Report on New Patented Drugs — Olmetec

Under its transparency initiative, the PMPRB publishes the results of the reviews of new patented drug products conducted by Board Staff for purposes of applying the Board's pre-2010 Guidelines for all new active substances introduced in Canada after January 1, 2002.

Brand Name: Olmetec

Generic Name: olmesartan medoxomil

DIN: 02318660 (20 mg per tablet)
02318679 (40 mg per tablet)

Patentee: Schering-Plough Canada Inc.

Indication – as per product monograph: Indicated for the treatment of mild to moderate essential hypertension.

Date of Issuance of First Patent Pertaining to the Medicine: January 19, 1999

Notice of Compliance: October 28, 2008

Date of First Sale: December 22, 2008

ATC Class: C09CA08
Cardiovascular System; Agents Acting on the Renin-Angiotensin System; Angiotensin II Antagonists, Plain; Angiotensin II antagonists, plain

Application of the Guidelines

Summary
The introductory prices of Olmetec were found to be within the pre-2010 Guidelines because the cost of therapy did not exceed the cost of therapy of existing drugs in the therapeutic class comparison and the prices did not exceed the range of prices in other comparator countries where Olmetec is sold.

Scientific Review
Olmetec is a new active substance and the PMPRB's Human Drug Advisory Panel (HDAP) recommended that Olmetec be classified as a category 3 new medicine (provides moderate, little or no therapeutic advantage over comparable existing drug products in the treatment of essential hypertension).

The Therapeutic Class Comparison (TCC) test of the pre-2010 Guidelines provides that the price of a category 3 new drug product cannot exceed the prices of other drug products that are clinically equivalent in treating the same disease or condition. Comparators are generally selected from among existing drug products in the same 4th level of the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) classification system. See the PMPRB's then *Compendium of Guidelines, Policies and Procedures "up to 2009"* for a more complete description of the Guidelines and the policies on TCCs.

The HDAP recommended losartan (Cozaar), eprosartan (Teveten), valsartan (Diovan), irbesartan (Avapro), candesartan (Atacand) and telmisartan (Micardis) as the most appropriate comparators to olmesartan medoxomil (Olmetec). All these agents share the same 4th level ATC classification, share the same indication and are clinically equivalent in addressing the approved indication of Olmetec.

The pre-2010 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 Olmetec and its comparable drug products have been selected based on their respective product monographs as well as the available clinical trials and reviews relevant to Olmetec.

Price Review

Under the pre-2010 Guidelines, the introductory price of a category 3 new drug product will be presumed to be excessive if it exceeds the price of all the comparable drug products based on the Therapeutic Class Comparison (TCC) test or if it exceeds the range of prices of the same drug product sold in the seven countries listed in the *Patented Medicines Regulations* (Regulations). At introduction, the costs of treatment of Olmetec were within the Guidelines, as the daily cost of therapy did not exceed the cost of therapy of the comparator medicines.

Name	DIN	Strength	Dosage Regimen/Day	Cost per Day
Olmetec (olmesartan medoxomil)	02318660	20 mg/tablet	1 tablet	$0.9900[1]
Cozaar (losartan)	02182882	100 mg/tablet	1 tablet	$1.1628[1]
Teveten (eprosartan)	02240432	400 mg/tablet	1/2 tablet	$0.3502[1]
Diovan (valsartan)	02244781	80 mg/tablet	1 tablet	$1.1000[1]
Avapro (irbesartan)	02237924	150 mg/tablet	1 tablet	$1.1416[1]
Atacand (candesartan)	02239091	8 mg/tablet	1 tablet	$1.1400[1]
Micardis (telmisartan)	02240769	40 mg/tablet	1 tablet	$1.1296[1]
Olmetec (olmesartan medoxomil)	02318679	40 mg/tablet	1 tablet	$0.9900[1]
Teveten (eprosartan)	02240432	400 mg/tablet	1 tablet	$0.7004[1]
Diovan (valsartan)	02244782	160 mg/tablet	1 tablet	$1.1000[1]
Avapro (irbesartan)	02237925	300 mg/tablet	1 tablet	$1.1416[1]
Atacand (candesartan)	02239092	16 mg/tablet	1 tablet	$1.1400[1]
Micardis (telmisartan)	02240770	80 mg/tablet	1 tablet	$1.1296[1]

Source:

1 La Régie de l'assurance maladie du Québec, June 2009.

At the time of introduction, Olmetec 20 mg and 40 mg were sold in six of the seven countries (i.e., France, Germany, Italy, Switzerland, United Kingdom and United States) listed in the Regulations. In compliance with the Guidelines, the price in Canada did not exceed the range of prices in these

countries. The price of Olmetec 20 mg was second highest of the six countries in which it was sold, above the median international price. Olmetec 40 mg was third lowest of the six countries in which it was sold, below the median international price.

The publication of Summary Reports is part of the PMPRB's commitment to make its price review process more transparent.

Where comparators and dosage regimens are referred to in the Summary Reports, they have been selected by the HDAP for the purpose of carrying out the PMPRB's regulatory mandate, which is to review the prices of patented drug products sold in Canada to ensure that such prices are not excessive.

