April 10, 2008

Decision: PMPRB-06-D3-ADDERALL XR - Merits

IN THE MATTER OF the *Patent Act* R.S.C. 1985, c. P-4, as amended

AND IN THE MATTER OF Shire BioChem Inc. (the "Respondent") and the medicine "Adderall XR"

Introduction

1. This proceeding before the Patented Medicine Prices Review Board (the "Board") concerns the pricing of "Adderall XR", a patented medicine sold in Canada by Shire BioChem Inc. ("Shire") for the treatment of attention deficit hyperactivity disorder ("ADHD"). The Staff of the Board ("Board Staff") allege that Adderall XR has been sold by Shire in Canada at excessive prices, in contravention of the provisions of the *Patent Act* (the "Act"). Shire denies this allegation. Janssen-Ortho Inc. ("Janssen-Ortho"), which markets the medicine "Concerta" for the treatment of ADHD, intervened in the proceeding because of the potential impact of the proceeding on the pricing of Concerta.

2. Board Staff and Shire each presented evidence, and they and Janssen-Ortho presented written and oral argument, to a panel of the Board (the "Panel") at a public hearing that lasted 11 days and heard evidence from 14 witnesses. The evidence was often extremely technical and complex from medical, scientific, economic and sociological perspectives. The proceeding raised important considerations of policy concerning the manner in which the Board should determine when a medicine is excessively priced.

3. After careful consideration of all of the evidence and argument – much of which is only very generally summarized in these reasons – the Panel has determined that Adderall XR was and is being sold by Shire at prices that are excessive under the terms of the Act. However, the Panel agrees with Shire that Adderall XR is a medicine with benefits relative to existing ADHD medicines that entitle Shire to sell Adderall XR at prices that are potentially higher than those that would be indicated by the Board's Excessive Price Guidelines (the "Guidelines".) That is to say, the Panel has established parameters for a maximum non-excessive price (MNE) for Adderall XR that allow the MNE of Adderall XR to exceed that indicated by the Guidelines.

4. It should be noted that the Panel has concluded that Board Staff correctly applied the Guidelines in establishing the MNE for Adderall XR, and that it was Board Staff's obligation to approach the pricing of Adderall XR in this manner. Board Staff does not have the discretion to depart from the Guidelines in the manner indicated by the conclusions of this Panel. Subject to some comments below concerning the weight that a hearing panel should give to the Guidelines, this case proceeded as this Panel considers appropriate for the operation of the Guidelines: Board Staff identified the pricing of a medicine that was higher than permitted by the Guidelines; the matter was brought to a hearing where Board Staff defended the Guidelines and demonstrated their contravention by the pricing of the medicine; the patentee defended the pricing of the medicine both within and regardless of the Guidelines, and the Panel considered the evidence, the Act and the Guidelines.

5. In this case, the Panel concluded that Board Staff was correct in its application of the Guidelines, but that, for Adderall XR, the Guidelines did not constitute an appropriate implementation of the terms of the Act. The price for Adderall XR advocated by Shire was considered by the Panel to be excessive, and the price for Adderall XR indicated by the Guidelines was considered to be below an excessive level. The Panel has established parameters for the non-excessive price of Adderall XR that falls between those two points.

Background

6. ADHD is the most common psychiatric disease of childhood, affecting 4-12% of young children. ADHD is characterized by its principal symptoms of inattention, hyperactivity and impulsivity. ADHD is often accompanied by other psychiatric disorders, such as depression, anxiety and conduct disorders.

7. For approximately fifty years, doctors have been aware that the symptoms of what is now referred to as ADHD are mitigated by psychostimulants, such as amphetamine. ADHD is believed to result from the impaired functioning of two chemical messengers – neurotransmitters – in the brain, and psychostimulants which improve the functioning of those neurotransmitters. Common amphetamine medicines that have been used in the treatment of ADHD are Benzedrine and Dexedrine. The ADHD medicine "Ritalin" uses a different stimulant – methylphenidate – which is the stimulant in Janssen-Ortho's ADHD medicine "Concerta".

8. Adderall XR is a formulation of amphetamine that is different from Benzedrine and Dexdrine in two ways. First, it is a unique mixture of the two forms of amphetamine, only one of which is used in Dexedrine and different proportions of which are used in Benzedrine. Second, and the topic of most of the evidence in this proceeding, the amphetamine in an Adderall XR capsule is encased in a series of coatings, with the effect that an appropriately fast delivery of amphetamine is delivered to the body when the capsule is taken in the morning, and then a more gradual release of the rest of the amphetamine is spread out over the course of the balance of the day.

