Canadian Drug Expert Committee
Final Recommendation – Plain Language Version

TELMISARTAN/AMLODIPINE
[Twynsta – Boehringer Ingelheim (Canada) Ltd]
Indication – Essential Hypertension

Recommendation:
The Canadian Drug Expert Committee (CDEC) recommends that Twynsta, which is a combination of telmisartan and amlodipine, be listed by Canada's publicly funded drug plans for the treatment of high blood pressure.

Reasons for the Recommendation:
1. Twynsta, at both the lowest and highest recommended doses, was shown to work the same way in the body as when each component is given separately.
2. At the submitted price, the cost of Twynsta ($0.68 daily) is less than telmisartan ($1.13 daily) plus amlodipine ($0.34 to $0.50 daily) given separately.

Of Note:
The Committee considered a statement in the Health Canada product monograph that specifies Twynsta is not to be used as a first treatment option, and that the dose of each medication (telmisartan and amlodipine) should be adjusted separately until the right dose of each is reached, before switching to the combination product Twynsta.

Background:
Twynsta tablets contain two medicinal ingredients called telmisartan and amlodipine. Both of these substances help to control high blood pressure.

- Telmisartan belongs to a group of substances called "angiotensin-II receptor antagonists." Angiotensin II is a substance produced in the body that causes blood vessels to narrow; thus, increasing blood pressure. Telmisartan works by blocking the effect of angiotensin II.
- Amlodipine belongs to a group of substances called "calcium channel blockers." Amlodipine stops calcium from moving into the blood vessel wall, which stops the blood vessels from tightening.

These two medicinal ingredients work together to help stop the blood vessels from tightening. As a result, the blood vessels relax and blood pressure is lowered.

Twynsta is approved by Health Canada for the treatment of high blood pressure in patients who already receive telmisartan and amlodipine from separate tablets and who instead wish to take

the same doses in one tablet once daily for convenience. This combination product is not to be used as a first treatment option for high blood pressure.

Twynsta 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.

Summary of CDEC Considerations:
To make their decision, the Committee considered the following information prepared by the Common Drug Review (CDR): a review of clinical information submitted by the manufacturer (including the reasoning behind the combination, bioequivalence [availability in the body], place in therapy, and harms information) and a cost evaluation. No patient groups responded to the CDR Call for Patient Input.

Summary of Findings
The guidelines for the treatment of high blood pressure recommend that patients should receive combination treatment if a single treatment is not working. There is a good reason for this in the case of telmisartan and amlodipine as they work in different ways to relax the blood vessels; thus, lowering the blood pressure. Also, giving patients combination therapy may lower the chance of them not taking medication as prescribed. Finally, taking a combination pill may also decrease the amount of side effects, because when two medications are used together they may be used at lower doses than if either was used alone.

Two medical studies showed that when the medications are given together, as Twynsta, at both the lowest and highest dose, the medication works the same way in the body as when each of the medications are given separately. The manufacturer provided North American data showing that telmisartan and amlodipine are used together in clinical practice.

Safety data included two medical studies in which Twynsta was assessed in patients for whom amlodipine had not worked previously; one medical study comparing Twynsta to the individual components given separately as a first treatment for patients likely to need more than one medication to control their blood pressure; and combined data from five medical studies of Twynsta in healthy persons (who did not have high blood pressure). The data did not show any new safety concerns; however, side effects possibly related to the blood pressure lowering were more frequent when Twynsta was used as a first treatment. In some studies, there was a lower chance of edema (swelling) with Twynsta compared with the maximum dose of amlodipine used alone.

Cost and Cost-Effectiveness
Twynsta (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 taking the upcoming patent expiry of telmisartan into account. Twynsta is either comparable in cost or less costly than other 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 Twynsta 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
The information contained within this plain language version of the Canadian Drug Expert Committee (CDEC) Recommendation about this drug is based on the information found within the corresponding technical version of the CDEC Recommendation.

In making its recommendation, CDEC considered the best clinical and pharmacoeconomic evidence available, up to that time. Health care professionals and those requiring more detailed information are advised to refer to the technical version available in the CDR Drug Database on the CADTH website (www.cadth.ca).

Background on CDEC
CDEC is a committee of the Canadian Agency for Drugs and Technologies in Health (CADTH). The Committee is made up of drug evaluation experts and public members. CDEC provides recommendations about whether or not drugs should be listed for coverage through the participating publicly funded drug plans; however, the individual drug plans make their own decision about whether or not to cover a drug.

In making its recommendations, CDEC decides if the drug under review ought to be covered by the participating public drug plans based on an evidence-informed review of the medication's effectiveness and safety, and based on an assessment of its cost-effectiveness in comparison with other available treatments. Patient information submitted by Canadian patient groups is included in the CDR reviews and used in the CDEC deliberations.

The CDEC Recommendation neither takes the place of a medical professional providing care to a particular patient, nor is it intended to replace professional advice. CADTH is not legally responsible for any damages arising from the use or misuse of any information contained in or implied by the contents of this document.

The statements, conclusions, and views expressed herein do not necessarily represent the views of Health Canada, the federal government, any provincial or territorial government, or any pharmaceutical manufacturer.

The manufacturer has reviewed this document and has not requested the deletion of any confidential information.