PATENTED MEDICINE PRICES REVIEW BOARD

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

AND IN THE MATTER OF Leo Pharma Inc., (the "Respondent") and the medicine "Dovobet"

STATEMENT OF ALLEGATIONS OF BOARD STAFF

INTRODUCTION

1. This Statement of Allegations results from an investigation by Board Staff into the price of Dovobet (calcipotriol/betamethasone dipropionate) 50 mcg / 0.5 mg per gram ointment (DIN 02244126), a patented medicine sold in Canada by Leo Pharma Inc. ("Leo Pharma").

THE MEDICINE

2. Dovobet is a medicine indicated for the topical treatment of active lesions of psoriasis vulgaris in adult patients. **(Attachment 1)** It is a new combination of substances currently sold as individual components in Canada: Dovonex (calcipotriol 50 mcg/g) and Diprosone or Diprolene (betamethasone dipropionate 0.5 mcg/g). Its ATC classification is D05AX52.

3. Health Canada issued a Notice of Compliance for Dovobet on June 11, 2001. **(Attachment 2)**

4. Leo Pharma began selling Dovobet in Canada on December 17, 2001.

THE PATENT

5. Canadian Patent 1,307,288 pertains to Dovobet. **(Attachment 3)** This patent was granted to Leo Pharmaceutical Products Ltd. on September 8, 1992 and will expire on September 8, 2009. Leo Pharma Inc. is a wholly-owned subsidiary of Leo Pharmaceutical Products Ltd. and for the purposes of the Patented Medicine Prices Review Board ("PMPRB") is considered to be the "patentee".

6. Canadian Patent Application 2,370,565 pertains to Dovobet. **(Attachment 4)** This patent application filed by Leo Pharmaceutical Products Ltd. is still pending.

THE PRICE REVIEW

7. In accordance with the *Patented Medicines Regulations, 1994* ("the Regulations"), Leo Pharma filed price and sales information in February 2002 for the December 17, 2001 to January 16, 2002 filing period and in July 2002 for the January to June 2002 filing period. During this introductory period, Leo Pharma was selling Dovobet at a price of $1.60 per gram.

8. Following the procedures outlined in the PMPRB's Guidelines for new medicines, Board Staff conducted its review of Dovobet during the fall 2002 to determine its categorization as a new medicine and to review its price to determine whether the price of Dovobet of $1.60 per gram was within the Guidelines.

APPLICABLE GUIDELINES

Category

9. The Guidelines provide the following guidance with respect to determining categorization for a new active substance:

> 3.1 A Category 1 drug product is a new DIN of an existing dosage form of an existing medicine, or a new DIN of another dosage form of the medicine that is comparable to the existing dosage form as per Schedule 7.
>
> 3.2 A Category 2 drug product is one that provides a breakthrough or substantial improvement. It is a new DIN of a non-comparable dosage form of an existing medicine or the first DIN of a new chemical entity.
>
> 3.3 A Category 3 drug product is a new DIN of a non-comparable dosage form of an existing medicine or the first DIN of a new chemical entity. These DINs provide moderate, little or no therapeutic advantage over comparable medicines. This group includes those new drug products that are not included in Category 2 above.

10. Based on the above Guidelines, Board Staff classified Dovobet as a category 3 drug product **(Attachment 5**). The same category had been proposed by the patentee to Board Staff.

Comparable Medicines & Dosage Regimens

11. With respect to the selection of comparable medicines, the Guidelines provide as follows:

> 9.1 Comparable drug products are selected by identifying both comparable medicines and comparable dosage forms.
>
> 9.2 Comparable medicines are clinically equivalent in addressing the approved indication that is anticipated to be the primary use of the new drug product under review. The PMPRB refers to the World Health Organization (WHO) Drug Utilization Research Group's Anatomical Therapeutic Chemical Classification System (ATC) as the starting point for the selection of comparable medicines.
>
> 9.3 Comparable medicines will typically be those identified under the ATC classification system at the sub-class level above the single chemical substance. This will normally be the fourth sub-class level. If the appropriate comparable medicines are not identified at this level, then the PMPRB may choose from the next higher sub-class or another sub-class. In some instances, it may be appropriate to select from the fifth or single chemical substance level. Selection criteria will include the indication and therapeutic use, and could include other factors such as mode of action, spectrum of activity or chemical family.
>
> 9.4 The PMPRB may omit from the comparison a chemical substance or a drug product of the same ATC therapeutic class as the drug product under review if, in the panels' or staff's opinion, it is not clinically equivalent or is unsuitable for comparison. For example, drug products with primary uses other than to address the indication anticipated to be the primary use of the drug product under review may be omitted from the comparison. Similarly, the PMPRB may choose to add products from other ATC classes if they are clinically equivalent for the appropriate indication to the drug product under review.