9. As a consequence of the gradual release of amphetamine from a capsule of Adderall XR, only one capsule per day is required for the patient to have an adequate level of the medicine in his or her blood from the beginning to the end of the day. In contrast, the older amphetamine medicines for ADHD, which release all of their active ingredient shortly after the medicine is taken, require two or three doses per day, depending on how late in the day the patient is to be medicated.

10. The once-daily dosing regimen for Adderall XR is argued by Shire (and by Janssen-Ortho with respect to Concerta) to have a number of beneficial effects for the patient, the patient's parents and teachers, and for society generally. These benefits, described more fully below, include a more constant level of amphetamine in the body over the course of the day, the convenience, societal cost-savings and reduced patient stigmatization resulting from the patient not needing mid-day medication (typically in school), and reduced potential for diversion of the medicine for recreational use.

11. Shire and Janssen-Ortho argue that these benefits are relevant to the manner in which the Board should determine whether the price of Adderall XR is excessive within the terms of the Act. In accordance with the framework described below, and speaking in very general terms for the purpose of this introduction, the regime under which the Board determines whether a medicine is being sold at an excessive price within the terms of the Act, allows that a medicine has the potential to be sold at a higher price than existing medicines for the same disease, without that price being excessive, if it represents a "substantial improvement" over the existing medicines. If the improvement over existing medicines is less than substantial, its price must be in line with the existing medicines.

The Legal Framework

a) Section 85 of the Act

12. Section 85 of the Act instructs the Board to determine whether the price of a medicine sold in Canada is excessive by reference to a series of factors that can be expressed in a summary fashion as a comparison between the price of the medicine with (1) the prices of comparable medicines; and (2) the price of the medicine in other countries. Though it is not relevant to this proceeding, section 85 also requires reference to increases in the price of the medicine over time.

b) The role of the Guidelines

13. As the Board discussed in the *LEO Pharma* decision, it is evident that Parliament intentionally framed the factors in section 85 of the Act in very broad terms. The Act, in section 96, contemplates the Board establishing guidelines, and the Board did so with respect to the specific implementation of the general factors listed in section 85 (the "Guidelines").

14. It is important to correctly characterize the significance of the Guidelines; their role should neither be understated nor overstated. As noted in the *LEO Pharma* decision, some guidelines are absolutely essential for the implementation of the general factors listed in section 85. In the *LEO Pharma* decision, articulating principles cited with agreement by the Federal Court on judicial review of that decision, the Board said:

> To simplify the terminology in subsection 85(1), it can be said that it requires the Board to determine whether or not the price of a medicine in Canada is excessive (taking into account changes in the Consumer Price Index) by comparing the price of the medicine in Canada [85(1)(a)] to:
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> 1) the price of comparable medicines in Canada [85(1)(b)];
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> 2) the price of the medicine in other countries [85(1)(c)]; and
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> 3) the price of comparable medicines in other countries [85(1)(c)].
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> The factors set out in subsection 85(1) are exhaustive of the factors that the Board may consider and the Board must give due consideration to each of them when reviewing the price of a medicine for the purposes of a potential order under section 83 of the Act.

However, having directed the Board to the factors it must consider, section 85 does not stipulate how those factors must be used or weighed to assess whether or not the price of a medicine is excessive. In other words, section 85 does not provide a formula into which the Board can feed pricing information to calculate the MNE for a medicine.

In particular, two features of subsection 85(1) require the Board to exercise discretion, to apply judgment and expertise, and if appropriate to give consideration to the stakeholder input and compromise that went into the development of the Guidelines, when determining whether or not the factors in section 85 indicate that the price of a medicine is excessive. First, performing a comparison does not dictate a conclusion that must result from that comparison. Section 85 leaves it within the discretion of the Board to determine the relevance of each comparison and of all of the comparisons taken together. For example, section 85 does not stipulate that if the price of a medicine is higher in Canada than in other countries it must be found to be excessive, nor that if it is lower in Canada than in other countries it must be found not to be excessive. The comparison of the price of the medicine in Canada with its price in other countries must be made, and then the relevance of that comparison must be assessed. So too with each of the other comparisons and then all of the comparisons taken together.
A second and related point is that each of the comparisons listed in section 85 could lead the Board towards a different conclusion. There are a number of permutations. For example, a medicine might be sold in Canada at a lower price than in other countries but at a higher price than comparable medicines sold in Canada, or vice versa. Each of the three comparisons must be considered, and then the weight to be given to each of them, and how they should relate to each other, must be determined.
…

The need for balancing is evident in the application of section 85 of the Act because each of the factors taken on its own does not merely pull directionally but, depending on the relevance of the comparison itself, could lead to a different conclusion. It could be logically impossible for the Board to give each of the factors equal weight, or it could be logical after consideration of all factors to give one or more factors primary or decisive weight, as otherwise there could be irreconcilable conflicts in the conclusions to be drawn from each of the factors.

