screening criteria. A patented medicine may also be recategorized from Category II to Category I if its revenues increase above the annual Market Size Threshold contrary to the initial market size estimate filed by the patentee. In either case, the category change will result in the patented medicine being given an MRP.

66. A Category I patented medicine that has had its MRP set based on an estimated total prevalence no greater than 1 in 2,000 across all indications may have this MRP reassessed if total prevalence increases above this threshold.

67. For all patented medicines, including grandfathered patented medicines, if the MLP is set by the MIP and, in subsequent periods, the prevailing MIP is lower than the MLP by more than 10%, the MLP will be reset by the prevailing MIP. If the patented medicine has additional DINs whose MLPs were set by the RR test (see Appendix B) in reference to this MLP, those MLPs will be adjusted accordingly.

68. The patentee will be notified in the event that the MLP and/or MRP for a patented medicine will be adjusted following a reassessment. Following such notice, the patentee will be granted until the next reporting period for the MLP, and until the end of the subsequent reporting period for the MRP to ensure that prices are adjusted such that the patented medicine is not priced higher than the modified price ceiling(s), failing which the price may be subject to additional review or investigation by Staff.

VII Investigations

69. An investigation is an in-depth review of the price of a patented medicine by Staff. As part of an investigation, information provided by the patentee and information that may be obtained from other sources is reviewed by Staff. Investigations are purely administrative in nature and conducted solely by Staff. No Board members are involved in this process. If an investigation results in a hearing, the Hearing Panel must undertake an independent *de novo* review of the price of the patented medicine to determine whether it is excessive under the section 83 of the Act. Accordingly, the positions taken by Staff or the patentee(s) during the investigation may differ from those taken during the hearing.

70. The criteria for commencing an investigation have been developed with the intention of making the most efficient use of the PMPRB's human and financial resources. The fact that the price of a patented medicine is not subject to an investigation does not necessarily mean that the price is not excessive. It only means that the investigation criteria have not been met in the particular circumstances.

A. Investigation Criteria

71. In general, an investigation will be commenced by Staff when any of the following situations occur:

- the price of any dosage form or strength of a patented medicine appears to be above the corresponding applicable price ceiling by more than 5%; or
- the cumulative potential revenues earned as a result of pricing above applicable ceiling(s) ("**potential excess revenues**") appears to exceed $50,000 for the patented medicine (i.e., across all dosage forms and strengths of the medicine) in a calendar year; or
- A complaint is received.

72. When the price of a patented medicine is higher than the applicable ceilings under the Guidelines but does not meet the criteria for commencing an investigation, the patentee will be notified and the patented medicine will be reported in the PMPRB's Annual Report as "Does Not Trigger Investigation." In such an instance, no immediate action will be taken by Staff; however, the patentee must ensure that its price is reduced to a level no higher than the applicable ceiling price and offset any revenues that may have accrued in accordance with section B.2, "Calculation of potential excess revenues", failing which the price may be subject to eventual investigation by Staff.

B. Investigation Process

73. When an investigation is commenced by Staff, the patentee will be notified and the patented medicine will be reported in the PMPRB's Annual Report as "Under Investigation." Price reviews and investigations cannot result in a legal determination that the price of a patented medicine is excessive under the Act. Such a determination can only be made by a Hearing Panel after the patentee or former patentee has been provided with a reasonable opportunity to be heard, as required by section 83 of the Act.

1. ADDITIONAL REVIEW OF FILINGS

74. When a patented medicine comes under investigation, its pricing history from introduction will be reviewed by Staff. All information filed by the patentee is analysed and further clarification may be sought. For example, if a price seems to be in error or unexpected, or if there are discrepancies in the patentee's filings, the patentee may be asked for an explanation or to provide additional supporting materials. Any relevant materials not filed by the patentee, such as dTCC and iTCC List Prices, may also be considered by Staff. In addition, an analysis of the appropriateness of the applicable tests is conducted by Staff to take into account the facts of the case and the particularities of the relevant markets in which the patented medicine is sold.

