Guidelines for PMPRB Staff

Administrative Process for Excessive Price Hearing Recommendation

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

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The Role of These Guidelines

1. The Patented Medicine Prices Review Board ("PMPRB") was established via amendments to the *Patent Act* (the "Act") in 1987 as the response to a major set of reforms to the Act which strengthened Canada's patent protection for medicines. The PMPRB is an independent quasi-judicial statutory body with a mandate to monitor the prices of patented medicines sold in Canada to ensure that they are not excessive. The PMPRB fulfills its mandate by holding public hearings to determine whether the prices of specific patented medicines are excessive. The PMPRB is also empowered to issue non-binding Guidelines on matters within its jurisdiction.

2. In 2019, the Government proposed to amend the Patented Medicines Regulations ("Regulations") to introduce new price review factors (pharmacoeconomic value, market size and gross domestic product) for the PMPRB to consider when monitoring for excessive pricing, changed the schedule of countries for which Rights Holders are to report price information to the PMPRB and also required Rights Holders to file information net of all price adjustments, including rebates provided through product listing agreements.

3. The proposed amendments were challenged in both provincial and federal courts, resulting in new judicial guidance in two court proceedings – *Merck Canada Inc*. c. *Procureur general du Canada* and *Innovative Medicines Canada* v. *Canada* (*Attorney General*)[1]- as to the scope of the PMPRB's mandate and authority. Subsequently the Governor in Council decided not to proceed with the amendments related to the new price review factors and the net price information filing. Instead, the Government moved forward only with the implementation of the updated schedule of eleven countries ("PMPRB11") and reduced reporting requirements for medicines believed to be at the lowest risk of excessive pricing: changes which were upheld as both

[1] *Merck Canada inc. c. Procureur général du Canada*, 2022 QCCA 240 ; *Innovative Medicines Canada v. Canada (Attorney General)*, 2022 FCA 210.

constitutional and vires the Act in the Court proceedings. These two regulatory changes came into force on July 1, 2022.

4. These non-binding Guidelines have been developed to address the amendments to the Regulations, and to reflect the guidance provided by the case law. These Guidelines are directed to PMPRB Staff ("Staff") and are intended to provide transparency to interested parties regarding the process the Staff uses to identify potential candidates to recommend that the Chairperson consider for hearings. These Guidelines are designed to ensure procedural fairness and consistency in that all similarly placed Rights Holders are subject to the same process and process timelines. The process described in these Guidelines consists of two "screening" steps designed to prioritize the cases that are advanced for recommendation for a hearing. The goal of the process is to allow the PMPRB to focus its limited hearings-related resources most efficiently. The first screening step – Initial Review and Annual Review – prioritizes cases for In-Depth Review. The second screening step – In-Depth Review – prioritizes cases for recommendation for hearing. Neither step determines whether a price is excessive. The steps only determine which cases Staff recommends to the Chairperson for a hearing. In all cases, the discretion to determine whether to issue a Notice of Hearing rests with the Chairperson and not with the Staff. At all times, the discretion to determine whether a given price is excessive remains with the panel of Board members assigned to an excessive price hearing ("Hearing Panel").

5. These Guidelines are not intended to be a pricing framework. They are not directed at Rights Holders, nor are they intended to provide certainty on ultimate outcomes for particular cases, suggest or set prices in Canada, or encourage "compliance" with any tests or price ceilings. These Guidelines do not calculate "price ceilings", "non-excessive prices", or "potential excess revenues" either at introduction or at any subsequent point nor do they deem or presume any prices or price thresholds to be excessive or not excessive.

6. The PMPRB can neither define the term "excessive" nor decide whether the price of any given patented medicine is or is not excessive through general Guidelines. a Hearing Panel of the Board can only decide that prices are excessive and order price reductions to a maximum ceiling and/or order excess revenue payments on a case-by-

case basis, based on the factors enumerated in the Act, in the context of a public hearing. During hearings, a Hearing Panel of the Board cannot be fettered in its discretion by the Guidelines, including with respect to the calculation of the amount of excess revenues or the determination of the period during which a medicine may have been excessively priced.

7. The Board recognizes that the approach presented in these Guidelines is a departure from its historical practice of issuing Guidelines directed to Rights Holders to encourage "voluntary compliance" with specific price ceilings identified through the Guidelines. The Board has chosen this new approach based on the recent litigation and jurisprudence regarding its mandate and powers, and the input of interested parties during consultation processes the Board has undertaken with respect to the Guidelines over the past several years.

8. As per the Act, unless they are subject to an order of the Board after a hearing into the price of a particular patented medicine, Rights Holders may price their patented medicines in Canada as they see fit at any time. Rights Holders do not require any "approval" from the PMPRB, or "compliance" with the Guidelines, to sell their patented medicines in Canada. The PMPRB cannot and does not authorize or approve prices.

9. Certain aspects of these Guidelines may be revisited by the PMPRB as circumstances change. If any changes to the Guidelines are contemplated because of an internal review, interested parties will be consulted by the PMPRB as per subsection 96(5) of the Act.

Overview of the PMPRB and its Legislation

Mandate

10. The PMPRB's mandate and jurisdiction are set out in sections 79-103 of the Act. The PMPRB's principal mandate is to ensure that the prices of patented medicines sold in Canada are not excessive. In this regard, the PMPRB monitors and reviews the prices of patented medicines and conducts price hearings which may result in orders to reduce prices to a non-excessive level.

11. The Act does not define what an "excessive" price is. Instead, subsection 85(1) of the Act sets out factors that a Hearing Panel of the Board must take into consideration when it is holding a hearing to determine whether a patented medicine is being sold or has been sold at an excessive price "in any market" in Canada by a Rights Holder or former Rights Holder. These factors are:

    a. The prices at which the medicine has been sold in the relevant market;

    b. The prices at which other medicines in the same therapeutic class have been sold in the relevant market;

    c. The prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada;

    d. Changes in the Consumer Price Index; and

    e. Such other factors as may be specified in any regulations made for the purposes of this subsection.[2]

12. If after considering the above factors, the Board is unable to determine if a price is excessive, subsection 85(2) of the Act stipulates that it may consider the costs of making and marketing the medicine, as well as other factors which can be specified by regulations[3] or that the Board considers relevant in the circumstances.

13. In addition to ensuring that the prices of patented medicines sold in Canada are not excessive, the PMPRB is mandated to provide information on pricing trends in the pharmaceutical industry via its Annual Reports. Moreover, further to a request from the Minister of Health under section 90 of the Act, the PMPRB also prepares reports to the

[2] None apply at this time.
[3] None apply at this time.

Minister on a variety of subject matter related to pharmaceutical pricing and usage. These reports, also known as the National Prescription Drug Utilization Information System (NPDUIS) reports, are available on the PMPRB's website. Information filed by Rights Holders with the PMPRB is not used for these reports to the Minister.

Structure and Administrative Operation

14. The PMPRB is composed of up to five Board members, appointed by the Governor–in-Council pursuant to subsection 91(1) of the Act. One of the Board members is also designated as the Chairperson of the Board and, in that capacity, acts as the Chief Executive Officer ("CEO") of the PMPRB. In addition to their role as a Board member, the Chairperson is responsible for administrative supervision over and direction of the work of the Board, including issuing Notices of Hearing, appointing members of the Board to serve as panel members on hearings, and the management of the PMPRB's internal affairs and the duties of its staff. Another Board member is designated as a Vice-Chairperson and, in that capacity, is empowered to assume the powers and functions of the Chairperson during their absence, incapacity or in case of a vacancy.

15. Collectively, the PMPRB Board members issue the Guidelines and PMPRB reports. In addition, Board members assigned to a Hearing Panel constitute the Board for the purpose of the hearing. Only Board members assigned to a Hearing Panel have the discretion to exercise the PMPRB's powers to conduct hearings and issue binding orders, including making decisions on whether a price is excessive under section 85 of the Act and ordering appropriate remedies under the Act. Outside the issuance of Guidelines and by-laws, Board members other than the Chairperson do not direct or instruct Staff on its day-to-day work.

16. Orders issued by the PMPRB's Hearing Panels 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.

17. The PMPRB's Staff consists of civil servants appointed pursuant to subsection 94(1) of the Act. The role of Staff is to assist with the proper conduct of the work of the PMPRB.

Staff is headed by a Director General, who reports to the Chairperson of the PMPRB. Staff has no discretionary power to issue Guidelines, commence hearings, make decisions regarding whether a patented medicine is priced excessively, issue binding orders or directions, or to compel Rights Holders to comply with legislation. All such discretion resides with the Board as a whole, the Chairperson, or Board members sitting on a Hearing Panel as per the applicable provisions in the Act.

18. Because the PMPRB is established under the Act as an independent, quasi-judicial body, it maintains an arm's length relationship from the rest of the Federal Government, including the Minister of Health (who is responsible for the sections of the Act pertaining to the PMPRB), and the Minister of Innovation, Science and Economic Development (who is responsible for the Act as a whole) with regard to the exercise of its mandate. Under the *Patent Act*, the PMPRB has no specific authority or obligation to align itself with any other policy of government relating to pharmaceuticals or the life-sciences ecosystem in Canada. Equally, 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 price monitoring function. That said, the PMPRB is part of the Federal Government, and the Minister of Health is the designated Minister for the PMPRB for the purposes of the Financial Administration Act, in addition to having specific limited duties and authorities vis-a-vis the PMPRB as set out in the *Patent Act*.

19. Internally, the PMPRB is structured in a manner that separates the work and functions of Staff, the Chairperson and Board Members. Adjudication functions are reserved for Board Members sitting in a Hearing Panel. Internal administrative functions, including reviews of information filed by Rights Holders, are performed by Staff under the direction of the Chairperson as the CEO. The Board Secretariat operates separately and independently from other Staff with respect to hearings and other confidential matters related to the operation of the Board. It is responsible for managing the activities of the Board, including Board meetings, consultations, hearings and other related processes.

