CDEC FINAL RECOMMENDATION

TELMISARTAN/AMLODIPINE
(Twynsta – Boehringer Ingelheim Canada Ltd.)
Indication: Essential Hypertension

Recommendation:
The Canadian Drug Expert Committee (CDEC) recommends that telmisartan/amlodipine fixed-dose combination (FDC) (Twynsta) be listed.

Reasons for the Recommendation:
1. Telmisartan/amlodipine FDC, at both the lowest and highest recommended doses, was demonstrated to be bioequivalent to the same doses of its individual components given separately.
2. At the submitted price, the cost of telmisartan/amlodipine FDC ($0.68 daily) is less than telmisartan ($1.13 daily) plus amlodipine ($0.34 to $0.50 daily) given separately.

Of Note:
The Committee gave consideration to the provision in the Health Canada product monograph which states that telmisartan/amlodipine FDC is not indicated for initial therapy, and that patients should be titrated on the individual components.

Background:
Telmisartan/amlodipine FDC has a Health Canada indication for treatment of mild to moderate essential hypertension in patients for whom combination therapy is appropriate. Telmisartan is an angiotensin II receptor blocker and amlodipine is a calcium channel blocker.

Telmisartan/amlodipine FDC is not indicated for initial therapy. It is available as oral tablets in the following dose combinations of telmisartan/amlodipine: 40 mg/5 mg, 40 mg/10 mg, 80 mg/5 mg, and 80 mg/10 mg.

Health Canada recommends that patients should be titrated on the individual components. Patients receiving telmisartan and amlodipine from separate tablets can instead receive telmisartan/amlodipine FDC containing the same component doses in one tablet once daily.

Summary of CDEC Considerations:
The Committee considered the following information prepared by the Common Drug Review (CDR): a critique of the manufacturer's clinical evaluation (including the rationale for the combination, bioequivalence, place in therapy, and harms information) and pharmacoeconomic evaluation, and patient group-submitted information about outcomes and issues important to patients.

Summary of Findings
Treatment guidelines support combination therapy of hypertension if target blood pressure levels are not achieved with standard-dose monotherapy. There is a good pharmacological rationale for the reviewed combination, given that telmisartan and amlodipine display different and complementary mechanisms of action on smooth muscle contraction and cooperate in inducing vasodilation and lowering blood pressure. Combination therapy may potentially decrease the risk of medication non-compliance and minimize the incidence of adverse events by allowing the use of two drugs at a lower dose than would be required for monotherapy.

Bioequivalence to the individual marketed tablets administered together was demonstrated in two phase 1 studies conducted with the highest- and lowest-dose strengths of telmisartan/amlodipine FDC. The manufacturer provided North American utilization data indicating that telmisartan and amlodipine are used together in clinical practice.

Safety data included two double-blind randomized controlled trials (RCTs) in which telmisartan/amlodipine FDC was assessed in patients who had not responded previously to amlodipine; one placebo-controlled double-blind RCT in which the combination of single-entity tablets was compared with the respective monotherapy components as initial therapy in patients likely to need multiple drugs to achieve blood pressure goals; and pooled data from five phase 1 trials in healthy subjects. The data did not yield any new safety concerns; however, adverse events potentially related to blood pressure-lowering were modestly increased when the combination was used as initial therapy. There was a lower incidence of oedema compared with the maximum dose of amlodipine used in monotherapy in some studies.

Cost and Cost-Effectiveness
Telmisartan/amlodipine FDC (40 mg/5 mg, 40 mg/10 mg, 80 mg/5 mg, and 80 mg/10 mg tablets; $0.68 daily regardless of strength) is less costly than its individual components given separately (telmisartan $1.13 daily plus amlodipine, $0.34 to $0.50 daily), even after accounting for upcoming patent expiry of telmisartan. Telmisartan/amlodipine FDC is either comparable in cost or less costly than other fixed-dose combination products, with the exception of irbesartan/hydrochlorothiazide (HCTZ) ($0.29 daily), valsartan/HCTZ ($0.29 to $0.30 daily), ramipril/HCTZ ($0.23 to $0.29 daily), and lisinopril/HCTZ ($0.21 to $0.50 daily).

Patient Input Information:
No patient groups responded to the CDR Call for Patient Input.

Other Discussion Points:
- The Committee noted no additional safety concerns with telmisartan/amlodipine FDC compared with its individual components.

CDEC Members:
Dr. Robert Peterson (Chair), Dr. Lindsay Nicolle (Vice-Chair), Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Ms. Cate Dobhran, Mr. Frank Gavin, Dr. John Hawboldt, Dr. Peter Jamieson, Dr. Julia Lowe, Dr. Kerry Mansell, Dr. Irvin Mayers, Dr. Yvonne Shevchuk, Dr. James Silvius, and Dr. Adil Virani.

November 16, 2011 Meeting

Regrets:
One CDEC member did not attend.

Conflicts of Interest:
None

About this Document:
CDEC provides formulary listing recommendations to publicly funded drug plans. Both a technical recommendation and plain language version of the recommendation are posted on the CADTH website when available.

CDR clinical and pharmacoeconomic reviews are based on published and unpublished information available up to the time that CDEC made its recommendation. Patient information submitted by Canadian patient groups is included in the CDR reviews and used in the CDEC deliberations.

The manufacturer has reviewed this document and has not requested the removal of confidential information in conformity with the *CDR Confidentiality Guidelines*.

The Final CDEC Recommendation neither takes the place of a medical professional providing care to a particular patient nor is it intended to replace professional advice.

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