

## Report on New Patented Drugs - Lyrica

Under its transparency initiative, the PMPRB publishes the results of the reviews of new patented drugs by Board Staff, for purposes of applying the PMPRB's *Excessive Price Guidelines* (Guidelines) for all new active substances introduced in Canada after January 1, 2002.

**Brand Name:** Lyrica

**Generic Name:** (*pregabalin*)

**DIN:**

02268418	25 mg capsule
02268426	50 mg capsule
02268434	75 mg capsule
02268450	150 mg capsule
02268485	300 mg capsule

**Patentee:** Pfizer Canada Inc.

### Indication - as per product monograph:

For the treatment of peripheral neuropathy in adults.

As adjunctive therapy in the treatment of partial seizures with or without secondary generalization in patients 12 years of age and older.

**Date of Issuance of First Patent(s) Pertaining to the Medicine:** March 26, 2002

**Notice of Compliance:** June 3, 2005

**Date of First Sale:** August 4, 2005

**ATC Class:** N03AX16  
*Nervous System, Antiepileptics, Antiepileptics, Other Antiepileptics*

## APPLICATION OF THE GUIDELINES

### Summary

The introductory prices of Lyrica 50 mg, 75 mg, 150 mg, and 300 mg capsules were found to be within the Guidelines because the cost of therapy did not exceed the cost of therapy of existing comparable medicines and the prices did

not exceed the prices of the same medicine in the comparator countries where Lyrica 50 mg, 75 mg, 150 mg, and 300 mg capsules were sold.

The introductory price of Lyrica 25 mg capsule was found to be within the Guidelines because its price bore a reasonable relationship to the prices of the other strengths of Lyrica and the price did not exceed the prices in the comparator countries where Lyrica 25 mg capsule was sold.

### **Scientific Review**

The Guidelines provide that new DINs with multiple approved indications will be categorized based on the approved indication for which the medicine offers the greatest therapeutic advantage in relation to alternative therapies for the same indication in a significant population. Where there is no apparent single approved indication for which the medicine offers the greatest therapeutic advantage, the approved indication representing, potentially, the greatest proportion of sales will be the basis for categorization and selection of comparable medicines.

The PMPRB's Human Drug Advisory Panel (HDAP) could not establish for which indication the medicine offers the greatest therapeutic advantage in relation to alternative therapies. Epidemiologic data supports neuropathic pain as being more frequent in the Canadian population, with a greater disease burden than is reported for epilepsy. Therefore, the HDAP recommended the primary indication for Lyrica be neuropathic pain.

Lyrica is a new active substance and the HDAP recommended that Lyrica be classified as a category 3 new medicine (provides moderate, little or no therapeutic advantage over comparable medicines).

The Therapeutic Class Comparison (TCC) test of the Guidelines provides that the price of a category 3 new drug product cannot exceed the prices of other drugs that treat the same disease or condition. Comparators are generally selected from among existing drug products in the same 4<sup>th</sup> level of the Anatomical Therapeutic Chemical (ATC) System that are clinically equivalent in addressing the approved indication. See the PMPRB's *Compendium of Guidelines, Policies and Procedures* for a more complete description of the selection of the Guidelines and the policies on TCCs.

The HDAP identified Lamictal (*lamotrigine*), Neurontin (*gabapentin*), and Topamax (*topiramate*) as comparable medicines for Lyrica. These medicines share the same 4<sup>th</sup> level ATC and are currently used for the treatment of neuropathic pain.

The Guidelines provide that the dosage recommended for comparison purposes will normally not be higher than the maximum of the usual recommended

dosage. The recommended comparable dosage regimens for Lyrica and the comparable medicines are based on the respective product monographs and supported by clinical literature.

The HDAP could not derive a comparable dosage regimen for the Lyrica 25 mg strength and recommended that it be compared to the other strengths.

### Price Review

Under the Guidelines, the introductory price of a new category 3 drug product will be presumed to be excessive if it exceeds the price of all of the comparable drug products in the TCC test, or if the price in Canada exceed the range of the prices of the same medicine sold in the countries listed in the *Patented Medicines Regulations* (Regulations).