20. To preserve the impartiality of Board members, until a matter is brought before a Hearing Panel at a public hearing, no Board member other than the Chairperson is

informed of details of internal reviews of information filed by Rights Holders or of any recommendations made to the Chairperson. Once a hearing has commenced, Staff represents the public interest as the party opposing the Rights Holder in the hearing. As such, Staff does not engage in any *ex-parte* communication with the Hearing Panel members about the hearing, and only interacts with the Hearing Panel members in the manner set out in the *PMPRB Rules of Practice and Procedure*[4] for hearings. Similarly, Board members not on the Hearing Panel do not discuss the hearing with the Hearing Panel members.

General Role of Guidelines

21. Under subsection 96(4) of the Act, the PMPRB may, but is not obligated to, issue non-binding guidelines ("Guidelines") on matters within its jurisdiction.

22. The Board does not have the administrative capacity or resources to conduct hearings for each patented medicine under its jurisdiction. As a result, the Board needs a mechanism to prioritize the cases that are advanced for recommendation by Staff to the Chairperson for a hearing.

23. Consequently, as described in the Introduction, the Board has drafted these Guidelines to guide Staff and to provide transparency to interested parties regarding the process the Staff uses to identify potential cases to recommend that the Chairperson consider for hearings. They are designed to ensure procedural fairness and consistency in that all similarly placed Rights Holders are subject to the same process and process timelines.

24. Since the Act stipulates that the Board is to only consider the factors in subsection 85(2) if it is unable to determine whether the medicine is being sold or has been sold at an excessive price after considering the factors in subsection 85(1), these Guidelines are directed at only the subsection 85(1) factors and do not contemplate considerations which could only be raised pursuant to subsection 85(2).

25. Once Staff has followed the processes described in these Guidelines, it informs the Chairperson whether it recommends that a hearing into the price of a patented medicine be held and provides the Chairperson with all the relevant information that

[4] Rules of Practice and Procedure for Hearings - Canada.ca

relates to the recommendation. Subsequently, the Chairperson decides whether to issue a Notice of Hearing.

26. When deciding whether to issue a Notice of Hearing, the Chairperson's involvement takes place only in their management capacity as the CEO of the PMPRB, pursuant to subsection 93(2) of the Act, which is done solely for the purpose of determining whether a hearing is in the public interest, and not to determine whether the price of a patented medicine is excessive.

Jurisdiction of the PMPRB

27. The Act gives the PMPRB jurisdiction to determine whether a Rights Holder or former Rights Holder of an invention pertaining to a medicine is selling or has sold the medicine at an excessive price in any market in Canada if the following criteria are satisfied[5].

Rights Holder or Former Rights Holder

28. Subsection 79(1) of the Act defines a "Rights Holder" as "a patentee and the person for the time being entitled to the benefit of a certificate of supplementary protection for that invention, and includes, if any other person is entitled to exercise rights in relation to the certificate, that other person in respect of those rights."

29. The PMPRB also has jurisdiction over a former Rights Holder of an invention, while it was a Rights Holder (see, e.g. subsections 80(2), 83(3)).

Invention of the Patent pertains to the medicine

30. The case law to date has established the following principles regarding whether an invention pertains to the medicine:

    - A patented invention pertains to a medicine if it is "intended or capable of being used for medicine or for the preparation or production of the medicine";

[5] *ICN Pharmaceuticals, Inc. v. Canada (Patented Medicine Prices Review Board)* [1996] F.C.J. No 1065

- On the face of the patent, there must be a rational connection or nexus between the invention described in the patent and the medicine and that connection can be the medicine itself.[6];

Medicine

31. Subsection 79(1) of the Act provides that the term "medicine" "includes a drug, as defined in section 104, and a medicinal ingredient."

32. Section 104 of the Act defines a "drug" as "a substance or a mixture of substances manufactured, sold or represented for use in (a) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms, in human beings or animals; or (b) restoring, correcting or modifying organic functions in human beings or animals."

33. The PMPRB has historically interpreted these definitions to exclude medical devices per se (as opposed to active substances used in medical devices), in vitro diagnostic products and disinfectants that are not used in vivo.

Invention/Patent

34. Subsection 79(2) of the Act provides that "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."

35. Types of patented inventions that may pertain to a medicine include, but are not restricted or limited to:

- Patented inventions for active ingredients;
- Patented inventions for processes of manufacture;
- Patented inventions for a particular delivery system or dosage form that are integral to the delivery of the medicine;

[6] *ICN Pharmaceuticals, Inc. v. Canada (Patented Medicine Prices Review Board)* [1996] F.C.J. No 1065; *Galderma Canada Inc. v. Canada (Attorney General)*, 2017 FC 1023; *Canada (Attorney General) v Galderma Canada Inc*, 2019 FCA 196; *Galderma Canada Inc. v. Canada (Attorney General)*, 2024 FCA 208.

- Patented inventions for indications/uses; and
- Patented inventions for formulations.

Sale in any market in Canada

36. The Rights Holder or former Rights Holder must be selling or have sold the patented medicine "in any market" in Canada (see e.g. subsection 83(1)).

37. The PMPRB reviews the prices of patented medicines sold at arm's-length by Rights Holders. Sales in Canada may include, but are not limited to, patented medicines subject to a Notice of Compliance (NOC), Notice of Compliance with Conditions (NOC/c), the Special Access Programme ("SAP"), or the List of Drugs for an Urgent Public Health Need[7]. The PMPRB has no authority over prices charged by parties other than Rights Holders, such as prices charged by wholesalers or retailers, or over pharmacists' professional fees.

Filing Requirements and Protection of Filed Information

38. The Patented Medicines Regulations ("Regulations") set out the information that Rights Holders are to report to the PMPRB and the timeframes in which that information is to be provided. This includes information such as the identity of the medicine and information related to the price and sales of the medicine.

39. The Regulatory filing requirements are mandatory and neither the Board nor Staff have the authority to vary them, grant exceptions or extend deadlines set by the Regulations.

40. Evidence of failure to file any of the information set out in the Regulations in the manner prescribed therein may be brought to the attention of the Chairperson who may recommend that a panel of the Board be appointed to hold a hearing into whether to issue an order requiring production of this information.

41. In the alternative or in addition, the matter may be referred to the Attorney General of Canada to determine if summary conviction proceedings should be commenced under subsection 76.1(1) of the Act.

[7] e.g. *Celgene Corp. v. Canada (Attorney General)*, 2011 SCC 1.

42. Pursuant to subsection 87(1) of the Act, any information or document provided to the PMPRB under sections 80, 81 or 82 of the Act, or in any proceeding under section 83, is privileged, and cannot be disclosed without the authorization of the person who provided it, unless it has been disclosed at a public hearing under section 83. Additional protective measures set out in the *Access to Information Act* or the *Privacy Act* may apply.

43. Receipt of information or documents filed by Rights Holders does not constitute acceptance, verification, or approval of their contents by Staff or Board Members.

Review Process

44. The following diagram sets out the general review processes contemplated under these Guidelines and is separated into two steps or screens. The first step is an Initial Review or Annual Review and applies to all patented medicines sold in Canada, with certain limited exceptions (set out below under "Special Provisions on Complaints"). The result of the first step may either be (a) no further review; or (b) referral for In-Depth Review. The second step only applies to patented medicines who have gone through the first step (Initial Review or Annual Review) and been referred for In-Depth Review. The result of the second step is either (a) recommendation for closure of the In-Depth Review; or (b) recommendation for a hearing.

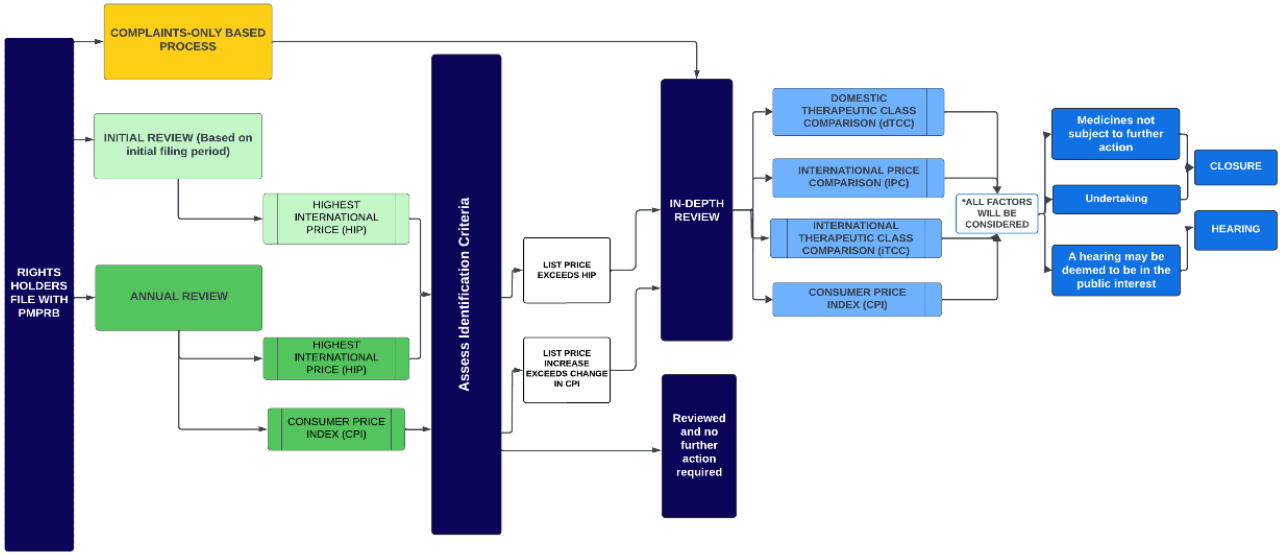


Figure 1. Review Process

45. Patented Medicines are reviewed by Staff at the DIN level in the Initial and Annual Reviews. If one DIN meets the criteria for In-Depth Review, all Associated DINs[8] sold by the Rights Holder are considered as part of the In-Depth Review. If multiple list prices are reported either in Canada or in a Schedule Country for a patented medicine, Staff considers the highest list price in the relevant market so long as the prices filed by the Rights Holder meet the requirements of the Regulations. In cases where there is

[8] "Associated DINs" are all DINs which the Rights Holder has identified in its filings with the PMPRB as pertaining to the same patented invention(s)as the DIN which is subject to In-Depth Review (see Patented Medicine Regulations s. 3(1)(g),(h) and (i)).

reason to believe that a price filed by the Rights Holder does not conform to the requirements of the Regulations (e.g., the reported price appears to be a public sale price as opposed to the ex-factory price required by the Regulations, or a typographic error is suspected), Staff may contact the Rights Holder to raise the issue of potential correction of the data.