2. CALCULATION OF POTENTIAL EXCESS REVENUES

75. In the event that the price of a patented medicine exceeds the ceilings established under the Guidelines, the patentee will be notified that its price(s) are "outside the thresholds set out in the Guidelines" and the applicable price ceilings will be indicated. Cumulative potential excess revenues will also begin to be calculated by Staff based on Net Prices filed by the patentee regardless of the type of price ceiling being used (iMLP, MLP, or MRP). Because the PMPRB has jurisdiction over the medicine in the pre-grant patent period, potential excess revenues related to its sales during that period will be included in the calculations.

76. In a hearing, Staff may seek a remedy in the form of excess revenues that may differ from the cumulative potential excess revenues calculated during an investigation. In addition, where Staff believes the patentee or former patentee has engaged in a policy of selling the patented medicine at an excessive price, it may seek an order that the patentee offset up to twice the amount of excess revenues.

3. INVESTIGATION OUTCOMES

77. Possible outcomes of an investigation include:

- A Voluntary Compliance Undertaking ("**VCU**"), as described in section VIII;
- The issuance of a Notice of Hearing, if, upon the recommendation of Staff, the Chairperson considers it to be in the public interest; and
- The closure of the investigation.

78. The closure of an investigation may follow from a VCU or a determination that further examination of the price of a patented medicine is not warranted at that point in time in view of facts and considerations that come to light during the investigation.

79. The closure of an investigation is an administrative act and does not constitute a legal determination or an admission by the PMPRB that the price of the patented medicine is not excessive. The closure of an investigation does not preclude the possibility of the opening or re-opening of further investigation(s) or the commencement of a hearing in the future.

VIII Voluntary Compliance Undertaking (VCU)

80. At any time prior to the issuance of a Notice of Hearing, a patentee may submit a VCU to Staff. A VCU is a promise by the patentee to reduce its price and/or offset any potential excess revenues from the sale of a patented medicine that is subject to an investigation. A proposed VCU does not constitute an admission by the patentee that the price of the patented medicine is excessive.

81. VCU negotiations with patentees are conducted by Staff and it is the PMPRB's policy that the Chairperson not be involved in those discussions. If negotiations result in a VCU proposal that Staff believes would be acceptable to the Chairperson, it will be referred to the Chairperson for his or her consideration. Staff cannot independently determine whether a VCU proposal is acceptable and cannot make any assurances to the patentee regarding the likelihood that the Chairperson will consider it acceptable.

82. The consideration of a VCU is an administrative procedure and does not constitute an admission or determination by the PMPRB that the price submitted by the patentee, or used to calculate a revenue offset, is not excessive. However, the acceptance of a VCU by the Chairperson will result in the closure of an investigation.

83. The PMPRB reports publicly on all VCUs that the Chairperson has accepted. In submitting a signed VCU a patentee must consent to its publication either in full or redacted form. The reported information can include disclosure of a copy of the VCU or terms included in the VCU. The reported information may appear in the PMPRB's Annual Report, on the PMPRB's website, in the PMPRB's publications such as the *NEWSletter*, and on social media platforms.

84. Requests for VCU negotiations or proposals "without prejudice" cannot be considered by Staff. VCUs are unilateral promises by patentees and not settlement agreements. However, discussions between patentees and Staff are subject to the protections set out in sections 87 and 88 of the *Patent Act* and in the *Access to Information Act*.

85. If a Notice of Hearing has been issued, patentees may still pursue settlement through the negotiation of a settlement agreement, which must be approved by the Hearing Panel. Requests for settlement agreements or proposals are considered by Staff on a "without prejudice" basis.

IX Hearing Recommendation

86. When an investigation into the price of a patented medicine is completed and the matter is not resolved with the patentee, Staff may submit a report to the Chairperson. The Chairperson, in his or her capacity as the CEO of the PMPRB, may decide to issue a Notice of Hearing if he or she is of the opinion that it is in the public interest. A decision to issue a Notice of Hearing is not in any sense adjudicative and no analysis is undertaken by the Chairperson as to whether the facts alleged by Staff are, or will be, proven. Until a matter is brought before a Hearing Panel at a public hearing, no Board member (other than the Chairperson as per the procedure described above) is informed of the results of Staff's review into the price of a patented medicine.

87. The decision of whether the price of a patented medicine is excessive is made by the Hearing Panel alone after the public hearing is held.