The introductory prices of Lyrica 50 mg, 75 mg, 150 mg, and 300 mg capsules were within the Guidelines as the cost per treatment did not exceed the cost per treatment of the comparable medicines. The introductory price of Lyrica 25 mg capsule (\$0.7477<sup>1</sup>) was within the Guidelines based on the Reasonable Relationship test.

#### Lyrica 50 mg capsule – Introductory Period (August to December 2005)

Name	Strength	Dosage Regimen	Unit Price	Cost per Day
Lyrica	50 mg capsule	3 capsules	\$1.1730 <sup>1</sup>	\$3.5190
Lamictal	100 mg tablet	2 tablets	\$1.3260 <sup>2</sup>	\$2.6520
Neurontin	300 mg capsule	3 capsules	<sup>3</sup>	<sup>3</sup>
Topamax	100 mg tablet	2 tablets	\$1.9900 <sup>2</sup>	\$3.9800

#### Lyrica 75 mg capsule – Introductory Period (August to December 2005)

Name	Strength	Dosage Regimen	Unit Price	Cost per Day
Lyrica	75 mg capsule	2 capsules	\$1.5178 <sup>1</sup>	\$3.0356
Lamictal	100 mg tablet	2 tablets	\$1.3260 <sup>2</sup>	\$2.6520
Neurontin	300 mg capsule	3 capsules	<sup>3</sup>	<sup>3</sup>
Topamax	200 mg tablet	1 tablet	\$3.1500 <sup>2</sup>	\$3.1500

**Lyrica 150 mg capsule – Introductory Period (August to December 2005)**

Name	Strength	Dosage Regimen	Unit Price	Cost per Day
Lyrica	150 mg capsule	2 capsules	\$2.3218 <sup>1</sup>	\$4.6436
Lamictal	100 mg tablet	4 tablets	\$1.3260 <sup>2</sup>	\$5.3040
Neurontin	600 mg capsule	3 capsules	<sup>3</sup>	<sup>3</sup>
Topamax	200 mg tablet	2 tablets	\$3.1500 <sup>2</sup>	\$6.3000

**Lyrica 300 mg capsule – Introductory Period (August to December 2005)**

Name	Strength	Dosage Regimen	Unit Price	Cost per Day
Lyrica	300 mg capsule	2 capsules	\$2.3218 <sup>1</sup>	\$4.6436
Lamictal	100 mg tablet	4 tablets	\$1.3260 <sup>2</sup>	\$5.3040
Neurontin	600 mg capsule	6 capsules	<sup>3</sup>	<sup>3</sup>
Neurontin	800 mg capsule + 400 mg capsule	3 capsules + 3 capsules	<sup>3</sup>	<sup>3</sup>
Topamax	200 mg tablet	4 tablets	\$3.1500 <sup>2</sup>	\$12.6000

<sup>1</sup> Publicly available price as per the Patented Medicines Regulations

<sup>2</sup> Ontario Drug Benefit Formulary, September 22, 2005

<sup>3</sup> At publication of this report, the price of Neurontin is under review

In 2005, Lyrica 25 mg, 50 mg and 300 mg capsules were being sold in six of the seven countries listed in the Regulations, namely Germany, Italy, Sweden, Switzerland, the United Kingdom, and the United States. In compliance with the Guidelines, the prices in Canada did not exceed the range of prices in those countries. The price of Lyrica 25 mg capsule was the 4<sup>th</sup> highest price, below the median international price; the price of Lyrica 50 mg capsule was the 5<sup>th</sup> highest price, below the median international price; and the price of Lyrica 300 mg capsule was the 6<sup>th</sup> highest price, below the median international price.

In 2005, Lyrica 75 mg and 150 mg capsules were being sold in the seven countries listed in the Regulations, namely France, Germany, Italy, Sweden, Switzerland, the United Kingdom, and the United States. In compliance with the Guidelines, the prices in Canada did not exceed the range of prices in those countries. The price of Lyrica 75 mg capsule was the 4<sup>th</sup> highest price, above the median international price and the price of Lyrica 150 mg capsule was the 2<sup>nd</sup> highest price, above the median international price.