46. When selecting the list price for any therapeutic comparators, Staff considers the highest publicly-available list price for each comparator. The information about the prices of comparators used by Staff comes from public sources, not Rights Holder filings. Provincial formularies are typically the starting point for Canadian prices, while official formularies for the Schedule Countries (where available) are typically used for international prices. In the event of a hearing, however, all prices for the patented medicine and its comparators – not just the highest – may be considered by a Hearing Panel.

47. For prices filed by Rights Holders for the Schedule Countries, Staff converts local currency prices filed for the Schedule Countries 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 as published by the Bank of Canada. During a patented medicine's Initial Review, the thirty-six (36) months ending in the second month of the previous reporting period (i.e., February or August) is generally used. In Annual Reviews, the thirty-six (36) months ending in the second month of the reporting period under review is generally used to convert prices filed by the Rights Holders.

48. No "margins" are provided to account for exchange rate or other temporary price fluctuations when determining whether a patented medicine meets the criteria for In-Depth Review, but issues around foreign exchange fluctuations may be considered by Staff as part of the In-Depth Review.

First Step

Initial Review

49. Staff uses a patented medicine's first semi-annual price filing to conduct an Initial Review against the highest international price("HIP") among the Schedule Countries filed by the Rights Holder based on paragraph 85(1)(c) of the Act. The review compares

the list price(s) of a patented medicine in Canada with the information the Rights Holder files regarding the list price(s) of the medicine in the Schedule Countries. "New medicines"[9] will be subject to the Initial Review process immediately after these Guidelines come into effect. "Existing medicines"[10] will be subject to the transitional measures outlined in the Annual Review process (see paras. 53-54).

50. Patented medicines whose prices are above the HIP threshold are subject to an In-Depth Review. As noted above, while Staff reviews patented medicines at the DIN level, if one DIN meets the criteria to commence an In-Depth Review, Associated DINs are considered as part of the In-Depth Review.

51. If an International Price Comparison ("IPC") cannot be conducted during the Initial Review because no list prices are filed for the medicine in any of the Schedule Countries, the list price is considered reviewed for the purpose of the Initial Review and is not reviewed again until the Annual Review. For further clarity, an IPC is conducted if one or more list prices are filed for the medicine in any of the Schedule Countries.

52. The Initial Review service standard for Staff is to advise Rights Holders whether their patented medicine(s) is subject to an In-Depth Review within 60 days of the filing deadline for their first semi-annual filing.

Annual Review

53. Staff conducts an Annual Review of list price for each patented medicine under the PMPRB's jurisdiction beginning in January of each year to see whether they should be subject to an In-Depth Review. New medicines and Existing medicines are subject to the same Annual Review process, although existing medicines will be reviewed starting two (2) years from the date these Guidelines go into effect.

54. Transitional measures: For the first Annual Review for existing medicines, occurring two (2) years from the date these Guidelines go into effect, Staff will only apply the IPC identification criterion (the HIP). The application of the Consumer Price Index (CPI) identification criterion will begin during the following Annual Review. Existing

[9] New Medicine: Patented medicines first sold on or after July 1, 2022
[10] Existing Medicine: Patented medicines first sold before July 1, 2022

medicines will only become subject to In-Depth Review during this two-year period if they are the subject of a complaint (set out below under "Special Provisions on Complaints") or if they are an Associated DIN of a medicine that is subject to In-Depth Review.

55. As in the Initial Review, the service standard for Staff is that Rights Holders are advised whether any of their patented medicines are subject to In-Depth Review within 60 days of the filing deadline for their semi-annual filing in January. The Annual Review applies the same IPC identification criteria (the HIP) and methodology (e.g. foreign exchange, selection of price when multiple prices are filed for a country, etc.) used during the Initial Review, but focuses on the most recently filed domestic and international pricing data.

56. Note that since the Annual Review will compare the list price(s) of a patented medicine against the HIP based on the prevailing list prices in the Schedule Countries, changes in the HIP could render the applicable threshold lower or higher in subsequent years than it was at introduction, depending on how the international landscape evolves. For example, if a patented medicine which was previously listed in only some of the Schedule Countries is subsequently listed in another Schedule Country at a higher price point than the original countries, the price threshold for initiating an In-Depth Review could rise accordingly. Likewise, if the highest price for the medicine in the other Schedule Countries where it is available declines, this could mean that the threshold becomes lower over time. Any such shifts are considered in the context of the In-Depth Review.

57. During an Annual Review, Staff also compares the price change of each patented medicine against changes in the CPI as an identification criterion to prioritize medicines that warrant an In-Depth Review.

58. If an IPC cannot be conducted because no list prices are filed for the patented medicine in the Schedule Countries, an In-Depth Review is only initiated based on the change in the CPI, or in response to a complaint.

59. If an In-Depth Review for a given patented medicine is still open at the beginning of a subsequent Annual Review period, the medicine does not trigger a new Annual Review at that time.

60. A patented medicine that has been subject to an In-Depth Review which has been closed will not be subject to another In-Depth Review for at least the two subsequent filing periods.

Changes in the Consumer Price Index (CPI)

61. List prices are reviewed against the change in the CPI each year using the one-year lagged CPI (e.g. for patented medicines reviewed in 2028, Staff will compare list price increases taken in 2027 against the 2026 CPI factors, published by Statistics Canada in January 2027). If a Rights Holder increases the list price of a patented medicine by an amount greater than the change in the CPI in any given year, Staff opens an In-Depth Review into the medicine unless the Rights Holder did not take a list price increase in the previous year and the increase in the second year is lower than or equal to the total change in CPI over those two years. Staff does not consider the total changes to the CPI for more than the most recent two years in determining whether to open an In-Depth Review, but the total change in the CPI for more than two years may be a relevant consideration during an In-Depth Review.

62. The source Staff uses to calculate the CPI is the "Consumer Price Index, monthly, not seasonally adjusted" as published by Statistics Canada.[11]

63. An In-Depth Review commenced due to the list price increases above the CPI described above subsequently proceeds in the same manner as all other In-Depth Reviews.

Special Provisions on Complaints

64. The complaints process is an administrative monitoring safeguard intended to capture situations which may not be flagged by the typical review process. The PMPRB uses

[11] Consumer Price Index, monthly, not seasonally adjusted (statcan.gc.ca). This is the same source Staff has historically used in previous iterations of the Guidelines.

this mechanism as a substitute for periodically conducting In-Depth Reviews of a random selection of medicines.

65. Patented generic medicines, over the counter medicines and veterinary medicines are only subject to In-Depth Review if a complaint is received from an approved individual or organization (see para. 68).

66. In addition, for all other patented medicines, the receipt of a complaint from an approved individual or organization (see para. 68) who believes that the price of a patented medicine may be excessive in any market in Canada will automatically lead to an In-Depth Review. This applies even if the Initial Review or Annual Review criteria have not otherwise been met, provided it is determined that the medicine is subject to the PMPRB's jurisdiction.

67. The complaints process will take effect once the Guidelines come into force and will apply to both new and existing medicines. For clarity, any complaints received for existing medicines before they become subject to Annual Reviews (see para. 53, above) will result in an In-Depth Review, provided the medicine falls under the PMPRB's jurisdiction.

68. The approved individuals or organizations whose complaints lead to In-Depth Reviews are set out below:

- the Federal Minister of Health or any of their Provincial or Territorial counterparts; or
- Senior officials who are authorized to represent Canadian publicly-funded drug programs.

69. The Federal Minister of Health and their Provincial counterparts are approved complainants consistent with their special status under sections 86(2) and 87(2)(a) of the Patent Act. Canadian publicly-funded drug programs typically operate under the authority of their respective Minister of Health or equivalent.

70. Complaints from other parties do not lead to In-Depth Reviews. Other parties who have concerns about the list prices of specific patented medicines are encouraged to raise their concerns with their relevant Minister(s) of Health or Canadian publicly-

funded drug program, who may choose to make a complaint to the PMPRB on their behalf.

71. Approved individuals and organizations may submit a complaint by following the process available on the "How to Make a Complaint" page of the PMPRB's website. Information about the complainant is not provided to the Rights Holder of the patented medicine subject to complaint, unless required by law. Neither the information about the complainant, nor the patented medicine subject to complaint and corresponding Rights Holder is made public by the PMPRB, unless the matter results in a Hearing or as otherwise required by law. The complainant is not required to provide any documents or evidence to the PMPRB and if they choose to do so, Staff only consider any information which is relevant to the subsection 85(1) factors.

72. Due to limitations on disclosure set out in section 87 and section 88 of the Act and in the *Access to Information Act*, the complainant is only informed that the complaint has been received, and of the outcome of an In-Depth Review if the process results in an Undertaking or a Notice of Hearing. For clarity, due to these confidentiality obligations, if an In-Depth Review is concluded with no further action being taken (i.e., it is closed by the Chairperson), only the Rights Holder is advised and not the complainant.