X Excessive Price Hearing Process and Remedies

88. PMPRB hearings are public proceedings. During a hearing, submissions and evidence from the parties are heard by a Hearing Panel consisting of at least two Board members. The Hearing Panel determines whether a patented medicine is being or has been sold at an excessive price in any market in Canada by taking into consideration the available information relating to the factors set out in section 85 of the Act.

89. For more information about hearings, please consult the *PMPRB Rules of Practice and Procedure*, the published standard set of procedures to be followed by all participants in hearings before the Board. The *Rules* set out the Board's procedures in accordance with the requirement under the Act to resolve matters as informally and expeditiously as the circumstances and considerations of fairness permit. Practice directions and further information about previous and ongoing hearings are also publicly available on the PMPRB's website.

90. Under the Act, the PMPRB is empowered to make remedial orders when it is found, following a hearing, that a patentee (or former patentee) is selling, or has sold, a patented medicine in any market in Canada at an excessive price.[16]

91. In broad terms, the PMPRB has the power to impose two main forms of remedy after a hearing: (i) orders directing the patentee to cause the maximum price at which the patentee sells the medicine in that market to be reduced to such level as the Board considers not to be excessive; and (ii) orders directing the patentee to offset the amount of the excess revenues estimated by it to have been derived by the patentee from the sale of the medicine at an excessive price by either (a) reducing the price at which the patentee sells the medicine; (b) reducing the price at which the patentee sells one other medicine to which a patented invention of the patentee pertains; or (c) paying to Her Majesty in right of Canada an amount specified in the order.

92. If a Hearing Panel finds that the patentee or former patentee has engaged in a policy of selling the patented medicine at an excessive price, it may order the patentee to offset up to twice the amount of excess revenues estimated by it to have been derived from the sale of the patented medicine at an excessive price. The extent and duration of sales of the patented medicine at an excessive price will be considered by the Board in making this finding and order.

16 Pursuant to ss. 81(3) of the *Patent Act*, the PMPRB may make remedial orders against former patentees for up to three (3) years from the day on which the former patentee ceased to be entitled to the benefit of the patent or to exercise any rights in relation to the patent.

XI Failure to File Hearing

93. When it is the opinion of Staff that a patentee has failed or refused to provide the PMPRB with the pricing, sales or revenues and like information required by law, the Chairperson will receive a recommendation from Staff to hold a public hearing to determine whether the patentee has, in fact, breached the reporting requirements of the Act and Regulations. If, as the result of such a hearing, the Hearing Panel finds that the patentee is in breach of its reporting requirements, it may order the patentee to provide the PMPRB with the required information and documents as per section 81 and/or section 88 of the Act.

94. In addition, as per subsection 76.1(1) of the Act, every person who contravenes or fails to comply with the filing requirements set out in section 80, 81, 82 or 88, or any order made thereunder, is guilty of an offence punishable on summary conviction and liable to a fine or to imprisonment.

XII Complaints

95. Any individual or group who believes that the price of a patented medicine is excessive may submit a complaint to the PMPRB. A complaint may be submitted by telephone, in writing, or electronically using the contact information available on the PMRPB's "How to Make a Complaint" page.

96. Complaints are a trigger for an investigation by Staff into the price of a patented medicine. The complainant is not part of that investigation or of any resulting hearing (unless the complainant applies to become an intervener in the hearing). The complainant is not required to provide any documents or evidence to the PMPRB. Any investigation will be based on materials provided by the patentee or otherwise obtained by Staff.

97. Due to limitations on disclosure set out in sections 87 and 88 of the *Patent Act* and in the *Access to Information Act*, the complainant will be only be informed of the outcome of the investigation if the process results in a VCU or a Notice of Hearing.

XIII Appendices

A. Domestic Therapeutic Class Comparison (dTCC) and International Therapeutic Class Comparison (iTCC)

dTCC TEST

As described in section V of these Guidelines, the domestic Therapeutic Class Comparison ("dTCC") test is used as part of the calculation of a patented medicine's MLP, and in some cases, its MRP. The dTCC test compares a patented medicine's List Price with the list prices of other medicines identified by scientific review for comparison purposes.

Identification of medicines for comparison purposes

The World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology's Anatomical Therapeutic Chemical (ATC) Classification System is used in the selection of medicines to be used for comparison purposes.