In other words, the Board must come to a single specific price that is the MNE for a medicine, and, needless to say, the three different factors stipulated by subsection 85(1) do not generate that single figure, for both of the reasons

mentioned: the act of comparing does not entail any specific conclusion, and for a given medicine each of the three factors could suggest an MNE that is different in direction and/or degree.

15. The Guidelines were established after consultation with stakeholders, as mandated by subsection 96(5) of the Act. The Guidelines aim to provide a structure for the necessary particularization and integration of the general factors listed in section 85, to provide fairness through consistent treatment among patentees, and to give patentees guidance on the process that will be used in establishing the MNE for their medicines, both when the medicines are first introduced to a market in Canada and each year thereafter that they are sold in Canada.

16. On the other hand, the Guidelines are not binding on the Board. Furthermore, situations could arise that are not contemplated by the Guidelines, or changes in medicine or the marketing of medicines in Canada could give rise to situations that are no longer covered appropriately by the Guidelines. In each case where the review of the pricing of a medicine comes before a panel of the Board, the panel must determine whether the medicine is priced excessively with in the terms of section 85 of the Act. To the extent that the Guidelines speak to this issue, the panel must determine whether the Guidelines provide for an appropriate and reasonable implementation of the factors in section 85 of the Act before establishing an MNE by the terms of the Guidelines. If the Guidelines do not result in an appropriate implementation of section 85 of the Act, the panel must depart from the Guidelines.

17. Board Staff suggested in final argument that the Guidelines establish an MNE for a medicine that should be presumed by a panel of the Board, in a price review hearing, to be excessive unless the patentee can satisfy the Board otherwise. The Panel believes that this over-states the role of the Guidelines. In each case a hearing panel must be satisfied, through evidence, argument, the application of its own expertise and judgment or a combination of all of those factors that the Guidelines provide for a reasonable implementation of section 85 of the Act. In deciding whether to reach this conclusion, appropriate weight will be given to the provenance and role of the Guidelines, but they will not be presumed to correctly implement the Act.

18. The final arguments of Janssen-Ortho and Shire tended to under-play the significance of the Guidelines in a price review hearing. The Panel does not believe that, as soon as the pricing of a medicine moves from the routine administration of the Guidelines by Board Staff, to a hearing before a panel of the Board, the hearing panel is without guidance from the Guidelines, and forced to reconcile the very general factors listed in section 85 with the particulars of each case on an ad hoc

basis. Nor can it be that the set of principles that applies to patentees who comply with the Guidelines has no potential application in a price review hearing. There is not a Guidelines regime for patentees who allow their MNEs to be set by the Guidelines and a separate section 85 regime for patentees who bring a matter to price review hearing.

19. Rather, for all patentees, section 85 of the Act governs, as particularized by the Guidelines (assuming that there are applicable provisions in the Guidelines), unless, in a matter brought to price review hearing, Board Staff is unable to satisfy the Board as to the reasonableness of the Guidelines in the circumstances of that case.

20. The onus is on Board Staff to satisfy the hearing panel on two points before a finding of excessive pricing is reached on the basis of section 85 insofar as it is implemented in the Guidelines: (1) that the Guidelines represent an appropriate implementation and particularization of section 85 of the Act; and (2) that the pricing of the medicine exceeds the Guidelines. In meeting its burden on the first point, Board Staff will doubtless make reference to the provenance of the Guidelines, and the fairness and practicality of a regime guided by principles and practices such as those in the Guidelines. Ultimately, however, the hearing panel must be satisfied that the Guidelines provide for an appropriate application of the terms of section 85 of the Act in the circumstances of the case before it.

c) The operation of the Guidelines

21. The Guidelines provide a methodology for the comparisons of the price of the medicine under review with those of other medicines in the same therapeutic class through a two stage process. There are at least two objectives to this process. First, the Guidelines embody the principle that a patentee should be rewarded for creating a medicine that constitutes a breakthrough in the treatment of a condition or, perhaps as importantly for a particular disease, a medicine that marks a substantial improvement over other medicines used to treat a condition. Such a medicine is referred to as a "Category 2" medicine.[1]

22. If the medicine does not represent a breakthrough or provides an improvement that is less than a substantial improvement (termed by the Guidelines as "no, little or moderate" improvement) it is designated a Category 3 medicine.