73. An In-Depth Review commenced due a complaint subsequently proceeds in the same manner as all other In-Depth Reviews.

Second Step

In-Depth Review

74. In-Depth Review is the process by which Staff analyses and balances all the information related to the section 85 factors to prepare a recommendation to the Chairperson on whether a matter should be brought to a hearing. This Section as well as the following Sections ("Scientific Review: Therapeutic Class Comparison Selection and Analysis" and "Price Review") provide further details on In-Depth Review.

75. Note that the selection of the HIP as an identification criterion for Initial Review and Annual Review is based on administrative efficiency and resource prioritization and does not pre-suppose that prices above or below the HIP are excessive or not

excessive. The Board recognizes that the determination of whether a price is excessive can only be made by Hearing Panels in hearings and must consider all the factors set out in subsection 85(1) of the Act. As such, it is possible that a price above or below the HIP could be found to be excessive or non-excessive, depending on how the factors and related information are weighted by a Hearing Panel in the circumstances of a specific case.[12] Staff keeps these principles in mind when conducting an In-Depth Review, and considers all available prices in the Schedule Countries as part of an In-Depth Review.

Deferral Letters

76. In the event of resource constraints, Staff will prioritize patented medicines with list prices significantly above the HIP or whose list price increases are significantly above the CPI. Depending on the PMPRB's internal resources, other patented medicines may receive deferral letters. It is possible that some patented medicines with list prices above the HIP may be deferred multiple times depending on the PMPRB's internal resources. Deferral letters do not provide relief from any calculation of excess revenue by a Hearing Panel that may be potentially accruing during the period of deferral as the amount and applicable time-frame for the calculation of excess revenues can only be determined by a Hearing Panel following a hearing.

Scientific Review: Therapeutic Class Comparison Selection and Analysis

77. The Staff scientific team is composed of health care professionals with significant education, background, and experience in a variety of areas of clinical practice, drug evaluation, and drug utilization. Once an In-Depth Review is initiated, the Staff scientific team identifies the comparators for the purpose of conducting a Therapeutic Class Comparison ("TCC"). Comparators are identified for each approved indication or use of the patented medicine under In-Depth Review at the time the In-Depth Review is initiated. To best prioritize the resources of the Staff scientific team, only the approved indications or uses of the patented medicine under review will be considered for the purpose of populating the TCC during In-Depth Reviews. If there is evidence to demonstrate that the patented medicine is used for other indications which have not

[12] April 10, 2008 Decision: PMPRB-06-D3-ADDERALL XR – Merits; September 1, 2022 Decision: Procysbi (Re)

been approved, those other indications could potentially be relevant in the case of a hearing.

78. All products having the same indication or use as the medicine under review will be identified for the purposes of a TCC. TCC assessments are conducted from a population therapeutics perspective for each indication rather than from the perspective of the needs of individual patients and are not intended to address all possible unique patient circumstances or needs. TCC assessments are only intended for use in internal PMPRB price reviews under the Guidelines and are not intended for use in PMPRB hearings or in third-party clinical, medical, or drug evaluation settings. TCC assessments are confidential to the Rights Holder and will not be shared with third parties by the PMPRB, unless required by law.

79. Each comparator is assigned a level of similarity to the patented medicine subject to In-Depth Review in accordance with the following two-step framework. Comparability is assigned for each comparator identified for a single indication. Comparable dosage forms are also established at this stage. The most appropriate strength of the drug product is chosen for a particular dosage regimen. Generally, a dosage regimen based on a course of treatment is applicable to acute indications, while a per-day regimen (based on a maintenance dose) is applicable for chronic indications.

Step 1: Qualitative Assessment

Qualitative Class	**Example Rationale**[13]
A	**Comparable**: comparable safety and efficacy demonstrated in high quality head-to-head trials or meta-analyses. Recommended or used in the same place in therapy as the patented medicine under review.
B	**Less comparable**: efficacy, safety or patient-assessed outcomes are meaningfully different (either better or worse) than the patented medicine under review based on published literature. Recommended or used in a similar place in therapy as the medicine under review.
C	**Undetermined comparability**: could be used alternatively or in place of the patented medicine under review in many circumstances but comparability is unclear based on available published literature.

[13] Note: The rationale will be summarized by the scientific officer in their report and is not limited to the examples shown.

D	**No data**: No quality published data available to assess comparability to the patented medicine under review.
X	**No comparators.** Do ***not*** proceed to step 2.*

**Note: for the purposes of a TCC, a patented medicine that is identified as the only effective treatment sold in Canada for a particular illness or indication is designated as a Qualitative Class X. This medicine therefore has no comparators.*

Step 2: Grouping Assessment

Group	Description of the comparator
1	Same 4th level ATC†, materially similar approved indication or use as the patented medicine under review as per Health Canada.
2	Different 4th level ATC, materially similar approved indication as the patented medicine under review as per Health Canada.
3	Same 4th level ATC, used in Canada for a materially similar indication or use as the patented medicine under review as per published literature but not indicated by Health Canada.
4	Different 4th level ATC, used in Canada for a materially similar indication or use as the patented medicine under review as per published literature but not indicated by Health Canada.
†Anatomic and Therapeutic Classification System as published by the World Health Organization	

80. For example, if there are three comparators identified, one may be described as a B2 comparator, another could be an A1 comparator, and another as a D2 comparator.

81. Rights Holders are generally notified regarding the selection of comparators for each approved indication or use within 8 months of the initiation of the In-Depth Review (potentially longer if Staff decides to consult the Human Drug Advisory Panel (HDAP)).

82. Note that the Scientific Review does not consider the pricing of either the patented medicine under In-Depth Review or the comparators as part of this assessment. The purpose of this part of the analysis is to determine how comparable medicines of the same therapeutic class are to the patented medicine under In-Depth Review in order to provide context for the comparators used in the TCC as a paragraph 85(1)(b) factor.

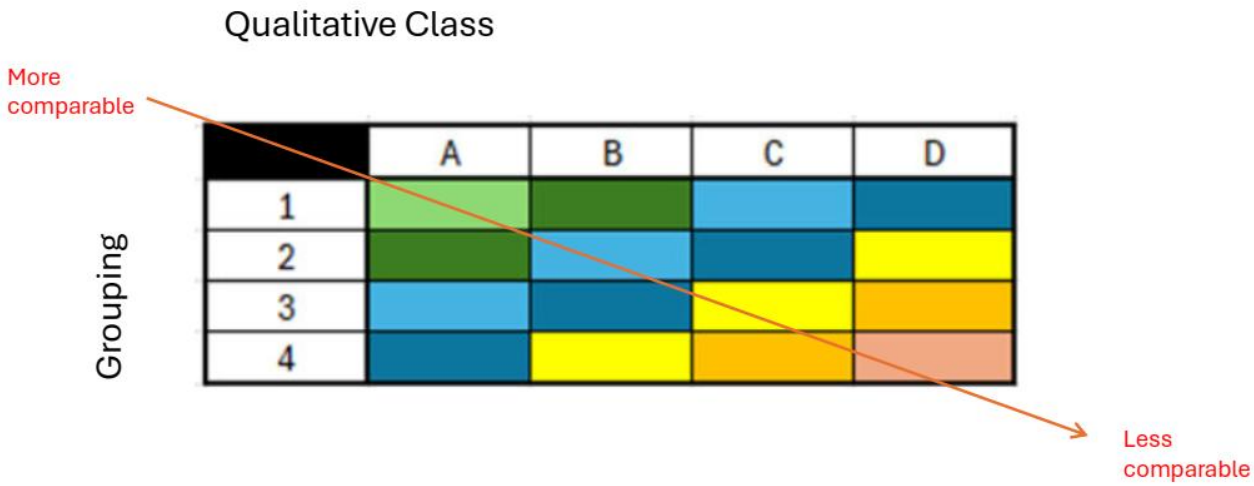


Figure 2. Visual representation of comparability

High comparability	Medium comparability	Low comparability
• A1, A2 or B1 • Science is relatively solid • High proportion of comparators with these rankings means a reasonably solid TCC • TCC should be an important factor in considering a hearing	• A3, A4, B2, B3, C1, C2, D1 • Science is developing or unclear • High proportion of comparators with these classifications means a less solid TCC • TCC might be relevant when considering a hearing	• B4, C3, C4, D2, D3, D4 • Science is poor quality or unavailable • High proportion of comparators with these classifications means less certainty in the TCC • TCC could have less weight when considering a hearing

Figure 3. Non-exclusive examples of potential features for inclusion in comparability categories

Domestic TCC (dTCC)

83. The Scientific Review of the dTCC involves a separate evaluation of each approved indication or use of the patented medicine subject to In-Depth Review at the time the In-Depth Review is conducted. If approved indications or uses in Canada change over time, this is reflected in any subsequent In-Depth Review. A separate dTCC assessment is prepared for each approved indication or use. Medicines used for the

treatment of the indication under review may form part of the dTCC for a given patented medicine, regardless of their approved indication(s) or use(s), if there is appropriate evidence to support their inclusion. For clarity, comparators which are generic products or biosimilars (patented or otherwise) may be included in the dTCC if considered appropriate based on the available evidence.

International TCC (iTCC)

84. In general, the Staff scientific team uses the comparators identified in the dTCC to populate the iTCC. This approach is the fastest and easiest to operationalize and therefore best prioritizes the Board's use of resources, but it may not necessarily reflect the therapeutic comparators available in each of the Schedule Countries.

85. In some cases, the Staff scientific team may also populate an iTCC which identifies lists of comparators for each relevant Schedule Country. The Staff scientific team is more likely to conduct individual reviews of the comparators in each Schedule Country in situations where the science is particularly complex; the therapeutic class could differ significantly across the Schedule Countries due to the indication(s) of the patented medicine under In-Depth Review; and/or if the analysis of the other subsection 85(1) factors suggests the case may be a candidate for a hearing and the more comprehensive analysis is worth the additional expenditure of resources.

