July 2006

Report on New Patented Drugs

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 after January 1, 2002.

Brand Name: Tarceva

Generic Name: *(erlotinib)*

DIN: 02269023 150 mg/tablet
02269015 100 mg/tablet

Patentee: Hoffmann-La Roche Limited, Canada

Indication - as per product monograph:

For the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of at least one prior chemotherapy regimen, and whose EGFR expression status is positive or unknown.

Date of Issuance of First Patent(s) Pertaining to the Medicine: February 17, 2004

Notice of Compliance: July 7, 2005

Date of First Sale: July 19, 2005 (150 mg/tablet)
July 20, 2005 (100 mg/tablet)

ATC Class: L01XX34
Antineoplastic and Immunomodulating Agents, Antineoplastic Agents, Other Antineoplastic Agents

APPLICATION OF THE GUIDELINES

Summary

The introductory price of Tarceva 150 mg/tablet was found to be within the Guidelines because the cost of therapy did not exceed the cost of therapy of existing drugs in the therapeutic class comparison and the price did not exceed the prices in the other comparator countries where Tarceva 150 mg was sold.

The introductory price of Tarceva 100 mg/tablet was found to be within the Guidelines because its price bore a reasonable relationship to the price of Tarceva 150 mg/tablet and the price did not exceed the prices in the other comparator countries where Tarceva 100 mg was sold.

Scientific Review

The PMPRB's Human Drug Advisory Panel (HDAP) recommended that Tarceva be reviewed 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 4th 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 Guidelines and the policies on TCCs.

The HDAP identified Taxotere (*docetaxel*), Alimta (*pemetrexed*) and Taxol (*paclitaxel*) as the most appropriate comparators for Tarceva. Based on clinical studies and available guidelines, these agents have proven efficacy rates in the second line treatment of advanced lung cancer after the failure of first line platinum-based therapy.

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 Tarceva and the comparators are based on their respective product monographs, available comparative clinical trial information as well as guidelines relevant to the subject matter.

Because Tarceva 100 mg/tablet represents a titration strength for dose adjustment, a clinically equivalent therapeutic class comparison could not be established. The HDAP recommended that this strength should be compared to the 150 mg/tablet on a mg to mg basis.

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 prices of all of the comparable drug products in the TCC test, or if it exceeds the prices of the same medicine in the seven countries listed in the *Patented Medicines Regulations*. The price of Tarceva 150 mg/tablet was within the Guidelines as the cost per treatment did

not exceed the cost per treatment with the comparator medicines. The price of Tarceva 100 mg/tablet was within the Guidelines as the price of $53.3333[1] per tablet did not exceed the price of Tarceva 150 mg when compared on a mg to mg basis, as recommended by the HDAP.

Introductory Period (July to December 2005)			
Name	**Strength**	**Dosage Regimen**	**Cost per Treatment**
Tarceva (*erlotinib*)	**150 mg/tab**	**150 mg daily PO**	**$1,680.0000 [1]**
Taxotere (*docetaxel*)	80 mg/vial + 20 mg/vial	100 mg/m^2 every 3 weeks	$1,804.2525 [2]
Alimta (*pemetrexed*)	500 mg/vial	500 mg/m^2 every 3 weeks	$3,617.0000 [2]
Taxol (*paclitaxel*)	6 mg/ml	175 mg/m^2 every 3 weeks	$ 904.3415 [2]

1. *Association québécoise des pharmaciens propriétaires* (AQPP), October 2005
2. IMS, December 2005

In 2005, Tarceva 150 mg/tablet and 100 mg/tablet were being sold in two of the seven countries listed in the Regulations, namely Switzerland and the United States. In compliance with the Guidelines, the prices in Canada did not exceed the range of prices in those countries; the prices of Tarceva in Canada were the lowest of those countries, below 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 – Tarceva

1. Hanna N, et al. Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small-cell lung cancer previously treated with chemotherapy. J Clin Oncol. 2004 May 1; 22(9):1589-97.

2. National Comprehensive Cancer Network [homepage on the Internet]. Clinical practice guidelines in oncology – v.2.2005: Non-small cell lung cancer.