The medicines used for comparison purposes will typically be those identified under the ATC classification system at the sub-class level above the single chemical substance. This will normally be the fourth sub-class level but could include the next higher sub-class or another sub-class. In some instances, it may be appropriate to select from the fifth or single chemical substance level.

A medicine of the same ATC therapeutic class as the medicine under review may be omitted if it is unsuitable for comparison. For example, a medicine with a primary indication other than the primary indication of the patented medicine under review may be omitted from the comparison.

All medicines identified for comparison that have the same approved indication as the Relevant Indication of the patented medicine under review will be included in the review. This review is based on Staff research and may include additional research by a Drug Information Centre (DIC) or consideration of evidence submitted by patentees. In some cases, Staff may also seek non-binding advice from the Human Drug Advisory Panel (HDAP).

For a patented medicine that is a new dosage form or strength of the same medicinal ingredient as one or more existing medicines, its comparators will be those existing medicines that are available in the same or comparable dosage form and have the same indication. This will apply regardless of whether the dosage regimens of the new and existing medicines are the same or differ materially.

For a product that is a combination of medicines, where each of the medicines of the combination are sold in Canada and have the same indication, its comparators will be limited to the component medicines.

Comparable dosage regimens

The comparable dosage regimen used for comparison purposes will normally be the maximum of the usual recommended dosage in the Product Monograph (or similar information) taking into account relevant clinical variables. The most appropriate strength of the medicine will be chosen for a particular dosage regimen. Generally, a dosage regimen based on a course of treatment will be applicable to acute indications, while a per-day regimen (based on maintenance dose) will be applicable to chronic indications.

Price sources

Patentees do not file prices for the patented medicine's comparators. Public sources will be used for the prices of the medicines used for comparison purposes in order to conduct a dTCC test. Provincial formularies will be the starting point in Staff's identification of public prices. The lowest public price for each of the medicines identified for comparison purposes will be used. Any medicine (patented or non patented) identified for comparison purposes may be excluded from a dTCC test if Staff has reason to believe it is being sold at an excessive price.

dTCC test

Following the identification of medicines for comparison purposes and of their lowest public price for each medicine, the cost of comparable courses of treatment for each medicine will be calculated. These costs of treatment will be ordered and the median identified. In the event of an even number of medicines used for comparison purposes, the median will be the simple average of the middle two costs of treatment. This median cost of treatment will then be divided by the constituent units of the comparable course of treatment for the medicine under review to establish a per-unit price.

iTCC TEST

As described in section V of these Guidelines, the international Therapeutic Class Comparison ("iTCC") test may be used as part of the calculation of a patented medicine's MRP. The iTCC test compares a patented medicine's List Price with the list prices of other medicines identified by scientific review for comparison purposes in the eleven (11) comparator countries listed in the Regulations.

Identification of medicines for comparison purposes and comparable dosage regimens

The iTCC test uses the same medicines identified for comparison purposes and comparable dosage regimens as the dTCC test, following the procedures set out above. In cases where no domestic comparators have been identified, Staff may assess whether there are additional medicines approved for the same approved indication as the medicine under review in any of the comparator countries.

Price sources

Patentees do not file international prices for the international comparators to the patented medicine. National formularies will be the starting point in Staff's identification of public prices. Publicly available ex-factory prices for the comparator medicines will be used in order to conduct an iTCC test. The lowest public price for each of the medicines identified for comparison purposes will be used.

Any medicine (patented or non patented) identified for comparison purposes may be excluded from an iTCC test if Staff has reason to believe it is being sold at an excessive price.

iTCC test

Following the identification of medicines for comparison purposes and of the lowest public price for each medicine, the cost of comparable courses of treatment for each comparator medicine in each comparator country will be calculated. These costs of treatment will be ordered and the median identified for each country. In the event of an even number of comparator medicines used for comparison purposes, the median will be the simple average of the middle two costs of treatment. These medians will be ordered in a "median of the medians" will be identified. This median cost of treatment will then be divided by the constituent units of the comparable course of treatment for the medicine under review to establish a per-unit price. Local currencies will be converted to Canadian dollars using the methodology described in section V of these Guidelines.