[1] It is not necessary, for the purposes of this decision, to describe Category 1 medicines, though dosages of Adderall XR introduced after the first sale of Adderall XR in Canada are properly categorized as Category 1 medicines.

23. Second, after categorization, medicines comparable to the medicine under review are identified, and in this process the "therapeutic class" of the medicine under review is established.[2]

24. The process of categorizing medicines as Category 2 or Category 3, and the different pricing tests (discussed below) applicable to each category, provide an important threshold for the level of accomplishment by a patentee that should entitle the patentee to charge more for a medicine under review than existing medicines for the same condition. The process of categorization can be viewed two ways. It allows a patentee the potential to charge a higher price for a medicine that represents a substantial improvement over other medicines for the same condition.

25. For a Category 3 medicine (that does not constitute a breakthrough or a substantial improvement over existing medicines for the condition in question), its MNE is the highest of the prices of the other medicines in its therapeutic class sold in Canada (hereafter referred to as the domestic therapeutic class comparison, or "DTCC").

26. For a Category 2 medicine (that does constitute a breakthrough or a substantial improvement), its MNE is not necessarily limited by the prices of existing medicines, but rather by the higher of (1) the price generated by a DTCC[3]; and (2) the median international price of the medicine itself (the median international price comparison, or MIPC). The latter ceiling, generated by the MIPC, will often be higher than that generated by the DTCC, given the fact that patented medicines sold in Canada are also often sold at unregulated prices, especially in the United States,

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[2] The Guidelines imply that a therapeutic class is to be established for Category 2 medicines [Compendium of Guidelines, Policies and Procedures, Chapter 1 – Excessive Price Guidelines]:

> 8.4 The introductory price of a Category 2 new drug product will be presumed to be excessive if it exceeds the prices of all comparable drug products, based on a Therapeutic Class Comparison Test, and the median of the international prices identified in an International Price Comparison Test.

The Panel is doubtful that this formulation will often be reasonable. A therapeutic class comparison is undertaken by reference to therapeutic equivalence. By definition, if a medicine is a breakthrough, or even if it represents a substantial improvement over existing medicines, it could be unreasonable to attempt to establish a therapeutic class based on therapeutic equivalence. This section of the Guidelines might be more workable if it were worded along the following lines, which the Panel believes capture the intent of the Guidelines:

> 8.4 The introductory price of a Category 2 new drug product will be presumed to be excessive if it exceeds the prices of (1) any drug products that would be in its therapeutic class but for the characteristics by which it is categorized as a Category 2 medicine; and (2) the median of the international prices identified in an International Price Comparison Test.

That said, the Panel is satisfied, for the reasons herein that Adderall XR (and Concerta) would be in the same therapeutic class as the existing ADHD medicines based on a therapeutic class comparison, given that there is no reliable evidence of a material difference in therapeutic equivalency among the old and the new medicines.

[3] See footnote 2.

that are higher than those in Canada. If, as with Adderall XR, the patentee is selling the medicine under review at a higher price internationally than the prices of existing medicines in Canada, its median international price can be higher than the highest price of existing medicines in Canada.

27. Looked at from another perspective, the Guidelines provide that, to have the opportunity to price a medicine under review beyond the level of the prices of the existing medicines sold in Canada for a given condition, a patentee must do more than simply "tweak" an existing medicine; a patentee must do more than introduce a new medicine that does not distinguish itself from existing medicines by any substantial improvement in its treatment of the condition in question.

The consideration of the Act and the Guidelines

28. It can be seen from the foregoing description of the Act and the Guidelines why a central focus of the debate in this proceeding was the question of whether or not Adderall XR represents a substantial improvement relative to the multiple daily dose medicines for ADHD. Board Staff witnesses agreed that Adderall XR provides a moderate improvement relative to the existing multiple daily dose medicines for ADHD, but not a substantial improvement.

29. Shire and its witnesses argued that the benefits of Adderall XR relative to existing multiple daily dose medicines did amount to a substantial improvement over those medicines. Alternatively, Shire argued that a comparison to the international prices of the existing ADHD medicines indicated that the MNE for Adderall XR should be higher than the MNE generated by the DTCC. In all events, given both the benefits of Adderall XR and its relatively higher international pricing, Shire argued, the benefits of Adderall XR relative to the existing multiple daily dose medicines for ADHD warranted a price premium over the MNE generated by the DTCC.