*Where comparators and dosage regimens are referred to in the Summary Reports, they have been selected by the PMPRB Staff and the HDAP for the purpose of carrying out the PMPRB's regulatory mandate, which is to review the prices of patented medicines sold in Canada to ensure that such prices are not excessive. The publication of these reports is also part of the PMPRB's commitment to make its price review process more transparent.*

*The information contained in the PMPRB's Summary Reports should not be relied upon for any purpose other than its stated purpose and is not to be interpreted as an endorsement, recommendation or approval of any drug nor is it intended to be relied upon as a substitute for seeking appropriate advice from a qualified health care practitioner.*

### **References – Lyrica**

1. Anon. Drugs for epilepsy. *Treat Guidel Med Lett*. 2003 May;1(9):57-64.
2. Arroyo S, Anhut H, Kugler AR, Lee CM, Knapp LE, Garofalo EA, et al. Pregabalin add-on treatment: a randomized, double-blind, placebo-controlled, dose-response study in adults with partial seizures. *Epilepsia*. 2004 Jan;45(1):20-7.
3. Backonja M et al. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus: a randomized controlled trial. *JAMA* 1998;280:1831-1836.
4. Ben-Menachem E. Pregabalin pharmacology and its relevance to clinical practice. *Epilepsia*. 2004;45 Suppl 6:13-8.
5. Beydoun A, Kugler AR, Greiner MJ, Lee CM, Anhut H, Knapp LE, et al. Safety and sustained long-term efficacy of pregabalin for partial-onset seizures. *Epilepsia* 2003;44(Suppl 9):Abstract 2.240. Available from: [http://www.aesnet.org/Visitors/AnnualMeeting/Abstracts/dsp\\_Abstract.cfm?id=4496](http://www.aesnet.org/Visitors/AnnualMeeting/Abstracts/dsp_Abstract.cfm?id=4496) (accessed 6 Apr 2005).
6. Beydoun A, Uthman BM, Kugler AR, Greiner MJ, Knapp LE, Garofalo EA. Safety and efficacy of two pregabalin regimens for add-on treatment of partial epilepsy. *Neurology*. 2005 Feb 8;64(3):475-80.
7. Dubinsky RM, Kabbani H, El-Chami Z, Boutwell C, Ali H. Practice parameter: treatment of postherpetic neuralgia: an evidence-based report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2004 Sep 28;63(6):959-65.
8. Dworkin R, Sharma U, Stacey B, Chambers R, Siffert J. Long-term treatment of neuropathic pain and fibromyalgia syndrome with pregabalin

- in treatment-refractory patients. Presentation at the 24<sup>th</sup> annual scientific meeting of the American Pain Society; 2005 Mar 30 – Apr 2: Boston. Abstract no 686. Available from:  
<http://www.ampainsoc.org/abstract/2005/data/686/index.html>  
(accessed 5 Apr 2005).
9. Dworkin RH et al. Pregabalin for the treatment of postherpetic neuralgia: a randomized, placebo-controlled trial. *Neurology* 2003;60:1274-1283.
  10. Dworkin RH, Backonja M, Rowbotham MC, Allen RR, Argoff CR, Bennett GJ, et al. Advances in neuropathic pain: diagnosis, mechanisms, and treatment recommendations. *Arch Neurol*. 2003 Nov;60(11):1524-34.
  11. Dworkin RH, Corbin AE, Young JP Jr, Sharma U, LaMoreaux L, Bockbrader H, Garofalo EA, Poole RM. Pregabalin for the treatment of postherpetic neuralgia: a randomized, placebo-controlled trial. *Neurology*. 2003 Apr 22;60(8):1274-83.
  12. Frampton JE, Foster RH. Pregabalin: in the treatment of postherpetic neuralgia. *Drugs*. 2005;65(1):111-8.
  13. Frampton JE, Scott LJ. Pregabalin: in the treatment of painful diabetic peripheral neuropathy. *Drugs*. 2004;64(24):2813-20.
  14. French JA, Kanner AM, Bautista J, Abou-Khalil B, Browne T, Harden CL, et al. Efficacy and tolerability of the new antiepileptic drugs I: treatment of new onset epilepsy: report of the Therapeutics and Technology Assessment Subcommittee and Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology*. 2004 Apr 27;62(8):1252-60.
  15. French JA, Kanner AM, Bautista J, Abou-Khalil B, Browne T, Harden CL, et al. Efficacy and tolerability of the new antiepileptic drugs II: treatment of refractory epilepsy: report of the Therapeutics and Technology Assessment Subcommittee and Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology*. 2004 Apr 27;62(8):1261-73.
  16. French JA, Kugler AR, Robbins JL, Knapp LE, Garofalo EA. Dose-response trial of pregabalin adjunctive therapy in patients with partial seizures. *Neurology*. 2003 May 27;60(10):1631-7.
  17. Goodman F et al. Drug class review on antiepileptic drugs in bipolar mood disorder and neuropathic pain: executive summary. Oregon Health Services University. Oregon Health Services Commission. December 2004.