The PMPRB reserves the right to exclude from the therapeutic class comparison test any drug product it has reason to believe is being sold at an excessive price.

In Summary Reports under the pre-2010 Guidelines, the PMPRB refers to the publicly available prices of comparators, provided that such prices are not more than 10% above a non-excessive price, in which case no price will be made available. Publication of these prices is for information only and should not be construed as indicating that the public prices are considered to be within the pre-2010 Guidelines.

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

References – Olmetec

Ball K. A multi-centre, double-blind, efficacy, tolerability and safety study of the oral angiotensin II-antagonist olmesartan medoxomil versus losartan in patients with mild to moderate essential hypertension (abstract no. P2.176). J Hypertens 2001;19:S153.

Ball KJ, Williams PA, Stumpe KO. Relative efficacy of an angiotensin II antagonist compared with other antihypertensive agents. Olmesartan medoxomil versus antihypertensives. J Hypertens 2001;19:S49-S56.

Barrios V, Boccanelli A, Ewald S, et al. Efficacy and tolerability of olmesartan medoxomil in patients with mild to moderate essential hypertension. Clin Drug Invest 2007;27:545-58.

Böhm M, Ewald S, et al. Blood pressure reduction with olmesartan in mild-to-moderate essential hypertension: a planned interim analysis of an open label sub-study in German patients. Curr Med Res Opin 2006;22:1375-80.

Brunner HR, Arakawa K. Antihypertensive efficacy of olmesartan medoxomil and candesartan cilexetil in achieving 24-hour blood pressure reductions and ambulatory blood pressure goals. Clin Drug Invest 2006;26:185-93.

Brunner HR, Stumpe KO, Januszewicz A. Antihypertensive efficacy of olmesartan medoxomil and candesartan cilexetil assessed by 24-hour ambulatory blood pressure monitoring in patients with essential hypertension. Clin Drug Invest 2003;23:419-30.

Brunner HR. Olmesartan medoxomil: current status of its use in monotherapy. Vasc Health Risk Manag 2006;2:327-40.

Campbell NR. Hypertension. In: Gray, J, ed. Therapeutic Choices, 5th edition. Ottawa, ON: Canadian Pharmacists Association, 2007:405-31.

Canadian Hypertension Education Program. 2008 CHEP recommendations for the management of hypertension.

Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood P ressure. JAMA 2003;289:2560-72.

Chrysant SG, Dimas B, Shiraz M. Treatment of hypertension with olmesartan medoxomil, alone and in combination with a diuretic: an update. J Hum Hypertens 2007;21:699-708.

Chrysant SG, Marbury TC, Robinson TD. Antihypertensive efficacy and safety of olmesartan medoxomil compared with amlodipine for mild-to-moderate hypertension. J Hum Hypertens 2003;17:425-32.

Chrysant SG, Marbury TC, Silfani TN, et al. Use of 24-h ambulatory blood pressure monitoring to assess blood pressure control: a comparison of olmesartan medoxomil and amlodipine besylate. Blood Press Monit 2006;11:135-41.

Chrysant SG, Weber MA, Wang AC, et al. Evaluation of antihypertensive therapy with the combination of olmesartan medoxomil and hydrochlorothiazide. Am J Hypertens 2004;17:252-9.

Destro M, Scabrosetti R, Vanasia A, et al. Comparative efficacy of valsartan and olmesartan in mild-to-moderate hypertension: results of 24-hour ambulatory blood pressure monitoring. Adv Ther 2005;22:32-43.

Ewald S. OLMEPAS-study: results of the OLMER3B-substudy (olmesartan real life responder rate in Belgium) (abstract no. P1.44). J Hypertens 2006;25:S36.

Giles TD, Oparil S, Silfani TN, et al. Comparison of increasing doses of olmesartan medoxomil, losartan potassium, and valsartan in patients with essential hypertension. J Clin Hypertens 2007;9:187-95.

Giles TD, Robinson TD. Effects of olmesartan medoxomil on systolic blood pressure and pulse pressure in the management of hypertension. Am J Hypertens 2004;17:690-5.

Hasler C, Nussberger J, Maillard M, et al. Sustained 24-hour blockade of the renin-angiotensin system: a high dose of a long-acting blocker is as effective as a lower dose combined with an angiotensin-converting enzyme inhibitor. Clin Pharmacol Ther 2005;78:501-7.

Ichikawa S, Takayama Y. Long-term effects of olmesartan, an ang II receptor antagonist, on blood pressure and the renin-angiotensin-aldosterone system in hypertensive patients. Hypertens Res 2001;24:641-6.

Izzo JL, Neutel JM, Silfani T, et al. Efficacy and safety of treating stage 2 systolic hypertension with olmesartan and olmesartan/HCTZ : results of an open-label titration study. J Clin Hypertens 2007;9:36-44.

Liau CS, Lee CM, Sheu SH, et al. Efficacy and safety of olmesartan in the treatment of mild-to-moderate essential hypertension in Chinese patients. Clin Drug Invest 2005;25:473-9.