B. Reasonable Relationship Test and Comparable Dosage Forms

REASONABLE RELATIONSHIP TEST

The Reasonable Relationship (RR) test may be conducted to determine the MLP or MRP of a new or additional strength of a patented medicine with other existing strengths, where the new or additional strength has the same medicinal ingredient, indication, dosage regimen, and same or comparable dosage form as the existing strength(s).

When a new strength of a medicine that is currently sold in Canada is introduced and meets the above requirements of the RR test, the MLP or MRP of the new strength will be set to be equivalent to the price per standard unit of the existing strength(s). This approach will also be applied when multiple strengths of a new medicine are first sold simultaneously and some strengths are identified specifically as loading, titration, or reduction doses.

COMPARABLE DOSAGE FORMS

The following are considered comparable dosage forms for the purpose of the RR test. Formulations within each group are considered comparable, but dosage forms in a different group are not.

TOPICAL (T)

- Aerosol
- Aerosol (foam)
- Cream
- Disc (extended release)
- Disc
- Dressings
- Gel
- Gel (controlled release)
- Liposomes
- Liquid
- Lotion
- Ointment
- Pad
- Paint
- Paste
- Patch
- Patch (extended release)
- Pencil
- Plaster
- Powder
- Shampoo
- Soap Bar
- Solution
- Sponge
- Spray
- Spray (bag-on-valve)
- Spray (metered dose)
- Stick
- Strip
- Swab
- Tincture

NASAL (N) / PULMONARY (P)

- Aerosol
- Aerosol-metered dose
- Drops
- Gas
- Metered dose preparation
- Powder
- Powder (metered dose)
- Solution
- Solution (extended release)
- Spray
- Spray (metered dose)
- Stick

ORAL SOLID (S)

- Bar (chewable)
- Caplet
- Capsule
- Effervescent granules
- Effervescent powder
- Effervescent tablet
- Film (soluble)
- Globules
- Granules
- Gum
- Lozenge
- Modified release caplet
- Modified release capsule
- Modified release tablet
- Pellet
- Piece (chewable)
- Powder (extended release)
- Strip
- Tablet
- Tablet (chewable)
- Tablet (oral disintegrating)
- Tablet for suspension
- Wafer

ORAL LIQUID (L)

- Drops
- Elixir
- Emulsion
- Gel
- Granules for solution
- Granules for suspension
- Granules for suspension (delayed release)
- Granules for suspension (extended release)
- Liquid
- Modified release liquid
- Powder (extended release)
- Powder for solution
- Powder for suspension
- Solution
- Solution (extended release)
- Spray
- Suspension
- Suspension (extended release)
- Syrup
- Syrup (extended release)
- Tea (herbal)
- Tincture

VAGINAL (V)

- Cone
- Cream
- Douche
- Foam
- Gel
- Gel (controlled release)
- Implant
- Insert
- Insert (extended release)
- Ovule
- Pellet
- Ring (slow release)
- Sponge
- Suppository
- Suppository (sustained release)
- Tampon
- Vaginal tablet
- Vaginal tablet (effervescent)

PARENTERAL (J)

- Bolus
- Implant
- Kit
- Liposomes
- Modified release injection
- Pellet (implantable)
- Powder for solution
- Powder for suspension (sustained-release)
- Solution
- Solution (extended release)
- Suspension for emulsion
- Suspension (extended release)

OTIC (E) / OPTHALMIC (Y)

- Drops
- Gel
- Gel (controlled release)
- Implant
- Insert
- Insert (extended release)
- Liquid
- Modified release ocular device
- Ointment
- Powder for solution
- Solution
- Solution (extended release)
- Suspension

RECTAL (R)

- Cream
- Enema
- Foam
- Insert
- Ointment
- Ovule
- Stick
- Suppository
- Suppository (sustained release)
- Suspension
- Suspension (extended release)

DENTAL/SUBLINGUAL BUCCAL (M)

- Emulsion
- Film (soluble)
- Floss
- Gel
- Gel (controlled release)
- Gum
- Lozenge
- Metered-dose pump
- Modified release buccal tablet
- Mouthwash (gargle)
- Paste
- Powder (effervescent)
- Powder for suspension
- Solution
- Solution (extended release)
- Spray – buccal
- Spray – sublingual
- Stick
- Strip
- Sublingual tablet
- Suspension
- Suspension (extended release)
- Swab
- Tablet (orally disintegrating)
- Tablet
- Tooth paste
- Tooth powder
- Wafer

C. Pharmacoeconomic Value Assessment

As described in section V of these Guidelines, a pharmacoeconomic value assessment is used as part of the calculation of the MRP. Under the Regulations, patentees are required to file prescribed information relating to all pharmacoeconomic analyses of a medicine prepared by publicly funded Canadian organizations if the pro-rated cost of the treatment for that medicine over a 12-month period is greater than or equal to 50% of GDP per capita at the time of the publication of the analysis.

