

# Committee to Evaluate Drugs (CED)

## Recommendations and Reasons

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### Eplerenone for heart failure

**Product:** eplerenone (Inspra®)

**Class of Drugs:** mineralocorticoid receptor antagonist (MRA)

**Reason for Use:** heart failure

**Manufacturer:** Pfizer Canada Inc.

**Date of Review:** May 14, 2014

### CED Recommendation

The CED recommended eplerenone (Inspra®) be funded for patients with New York Heart Association (NYHA) class II heart failure (HF) according to specific criteria. The evidence shows that eplerenone reduces morbidity and mortality in patients with NYHA class II HF compared to placebo. The cost-effectiveness of this treatment is uncertain.

### Executive Officer Decision\*

Based on the CED's recommendation and an agreement with the manufacturer to help address concerns raised by the CED, the Executive Officer decided to fund eplerenone (Inspra®) on the Ontario Drug Benefit Formulary as a Limited Use (LU) Benefit according to specific criteria.

### Funding Status\*

Funded through the Ontario Public Drug Programs as an LU benefit with criteria.

\* 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:

- A clinical study showed that eplerenone, compared with placebo, reduces morbidity and mortality in patients with New York Heart Association (NYHA) class II heart failure (HF).
- In the study, a similar proportion of patients in the placebo and eplerenone groups experienced adverse events. There is a lack of long-term safety data for eplerenone.
- There are no direct comparison studies between eplerenone and spironolactone, an alternative drug. The relative effectiveness and safety of these two treatments are unknown.
- Eplerenone costs \$2.61 per day. The cost-effectiveness of eplerenone compared with spironolactone, which costs \$0.14–\$0.28, is uncertain.

## Background:

Heart failure (HF) is a condition resulting from the heart's inability to meet the body's oxygen requirements and can be caused by a variety of heart abnormalities.

Severity of disease is categorized according to the New York Heart Association (NYHA) functional classification system. Class I indicates no limitations of physical activity, whereas Class IV indicates the inability to perform any physical activity without discomfort and the presence of symptoms at rest. Individuals may move among classes during periods of worsening and improvement.

Half of all HF patients have systolic HF, characterized by a reduced ejection fraction. Chronic systolic HF is treated with a combination of an angiotensin converting enzyme inhibitor (or angiotensin receptor blocker) and a beta-blocker, with the addition of diuretics and a mineralocorticoid receptor antagonist (MRA) if needed.

There are two MRAs marketed in Canada, eplerenone and spironolactone.

## 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;
  - One patient group submission.
- The CED evaluated one randomized, double-blind, placebo-controlled trial, the EMPHASIS-HF study, in patients with NYHA class II HF.
- The primary efficacy outcome was a composite of death from cardiovascular (CV) causes or first hospitalization for HF. The study also measured CV mortality, HF hospitalization, all-cause mortality and all-cause hospitalization.
- The primary composite outcome (i.e., composite of CV death or first HF hospitalization) occurred in 18.3% of patients in the eplerenone group and 25.9% in the placebo group. This translated into a statistically significant difference in the time to the primary outcome favouring eplerenone (HR, 0.63; 95% CI, 0.54-0.74).

- CV mortality occurred in 10.8% of patients in the eplerenone group and 13.5% in the placebo group. The difference in time-to-event was statistically significant favouring eplerenone (HR, 0.76; 95% CI, 0.61-0.94). The benefit on CV mortality was not observed in patients who are 75 years or older.
- For outcomes of HF hospitalization, all-cause mortality and all-cause hospitalization, the study results all favoured eplerenone.
- Adverse events occurred with similar frequency in the eplerenone (72.0%) and placebo (73.6%) groups.
- No quality of life data were collected in the EMPHASIS-HF study, and there was no analysis of changes in NYHA class over time.
- Since EMPHASIS-HF was stopped early (based on pre-specified stopping rules for the primary efficacy outcome), the long-term safety of eplerenone is uncertain.
- There are no direct head-to-head studies comparing eplerenone and spironolactone.
- Eplerenone costs \$2.61 per day. The cost-effectiveness of eplerenone compared with spironolactone, which costs \$0.14–\$0.28, cannot be determined based on the manufacturer’s economic analysis.
- One patient group submission highlighted the burden of illness associated with HF (e.g., complex treatment regimen, comorbidities, and frequent hospitalizations).
- Overall, the EMPHASIS-HF study showed that eplerenone, compared with placebo, reduced morbidity and mortality in patients with NYHA class II HF. The efficacy and cost-effectiveness of eplerenone compared with spironolactone are uncertain.

### **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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