Communications with Rights Holders on Comparability

86. Once the assessment of the comparators has been completed by the Staff scientific team, Rights Holders are provided with the list of comparators and their comparable dosage regimens (the dTCC and/or iTCC), the comparability score of each comparator, a list of references reviewed and a summary of the rationale used in the assessment of each comparator.

87. Rights Holders may, but are not obligated to, provide input on Staff's TCC assessment at the beginning of the Scientific Review, or after they receive the TCC assessment, or at both points at their discretion. Rights Holders are, however, encouraged to submit any relevant information they wish to be considered as soon as possible after being notified of an In-Depth Review. Rights Holders are not limited in the written input they may provide to the Scientific Review or in their response to the proposed TCC and may

provide any information they deem appropriate. It is anticipated that input could include (but is not required to include) commentary and analysis of the patented medicine from relevant sources. Submissions which clearly explain the rationale behind the Rights Holder's proposals for level of comparability, drug products for comparison purposes, and comparable dosage regimens are likely to be the most useful to the Staff scientific team. This may include evidence regarding the indication(s) of the patented medicine under review and its potential comparators, a brief description of the patented medicine and its place in therapy, and a summary of the available clinical evidence. High level clinical evidence may include phase III trials (or phase II trials in cases where phase III trials are not yet available), high quality meta-analyses or systematic reviews, and head-to-head comparisons with comparators used for the indication(s) under review.

Human Drug Advisory Panel (HDAP)

88. The HDAP is an advisory body comprised of a defined list of independent health professionals who are under contracted retainer with the PMPRB to assist with scientific evaluations, as needed, in view of their broad general knowledge of drug therapy, drug evaluation, drug utilization and clinical research methodology.

89. Staff may consult the full HDAP membership, or a subset thereof, on an ad hoc basis when Staff identifies specific issues or questions necessitating additional advice. The HDAP is not an adjudicatory body, and Rights Holders cannot request a review of their patented medicine by the HDAP. If Staff decides to consult the HDAP and the Rights Holder has submitted input for the Scientific Review prior to the HDAP reviewing the patented medicine, that input is provided to the HDAP. Staff may also, but is not obliged to, seek input from additional contracted experts or specialists outside of the HDAP list if they feel additional input is necessary.

90. The HDAP's role is not to adjudicate disputes between Staff and Rights Holders over the selection or relative weights of comparators, and it is not anticipated that the HDAP will typically be consulted more than once about a patented medicine during a particular In-Depth Review. Rather, HDAP's role is to provide recommendations on comparators and comparable dosage regimens to assist the PMPRB's scientific staff when needed.

Sources

91. When assembling and assigning a comparability rating to medicines in the TCC, the Staff scientific team consults the following sources:

    - ATC classification;
    - Approved indications or uses, or proposed indications, where applicable;
    - Available medical literature;
    - Clinical evaluations undertaken by recognized health technology assessment organizations (e.g. Canada's Drug Agency, INESSS, WHO, NICE, etc.);
    - Written input provided by the Rights Holder (if any);
    - Research by a Drug Information Centre (DIC) – Staff may use the services of various drug information centres to obtain scientific information, such as clinical trial information, clinical practice guidelines, etc. The basis of the review by the DIC is the product monograph (or information like that contained in a product monograph if a NOC has not been granted). Product monographs (and like information) are filed by Rights Holders pursuant to the Regulations;
    - Research by Staff – Staff may also update research and supplement data and evidence from the Rights Holder and DIC using other sources;
    - PMPRB Human Drug Advisory Panel (HDAP) – On an ad hoc basis, Staff may consult with the HDAP to provide clinical context pertaining to the scientific information that is being considered by Staff; and
    - Guidelines or consensus statements from recognized Canadian or foreign clinical groups pertaining to the treatment of the approved Health Canada indication of the patented medicine under review.

Price Review

92. In parallel with the Scientific Review, Staff commences its Price Review of the patented medicine in anticipation of the results of the Scientific Review. If they choose to, Rights Holders may provide input to the pricing team on issues relevant to the subsection 85(1) factors other than the TCC within three months of being notified that their patented medicine is subject to In-Depth Review. As with the Scientific Review, Rights Holders are not limited in terms of the information they may choose to provide to Staff as context for Staff's consideration of the subsection 85(1) factors. Information provided by Rights Holders which would only be relevant as part of a subsection 85(2) analysis or other material that is not relevant to the factors in subsection 85(1) of the

Act may not be considered by Staff as part of the In-Depth Review. Any relevant additional information provided by Rights Holders may form part of Staff's recommendation to the Chairperson.

93. Once the Scientific Review has been concluded, Staff adds pricing information to the TCC analysis. The pricing for medicines in the TCC takes account of the treatment regimen for each medicine and indication as identified in the Scientific Review.

94. Staff reviews and analyses all the information related to the patented medicine provided pursuant to section 3 of the Regulations and information related to the price of the patented medicine provided pursuant to section 4 of the Regulations or collected by Staff that relates to factors in section 85 of the Act, namely:

- information relating to the price of the medicine in Canada;
- information relating to the price of the medicine in the Schedule Countries;
- information relating to the TCC selection and analysis; and
- information relating to changes in the CPI over the relevant period.

95. Staff considers all the information collected and prepares a recommendation to the Chairperson that the In-Depth Review either be closed (with or without an Undertaking) or that a hearing be held. The Appendix "Assessment of individual s. 85(1) factors, separately" sets out examples of how Staff begins its assessment of the information collected by first considering the individual subsection 85(1) factors separately. The Appendix "Weighting of individual factors during In-Depth Review" sets out examples of how Staff typically balances the subsection 85(1) factors in preparing its Recommendation. Note that the result of the analysis is not a price ceiling, recommended price, or a decision on whether a price is or is likely to be excessive; rather it is a recommendation that a hearing be held or not.

96. In addition to the above information, the recommendation includes any input received from the Rights Holder, and any proposed Undertaking(s). Each recommendation is reviewed by the Senior Director of Regulatory Affairs & Outreach and the Director General of the PMPRB to ensure consistency in the analytical approach and resulting recommendation.

97. Generally, an In-Depth Review could take between 12 and 28 months to complete, depending on its complexity (e.g. number of comparators during the Scientific Review, IPC calculations).

98. Rights Holders whose patented medicines are identified for In-Depth Review cannot avoid or prematurely terminate this review by unilaterally changing their list prices once it is initiated, although Rights Holders may propose Undertakings for the Chairperson's consideration at any point between being advised that their patented medicine is subject to In-Depth Review and up to two months after being informed that Staff recommends a hearing. If a Rights Holder submits a proposed Undertaking early in the In-Depth Review, Staff may pause the review to manage resources while the Chairperson considers the Undertaking.

Recommendations

99. If the result of the In-Depth Review is a recommendation to the Chairperson to issue a Notice of Hearing, Staff informs the Rights Holder of that recommendation when it is submitted to the Chairperson. Rights Holders are not provided with details of Staff's analysis in the Pricing Review beyond what is provided in respect of the Scientific Review (see para. 86, above). The information provided about the Scientific Review, the change in the CPI (which is publicly available), and the prices for the patented medicine in the Schedule Countries (which are filed by the Rights Holder) should be sufficient to assist the Rights Holder in determining why its patented medicine is recommended for a hearing by Staff. Rights Holders have two months from the date they are informed of the recommendation to provide a proposed Undertaking they may wish for the Chairperson to consider in making their decision. The Chairperson will render their decision within one month of receiving a proposed Undertaking or within no more than three months after receiving Staff's recommendation.

100. If the Chairperson decides that an In-Depth Review should be closed, the Rights Holder is advised by Staff of the Chairperson's decision.

101. If the Chairperson decides that it is in the public interest that a Notice of Hearing be issued, the Rights Holder is advised of the Chairperson's decision. If a Rights Holder

against whom a Notice of Hearing has been issued would like to resolve the matter before a hearing is concluded, the Rights Holder may seek a settlement with the Hearing Panel.

Undertakings and Settlement Proposals

102. Undertakings are unilateral promises made by Rights Holders and are not binding agreements. As such, Undertakings and discussions related thereto are not covered by settlement privilege and are not treated on a "without prejudice" basis.

103. Rights Holders are advised if an In-Depth Review is commenced. Rights Holders may submit an Undertaking at any point during the In-Depth Review and for two months after they are advised that Staff recommends a hearing to the Chairperson. Any Undertaking submitted is referred to the Chairperson.

104. Because Undertakings are unilateral and these Guidelines are not designed as price compliance Guidelines, neither Staff nor the Chairperson provides Rights Holders with suggestions or guidance on the substance of any proposed Undertaking, nor negotiate the terms. The Chairperson considers all Undertakings received, and if they are of the view that the recommended hearing would not be in the public interest in view of the terms of the Undertaking, the Chairperson directs Staff to close the In-Depth Review, and the matter does not proceed to a Notice of Hearing. Undertakings accepted by the Chairperson are intended to resolve a specific In-Depth Review and are not intended to provide assurances about prices going forward. The prices of the patented medicine continue to be reviewed in accordance with the Guidelines for as long as it remains subject to the jurisdiction of the Board.

105. For clarity, Staff do not calculate potential excess revenues as part of the In-Depth Review, and such calculation is not a factor in the recommendation to the Chairperson, which is based on list price only. Should an Undertaking be proposed by a Rights Holder which includes a repayment of potential excess revenues, Staff reviews the excess revenue calculation provided by the Rights Holder based on the average price per package and/or net revenue (ATP) information filed by the Rights Holder pursuant to the Regulations, and not on list prices.