30. The position of Board Staff is premised on the fact that the types of benefits that the Guidelines stipulate as preconditions to a finding of "substantial improvement" are focused on improved therapeutic outcomes; that is, reduced symptoms of the ailment in question and/or fewer side effects from the medicine under review, relative to the existing medicines. The Guidelines also allow for a finding of substantial improvement where a new medicine results in significant savings to the health care system.

31. In the opinion of the witnesses for Board Staff, there was no sufficiently reliable evidence to support a conclusion that patients taking Adderall XR have materially reduced ADHD symptoms or reduced side effects from the medicine

relative to patients taking the older multiple daily dose medicines. While Shire presented evidence to the effect that one reasonably might expect improved therapeutic outcomes from the more even serum concentration of amphetamine resulting from the extended-release formulation of Adderall XR, and from improved compliance expected with a once-daily medicine, there are no comparative clinical trials establishing this. Indeed, the evidence of Board Staff was that patients might even benefit from the drug "holidays" that result from the valleys in serum concentration associated with the multiple daily dose medicines, and compliance among ADHD patients is very poor for both multiple daily dose medicines and once-daily medicines.

32. The witnesses for Board Staff argued that there simply is no reliable evidence on these topics. Shire called expert witnesses to give evidence of each of the benefits – to patients, to caregivers, to society – of Adderall XR relative to multiple daily dose medicines for ADHD. Expert witnesses for Board Staff countered by noting either that there was no scientific evidence of the benefits or their quantification, or by acknowledging that such benefits, even if established, would constitute only a moderate improvement relative to existing medications.

33. In considering the benefits described by Shire, Board Staff noted that the Guidelines not only identify the types of benefits that must be present for a medicine to constitute a substantial improvement over existing medicines, as summarized above, they specifically stipulate that the types of benefits identified by Shire as arising from the use of Adderall XR, such as convenience, are not to be considered as resulting in a substantial improvement over existing medicines.

Conclusions

34. The Panel has determined, for the reasons below, that it is appropriate to depart from the Guidelines when establishing the MNE for Adderall XR. However, it should be noted that, after careful consideration of this issue, the Panel agrees generally with the premise in the Guidelines that, in demonstrating a "substantial improvement" over existing medicines, a patentee should be required to demonstrate, with reliable evidence, a statistically and therapeutically significant improvement in therapeutic outcomes, or significant savings to the health care system. Improved therapeutic effects – improved efficacy in reducing symptoms or reductions in adverse side effects – and savings to the health care system, are the primary objectives in improving medicines and should be the primary indicia for the allowance of increased prices relative to existing medicines. The Panel also agrees, as a general matter, with the identification in the Guidelines of improvements that should not form the basis of a finding of substantial improvement. The Panel

considers these elements of the Guidelines to be appropriate implementations of the factors in section 85 of the Act.

35. The Panel also finds that, generally speaking, the distinction in the Guidelines between Category 1, Category 2 and Category 3 medicines, and the different pricing tests in the Guidelines for determining the maximum non-excessive prices of medicines in each category, are appropriate implementations of section 85 of the Act.

36. In deciding to depart from the Guidelines, the Panel was aware that Board Staff and patentees rely to some extent on the consistent application of the Guidelines to provide certainty and predictability in pricing and enforcement decisions. However, as noted earlier in these reasons, a hearing panel of the Board must be prepared to identify situations where the Guidelines do not accommodate the specific characteristics of a given medicine. Where it is determined that the Guidelines do not result in a reasonable implementation of the factors in section 85 of the Act, the panel must apply its judgment to those factors in the Act and apply them appropriately to the price of the medicine in question.

37. The departure from the Guidelines in this decision is specific to the combination of the unique features of the condition treated by Adderall XR and the relevance of the particular improvements brought by Adderall XR to that condition and its attendant circumstances for the individual and society. The non-therapeutic benefits of a once-daily medication for ADHD provide patients with real advantages that will improve their lives beyond the mere benefits of convenience. Because of the symptoms of ADHD and the circumstances of the patient population and its caregivers, these benefits can also materially improve the lives of the parents and teachers of ADHD patients. Finally, the Panel considered the virtual elimination of the potential for diversion of the amphetamine in Adderall XR to be a relevant factor in the Panel's conclusion.

38. The Panel believes that neither Category 2 nor Category 3, as they are described in the Guidelines, adequately captures the relationship between Adderall XR and the multiple daily dose ADHD medicines. For the reasons advocated by Shire and summarized above, the Panel believes that Adderall XR provides more than a moderate improvement over the multiple daily dose ADHD medicines. However, the Panel finds that there is no reliable evidence that there is a material therapeutic advantage over the multiple daily dose medicines, or significant savings to the health care system. Accordingly, the Panel does not believe that it can reasonably be said that Adderall XR represents a breakthrough or a substantial improvement relative to those medicines.

