

Committee to Evaluate Drugs (CED)

Recommendations and Reasons

Document Posted: January 2016

Nebivolol

Product: nebivolol (Bystolic®)

Class of Drugs: beta-blocker

Reason for Use: hypertension (high blood pressure)

Manufacturer: Forest Laboratories Canada Inc.

Date of Review: July 26, 2013 and April 9, 2014

CED Recommendation

The CED recommended nebivolol (Bystolic®) not be funded. Nebivolol has not been shown to provide greater efficacy or safety compared with other treatments for high blood pressure and it is more expensive.

Executive Officer Decision*

Based on the CED's recommendation, the Executive Officer decided not to fund nebivolol (Bystolic®).

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.*

Highlights of Recommendation:

- Clinical studies support that nebivolol is effective at reducing blood pressure.
- There is a lack of clinical trial data to show nebivolol improves clinically important outcomes, such as reducing stroke, heart attack or death.
- There are many medications available to treat hypertension. There is no compelling evidence to demonstrate that nebivolol is superior to the any of these.
- At a daily cost of \$1.20, nebivolol is more expensive than comparator agents from the same drug class.

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.

Nebivolol is a beta-blocker.

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 four randomized, double-blind, placebo-controlled trials and five randomized, beta-blocker-controlled trials in adults with mild to moderate essential hypertension.
- In general, nebivolol 5 mg to 20 mg once daily was more effective than placebo at reducing diastolic blood pressure (DBP) and systolic blood pressure (SBP) in patients with mild to moderate essential hypertension.
- In three of the placebo-controlled studies, all doses of nebivolol demonstrated statistically significant improvements in DBP relative to placebo. In the fourth placebo-controlled study,

combination therapy with nebivolol and hydrochlorothiazide showed greater DBP and SBP reductions compared with placebo and hydrochlorothiazide.

- Of the five beta-blocker-controlled studies, only one trial reported a statistically significant difference in DBP favouring nebivolol (5 mg to 10 mg) over atenolol (50 mg to 100 mg daily) (-11.1 mmHg versus -8.5 mmHg, respectively, $p=0.003$). None of the other trials reported statistically significant differences in DBP between nebivolol and comparators.
- Adverse events occurred more frequently in nebivolol-treated patients compared with placebo, although serious adverse events were uncommon. Headache, dizziness and fatigue were the most common complaints. The data were insufficient to assess the comparative safety and tolerability of nebivolol with other beta-blockers or other antihypertensive drugs, especially in terms of sexual dysfunction, a recognized adverse event associated with beta-blockers.
- The CED noted there is no compelling evidence to demonstrate that nebivolol is superior in efficacy or safety compared with other antihypertensive drugs.
- There is a lack of clinical trial data to show nebivolol improves clinically important outcomes, such as cardiovascular events, mortality, or health-related quality of life.
- At \$1.20 per day, nebivolol costs significantly more than other beta-blockers.
- The CED reviewed one patient group submission that outlined the impact of high blood pressure on patients' health.
- Overall, nebivolol has not been shown to provide greater efficacy or safety compared with other beta-blockers 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.

For more information, please contact:

Ministry of Health and Long-Term Care

Ontario Public Drug Programs

Hepburn Block, 9th Floor

80 Grosvenor Street, Queen's Park

Toronto, Ontario M7A 1R3

www.health.gov.on.ca/en/pro/programs/drugs/