Model selection

The typical source of pharmacoeconomic analysis used for this assessment will be the Common Drug Review (CDR) Pharmacoeconomic Reports and pan-Canadian Oncology Drug Review (pCODR) Final Economic Guidance Reports of the Canadian Agency for Drugs and Technologies in Health (CADTH). Analyses developed by the *Institut national d'excellence en santé et services sociaux* (INESSS) in its *Évaluations aux fins d'inscription* will also be considered.

As part of this assessment, Staff calculations will rely on the base case reanalysis conducted by the public agency (i.e., CADTH and/or INESSS), as opposed to the analysis conducted with the base case model submitted by the patentee. This will be a cost-utility analysis model in which health outcomes are expressed as QALYs. If the agency's report does not include a cost-utility analysis, a cost-minimization model may be used. For medicines with multiple indications, the pharmacoeconomic assessment for the Relevant Indication, as determined by the procedure in section V of these Guidelines, will be used.

Calculation of the Pharmacoeconomic Price (PEP)

The PMPRB relies on agencies to publish estimates enabling the calculation of the PEP in their reporting.

For medicines that provide health benefits relative to current care, the PEP is calculated as:

$$\text{PEP} = \frac{P_1\,(\text{PVT} * \text{Incremental QALYs} + \text{Treatment Cost} - \text{Incremental Costs})}{\text{Treatment Cost}}$$

For the purpose of this calculation:

- **PVT** is the Pharmacoeconomic Value Threshold of $60,000/QALY;[17]
- **P_1** is the list price of the medicine used in the agency's reporting;
- **Incremental QALYs** are the point estimate of incremental QALY gains of the medicine over the comparator in the agency's base case cost-utility analysis model, expressed in present value;
- **Incremental Costs** are the point estimate of incremental costs of the medicine over the comparator, expressed in present value; and
- **Treatment Cost** is the point estimate of the costs per patient of the medicine over the time horizon studied by the agency's report, expressed in present value. This value is limited to the medicine being assessed and excludes the cost of other medicines used jointly with the medicine being assessed or of medicines used to treat side effects.

17 This threshold may be adjusted from time to time, and at least every five years, based on empirical evidence and/or to reflect changes in GDP.

For medicines that do not provide health benefits relative to existing treatments, the PEP can be determined in one of two ways:

- In cases in which the medicine's associated costs of publicly funded health care resources differ from current care, the PEP is calculated as:

$$\text{PEP} = \frac{P_1\,(\text{Treatment Cost} - \text{Incremental Costs})}{\text{Treatment Cost}}$$

- In cases where the medicine's associated costs of publicly funded health care resources are equivalent to current care, the PEP will be equivalent to the domestic therapeutic class comparator (dTCC).

Multiple patient populations

In some cases, the agency may calculate multiple PEPs based on distinct subpopulations. In these cases, Staff will calculate a weighted average PEP using all base case models which cover a significant proportion (10% and over) of the total target population. In cases in which the PEP of an outlier subpopulation tends toward zero or infinity, the PMPRB may exclude them from the weighted average. Because the target population is the population that may benefit from the medicine for the Relevant Indication in Canada, the weighted average also excludes patient groups for which health outcomes are estimated to be worse than current care by the agency's model.