12. For purposes of conducting the Therapeutic Class Comparison ("TCC"), usual practice is for Board Staff to compare combination products, such as Dovobet, to the existing component products, when the component products are available in Canada. Accordingly, Board Staff compared Dovobet to its individual components: Dovonex (calcipotriol 50 mcg/g) and Diprosone or Diprolene (betamethasone dipropionate 0.5 mcg/g).

THE MAXIMUM NON-EXCESSIVE PRICE

13. The Guidelines set out the appropriate price test for a category 3 new drug product as follows:

> 8.5 In addition to the Guideline applicable to all patented drug products detailed in Section 7, the introductory price of a Category 3 new drug product will be presumed to be excessive if it exceeds the prices of all of the comparable drug products based on a Therapeutic Class Comparison Test (Schedule 2).
>
> 8.6 When it is inappropriate or impossible to conduct a Therapeutic Class Comparison Test, Board Staff will give primary weight to the median of the international prices identified in an International Price Comparison Test (Schedule 3) to determine if the introductory price of the new DIN is excessive.

14. Subsection 7.1 of the Guidelines (Chapter 1, Excessive Price Guidelines) further provides that:

> The price of a new or existing patented drug product will be presumed to be excessive if it exceeds the prices of the same medicine sold in all countries listed in the Regulations. These prices will be determined using the International Price Comparison Test described in *Schedule 3*.

15. As per the above Guidelines, Board Staff conducted a TCC test comparing Dovobet to Dovonex ointment (calcipotriol) plus Diprolene (betamethasone dipropionate). The results of the TCC test indicated that the introductory price of $1.6000 per gram exceeded the maximum non-excessive ("MNE") price of $1.2132 per gram.

16. Furthermore, the results of the International Price Comparison ("IPC") test indicated that the price of $1.6000 per gram of Dovobet was higher than the prices of Dovobet in the comparator countries in which it was sold at the time of introduction (Sweden and the United Kingdom). As of today, Dovobet is authorized for sale and has been sold in six of the seven

comparator countries and the Canadian price for Dovobet remains the highest of the said comparator countries.

17. By letter dated January 10, 2003, Board Staff advised Leo Pharma of the results of the price review of Dovobet and that an investigation was commenced into the introductory price of Dovobet. **(Attachment 6)**

18. In response, Leo Pharma filed a supplementary submission with Board Staff recommending the expansion of the TCC beyond the two components of Dovobet. **(Attachment 7)**

19. In light of the new scientific submission, Board Staff referred the medicine Dovobet to the Human Drug Advisory Panel ("HDAP") for its review. The HDAP was asked for its recommendation as to whether to expand the TCC of Dovobet beyond the individual component products, calcipotriol and betamethasone dipropionate. If so, the HDAP was asked to recommend the comparators for inclusion in the TCC and the comparable dosage regimens.

20. In a report dated November 17, 2003 **(Attachment 8)** , the HDAP recommended that the appropriate comparators for purposes of conducting a Therapeutic Class Comparison ("TCC") under the Guidelines were the individual components of Dovobet:

Drug
Dovobet (calcipotriol 50mcg/g / betamethasone dipropionate 0.5mg/g)
Dovonex ointment (calcipotriol 50 mcg/g) **plus** Diprosone or Diprolene ointments (betamethasone dipropionate 0.5mg/g)

21. By letter dated January 28, 2004, Board Staff informed Leo Pharma of the HDAP's recommendation against expanding the therapeutic class beyond the individual components of Dovobet. Further, Board Staff confirmed its conclusion that the introductory price of $1.6000 per gram continued to exceed the Guidelines. **(Attachment 9)**

22. Following a meeting between Board Staff and Leo Pharma on or about July 12, 2004, Leo Pharma filed additional material for Board Staff's consideration on the expansion of the therapeutic class. **(Attachment 10)**

23. By letter dated August 6, 2004, Board Staff advised Leo Pharma it would review their submission to expand the therapeutic class, and also advised Leo Pharma that the price of Dovobet in Canada continued to remain

higher than the price of Dovobet in all comparator countries in which it was sold. **(Attachment 11)** In fact, based on publicly-available information in 2004, the price of Dovobet in Canada, $1.6000 per gram, exceeded the highest international price of $1.2840 per gram and the median international price of $1.2370.

24. By letter dated September 17, 2004, Board Staff advised Leo Pharma that it had concluded its investigation and that the price of Dovobet of $1.6000 per gram continued to be above the MNE price of $ 1.2702 in 2004. **(Attachment 12)**

POLICY OF EXCESSIVE PRICING

25. Subsection 83(4) of the *Patent Act* provides that:

> "Where the Board, having regard to the extent and duration of the sales of the medicine at an excessive price, is of the opinion that the patentee or former patentee has engaged in a policy of selling the medicine at an excessive price the Board may, by order, in lieu of any order it may make under subsection (2) or (3), as the case may be, direct the patentee or former patentee to do any one or more of the things referred to in that subsection as will in the Board's opinion offset not more than twice the amount of the excess revenues estimated by it to have been derived by the patentee or the former patentee from the sale of the medicine at an excessive price.