18. Hadj Tahar A. Pregabalin for peripheral neuropathic pain. *Issues Emerg Health Technol.* 2005 Mar;(67):1-4.
19. Hufnagel A, Anhut H, Lee C, Messmer S. Evaluation of pregabalin as add-on treatment of partial seizures comparing fixed and flexible dosing in a randomized, double-blind, placebo-controlled trial. Presentation at the 8<sup>th</sup> Congress of the European Federation of Neurological Sciences; 2004 Sep 4: Paris. Abstract no P1169. Available from: <http://www.kenes.com/efns2004/program/session1.asp?SessionId=POS3&SSessionDate=9/5/2004> (accessed 5 Apr 2005).
20. Janssen-Ortho Inc. Topamax Product Monograph. Toronto, Ontario. March 6, 1997; revised January 4, 2005. Available from: <http://www.janssen-ortho.com/JOI/en/product/products.asp> (accessed 30 Mar 2005).
21. Lesser H, Sharma U, LaMoreaux L, Poole RM. Pregabalin relieves symptoms of painful diabetic neuropathy: a randomized controlled trial. *Neurology.* 2004 Dec 14;63(11):2104-10.
22. Lesser H et al. Pregabalin relieves symptoms of painful diabetic neuropathy. *Neurology* 2004;63:2104-2110.
23. Lyrica. Annex I. Summary of Product Characteristics (SPC). European Union. December 16, 2004.
24. Maizels M, McCarberg B. Antidepressants and antiepileptic drugs for chronic non-cancer pain. *Am Fam Physician.* 2005 Feb 1;71(3):483-90.
25. Namaka M, Gramlich CR, Ruhlen D, Melanson M, Sutton I, Major J. A treatment algorithm for neuropathic pain. *Clin Ther.* 2004 Jul;26(7):951-79.
26. Pfizer Canada Inc., Lyrica Product Monograph.
27. Pfizer Canada Inc. Neurontin Product Monograph. Kirkland, Quebec. January 9, 2001; revised October 29, 2003. Available from: <http://www.pfizer.ca/english/our%20products/prescription%20pharmaceuticals/default.asp?s=1> (accessed 30 Mar 2005).
28. Repchinsky C, editor. *Compendium of Pharmaceuticals and Specialties.* Ottawa: Canadian Pharmacists Association; 2004.

