



Canadian Agency for  
Drugs and Technologies  
in Health

# COMMON DRUG REVIEW

## CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

### RIVASTIGMINE PATCH

(Exelon™ Patch – Novartis Pharmaceuticals Canada Inc.)

#### Description:

Exelon™ Patch contains rivastigmine, a reversible cholinesterase inhibitor that is approved for the symptomatic treatment of patients with mild to moderate dementia of the Alzheimer's type.

#### Dosage Forms:

Exelon Patch 5 contains 9 mg/5 cm<sup>2</sup> and releases 4.6 mg/24 hours. Exelon Patch 10 contains 18 mg/10 cm<sup>2</sup> and releases 9.5 mg/24 hours. The recommended dose is one patch applied daily.

#### Recommendation:

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that Exelon Patch not be listed.

#### Reasons for the Recommendation:

1. Compared with placebo, Exelon Patch results in statistically significant, but clinically very small differences in some of the outcomes measures considered important in Alzheimer's disease.
2. Exelon Patch is associated with a higher incidence of treatment-related adverse events when compared with placebo.
3. The Committee had concerns regarding the cost-effectiveness of Exelon Patch relative to best supportive care.

#### Summary of Committee Considerations:

The Committee considered a systematic review of double-blind randomized controlled trials (RCTs) in patients with mild to moderate dementia of the Alzheimer's type. One trial of 24 weeks duration comparing Exelon Patch 10 with oral rivastigmine 6 mg given twice daily or placebo met the inclusion criteria for the systematic review. Outcome measures for patients treated with Exelon Patch 10 and rivastigmine oral were similar. Compared to placebo, Exelon Patch 10 resulted in statistically significant, but clinically small differences, in the following measures:

- Cognition: The mean change on the 70-point Alzheimer's Disease Assessment Scale – Cognitive (ADAS-Cog) was 1.6 units and on the 30-point Mini-Mental State Examination was 1.1 units. Previous studies of other cholinesterase inhibitors have reported mean changes in the ADAS-Cog of between 2.5 and 3.3 when compared with placebo.
- Daily function: The mean change on the 78-point Activities of Daily Living Scale was 2.2 units.

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- Global physician assessment: The mean change on the 7-point Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change scale was 0.3 units.

There were no statistically significant differences on the Neuropsychiatric Index, a measure of behaviour, and the Ten Point Clock-drawing test compared with placebo. Quality of life was not measured. A higher proportion of caregivers reported a preference for the patch over the oral formulation, although this preference may be related to ease of use, such as once daily administration and a simple titration schedule, which would be similar to oral cholinesterase inhibitors other than rivastigmine.

There were no statistically significant differences between groups in serious adverse events and withdrawals due to adverse events. There was a statistically significantly higher rate of patients experiencing at least one suspected treatment-related adverse event in the rivastigmine capsule group (44%) and the Exelon Patch 10 group (25%) than in the placebo group (16%). There was less nausea and vomiting with the Exelon Patch compared to rivastigmine capsules.

Exelon Patch costs \$4.29 per day, regardless of strength, which is less costly than rivastigmine capsules (\$4.88 per day), donepezil (\$4.78 per day), galantamine (\$4.73 per day) and memantine (\$4.59 per day).

**Of Note:**

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.
2. The Committee was aware of the lack of evidence to support the long-term benefits of cholinesterase inhibitors on clinically important outcomes and was concerned about their uncertain cost-effectiveness in the treatment of Alzheimer's disease.
3. It is anticipated that the patent for oral rivastigmine capsules will expire in 2009. As such, the projected cost savings by funding Exelon Patch may not be sustained.

**Background:**

CEDAC provides formulary listing recommendations to publicly funded drug plans. Recommendations are based on an evidence-based review of the medication's effectiveness and safety and an assessment of its cost-effectiveness in comparison to other available treatment options. For example, if a new medication is more expensive than other treatments, the Committee considers whether any advantages of the new medication justify the higher price. If the recommendation is not to list a drug, the Committee has concerns regarding the balance between benefit and harm for the medication, and/or concerns about whether the medication provides good value for public drug plans.

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