26. It is the position of Board Staff that Leo Pharma has engaged in a policy of selling Dovobet at an excessive price. Leo Pharma has been selling Dovobet since its introduction in Canada in December 2001 at a price per gram which Leo Pharma knew or ought to have known exceeded the MNE price calculated in accordance with the PMPRB's Guidelines. To date, Leo Pharma has failed and/or refused to lower the price of Dovobet to comply with the PMPRB's Guidelines.

OTHER

27. Board Staff reserves the right to make such other allegations and submissions and introduce other additional documents as Board Staff may advise and the Board may permit.

28. Pursuant to section 86 of the *Patent Act*, a hearing shall be held in public unless the Board orders otherwise. Board Staff submits that any hearing conducted by the Board into the price of Dovobet should be held in public and, subject to orders of the Board, all information and documents filed should form part of the public record.

ORDER REQUESTED

29. It is respectfully submitted that there are grounds for the Board to conclude pursuant to section 83 of the *Patent Act* that Leo Pharma is selling or has sold the medicine known as Dovobet in any market in Canada at a price which is or was excessive and that Leo Pharma engaged in a policy of selling Dovobet at an excessive price.

30. Board Staff seeks the issuance of an Order as against Leo Pharma, the terms of which would be as follows:

    a) The maximum non-excessive prices of Dovobet in Canada for the period December 17, 2001 to December 31, 2004 inclusive shall be the prices set out in **Attachment 13**.

    b) The maximum non-excessive price of Dovobet in Canada in future years shall be calculated in accordance with Schedule 4 of the Guidelines;

    c) In accordance with subsection 83(1) of the *Act*, Leo Pharma shall cause the maximum price at which it sells Dovobet in Canada to be reduced to the maximum non-excessive price effective on or before 30 days from the date of the Board's Order;

    d) In accordance with subsection 83(4) of the *Act*, and in lieu of an order under subsection 83(2), Leo Pharma shall offset twice the amount of excess revenues estimated to have been derived by Leo Pharma from the sale of Dovobet at an excessive price from December 17, 2001 until the date on which the price reduction referred to in paragraph c) above comes into effect:

        i) With respect to the period from December 17, 2001 to June 30, 2004, Leo Pharma shall pay to Her Majesty in right of Canada, within 30 days of the date of the Board's Order, an amount equal to twice the amount set out in **Attachment 13**; and

        ii) With respect to the period from July 1, 2004 to the date on which the price reduction referred to in paragraph b) comes into effect, Leo Pharma shall pay to Her Majesty in right of Canada, a further amount equal to twice the amount of the excess revenues estimated by the Board to have been derived by Leo Pharma from the sale of Dovobet at an excessive price; and make the payment

within 30 days of receipt of a notification from the Board of its estimate of excess revenues based on the information filed in response to paragraph e) below;

e) Leo Pharma shall, within 60 days of the date of the Board's Order:

i) Notify federal/provincial/territorial ministers of health or their representatives and all customers of the price decrease as required by the Board's Order (a copy of which shall be included in such notifications) and the effective date of such price decreases;

ii) Submit copies of the above-noted notifications and any other notice to the Board; and

iii) Provide to the Board information concerning the quantity of Dovobet sold and either the average price per package or the net revenue from sales of Dovobet in Canada, in the same form as required by subsection 4(1) of the *Patented Medicines Regulations, 1994* for the period July 1, 2004 to the date on which the price reduction referred to in paragraph c) comes into effect.

Dated at Ottawa this 24th day of November, 2004.

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LIST OF ATTACHMENTS

Attachment 1	Product Monograph for Dovobet dated March 4, 2002;
Attachment 2	Notices of Compliance – Prescription Pharmaceuticals for Human Use, Jan 1 – Dec 31 2001;
Attachment 3	Canadian Patent No. 1,307,288, granted September 8, 1992;
Attachment 4	Canadian Patent Application No. 2,370,565;
Attachment 5	New Medicine Scientific Review, dated September 11, 2002;
Attachment 6	Letter dated January 10, 2003 from Board Staff to Leo Pharma Inc.;
Attachment 7	Letter and accompanying submission dated August 26, 2003 from Leo Pharma Inc. to Board Staff;
Attachment 8	HDAP New Medicine Scientific Review dated November 17, 2003;
Attachment 9	Letter dated January 28, 2004 from Board Staff to Leo Pharma Inc.;
Attachment 10	Letter and supplementary information dated July 21, 2004 from Stikeman Elliott LLP to Board Staff;
Attachment 11	Letter dated August 6, 2004 from Board Staff to Leo Pharma Inc. and Letter dated September 3, 2004 from Stikeman Elliott LLP to Board Staff;
Attachment 12	Letter dated September 17, 2004 from Board Staff to Stikeman Elliott LLP;
Attachment 13	Dovobet – Calculation of Excess Revenues and International Prices.