39. Weighing all of the evidence, and allowing that this is a question involving some expertise, judgment and discretion, the Panel considers that, on the spectrum from “no improvement” to “substantial improvement”, Adderall XR can reasonably be said to be situated mid-way between moderate improvement and substantial improvement. The Panel considers Adderall XR to be in a fourth category that, on the findings of this Panel, is unique to once-daily medicines for ADHD.

40. The result of this conclusion is that the MNE of Adderall XR should have the potential to be higher than that generated by DTCC (applicable to moderate improvement medicines) but not as high as that generated by the MIPC (applicable to breakthrough and substantial improvement medicines.) In these circumstances, the Board considers it reasonable to set the MNE of Adderall XR at the mid-point between the MNEs that would be generated by the two tests.

41. Section 85 of the Act requires the Board to consider the international prices of medicines that are in the same therapeutic class as the medicine under review. The Panel considered carefully the evidence and argument presented by Shire with respect to the international prices of ADHD medicines other than Adderall XR. The Panel finds itself in agreement with the decision of the Board in the *LEO Pharma* case, in which the same issue was considered.

42. Comparisons of the price of the medicine under review with (1) the prices of comparable medicines in Canada, and (2) the price of the medicine in other countries, tend to provide compelling comparisons for the purposes of determining whether the price of a medicine in Canada is excessive. Once one makes the double-remove of going to international prices of comparable medicines, the comparison, while necessary and relevant, is potentially less compelling. Having considered the evidence on the international pricing of comparator medicines, and having weighed that evidence as stipulated in paragraph 85(1)(c) of the Act, the Panel was not persuaded that this factor should alter the conclusion that can be reached from the more reliable comparisons with the international prices of Adderall XR and the prices of comparable medicines in Canada. If the Panel had considered the evidence concerning the international pricing of comparable medicines to be influential in the context of the balance of the evidence in the proceeding, that influence would have been to support the same conclusion that the Panel has reached in this decision.

43. The Panel also gave careful consideration to the arguments of Janssen-Ortho to the effect that the Panel should establish a therapeutic class consisting of Adderall XR, Concerta and Strattera, and establish the MNEs for those medicines accordingly. However, the Panel accepts that the Guidelines are fundamentally sound in requiring a starting datum for the process of establishing a therapeutic

class and the MNEs of medicines within that therapeutic class. Though the result might turn out to be similar to that advocated by Janssen-Ortho, the Panel believes that the proper approach is to start with Adderall XR as the first medicine of its type sold in Canada, establish an MNE for Adderall XR as at the date of its first sale, and then add any other medicines, such as Concerta, to the therapeutic class of Adderall XR as at the date that those other medicines are first sold in Canada.

44. Accordingly, for the purposes of calculating the MNE for Adderall XR from its first sale in Canada onwards (which were sales of the 10, 20 and 30 mg strengths), the MNE of Adderall XR, will be the greater of:

(a) the MNE for Adderall XR that would be generated by the Domestic Therapeutic Class Comparison where the therapeutic class consists of Ritalin, Ritalin SR and Dexedrine tablets and spansules; and

(b) the mid-point between the MNE for Adderall XR that would be generated by the Domestic Therapeutic Class Comparison described in (a) and the MNE for Adderall XR that would be generated by the Median International Price Comparison.

45. The Panel finds that the 5, 15 and 25 mg strengths of Adderall XR, first sold on April 13, 2004, were medicines with new Drug Identification Numbers for existing or comparable dosage forms, and are thus correctly categorized as Category 1 medicines in accordance with the Guidelines. As noted above, the Panel considers the categorization of drug products as Category 1 medicines in the manner described in the Guidelines to be a reasonable implementation of section 85 of the Act. The Reasonable Relationship Test in the Guidelines establishes the MNE for new strengths of an existing medicine by a linear relationship between unit prices and strengths, and the Panel considers this too to be a reasonable implementation of section 85 of the Act. When the MNE for the 10, 20 and 30 mg strengths are established in accordance with this decision, the MNE for the 5, 15 and 25 mg strengths can be established using the Reasonable Relationship Test.