3. Perez-Soler R et al. Determinants of tumor response and survival with erlotinib in patients with non-small-cell lung cancer. J Clin Oncol. 2004 Aug 15;22(16):3238-47.

4. Pfister DG, et al. American Society of Clinical Oncology treatment of unresectable non-small-cell lung cancer guideline: update 2003. J Clin Oncol. 2004 Jan 15; 22(2):330-53.

5. Shepherd FA, et al. A randomized placebo-controlled trial of erlotinib in patients with advanced non-small cell lung cancer (NSCLC) following failure of 1st line or 2nd line chemotherapy. A National Cancer Institute of Canada Clinical Trials Group (NCIC CTG) trial. Proc Am Soc Clin Oncol; 2004 Jun. Abtract no 7022 and related slides.

6. Anon. Erlotinib (Tarceva) for advanced non-small cell lung cancer. Med Lett Drugs Ther. 2005 Mar 28; 47(1205):25-6.

7. Baker D, Levien TL, editors. Erlotinib [monograph on the Internet]. Philadelphia: Wolters Kluwer Health, Inc.; 2005.

8. BC Cancer Agency. Cancer Management Guidelines: Lung, (including Mesothelioma &Thymoma). Available from: http://www.bccancer.bc.ca/HPI/CancerManagementGuidelines/Lung/start.htm (accessed 19 Apr 2005)

9. Cancer Care Ontario [homepage on the Internet]. Chemotherapy in Stage IV (Metastatic) Non-Small Cell Lung Cancer. Practice Guideline Report #7-2. Available from: http://www.cancercare.on.ca/pdf/pebc7-2f.pdf (accessed 19 Apr 2005)

10. Cancer Care Ontario [homepage on the Internet]. The Role of Single-Agent Docetaxel (Taxotere®) as a Second-Line Treatment for Advanced Non-Small-Cell Lung Cancer. Practice Guideline Report #7-7-2. Available from: http://www.cancercare.on.ca/pdf/pebc7-7-2f.pdf (accessed 19 Apr 2005)

11. Cancer Care Ontario [homepage on the Internet]. Use of Gemcitabine in Non-Small Cell Lung Cancer. Practice Guideline Report # 7-8 (Version 2.2002). From: http://www.cancercare.on.ca/pdf/pebc7-8f.pdf (accessed 19 Apr 2005)

12. Cancer Care Ontario [homepage on the Internet]. Use of Vinorelbine in Non-Small Cell Lung Cancer. Practice Guideline Report # 7-5. From: http://www.cancercare.on.ca/pdf/pebc7-5f.pdf (accessed 19 Apr 2005)

13. Cancer Surveillance On-Line [database on the Internet]. Surveillance and Risk Assessment Division, CCDPC, Health Canada; Statistics Canada and the Canadian Council of Cancer Registries. Cancer of the lung and bronchus, both sexes combined, all ages, 2001. Available from: http://dsol-smed.phac-aspc.gc.ca/dsol-smed/cgi-bin/cancerchart2?3DLOOK=2D&CAUSE1=732&SEX1=3&YEAR1=01&DATA_TYPE=r&AGE1=0&CPROV1=View+Chart (accessed 13 Apr 2005)

14. Centre for Chronic Disease Prevention and Control, Public Health Agency of Canada [homepage on the Internet]. Lung cancer [last updated 29 Dec 2003]. Available from: http://www.phac-aspc.gc.ca/ccdpc-cpcmc/cancer/publications/lung_e.html (accessed 4 Apr 2005)

15. Georgoulias VA. Second-line chemotherapy in relapsing or refractory patients with non-small cell lung cancer. Lung Cancer. 2002 Dec; 38 Suppl 3:S61-6.

16. Hanna N, Shepherd FA, Fossella FV, Pereira JR, De Marinis F, von Pawel J, et al. Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small-cell lung cancer previously treated with chemotherapy. J Clin Oncol. 2004 May 1; 22(9):1589-97.

17. Herbst RS, Johnson DH, Mininberg E, Carbone DP, Henderson T, Kim ES, et al. Phase I/II trial evaluating the anti-vascular endothelial growth factor monoclonal antibody bevacizumab in combination with the HER-1/epidermal growth factor receptor tyrosine kinase inhibitor erlotinib for patients with recurrent non-small-cell lung cancer. J Clin Oncol. 2005 Apr 10; 23(11):2544-55.