D. Market Size Adjustment Methodology

As described in section V of the Guidelines, a market size adjustment is applied to Category I patented medicines with quantities sold such that annual revenues would exceed $25 million across all dosage forms and strengths of the medicine (i.e., all DINs combined) when priced at the MRP(s) set by the PEP. This adjustment will be applied annually to determine the MRP in accordance with the following table:

Market size adjustment for Category I medicines

Annual revenues	Incremental adjustment factor	MRP	
		Medicines with a PEP	Medicines without a PEP
<$25M	0%	PEP	Lower of LIP, dTCC, iTCC
$25M–$50M	-10%	PEP adjusted by applicable factor	Lower of LIP, dTCC, iTCC adjusted by applicable factor
$50M–$75M	-20%		
$75M–$100M	-30%		
$100M–$125M	-40%		
$125M+	-50%		

The market size adjustment to a patented medicine's MRP will be assessed annually based on actual quantity sold during the previous calendar year. This adjustment will be applied incrementally based on units sold in each tier over $25 million.[18]

For example, a patented medicine that would realize between $25 million and $50 million in revenues based on units sold at the MRP set by the PEP will have its MRP adjusted as follows:

$$MRP = \frac{\left[\$25M + 0.9 * PEP * \left(Units - \frac{\$25M}{PEP}\right)\right]}{Units}$$

Additional increments will be assessed for each additional revenue tier realized by the quantity sold. For example, a patented medicine that would realize between $50 million and $75 million in revenues based on units sold at the MRP based on the PEP would receive the following adjustment:

$$MRP = \frac{\left[\$25M + \$25M + 0.8 * PEP * \left(Units - \frac{\$25M}{PEP} - \frac{\$25M}{0.9 * PEP}\right)\right]}{Units}$$

After the initial market size adjustment, a patented medicine's MRP will only be readjusted following an increase in annual units sold. A patented medicine's MRP will not be readjusted following a decrease in annual units sold, or if its realized revenues fall into a lower tier.

For patented medicines with multiple DINs, each DIN's units will be converted into equivalent-strength units of the DIN for which the MRP was originally calculated. The market size adjustment will then be applied to this DIN using these total converted units. The resulting MRP will then be applied to each DIN on a price per standard unit basis using the RR test.

Rare disease or disorder medicines

For patented medicines that are screened into Category I, Staff will also assess the prevalence of the indicated condition(s). Patented medicines with an estimated total prevalence no greater than 1 in 2,000 across all approved indications will be designated as "rare disease or disorder" patented medicines. This assessment will be based on Staff research and may include additional research by a Drug Information Centre (DIC) or consideration of evidence submitted by patentees.

The MRP for these patented medicines will initially be calculated by identifying the Pharmacoeconomic Price (PEP) and applying an increase of 50%. For patented medicines that would realize revenues between $12.5 million and $25 million based on units sold during the previous calendar year, the MRP will subsequently be calculated by applying an incremental adjustment based on the PEP in the same manner as described above for other Category I medicines. The market size adjustment will subsequently be applied to revenues in each tier over $25 million.[19]

18 These tiers may also be adjusted from time to time, and at least every five years, to reflect changes in CPI and GDP.
19 These tiers may also be adjusted from time to time, and at least every five years, to reflect changes in CPI and GDP.

Market size adjustment for Category I rare disease or disorder patented medicines

Annual revenues	Incremental adjustment factor	MRP	
		Medicines with a PEP	Medicines without a PEP
<$12.5M	+50%	1.5 * PEP	Lower of LIP, dTCC, iTCC
$12.5M-$25M	0%	PEP	
$25M–$50M	-10%	PEP adjusted by applicable factor	Lower of LIP, dTCC, iTCC adjusted by applicable factor
$50M–$75M	-20%		
$75M–$100M	-30%		
$100M–$125M	-40%		
$125M+	-50%		

For example, a rare disease or disorder patented medicine that would realize between $12.5 million and $25 million in revenues based on units sold at the MRP set by the PEP will have its MRP adjusted as follows:

$$MRP = \frac{\left[\$12.5M + PEP * \left(Units - \frac{\$12.5M}{1.5 * PEP}\right)\right]}{Units}$$

Similarly, a rare disease or disorder patented medicine that would realize between $25 million and $50 million in revenues based on units sold at the MRP set by the PEP will have its MRP adjusted as follows:

$$MRP = \frac{\left[\$12.5M + \$12.5M + 0.9 * PEP * \left(Units - \frac{\$12.5M}{1.5 * PEP} - \frac{\$12.5M}{PEP}\right)\right]}{Units}$$

Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

Canada