Committee to Evaluate Drugs (CED)

Recommendations and Reasons

Document Posted: May 2015

Perampanel

Product: perampanel (Fycompa®)

Class of Drugs: antiepileptic

Reason for Use: adjunctive therapy of partial-onset seizures

Manufacturer: Eisai Limited

Date of Review: November 13, 2013

CED Recommendation

The CED recommended that perampanel (Fycompa®) be funded as an add-on treatment for partial-onset seizures according to specific criteria, in patients with epilepsy who are not satisfactorily controlled with conventional therapy. Perampanel has been shown to provide clinical benefit and, at the submitted confidential price, it costs less than its most relevant comparator.

Executive Officer Decision*

Based on the CED's recommendation and an agreement with the manufacturer, the Executive Officer decided to fund perampanel (Fycompa®) on the Ontario Drug Benefit Formulary as a Limited Use Benefit.

Funding Status*

Funded on the Ontario Drug Benefit Formulary as a Limited Use Benefit.

* *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.*

Ontario

Highlights of Recommendation:

- Three clinical trials, Study 304, Study 305 and Study 306, demonstrated that perampanel, compared to placebo, reduced seizure frequency when used as an add-on therapy in patients with partial-onset seizures.
- Perampanel use is associated with neuropsychiatric side effects.
- There is a lack of data on the long-term safety and efficacy of perampanel. There is also a lack of direct comparison studies of perampanel to other antiepileptic drugs, especially newer agents.
- Based on the manufacturer's submitted confidential price, perampanel costs less than its most relevant comparator.

Background:

Epilepsy is a chronic neurological disorder that manifests as a variety of seizure types and syndromes. There are two broad categories of epileptic seizures: partial-onset seizures (which affect 60% of patients) and generalized seizures.

The goals of treatment in epilepsy are to control seizures, avoid treatment side effects, and to maintain or restore quality of life. If seizure control is not accomplished with the initial choice of antiepileptic drug (AED), the dose of the drug may be increased (if there has been some improvement) or a second AED may be tried. Approximately 50% of patients with partial-onset seizures respond to their first trial of AED treatment, and another 20% respond to a combination of two or three AEDs. The remaining 25 to 30% of patients are considered medication resistant and are potentially candidates for epilepsy surgery. There are few effective AEDs available for patients with resistant epilepsy.

Perampanel is an oral once-daily AED indicated as adjunctive therapy in the management of partial-onset seizures in adult patients who are not satisfactorily controlled with conventional therapy.

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;
    - Submissions from three patient groups.
- The CED evaluated three double-blind, randomized, placebo-controlled, phase III superiority trials, Study 304, Study 305 and Study 306. The results of the trials demonstrated that the median percent reductions in seizure frequency per 28 days relative to baseline were statistically greater with perampanel (all doses) compared with placebo, except in the 2 mg group in Study 306.
- No statistical analyses were conducted to compare differences in quality-of- life between treatment groups.

- Perampanel is associated with neuropsychiatric disorders. The perampanel product monograph contains a warning statement regarding serious psychiatric and behavioural reactions.
- There is a lack of direct head-to-head studies comparing perampanel to other AEDs, especially newer AEDs.
- There is a lack of data on the long-term safety and efficacy of perampanel. Data are expected from an ongoing open-label extension study (307) that enrolled patients from Studies 304, 305 and 306.
- There are limited data regarding the maximum effective perampanel dose for patients who are receiving concomitant AEDs that interact with perampanel.
- Based on the confidential submitted prices for perampanel, the annual drug cost for perampanel is lower than its most relevant comparator.
- The CED considered patient input received by the CDR. The patient submissions highlighted the impact of the disease and patients' wishes for a new treatment option that will provide improved seizure control and less adverse effects than currently available alternatives. Many patients are willing to tolerate some adverse effects if they are able to obtain seizure control and return to their normal life activities.
- Overall, there is evidence from three trials to demonstrate statistically significant reductions in seizure frequency per 28 days with perampanel compared to placebo when used as an add-on therapy in the management of partial-onset seizures. At the confidential submitted price, the cost of perampanel is lower than its most relevant comparator.

Committee to Evaluate Drugs (CED)

The Committee to Evaluate Drugs (CED) is comprised of practicing physicians, pharmacists, health economics experts, 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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