106. Once a Notice of Hearing is issued, the matter can only be resolved by a settlement or the conclusion of proceedings before the Hearing Panel. Undertakings are no longer an available option. After a Notice of Hearing has been issued, a Rights Holder may only seek to settle the matter through a formal settlement approved by the designated Hearing Panel. All proposed settlements must be presented to and approved by the Hearing Panel. This is usually done through a motion for discontinuance based on the proposed settlement. Negotiations and discussions with Staff regarding a settlement proposal after the issuance of a Notice of Hearing may be conducted on a without prejudice basis and are subject to settlement privilege (see detailed discussion of hearing processes in Section "Price Hearings", below).

107. The PMPRB reports publicly on all Undertakings accepted by the Chairperson and all settlements accepted by Hearing Panels. The information reported ordinarily includes the name of the patented medicine and/or the rights holder and such other information as is considered appropriate. This information is included in the PMPRB's Annual Report and published on the PMPRB website. It may also be published in the NEWSletter or other publications.

Price Hearings

108. PMPRB hearings are commenced by the issuance of a Notice of Hearing which is provided to the relevant parties under the Act.

109. PMPRB hearings are public and are "de novo" proceedings, meaning that the Hearing Panel considers all the law and evidence from a blank slate. PMPRB hearings are not reviews of the application of the Guidelines or of Staff's actions prior to the issuance of the Notice of Hearing. 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. The Hearing Panel

cannot be bound or fettered in its discretion by these Guidelines or their application to the patented medicine that is the subject of the hearing[14].

110. For more information about hearings, please consult the *PMPRB Rules of Practice and Procedure*[15], the published standard set of procedures to be followed by all participants in hearings before the PMPRB. The Rules set out the PMPRB'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.

111. As per section 83 of the Act, where, following a hearing, the Board finds that a Rights Holder is selling a patented medicine in any market in Canada at an excessive price, the Board may order the Rights Holder to reduce the maximum price at which the Rights Holder sells the medicine in that market.

112. In addition, where, following a hearing, the Board finds that a Rights Holder or former Rights Holder, while a Rights Holder, has sold a patented medicine in any market in Canada at an excessive price, the Board may order the Rights Holder or former Rights Holder to offset the amount of excess revenues estimated by it to have been derived by the Rights Holder or former Rights Holder from the sale of the medicine at an excessive price. While these Guidelines require Staff to assess a patented medicine's list price against certain criteria, historically, when the Board has issued an order requiring the repayment of excess revenues, that calculation has taken the medicine's net or average transaction price into account.

113. Where, following a hearing, the Board finds that the Rights Holder or former Rights Holder has engaged in a policy of selling the patented medicine at an excessive price "having regard to the extent and duration of the sales of the medicine at the excessive price" (see subsection 83(4) of the Act), the Board may order the Rights Holder or former Rights Holder to offset up to twice the amount of excess revenues estimated by it to have been derived by the Rights Holder or former Rights Holder from the sale of

[14] *Alexion Pharmaceuticals Inc. v. Canada (Attorney General)*, 2021 FCA 157.
[15] Rules of Practice and Procedure for Hearings - Canada.ca

the medicine at an excessive price. As above, these calculations consider the net or average transaction price(s) of the patented medicine(s).

114. To offset excess revenues, the Board may order a Rights Holder or former Rights Holder to:

- reduce the price at which the Rights Holder or former Rights Holder sells the medicine in any market in Canada;
- reduce the price at which the Rights Holder or former Rights Holder sells another patented medicine in any market in Canada; and/or
- make a payment to His Majesty in right of Canada.

Glossary and list of Acronyms and Abbreviations

The following definitions are provided for general assistance only and are limited to terms that are not already defined in section 79 of the Act; they have no legal force and should be read in conjunction with the applicable legislation.

Associated DINs: all DINs which the Rights Holder has identified in its filings with the PMPRB as pertaining to the same patented invention(s)as the DIN which is subject to In-Depth Review (see Patented Medicine Regulations s. 3(1)(g),(h) and (i)).

ATC: Anatomic Therapeutic Classification as outlined by the World Health Organization.

CPI: Consumer Price Index

DIN: drug identification number as assigned by Health Canada.

dTCC: domestic Therapeutic Class Comparison

Existing Medicine: Patented medicines first sold before July 1, 2022.

HDAP: Human Drug Advisory Panel

HIP: The highest price of the same strength and dosage form of the same patented medicine among the Schedule Countries.

IPC: International Price Comparison

iTCC: international Therapeutic Class Comparison

List Price: the gross price (before any rebates or discounts) at the ex-factory level filed by the Rights Holder pursuant to paragraph 4(1)(f)(i) or (ii) of the Regulations.

New Medicine: Patented medicines first sold on or after July 1, 2022.

PMPRB11: Australia, Belgium, France, Germany, Italy, Japan, the Netherlands, Norway, Spain, Sweden, and the United Kingdom.

Schedule Countries: The countries currently set out in the Schedule to the Patented Medicines Regulations.

TCC: Therapeutic Class Comparison

Appendices

Assessment of individual subsection 85(1) factors, separately

The purpose of Appendix "Assessment of individual s. 85(1) factors, separately" and Appendix "Weighting of individual factors during In-Depth Review" is to provide a degree of transparency and predictability on the *process* to ensure consistency across In-Depth Reviews. It is not intended to address the *outcomes* for specific In-Depth Reviews.

When initiating an In-Depth Review, Staff begins by considering the individual subsection 85(1) factors separately. Information considered by Staff during this phase of the review may include but is not limited to the following:

85(1)(a) – the prices at which the medicine has been sold in the relevant market:

- How many different list prices have been reported by the Rights Holder for the medicine?
- Is there differential pricing across markets? How big is the difference?
- How have the list prices changed over time? Increased? Decreased?
- Are there other strengths of this medicine available in Canada? Are they level priced? Proportionally priced? Linearly priced?
- How do the average price per package or net revenue reported by the Rights Holder compare to the list price(s)? Have benefits been reported?
- Is this medicine a tendered product? Has the Rights Holder reported contract sales?
- Has this medicine been genericized? Is the generic version "authorized" by the Rights Holder? How does its price compare to the generic version?
- Is the medicine subject to an Undertaking (or a Voluntary Compliance Undertaking based on former Guidelines) and if so, is the price consistent with the terms of the Undertaking?
- Is the medicine subject to an Order by a panel of the Board, and if so, is it compliant with the Order?

85(1)(b) – the prices at which other medicines in the same therapeutic class have been sold in the relevant market:

- Is this medicine a line extension? A combination product? A biosimilar? A patented generic?
- How many indications is this medicine approved for?
- How many comparators were identified during the Scientific Review?
- Do the comparators share the same indication as the medicine, or are used in the same way without a shared approved indication?
- How strong are the levels of similarity across the comparators?
- What is the range in treatment costs? Tight? Narrow?
- Are there any high or low outliers among the treatment costs?
- Have any of the comparators been genericized?
- If the medicine is a patented biologic, are any of the comparators biosimilars?
- Did the Rights Holder express disagreement with any aspect of the Scientific Review? If so, on what grounds?

85(1)(c) – the prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada:

- If the In-Depth Review was triggered by the list price being above the HIP, by how much?
- How many comparator countries have been reported for the medicine?
- What is the range in prices for the medicine across the Schedule Countries? Tight? Narrow?
- How does the price of the medicine in Canada compare with other prices in the Schedule Countries generally?
- Has the number of comparator countries changed over time? If so, how?
- Do we anticipate additional countries to be reported in the future? If so, why?
- Has a price reduction (in local currency) been reported for any of the comparator countries?
- Has a price increase (in local currency) been reported for any of the comparator countries?
- Has there been an impact of exchange rates on the HIP?

- Are the comparators identified during the Scientific Review available across the Schedule Countries?
- How do the treatment costs of this medicine compare to the treatment costs of its comparators across the basket of comparator countries?
- If the medicine is consistently higher or lower priced than its comparators internationally, how does that compare to the dTCC?

85(1)(d) – changes in the Consumer Price Index:

- If the In-Depth Review was triggered by the list price increase being greater than CPI, by how much?
- Is there a difference between the one-year lagged CPI value used as the trigger and the CPI from the year in which the list price increase was taken? If so, how does the list price increase compare to both CPI factors?
- How many list price increases have been taken for this medicine, and how do each of those list prices increases compare to CPI?
- How does the cumulative increase since introduction compare to cumulative CPI over the same period?

Other possible considerations:

- How does the change in CPI and corresponding list price increase compare to the changes in the list prices in the Schedule Countries?
- Has this medicine previously been subject to In-Depth Review? If so, what was the outcome of that In-Depth Review? Are circumstances different? The same?
- When is the last reported patent for this medicine set to expire?
- Does the Rights Holder have a Certificate of Supplementary Protection for this medicine? If so, when does it expire?
- Has a complaint been received regarding the price of this medicine?
- Was there any additional information shared by the Rights Holder that is within the scope of the factors that the Chairperson should be aware of?

Weighting of individual factors during In-Depth Review

The purpose of this Appendix "Weighting of individual factors during In-Depth Review" is to provide general information about how Staff may balance the information related to the subsection 85(1) factors in an In-Depth Review.

All recommendations arising from In-Depth Reviews are vetted for consistency by the Senior Director of Regulatory Affairs & Outreach and the Director General before they are presented to the Chairperson for consideration.

Based on the results of the Staff's analysis of each case (see example questions in Appendix "Assessment of individual s. 85(1) factors, separately"), Staff makes a recommendation to the Chairperson on whether a Notice of Hearing should be issued or the In-Depth Review should be closed based on a balancing of the information related to the subsection 85(1) factors obtained during the In-Depth Review. The Staff's recommendation to the Chairperson is merely advice, and the Chairperson retains the sole discretion on the ultimate decision as to whether to issue a Notice of Hearing or to close the In-Depth Review.

In-Depth Reviews are conducted on a case-by-case basis, consequently it is impossible to anticipate all possible scenarios Staff may encounter and some individual cases may be subject to deviations from the general approach.