18. Hoffman-La Roche Limited. Tarceva Product Monograph (draft). Mississauga, Ontario. October 22, 2004.

19. Langer CJ. Emerging role of epidermal growth factor receptor inhibition in therapy for advanced malignancy: focus on NSCLC. Int J Radiat Oncol Biol Phys. 2004 Mar 1; 58(3):991-1002.

20. Nakanishi Y, Takayama K, Takano K, Inoue K, Osaki S, Wataya H, Takaki Y, Minami T, Kawasaki M, Hara N. Second-line chemotherapy with weekly cisplatin and irinotecan in patients with refractory lung cancer. Am J Clin Oncol. 1999 Aug; 22(4):399-402.

21. National Collaborating Centre for Acute Care. The Diagnosis and Treatment of Lung Cancer: Methods, Evidence & Guidance (CG24 Lung cancer - Full guideline). February 2005. Available from: http://www.nice.org.uk/pdf/cg024fullguideline.pdf (accessed 19 Apr 2005)

22. National Cancer Institute [homepage on the Internet]. Non-small cell lung cancer (PDQ®): Treatment. Recurrent non-small cell lung cancer [updated 23 Mar 2005]. Available from: http://cancernet.nci.nih.gov/cancertopics/pdq/treatment/non-small-cell-lung/HealthProfessional/page12 (accessed 12 Apr 2005)

23. National Comprehensive Cancer Network [homepage on the Internet]. Clinical practice guidelines in oncology – v.2.2005: Non-small cell lung cancer. Available from: http://www.nccn.org/professionals/physician_gls/PDF/nscl.pdf (accessed 11 Apr 2005)

24. Perez-Soler R, Chachoua A, Hammond LA, Rowinsky EK, Huberman M, Karp D, et al. Determinants of tumor response and survival with erlotinib in patients with non-small-cell lung cancer. J Clin Oncol. 2004 Aug 15; 22(16):3238-47.

25. Pfister DG, Johnson DH, Azzoli CG, Sause W, Smith TJ, Baker S Jr, et al. American Society of Clinical Oncology treatment of unresectable non-small-cell lung cancer guideline: update 2003. J Clin Oncol. 2004 Jan 15; 22(2):330-53.

26. Reck M, Gatzemeier U. Chemotherapy in stage-IV NSCLC. Lung Cancer. 2004 Aug; 45 Suppl 2:S217-22.

27. Repchinsky C, editor. Compendium of Pharmaceuticals and Specialties. Ottawa: Canadian Pharmacists Association; 2005.

28. Shepherd FA, Pereira J, Ciuleanu TE, Tan EH, Hirsh V, Thongprasert S, et al. A randomized placebo-controlled trial of erlotinib in patients with advanced non-small cell lung cancer (NSCLC) following failure of 1st line or 2nd line chemotherapy. A National Cancer Institute of Canada Clinical Trials Group (NCIC CTG) trial. Proc Am Soc Clin Oncol; 2004 Jun. Abtract no 7022. Available from: http://www.asco.org/ac/1,1003,_12-002627-00_18-0026-00_19-00678,00.asp (accessed 1 Apr 2005)

29. Socinski MA. Cytotoxic chemotherapy in advanced non-small cell lung cancer: a review of standard treatment paradigms. Clin Cancer Res. 2004 Jun 15; 10(12 Pt 2):4210s-4214s.

30. Therapeutic Products Directorate, Health Canada. Drug Product Database [database on the Internet; cited 13 Apr 2005]. Available from: http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/dpd_index_e.html

31. Therapeutic Products Directorate, Health Canada. Notice of Compliance Listings [database on the Internet; cited 13 Apr 2005]. Available from: http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_drugs_noc_e.html

32. WHO Collaborating Centre for Drug Statistics Methodology. ATC Index [database on the Internet; cited 13 Apr 2005]. Available from: http://www.whocc.no/atcddd/

33. Massarelli et al. A retrospecitve analysis of the outcome of patients who have received two prior chemotherapy regimens including platinum and docetaxel for recurrent non-small-cell lung cancer. Lung Cancer 39(2003);55-61