

# Committee to Evaluate Drugs (CED)

## Recommendations and Reasons

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### Azilsartan medoxomil / chlorthalidone

**Product:** azilsartan medoxomil / chlorthalidone (Edarbyclor®)

**Class of Drugs:** angiotensin II receptor blocker / diuretic

**Reason for Use:** hypertension (high blood pressure)

**Manufacturer:** Takeda Canada Inc.

**Date of Review:** January 15, 2014

### CED Recommendation

The CED recommended that azilsartan medoxomil / chlorthalidone (Edarbyclor®) not be funded. Although azilsartan medoxomil / chlorthalidone has been shown to be effective in reducing blood pressure, there are no clinical trial data to demonstrate this drug improves clinically important outcomes such as reduction in mortality, heart attack and stroke. The Committee noted that some of the other less expensive funded alternatives are supported by more robust outcome data, and therefore, this drug does not fill any clinical care gap.

### Executive Officer Decision\*

Based on the CED's recommendation, the Executive Officer decided not to fund azilsartan medoxomil / chlorthalidone (Edarbyclor®).

### Funding Status\*

Not funded through the Ontario Public Drug Programs.

*\* This information is current as of the posting date of the document. For the most up-to-date information on Executive Officer decision and funding status, see: [www.health.gov.on.ca/en/pro/programs/drugs/status\\_single\\_source\\_subm.aspx](http://www.health.gov.on.ca/en/pro/programs/drugs/status_single_source_subm.aspx).*

## Highlights of Recommendation:

- One 12-week clinical study in adult patients with moderate to severe essential hypertension support that azilsartan medoxomil/chlorthalidone (AZL-M/CLD) is effective in reducing blood pressure.
- There are no clinical trials to show that AZL-M/CLD improves clinically important outcomes such as reducing heart attack, stroke or death.
- At the submitted price, AZL-M/CLD costs \$1.19 per day, which is more expensive than other combination drugs for hypertension.
- Many blood pressure medications are already funded and AZL-M/CLD does not fill any clinical care gap.

## Background:

High blood pressure (hypertension) affects one in five Canadians. Untreated, high blood pressure can lead to heart attack, stroke and kidney failure. Risk factors include excess weight, lack of exercise, unhealthy diet, stress, and excessive alcohol consumption. Modifying these risk factors is the first approach in managing high blood pressure. Medications are used to manage patients who have high blood pressure despite lifestyle changes.

There are several types of medication used to treat high blood pressure. These include diuretics, beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin-II receptor blockers (ARBs), calcium channel blockers, alpha-blockers, vasodilators and central-acting agents. The standard approach is to prescribe one drug at a time. A second drug is usually added only if the first drug is not effective or the patient experiences side effects at higher doses of the first drug.

## Detailed Discussions:

- For this evaluation, the CED considered:
  - Findings from the Common Drug Review (CDR) and the recommendation of the Canadian Drug Expert Committee (CDEC);
  - Information in the manufacturer's submission;
  - A patient group submission received by the CDR;
- The CED reviewed one 12-week, randomized double-blind trial, Study 303. Adult patients with moderate to severe essential hypertension were randomized to one of three treatment groups: azilsartan medoxomil/chlorthalidone (AZL-M/CLD) 40 mg/25 mg, AZL-M/CLD 80 mg/25 mg, or olmesartan/hydrochlorothiazide (OLM/HCTZ) 40 mg/25 mg.
- At 12 weeks, both groups of patients who received AZL-M/CLD showed mean reductions in systolic blood pressure (SBP) from baseline of approximately 40 mmHg. Compared with the patient group on OLM/HCTZ, patients in the AZL-M/CLD groups showed statistically significantly greater reductions in clinic SBP from baseline.
- The Committee identified several limitations with the study. Only a small proportion of the study patients had severe hypertension, even though the drug is marketed as an initial

treatment for severe hypertension. In addition, the study was short-term; it is unknown if the observed reductions in blood pressure would be sustained beyond the study period.

- There are no clinical trials evaluating the effect of AZL-M/CLD on clinical important outcomes such as reduction in mortality, heart attack and stroke. The CED noted that clinical outcomes data are available to support the use of some of the other funded options.
- Many alternative combination drugs for hypertension are available and AZL-M/CLD does not fill any care gap.
- At the submitted price, AZL-M/CLD costs \$1.19 per day, which is more expensive than other combination drugs for hypertension.
- The CED reviewed one patient group submission received by the CDR. The patient submission outlined the health risks associated with high blood pressure and emphasized the need for patient adherence to treatment.
- Overall, although AZL-M/CLD has been shown to be effective in reducing blood pressure, there are no clinical trial data to demonstrate this drug improves clinically important outcomes such as reduction in mortality, heart attack and stroke. Some of the other funded alternatives are supported by more robust data, this drug does not fill any clinical care gap, and it is more expensive.

#### **Committee to Evaluate Drugs (CED)**

The Committee to Evaluate Drugs (CED) is comprised of practicing physicians, pharmacists, health economists, and patient representatives. In conducting its review, the CED considers data contained in the drug manufacturer's submission, input provided by patient groups, findings from the national Common Drug Review and the pan-Canadian Oncology Drug Review, and other scientific information as necessary.

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