See the "Case Studies" Appendix for illustrative case studies of the general approach for this Appendix.

Recommendation for Hearing

More particularly, scenarios that *likely* tilt the balance towards a recommendation for a hearing include:

- Cases where both IPC and TCC are available, and the Canadian list price(s) is/are above both.
- Cases that suggest a "policy of selling the medicine at an excessive price" as per the terms of subsection 83(4) of the *Patent Act*.
- Where both IPC and TCC are available, and the Canadian list price(s) is/are between them: significant differential between the price(s) of the most similar

comparator(s) and the IPC, especially if the comparator(s) is/are very similar and priced below the IPC.

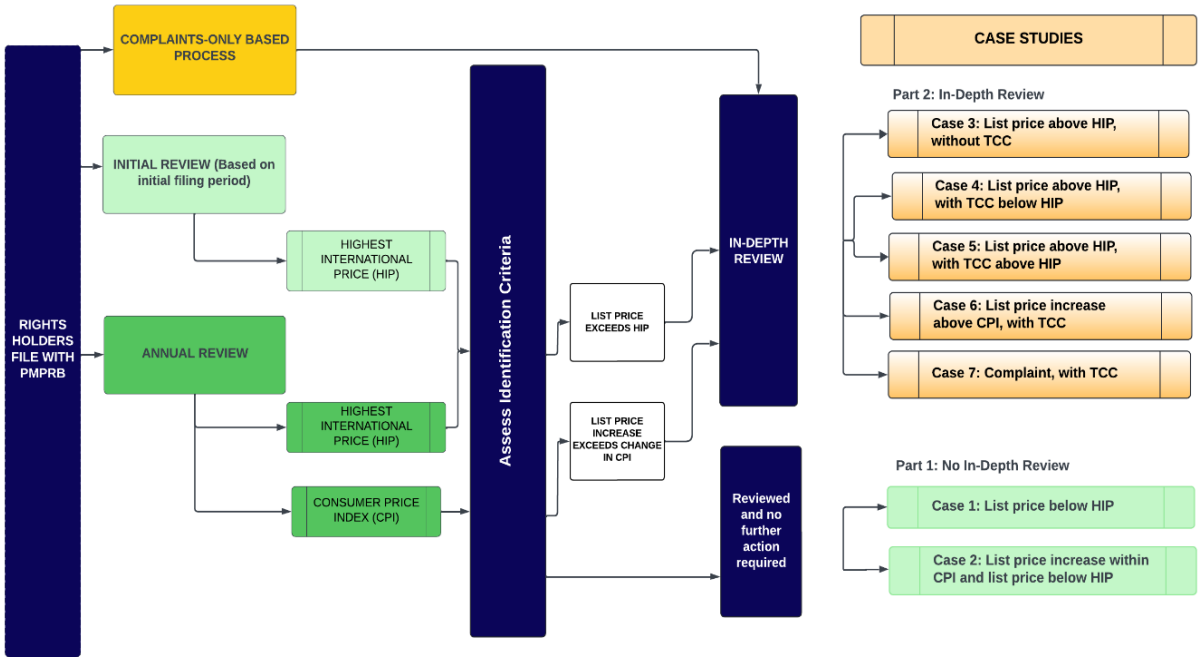
- Where TCC is not possible (no comparators) and the Canadian list price(s) is/are above the IPC: significant differential between the IPC price and the Canadian list price(s), especially when the differential does not appear to relate to exchange rate shifts.
- Where the IPC is not possible (no international prices) but TCC is possible (there are comparators) and the Canadian list price(s) is/are above the TCC: significant differential between the price of the most similar comparator(s) and the Canadian list price(s), especially if the comparator(s) is/are very similar.

Recommendation for Closure

Scenarios that *likely* tilt the balance towards a recommendation for closure include:

- Cases where both IPC and TCC are available, and the Canadian list price(s) is/are below both.
- Where both IPC and TCC are available, and the Canadian list price(s) is/are between them: de minimis differential between the price of the most similar comparator(s) and the IPC.
- Where TCC is not possible (no comparators) and the Canadian list price(s) is/are above the IPC: de minimis differential between the IPC price and the Canadian list price(s), especially when the differential appears to relate to exchange rate shifts.
- Where the IPC is not possible (no international prices) but TCC is possible (there are comparators) and the Canadian list price(s) is/are above the TCC: de minimis differential between the price(s) of the most similar comparator(s) and the Canadian list price(s).
- Where the IPC is not possible (no international prices) but TCC is possible (there are comparators): where the most similar comparator(s) is/are not very high on the comparability scale to the medicine under review.
- Cases that suggest that data filing errors or other unusual circumstances are causing a price fluctuation that is temporary and will likely be resolved within 1 filing period.
- Cases where the Rights Holder has submitted an Undertaking that would result in one of the above situations.

Case Studies



To help interested parties understand how Staff may weigh the factors during the in-depth review process in order to arrive at a recommendation to the Chairperson, several case studies have been prepared for illustration purposes.

The case studies are distinguished into two parts: Part 1 represents scenarios where the identification criteria are not met and thus no In-Depth Reviews were commenced. Part 2 includes scenarios where an In-Depth Review is initiated. In these scenarios, the case studies illustrate the decision-making framework that may be applied by PMPRB Staff in their recommendation to the Chairperson based on how the available information about the relevant factors from subsection 85(1) may appear in a given situation.

These case studies are not exhaustive and are not intended to cover all possible permutations of scenarios that may appear in In-Depth Reviews. They are for illustration purposes only. In particular, the magnitude differential represented by the lines and the distance between them should be ignored, as the examples only seek to represent the relative positions of the lines, not the distance between them or specific weight.

Part	Case Study
1. No In-Depth Review	**Case Study 1:** List price below HIP
	Case Study 2: List price increase within CPI and list price below HIP
2. In-Depth Review	**Case Study 3**: List price above HIP, without TCC

	Case Study 4: List price above HIP, with TCC below HIP
	Case Study 5: List price above HIP, with TCC above HIP
	Case Study 6: List price increase above CPI, with TCC
	Case Study 7: Complaint, with TCC

Given that the TCC figures prominently in the case studies in Part 2, it is important to be familiar with the process described in the "Scientific Review: Therapeutic Class Comparison Selection and Analysis" section. In any given review, multiple comparators will be identified and classified by their level of comparability. The case studies presented represent simplified scenarios.

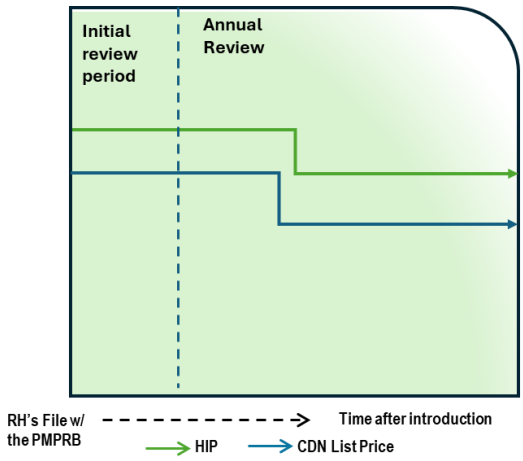
These examples are not intended to bind the Staff or the Board in any In-Depth Review or hearing and the analytical approach may be departed from based on the facts available during the review. All recommendations from the Staff and decisions from the Chairperson/Board will depend on the particular circumstances of the matter in question.

Part 1 (No In-Depth Reviews)

Case Study 1: List price below HIP

Issue/Facts:

- During the Initial Review, the Canadian list price is less than the HIP.
- The HIP trends downward with time, but the Canadian list price also decreases.
- With no list price increases occurring, changes in CPI are not a consideration.
- No complaint is received regarding this medicine.



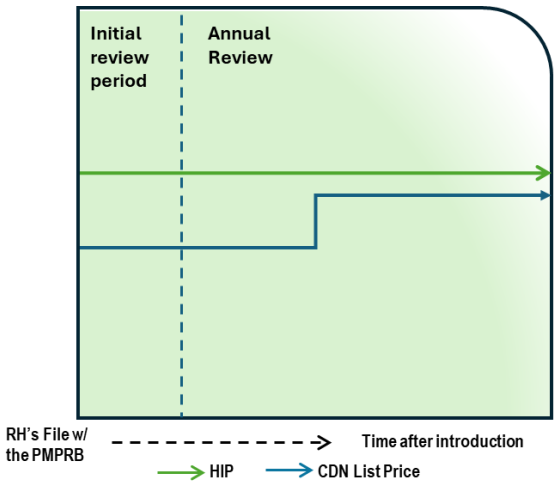
Analysis:

- No additional analysis is required, as the medicine does not trigger an In-Depth Review.

Potential Recommendation:

- N/A – medicine not subject to In-Depth Review.

Case Study 2: List price increase within CPI and list price below HIP



Issue/Facts:

- During the Initial Review, the Canadian list price is less than the HIP.
- The HIP is constant over time, but the Canadian list price increases.
- The list price increase is less than CPI.
- No complaint is received regarding this medicine.

Analysis:

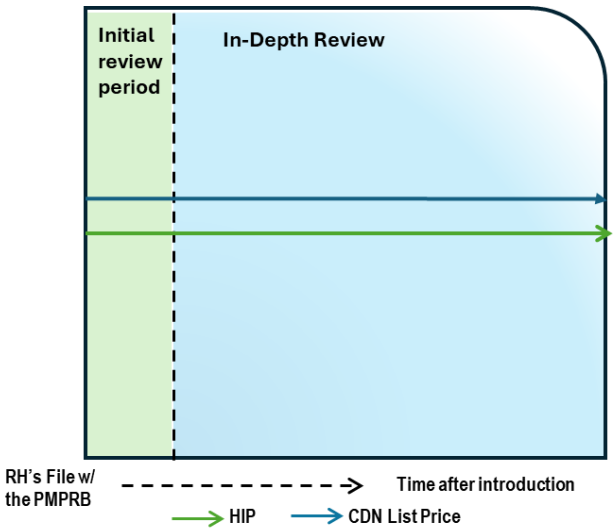
- No additional analysis is required, as the medicine does not trigger an In-Depth Review.