46. If the MNE for Adderall XR had been established by the principles enunciated in this decision from the time of its first sales in Canada, Shire would have been permitted to increase the price of Adderall XR, and correspondingly its MNE, in accordance with the CPI methodology in the Guidelines. It is impossible to say whether Shire would have done so, but the Panel considers it appropriate to give Shire the benefit of that doubt. Accordingly, the MNE for Adderall XR will be deemed to have risen by the increases in the consumer price index (CPI) in each calendar year from 2003 to 2008 inclusive, after which the CPI provisions of the

Guidelines will apply. This deviation from the CPI provisions of the Guidelines is specific to Adderall XR[4] for period described.

Impact of this decision on the Guidelines and other medicines

47. The Panel has noted that this finding is specific to once-daily medicines for ADHD, and is applicable because of the relationship between the symptoms of that condition and the consequent unique advantages of once-daily medication for the treatment of the condition, together with the collateral advantages, such as the avoidance of illegal diversion.

48. There could be other medicines that otherwise represent more than a moderate improvement, but less than a substantial improvement, over existing medicines, and thus arguably warrant pricing tests that are more liberal than those applicable to Category 3 medicines. However, the finding of this Panel is specific to Adderall XR.

49. The Panel appreciates that a great deal of effort went into the drafting of the Guidelines, and their evolution over time, to reconcile their various features and minimize conflicts or ambiguities in outcomes. There are already complex interactions between the provisions of the Guidelines without panels of the Board making unilateral adjustments for particular medicines. It could be that there is a superior methodology to make the accommodation that the Panel has concluded is appropriate for Adderall XR, and it could be that the current review of the Guidelines will generate a methodology.

50. This Panel does not have the authority to amend the Guidelines as they might apply to medicines other than those under review, and the decisions of this Panel are not binding on the Board or any other Panel of the Board. However, the Guidelines are under review by the Board, and it will be open to the Board to generalize or to reject, in amended Guidelines, a fourth category such as that described in this decision or, as noted, to develop a superior approach to the particular situation identified in this proceeding. Absent or pending such amendments, patentees and Board Staff may consider voluntary compliance undertakings when dealing with other medicines that are considered to belong in the fourth category described above.

[4] And, if applicable, Concerta and Strattera – see below.

The commencement of the Board's jurisdiction

a. The pre-patent issue

51. During this proceeding, Shire brought a motion for an order declaring that the Board did not have jurisdiction to make a remedial order concerning the pricing of Adderall XR for any period before the issuance, on April 13, 2004, of the Canadian patent held by Shire pertaining to Adderall XR. On that motion, Board Staff argued that the Board had jurisdiction to make a remedial order concerning the pricing of Adderall XR from and after the date on which Shire's Canadian patent pertaining to Adderall XR was laid open to the public, i.e., April 27, 2000.

52. On December 18, 2006, the Board denied Shire's motion and ruled that it had jurisdiction to make a remedial order concerning any sales of Adderall XR after April 27, 2000. Shire brought an application to the Federal Court for judicial review of this decision. That application was dismissed by the Federal Court on December 13, 2007, confirming the Board's jurisdiction, once a patent is issued, to make remedial orders concerning the laid-open period of a patent application. The Federal Court decision is under appeal.

53. Accordingly, this decision concerning the appropriate MNE for Adderall XR will apply to the pricing of Adderall XR from and after April 27, 2000.

b. Sales pursuant to the Special Access Program

54. Adderall XR was first sold in Canada in September 2002 pursuant to Health Canada's Special Access Program (the "SAP"). Shire argued that, inasmuch as Shire was not issued a Notice of Compliance ("NOC") for Adderall XR until January 2004, at which point it was entitled to market Adderall XR, the Board does not have jurisdiction to make a remedial order pertaining to the pricing of Adderall XR for any period before the issuance of that NOC. Board Staff argued that the Board had jurisdiction to make a remedial order concerning the price of Adderall XR from the date of first sale pursuant to the SAP.

55. Subsequent to the submissions of the parties in this proceeding, a panel of the Board considered this issue at some length in response to an application by Board Staff in relation to the medicine Thalomid. In that proceeding, the panel concluded that the Board has jurisdiction to make a remedial order pertaining to the price of a medicine from the date of its first sale in Canada, whether such sale is pursuant to the SAP or an NOC.

56. That decision is not binding on this Panel, though it appears from the reasons for the decision that the arguments of Board Staff and the patentee were very similar to those raised by Board Staff and Shire in this proceeding. Having considered submissions of the parties in this proceeding, and having reviewed the decision of the panel in the Thalomid application, this Panel concludes that the Board has jurisdiction to make a remedial order pertaining to the price of Adderall XR from the date of its first sale in Canada, that is, September 12, 2002. This Panel agrees with and adopts the reasoning of the panel in its decision on the Thalomid application.