Mallion JM, Heagerty A, Laeis P. Systolic blood pressure reduction with olmesartan medoxomil versus nitrendipine in elderly patients with isolated systolic hypertension. J Hypertens 2007;25:2168-77.

Neutel JM, Elliott WJ, Izzo JL, et al. Antihypertensive efficacy of olmesartan medoxomil, a new angiotensin II receptor antagonist, as assessed by ambulatory blood pressure measurements. J Clin Hypertens 2002;4:325-31.

Neutel JM, Smith DH, Silfani TN, et al. Effects of a structured treatment algorithm on blood pressure goal rates in both stage 1 and stage 2 hypertension. J Hum Hypertens 2006;20:255-62.

Neutel JM, Smith DH, Weber MA, et al. Use of an olmesartan medoxomil-based treatment algorithm for hypertension control. J Clin Hypertens 2004;6:168-74.

Neutel JM. Clinical studies of CS-866, the newest angiotensin II receptor antagonist. Am J Cardiol 2001;87:37C-43C.

Oparil S, Williams D, Chrysant SG, et al. Comparative efficacy of olmesartan, losartan, valsartan, and irbesartan in the control of essential hypertension. J Clin Hypertens 2001;3:283-91.

Püchler K, Laeis P, Stumpe KO. A comparison of the efficacy and safety of the oral angiotensin II-antagonist olmesartan medoxomil with those of atenolol in patients with moderate to severe hypertension under continuous treatment with hydrochlorothiazide (abstract no. P2.175). J Hypertens 2001;19:S153.

Saito I, Kushiro T, Hirata K, et al. The use of olmesartan medoxomil as monotherapy or in combination with other antihypertensive agents in elderly hypertensive patients in Japan. J Clin Hypertens 2008;10:272-9.

Sasaki T, Noda Y, Yasuoka Y, et al. Comparison of the effects of telmisartan and olmesartan on home blood pressure, glucose, and lipid profiles in patients with hypertension, chronic heart failure, and metabolic syndrome. Hypertens Res 2008;31:921-9.

Schmidt AC, Bramlage P, Limberg R, et al. Quality of life in hypertension management using olmesartan in primary care. Expert Opin Pharmacother 2008;9:1641-53.

Scott LJ, McCormack PL. Olmesartan medoxomil. A review of its use in the management of hypertension. Drugs 2008;68:1239-72.

Sellin L, Rump LC. Addition of hydrochlorothiazide to olmesartan medoxomil increases proportions of patients achieving 24-hour ambulatory blood pressure goals (abstract no. P-67). J Clin Hypertens 2008;10:A33-4.
Sellin L, Stegbauer J, Laeis P, et al. Adding hydrochlorothiazide to olmesartan dose dependently improves 24-h blood pressure and response rates in mild-to-moderate hypertension. J Hypertens 2005;23:2083-92.

Smith D, Bailey W, Jones M, et al. Efficacy of an olmesartan medoxomil (OLM)-based treatment algorithm in African American patients with hypertension (abstract no. P-124). J Clin Hypertens 2006;8:58-9.

Smith DH, Dubiel R, Jones M. Use of 24-hour ambulatory blood pressure monitoring to assess antihypertensive efficacy. Am J Cardiovasc Drugs 2005;5:41-50.

Smith DH. Comparison of angiotensin II type 1 receptor antagonists in the treatment of essential hypertension. Drugs 2008;68:1207-25.

Stumpe KO, Ludwig M. Antihypertensive efficacy of olmesartan compared with other antihypertensive drugs. J Hum Hypertens 2002;16:S24-28.

Tu K, Chen Z, Lipscombe LL. Mortality among patients with hypertension from 1995 to 2005: a population-based study. CMAJ 2008;178:1436-40.

Tu K, Chen Z, Lipscombe LL. Prevalence and incidence of hypertension from 1995 to 2005: a population-based study. CMAJ 2008;178:1429-35.

Van Mieghem W. A multi-centre, double-blind, efficacy, tolerability and safety study of the oral angiotensin II-antagonist olmesartan medoxomil versus atenolol in patients with mild to moderate essential hypertension (abstract no. P2.174). J Hypertens 2001;19:S152-3.

Williams PA. A multi-centre, double-blind, efficacy, tolerability and safety study of the oral angiotensin II-antagonist olmesartan medoxomil versus captopril in patients with mild to moderate essential hypertension (abstract no. 207). J Hypertens 2001;19:S300.

Zannad F, Fay R. Blood pressure-lowering efficacy of olmesartan relative to other angiotensin II receptor antagonists: an overview of randomized controlled studies. Fundam Clin Pharmacol 2007;21:181-90.

Atacand. Product Monograph. e-CPS 2009.

Avapro. Product Monograph. e-CPS 2009.

Cozaar. Product Monograph. e-CPS 2009.

Diovan. Product Monograph. e-CPS 2009.

Micardis. Product Monograph. e-CPS 2009.

Teveten. Product Monograph. e-CPS 2009.