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October 6, 2008

Sylvie Dupont
Secretary of the Board
Patented Medicines Prices Review Board
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Standard Life Centre
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Dear Ms. Dupont

Thank you for the opportunity to respond to the Draft Revised Excessive Price Guidelines released on August 20, 2008.

The almost 50 page Notice and Comment document released for discussion clearly represents a substantial amount of time and effort spent by the PMPRB Board, Board Staff and stakeholders. However, as noted in earlier correspondence, the rational and objectives for many of the proposed changes remains unclear to LEO Pharma. LEO Pharma has disagreed with repeated assertions by PMPRB that "the Dovobet Federal Judicial Ruling" required specific changes be made to the guidelines. The year end reviews released by the PMPRB have consistently shown that drug prices in Canada are stable and compliant within the existing guidelines. As noted many times in the annual report for 2007, the rate of Inflation / Consumer Price Index has exceeded the average increase in patented drug prices almost every year since 1988 (what other statistic could give greater certainty that drug price increases have not been excessive in Canada?). Among other unintended effects, it is incorrect of the PMPRB to think that some of the proposed changes will not have the effect of discouraging manufacturers' compassionate programs for patients. Such an outcome is curiously at odds with the Boards recent inclusion into their mandate of the phrase "…thereby protecting consumers and contributing to Canadian healthcare". The justification for the inclusion of this phrase in the Board's mandate is not clear.

Some comments on specific proposed changes to the guidelines are included below, listed in order as presented in the Draft Revised Excessive Price Guidelines document released on August 20, 2008.

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CHAPTER 1
Determining the Primary Indication/Use of a Drug Product
Section 4.2
For clarity, LEO Pharma recommends that the text be amended to include the italised phrase, as follows: "…offers the greatest therapeutic advantage, *as recognised at the time of introduction of the new medicine*, in relation to alternative therapies, *available at the time of introduction of the new medicine*, for the same indication….

Section 4.4
Again for clarity, LEO Pharma recommends that the text be amended to include similar changes as suggested for section 4.2, specifically: "…or use, representing, *as recognized at the time of introduction of the new medicine*, potentially, the greatest…"

Levels of Therapeutic improvement
Section 5.1
LEO Pharma agrees that adding a fourth category to this hierarchy of medicinal value is appropriate, in that it more accurately reflects the incremental increases in value / therapeutic improvement that characterise drug development.

Factors Considered in Determining the Level of Therapeutic Improvement
Section 6.1
It is unclear why the PMPRB deems it necessary to complicate and confine the advantage of medicines that offer compliance improvements with a need for "proof" that higher compliance leads to higher therapeutic efficacy.
It is also unclear how the PMPRB might distinguish between improvements in patient convenience, and improvements in compliance. Yet, only one of these requires the additional proof of higher therapeutic efficacy in order to be considered as a factor in the level of therapeutic improvement.
Finally, a product that is able to improve compliance seems to have a more solid claim on being a therapeutic advancement than one that is merely/only a new chemical entity. However, as presently written, the same demand for co-improvements in efficacy are made on each (see section 6.3) in order for them to be considered as a factor in determining the level of therapeutic improvement.

In summary, compliance improvements should be recognized as valuable of themselves.

CHAPTER 2
Excessive Price Tests
2.1
LEO Pharma notes the greater clarity now in the guidelines regarding the pricing of combination products.

2.3
Similar to the statements made concerning Chapter 1, sections 4.2 and 4.4, LEO Pharma suggests adding text to clarify that the re-conducting of the MIPC at a later time than its introduction would include only definitions and properties of comparators as recognized at the time of launch.

Review of prices of New Patented Drug Products
Section 3
(and Schedule 4 – TCC Test)
With regard to the evaluation of new, patented medicines against others in the domestic TCC, the proposed price test does not account for the fact that irrespective of whether a manufacturer has decided to "take" a PMPRB-allowable CPI price increase in any given year(s), a change (increase) in the CPI has occurred. The reference domestic TCC price of a given comparator should be the MNE price at introduction plus increases defined by each of the CPI adjustments that could have been available over the time since product introduction. This scheme would take into account cost of living increases that would be relevant to the development of the new agent.

Section 3.5
The term "any market" is used repeatedly in the document. However, unlike the term "class of customer", which is defined, no clear definition of "any market" is given.
In the "Introduction" section of the Notices and Comments document, sub-section "Working Group on Price Tests", page 8, a distinction seems to be made between "class of customer" and "Market" (…average prices in different markets (class of customer or province/territory)…"). This text suggests that there could be 4 (class of customers) plus 10 (provinces) plus 3 territories = 17 different markets.
However, in section 1.3 of Chapter 3, page 20, "class of customer" and "markets" seem to be the same ("…average prices in different markets (i.e., hospital, pharmacy, wholesaler).
Alternatively, if "any market" means any of the combinations of the 13 provinces/ territories and 4 classes of customers (52 potential markets), then this should be stated.

Perhaps linked to the lack of clear definitions for terms, the proposed criteria for when and how prices in any market could be examined are complicated and

unclear. LEO Pharma suggests that until greater clarity and simplicity can be described in a written document, “any market” reviews should not be completed.

Delinking
Section 4.2
(and schedule 8)
Similar to the situation regarding any market pricing reviews, the proposed strategy for delinking the MNE and ATP is too complex. A complete delinking of the MNE and ATP, with provision for year over year price increases on the original MNE up to the calculated CPI factor, and with a stated percentage maximum for year over year price increases (to limit year over year increases in specific situations) would be much more transparent. Again, until this matter can be simplified, this concept should not be presently implemented, and should be prioritized for further review.

SCHEDULES
TTC Test
Schedule 4
Section 3 – measuring the price
In the first paragraph, the last sentence deals with how the relevant pricing comparison will be made, distinguishing between “acute indications” and “chronic situations”. LEO Pharma suggests replacing the last sentence with the following “*Generally, the price per course of treatment will be applicable to indications and medicines wherein the treatment is given for relatively brief, finite periods of time, then stopped. Conversely, the price per day (based on maintenance dose) of medications will be applicable to indications and medicines given on a continuous basis for prolonged, indefinite periods*.” This wording distinguishes treatment of chronic diseases that are marked by periods of exacerbation requiring therapy, followed by relative quiescence wherein no therapy is given, from treatment of other chronic diseases that require continual therapy.

Schedule 6
Existing medicines with Unusual Circumstances
Changes in exchange rates, and the removal of a drug product priced highest in the world from the market should not be reasons for drug prices in Canada to be declared excessive, or to be required to be reduced. Neither situation is under the control of the manufacturer of the product in question, nor does either situation directly affect Canadian consumers after the introduction of the drug product onto the market. The limiting of price increases to the CPI adjustment factor protects Canadian consumers adequately. Finally, if exchange rates changed in an opposite direction in a situation wherein the HIPC

determined the MNE, there is no corresponding provision to allow price increases to exceed the CPI to account for exchange rate fluxations. This lack of “consistency” argues against any effect of changing exchange rates on allowable MNEs.

Thank you for this opportunity to comment on the draft guideline revisions.

Best regards
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LEO Pharma