29. Rosenstock J et al. Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo-controlled trial. *Pain* 2004;110:628-638.
30. Rosenstock J, Tuchman M, LaMoreaux L, Sharma U. Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo-controlled trial. *Pain*. 2004 Aug;110(3):628-38.
31. Rowbotham M et al. Gabapentin for the treatment of postherpetic neuralgia. *JAMA* 1998;280:1837-1842.
32. Sabatowski R, Galvez R, Cherry DA, Jacquot F, Vincent E, Maisonobe P, et al. Pregabalin reduces pain and improves sleep and mood disturbances in patients with post-herpetic neuralgia: results of a randomised, placebo-controlled clinical trial. *Pain*. 2004 May;109(1-2):26-35.
33. Sabatowski R et al. Pregabalin reduces pain and improves sleep and mood disturbances in patients with psot-herpetic neuralgia: results of a randomized, placebo-controlled clinical trial. *Pain* 2004;109:26-35.
34. Sander JW. The use of antiepileptic drugs: Principles and practice. *Epilepsia*. 2004;45 Suppl 6:28-34.
35. Scottish Intercollegiate Guidelines Network (SIGN). Diagnosis and management of epilepsy in adults. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2003 Apr. Available from: <http://www.sign.ac.uk/pdf/sign70.pdf> (accessed 6 Apr 2005).
36. Sharma U, Allen R, Glessner C, Hes M, Lamoreaux L, Poole RM. Pregabalin effectively relieves pain in patients with diabetic peripheral neuropathy [Abstract 686-P]. *Diabetes* 2000;49(Suppl 1):A167.
37. Sharma U, Moore J, LaMoreaux L, Corbin E, Garofalo E, Poole RM. Pregabalin relieves pain and reduces pain interference with sleep in patients with diabetic neuropathy [Abstract P578]. *J Neurol* 2002;249(Suppl 1):1/149.
38. Siddall P, Cousins M, Otte A, Phillips K, Griesing T. Pregabalin safely and efficaciously treats chronic central neuropathic pain after spinal cord injury. Presentation at the 24<sup>th</sup> annual scientific meeting of the American Pain Society; 2005 Mar 30 – Apr 2: Boston. Abstract no 665. Available from: <http://www.ampainsoc.org/abstract/2005/data/665/index.html> (accessed 5 Apr 2005).



39. Strojek K, Floter T, Balkenohl M, Xie F, Griesing T. Pregabalin in the management of chronic neuropathic pain: a novel evaluation of fixed and flexible dosing. Presentation at the 23d American Pain Society Annual Scientific Meeting; 2004 May 6-9: Vancouver. Poster no 804. Available from: <http://www.ampainsoc.org/abstract/2004/data/804/index.html> (accessed 5 Apr 2005).
40. Tellez-Zenteno JF, Pondal-Sordo M, Matijevic S, Wiebe S. National and regional prevalence of self-reported epilepsy in Canada. *Epilepsia*. 2004 Dec;45(12):1623-9.
41. Therapeutic Products Directorate, Health Canada. Drug Product Database [database on the Internet; cited 6 Apr 2005]. Available from: [http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/dpd\\_index\\_e.html](http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/dpd_index_e.html).
42. Toelle T, Versavel M, Glessner C, Trostmann U. A Novel Treatment for diabetic peripheral neuropathy: Pregabalin dose and pain relief. Presentation at the American Society of Anesthesiologists Annual Meeting; 2004 Oct 23-27: Las Vegas. Abstract A-967. Available from: <http://www.asaabstracts.com/strands/asaabstracts/abstract.htm;jsessionid=805F8EA9665F32EBCCB8D8700AC3E893?year=2004&index=12&absnum=2214> (accessed 5 Apr 2005).
43. Topol A. Pregabalin for epilepsy. *New Medicines Profile*. 2004 Nov;(04/12):1-3. Available from: <http://www.ukmi.nhs.uk/NewMaterial/html/docs/pregabalinpilepsyNMP1104.pdf> (accessed 5 Apr 2005).
44. Van Seventer R, Bladen C, Hoggart B, Martin S, Amphibia Ziekenhuis B. Pregabalin dosed twice a day (BID) efficaciously and safely treats neuropathic pain associated with postherpetic neuralgia. Presentation at the 23<sup>rd</sup> American Pain Society Annual Scientific Meeting; 2004 May 6-9: Vancouver. Abstract no 800. Available from <http://www.ampainsoc.org/abstract/2004/data/800/index.html> (accessed 5 Apr 2005).
45. Watson CPN. Neuropathic Pain. Chapter 12. In *Therapeutic Choices*, 3<sup>rd</sup> edition, 2003. Canadian Pharmacists Association, Ottawa, Canada.
46. WHO Collaborating Centre for Drug Statistics Methodology. ATC Index [database on the Internet; cited 5 Apr 2005]. Available from: <http://www.whocc.no/atcddd/>.
47. Wolfe GI, Rivedi JR. Painful peripheral neuropathy and its nonsurgical treatment. *Muscle Nerve* 2004;30:3-19.