Potential Recommendation:

- N/A – medicine not subject to In-Depth Review.

Part 2 (In-Depth Review)

Case Study 3: List price above HIP, without TCC



Issue/Facts:

- During the Initial Review, the Canadian list price is greater than the HIP. This results in an In-Depth Review.

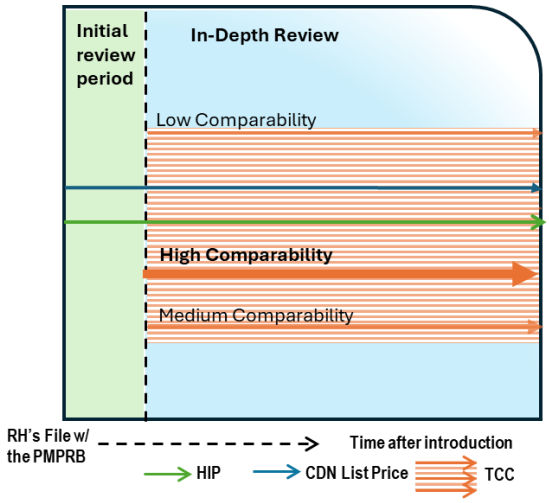
Analysis:

- The commencement of an In-Depth Review prompts a Scientific Review; however, there are no therapeutic comparators and a TCC analysis cannot be conducted.
- During the In-Depth Review, it is observed that the Canadian list price continues to be greater than the HIP, but no list price increases are taken by the Rights Holder.
- With no TCC and no list price increase to measure against CPI, the only 85(1) factor available for consideration is the HIP. PMPRB Staff may consider the difference between the Canadian list price and the HIP, the number of countries with a reported price for the medicine, as well as the range in prices across the PMPRB11.

Potential Recommendation:

- This case could result in a recommendation for closure or Notice of Hearing, depending upon how the Canadian list price is positioned relative to the more comprehensive analysis of the international market.

Case Study 4: List price above HIP, with TCC below HIP



Issue/Facts:

- During the Initial Review, the Canadian list price is greater than the HIP. This results in an In-depth Review.

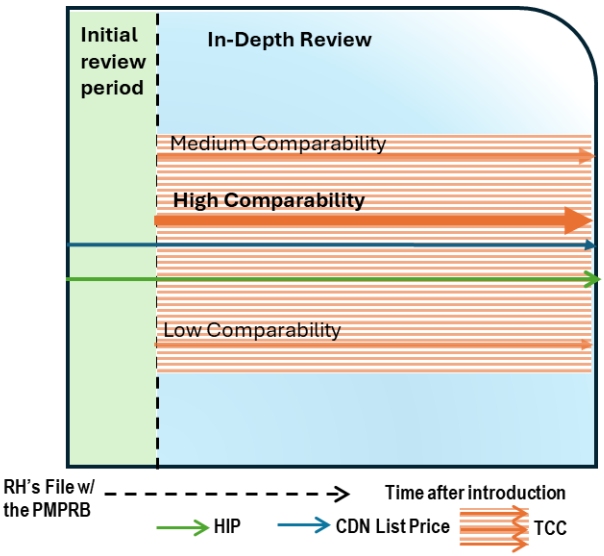
Analysis:

- The commencement of the In-Depth Review prompts a Scientific Review. This review identifies a therapeutic class containing multiple comparators with prices both higher and lower than the Canadian list price and the HIP. The Scientific Review will evaluate the comparators for their level of comparability to the medicine under review.
- While no list price increase has been taken by the Rights Holder, the analysis suggests that the Canadian list price is above both the HIP and TCC.
- PMPRB Staff may consider the strength of the TCC, as well as the difference between the Canadian list price and the HIP, the number of countries with a reported price for the medicine, and the range in prices across the PMPRB11.

Potential Recommendation:

- With the Canadian list price above both the HIP and certain TCC comparators, the case-specific context would need to be supportive of the price of the medicine for PMPRB Staff to recommend closure of this In-Depth Review. More likely, given the existence of a high comparability comparator whose price is lower than both the Canadian list price and the HIP, this case would result in the recommendation for a Notice of Hearing.

Case Study 5: List price above HIP, with TCC above HIP



Issue/Facts:

- During the Initial Review, the Canadian list price is greater than the HIP. This results in an In-Depth Review.

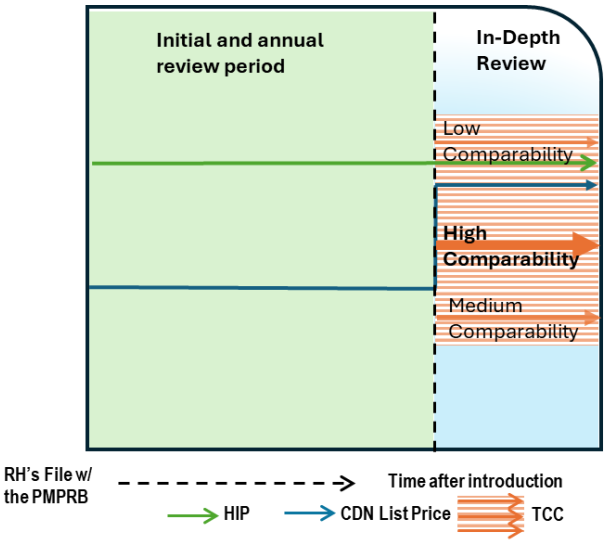
Analysis:

- The commencement of the In-Depth Review prompts a Scientific Review. This review identifies a therapeutic class containing multiple comparators with prices both higher and lower than the Canadian list price and the HIP. The Scientific Review will evaluate the comparators for their level of comparability to the medicine under review. A high comparability comparator priced above both the Canadian list price and the HIP was identified.
- No list price increase has been taken by the Rights Holder, as a result the CPI factor is not taken into consideration.
- PMPRB Staff may consider the strength of the TCC, as well as the difference between the Canadian list price and the HIP, the number of countries with a reported price for the medicine, and the range in prices across the PMPRB11.

Potential Recommendation:

With the Canadian list price above the HIP but below certain TCC comparators, the case-specific context would need to be supportive of the price of the medicine for PMPRB Staff to recommend closure of this In-Depth Review. Given the existence of a high comparability comparator whose price is higher than both the Canadian list price and the HIP, Staff will likely recommend a closure of the In-Depth Review.

Case Study 6: List price increase above CPI, with TCC below HIP



Issue/Facts:

- After a period of time on the market, the list price increases greater than CPI.

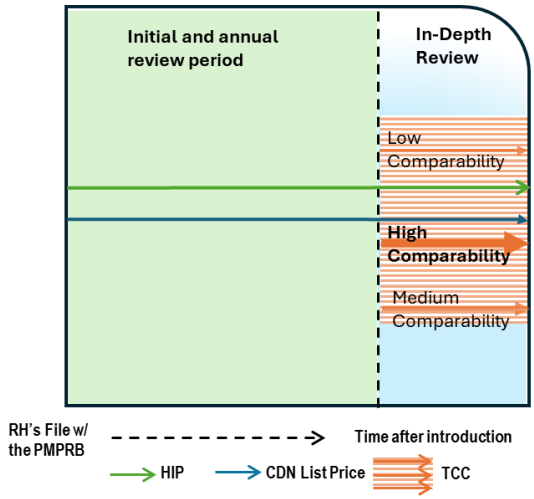
Analysis:

- The commencement of the In-Depth Review prompts a Scientific Review. This review identifies a therapeutic class containing multiple comparators with prices both higher and lower than the Canadian list price and the HIP. The Scientific Review will evaluate the comparators for their level of comparability to the medicine under review. A high comparability comparator priced below both the Canadian list price and the HIP was identified.
- PMPRB Staff may consider the strength of the TCC, as well as the difference between the Canadian list price and the HIP, the number of countries with a reported price for the medicine, and the range in prices across the PMPRB11.

Potential Recommendation:

- The Canadian list price is below the HIP. Given the increase above CPI and the lower TCC the case-specific context would need to be considered, including the difference between the Canadian list price and the HIP, the extent of the price increase and the relative comparability of the TCC. Given the existence of a high comparability comparator whose price is lower than both the Canadian list price and the HIP, this case would likely result in the recommendation for a Notice of Hearing.

Case Study 7: Complaint, with TCC



Issue/Facts

- Over time on the market, the Canadian list price and the HIP remain unchanged.
- A complaint is received. This will result in an In-Depth Review.

Analysis:

- The commencement of the In-Depth Review prompts a Scientific Review. This review identifies a therapeutic class containing multiple comparators with prices both higher and lower than the Canadian list price and the HIP. The Scientific Review will evaluate the comparators for their level of comparability to the medicine under review. A high comparability comparator priced below both the Canadian list price and the HIP was identified.
- Staff must take the TCC into account and weigh it against the HIP and the fact that the Canadian list price has not changed. Staff's recommendation will depend heavily on the TCC context and price differential magnitude.

Potential Recommendation:

- In this case, a high comparability comparator whose price is lower than both the Canadian List and the HIP was identified. This will have to be weighed against the fact that the Canadian list price is lower than the HIP. In a situation where the HIP has considerably more weight than the TCC given the context, Staff may recommend that the In-Depth Review be closed. If the reverse is the case, Staff may recommend that a Notice of Hearing be issued.

Comparable Dosage Forms

This Appendix identifies comparable dosage forms for the purpose of the Scientific Review for patented medicines. Formulations within each group are considered comparable, but dosage forms in a different group are not.

The PMPRB reviews the list of comparable dosage forms periodically to ensure that it includes those currently used.

Topical

- 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)/Ophthalmic (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