Concerta

57. This Panel is also the panel established to review the price of Concerta. In the Concerta proceeding, a consistent finding has been made, albeit on the evidence in that proceeding (some of which was evidence from this proceeding incorporated by reference into the Concerta proceeding). For the reasons discussed above concerning the first sale of Adderall XR in Canada, the Panel concludes that Concerta was first sold in Canada after Adderall XR, and in the Concerta proceeding Concerta is categorized as a Category 3 medicine, in that, at the time of its introduction in Canada, Concerta did not represent any appreciable improvement over Adderall XR. Concerta has been placed in the same therapeutic class as Adderall XR.

58. Accordingly, at its introduction, Concerta belonged in the same therapeutic class as Adderall XR, Ritalin, Ritalin SR and Dexedrine capsules and spansules. With that therapeutic class now containing Adderall XR, the MNE of which can rise to its median international price, and which is deemed by this decision to have risen in each calendar year from 2004 to 2008, Concerta (through the application of the DTCC) should have its MNE (subject to dosage comparisons) increased by operation of the same principles that have been applied to Adderall XR in this decision.

59. If the Panel had concluded that Adderall XR was first sold in a market in Canada in January of 2004 when its NOC was issued, then the same analysis that has been applied to Adderall XR would have been applied to Concerta, with Adderall XR being added to the therapeutic class containing Concerta, Ritalin, Ritalin SR and Dexedrine capsules and spansules.

Strattera

60. The Board has issued a Notice of Hearing in relation to the pricing of a third once-daily medication for ADHD, Strattera, and this Panel has been seized with that proceeding. Strattera differs from Adderall XR and Concerta in that its active ingredient is not a stimulant. The Panel invites Board Staff and the patentee of Strattera to consider whether there are any compelling reasons that Strattera would not fall into the same therapeutic class as Adderall XR and Concerta and, if there are no such reasons, to consider a voluntary compliance undertaking based on the findings in this proceeding.

Board Order

61. The Panel requests that the parties agree on the terms of an order that implement the conclusions in these reasons. The Panel remains fully seized of this matter in order to issue an order and, allowing that issues might arise as to the manner in which the intent of this decision should be implemented in an order of the Board, to hear further evidence or argument on issues if necessary.

62. To assist the parties in drafting the requisite order, the Panel wishes to advise parties that it found the structure and terms of the order proposed by Board Staff in its final written argument to be appropriate, subject of course to modifications of the MNEs of the various strengths of Adderall XR, which are to be calculated in accordance with this decision. It would appear that these modifications can be accomplished most expeditiously by retaining the terms of the Board Staff's proposed order but revising the proposed appendix to reflect MNEs calculated in accordance with this decision. The Board expects the parties to submit a proposed order on or before May 10, 2008.

Addendum

After the close of argument, the Panel received submissions from Shire, and responding submissions from Board Staff, concerning the potential implications on this case of the recent decision of a panel of the Board in the matter of the Celgene Corporation and the medicine Thalomid (the "Celgene case").[5] In particular, Shire argued that the Board's decision in the Celgene case argues for the position that Adderall XR was being sold in a "discrete market" when it was being sold pursuant to Health Canada's Special Access Program (SAP).

[5] PMPRB-07-D1-THALOMID, January 21, 2008

This Panel is not bound by the decision of the panel in the Celgene case, but in all events this Panel agrees with the submissions of Board Staff on this point, to the effect that the Celgene case does not argue for the position advanced by Shire. The panel in the Celgene case was addressing a narrow issue concerning the meaning of the phrase "in any market" in the *Patent Act*, and observed that SAP sales could hypothetically be considered either to be in a market of their own or as part of the market for medicines generally. The Board, in applying its judgment, expertise and discretion to this issue, has always considered SAP sales of each medicine sold pursuant to that program to take place in the Canadian market for medicines generally. This Panel agrees with that approach for the sales of Adderall XR. Accordingly, it is not necessary for the Board to deal with the further submissions of Shire regarding the pricing implications of a contrary finding by this Panel.

Board Members: Dr. Brien G. Benoit
Thomas (Tim) Armstrong

Board Counsel: Gordon Cameron

Appearances

For Board Staff: Barbara MacIsaac, Counsel
Benjamin Mills, Counsel

For the Respondent:
Malcolm Ruby, Counsel
Allan West, Counsel

For the Interveners: Martin Mason, Counsel
Graham Ragan, Counsel

Original signed by

Sylvie Dupont
Secretary of the Board