Report on New Patented Drugs — Olmetec Plus

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 Plus**

Generic Name: olmesartan medoxomil/hydrochlorothiazide

DIN: 02319616 (20 mg/12.5 mg per tablet)
02319624 (40 mg/12.5 mg per tablet)
02319632 (40 mg/25 mg per tablet)

Patentee: Schering-Plough Canada Inc.

Indication – as per product monograph: Indicated for the treatment of mild to moderate essential hypertension in patients for whom combination therapy is appropriate.

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

Notice of Compliance: November 21, 2008

Date of First Sale: December 22, 2008

ATC Class: C09DA08
Cardiovascular System; Agents Acting on the Renin-Angiotensin System; Angiotensin II Antagonist, Combinations; Angiotensin II antagonists and diuretics

Application of the Guidelines

Summary
The introductory prices of Olmetec Plus 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 Plus is sold.

Scientific Review

Olmetec Plus 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/hydrochlorothiazide (Hyzaar), valsartan/hydrochlorothiazide (Diovan-HCT), irbesartan/hydrochlorothiazide (Avalide), candesartan /hydrochlothiazide (Atacand Plus) and telmisartan/hydrochlorothiazide (Micardis Plus) as the most appropriate comparators to Olmetec Plus. The HDAP had also recommended eprosartan/ hydrochlorothiazide (Teveten Plus) as a comparator. However, a dosage regimen could not be derived for this agent. 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 Plus.

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 Plus 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 Plus.

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 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 Plus were within the Guidelines as the daily cost of therapy did not exceed the cost of therapy with the comparator medicines.

Name	DIN	Strength	Dosage Regimen/Day	Cost per Day
Olmetec Plus (olmesartan medoxomil/hydrochlorothiazide)	02319616	20/12.5 mg tablet	1 tablet	$0.9900[1]
Hyzaar (losartan potassium/hydrochlorothiazide)	02297841	100/12.5 mg tablet	1 tablet	$1.1490[2]
Diovan-HCT (valsartan/hydrochlorothiazide)	02241900	80/12.5 mg tablet	1 tablet	$1.1100[2]
Avalide (irbesartan/hydrochlorothiazide)	02241818	150/12.5 mg tablet	1 tablet	$1.1416[2]
Olmetec Plus (olmesartan medoxomil/hydrochlorothiazide)	02319624	40/12.5 mg tablet	1 tablet	$0.9900[1]
Diovan-HCT (valsartan/hydrochlorothiazide)	02241901	160/12.5 mg tablet	1 tablet	$1.1000[2]
Avalide (irbesartan/hydrochlorothiazide)	02241819	300/12.5 mg tablet	1 tablet	$1.1416[2]
Atacand Plus (candesartan cilexetil/hydrochlorothiazide)	02244021	16/12.5 mg tablet	1 tablet	$1.1400[2]

Micardis Plus (telmisartan/hydrochlorothiazide)	02244344	80/12.5 mg tablet	1 tablet	$1.1296[2]
Olmetec Plus (olmesartan medoxomil/hydrochlorothiazide)	02319632	40/25 mg tablet	1 tablet	$0.9900[1]
Diovan-HCT (valsartan/hydrochlorothiazide)	02246955	160/25 mg tablet	1 tablet	$1.1100[2]
Avalide (irbesartan/hydrochlorothiazide)	02280213	300/25 mg tablet	1 tablet	$1.1279[2]

Sources:

1 Publicly available price as per the *Patented Medicines Regulations*
2 La Régie de l'assurance maladie du Québec, June 2009.

At the time of introduction, Olmetec Plus 20 mg/12.5 mg tablet was sold in four of the seven countries (i.e., Germany, Switzerland, United Kingdom and United States) listed in the Regulations. Olmetec Plus 40 mg/12.5 mg and Olmetec Plus 40 mg/25 mg were sold in the United States only. In compliance with the Guidelines, the prices in Canada did not exceed the range of prices in these countries. The price of Olmetec 20 mg/12.5 mg was second highest of the four countries in which it was sold, above the median international price. Olmetec Plus 40 mg/12.5mg and 40 mg/25 mg were lower than the United States price.

References — Olmetec Plus

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

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

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

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

Fogari R, Zoppi A, Mugellini A, et al. Hydrochlorothiazide added to valsartan is more effective than when added to olmesartan in reducing blood pressure in moderately hypertensive patients inadequately controlled by monotherapy. *Adv Ther* 2006;23:680-95.

Rump LC, Ambrosioni E, Burnier M, et al. Initial combination therapy with olmesartan/hydrochlorothiazide in moderate-to-severe hypertension. *J Hum Hypertens* 2006;20:299-301.

Fogari R, Zoppi A, Mugellini A, et al. Effectiveness of hydrochlorothiazide in combination with telmisartan and olmesartan in adults with moderate hypertension not controlled with monotherapy: a prospective, randomized, open-label, blinded end point (PROBE), parallel-arm study. *Curr Ther Res Clin Exp* 2008;69:1-15.

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.

Kereiakes DJ, Neutel JM, Punzi HA, et al. Efficacy and safety of olmesartan medoxomil and hydrochlorothiazide compared with benazepril and amlodipine besylate. *Am J Cardiovasc Drugs* 2007;7:361-72.

Punzi H, Kereiakes D, Xu J, et al. Blood pressure (BP)-lowering efficacy of olmesartan medoxomil (OM)/hydrochlorothiazide (HCTZ) and benazepril (BN) + amlodipine (AML) in patients (pts) stratified by age and gender (abstract no. P-64). *J Clin Hypertens* 2008;10:A32.

Neutel J, Punzi H, Xu J, et al. Blood pressure (BP)-lowering efficacy of olmesartan medoxomil (OM)/hydrochlorothiazide (HCTZ) vs benazepril (BN) + amlodipine (AML) therapy in black and non-black patients (pts) with stage 2 hypertension (HT) (abstract no. P-54). *J Clin Hypertens* 2008;10:A28.

Fogari R, Derosa G, Zoppi A, et al. Effects of manidipine/delapril *versus* olmesartan/hydrochlorothiazide combination therapy in elderly hypertensive patients with type 2 diabetes mellitus. *Hypertens Res* 2008;31:43-50.

Fogari R, Derosa G, Zoppi A, et al. Effect of delapril/manidipine vs olmesartan/hydrochlorothiazide combination in insulin sensitivity and fibrinogen in obese hypertensive patients. *Inter Med* 2008;47:361-6.

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.

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.

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.

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.

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

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, 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.

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.

Izzo JL, Neutel JM, Silfani T, et al. Titration of HCTZ to 50 mg daily in individuals with stage 2 systolic hypertension pretreated with an angiotensin receptor blocker. *J Clin Hypertens* 2007;9:45-8.

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.

Barrios B, Escobar C. Olmesartan medoxomil plus hydrochlorothiazide for treating hypertension. *Expert Opin Pharmacother* 2008;9:129-36.

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.

Greathouse M. Olmesartan medoxomil combined with hydrochlorothiazide for the treatment of hypertension. *Vasc Health Risk Manag* 2006;2:401-9.

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

Canadian Hypertension Education Program. 2009 CHEP recommendations for the management of hypertension.

Hyzaar/Hyzaar DS. Product Monograph. e-CPS 2009.

Teveten Plus. Product Monograph. e-CPS 2009.

Diovan-HCT. Product Monograph. e-CPS 2009.

Avalide. Product Monograph. e-CPS 2009.

Atacand Plus. Product Monograph. e-CPS 2009.

Micardis Plus. Product Monograph. e-CPS 2009.