CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION

OLMESARTAN MEDOXOMIL /HYDROCHLOROTHIAZIDE (Olmetec Plus® – Schering-Plough Canada Inc.) Indication: Mild to Moderate Essential Hypertension

Description:
Olmetec Plus is a combination product containing an angiotensin II receptor blocker (ARB), olmesartan, and a thiazide diuretic, hydrochlorothiazide. Olmetec Plus is indicated for the treatment of mild to moderate essential hypertension in patients for whom combination therapy is appropriate. It is not indicated for the initial treatment of hypertension and patients should be titrated to a stable dose of the individual components prior to initiation of therapy with Olmetec Plus.

Dosage Forms:
Suppled as tablets containing olmesartan medoxomil/hydrochlorothiazide in the following ratio: 20 mg/12.5 mg, 40 mg/12.5 mg, 40 mg/25 mg.

Recommendation:
The Canadian Expert Drug Advisory Committee recommends that Olmetec Plus be listed in a similar manner as drug plans list other ARB/hydrochlorothiazide combination products.

Reasons for the Recommendation:
1. One double-blind randomized controlled trial was included in the systematic review and compared Olmetec Plus and losartan/hydrochlorothiazide. There were similar reductions in systolic blood pressure and diastolic blood pressure between the two products.
2. Olmetec Plus is similar in cost to its individual components given separately and the daily cost of Olmetec Plus is less than or similar to other ARB/hydrochlorothiazide combination products.

Summary of Committee Considerations:
The Committee considered the results of a systematic review that included one randomized controlled trial (RCT) evaluating the effects of olmesartan/hydrochlorothiazide for the treatment of moderate to severe essential hypertension.

The 12 week double-blind RCT enrolled 629 patients (mean baseline diastolic blood pressure of 104 mm Hg) and compared the combination of olmesartan 20 mg/hydrochlorothiazide 12.5 mg (n=315) to losartan 50 mg/hydrochlorothiazide 12.5 mg (n=314). The primary outcome of the study was the

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change from baseline in diastolic blood pressure. Pulse pressure and change in heart rate were also measured. Morbidity and target-organ damage were either not investigated or events were too infrequent to draw any conclusions.

The reduction in mean diastolic blood pressure was not statistically significantly different between Olmetec Plus and losartan/hydrochlorothiazide groups. The Olmetec Plus treated-group had a statistically significantly greater reduction in mean systolic blood pressure relative to losartan/hydrochlorothiazide, with a difference of 4-5 mm Hg. Olmetec Plus produced a statistically significant reduction in pulse pressure compared with losartan/hydrochlorothiazide. The change from baseline in heart rate was similar for each of the treatment groups.

Similar proportions of patients in each treatment group experienced a serious adverse event (1.6% in both groups). More Olmetec Plus patients experienced an adverse event compared with losartan/ hydrochlorothiazide patients (42% vs. 35%, p=0.05). A higher proportion of patients in the Olmetec Plus group withdrew due to an adverse event compared with the losartan/hydrochlorothiazide group (3.2% vs. 1.0%), but this difference was not statistically significant.

Olmetec Plus ($0.99, regardless of strength) is similar in cost to its individual components given separately (olmesartan $0.99 daily plus hydrochlorothiazide, $0.02 to $0.03 daily). Olmetec Plus is less expensive than other ARB/hydrochlorothiazide combinations ($1.03-$1.25) but is more expensive than many ACE inhibitors/hydrochlorothiazide fixed dose combinations (<$1 daily).

Of Note:

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.
2. Given that many ARB/hydrochlorothiazide products such as Olmetec Plus are more expensive than most ACE inhibitor/hydrochlorothiazide products, the full potential for cost savings will not be maximized if ARB/hydrochlorothiazide combinations are prescribed before ACE inhibitor/hydrochlorothiazide combinations. Therefore, the Committee suggests that drug plans consider a listing criteria that ARB/hydrochlorothiazide combinations only be used in patients who cannot tolerate ACE inhibitors.
3. The manufacturer has reviewed this document and has not requested the removal of any confidential information, in conformity with the CDR Confidentiality Guidelines.

Background:

CEDAC provides formulary listing recommendations to publicly funded drug plans. Recommendations are based on an evidence-based review of the medication's effectiveness and safety and an assessment of its cost-effectiveness in comparison to other available treatment options. For example, if a new medication is more expensive than other treatments, the Committee considers whether any advantages of the new medication justify the higher price. If the recommendation is not to list a drug, the Committee has concerns regarding the balance between benefit and harm for the medication, and/or concerns about whether the medication provides good value for public drug plans.

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