MEMANTINE  
(Ebixa - Lundbeck Canada Inc.)

Description:
Memantine is a noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist that, in part, inhibits activation of NMDA receptors by glutamate. Health Canada has granted memantine a Notice of Compliance with conditions as monotherapy or as adjunctive therapy with cholinesterase inhibitors for the symptomatic treatment of patients with moderate to severe dementia of the Alzheimer’s type.

Dosage Forms:
10 mg tablets.

Recommendation:
The Canadian Expert Drug Advisory Committee (CEDAC) recommends that memantine not be listed.

Reasons for the recommendation:
1. The committee considered the efficacy findings from three randomized controlled trials (RCTs), two comparing memantine to placebo (24 - 28 weeks) and one comparing memantine plus donepezil to donepezil alone (24 weeks) in patients with moderate to severe Alzheimer’s disease (MMSE 3-14) who were residing in the community. No randomized trials compared memantine to donepezil, galantamine or rivastigmine. Two of the three RCTs reported statistically significant, but numerically small, group mean improvement in instruments measuring activities of living and cognition. There is insufficient scientific evidence to establish the clinical importance of these small differences. One trial reported no statistically significant improvement in functional, cognitive, behavioural and global assessments.

2. Time to institutionalization was only reported in one study in which very low institutionalization rates were observed (1 of 90 patients on memantine vs 5 of 76 patients on placebo) during the six month study.

3. The pharmacoeconomic model submitted by the manufacturer, comparing memantine to standard care, was based on two important assumptions: reduced hospitalization and
institutionalization for patients treated with memantine. However, the RCTs did not find any differences in these clinical endpoints in favour of memantine.

**Of Note:**
1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.

2. Health Canada has granted a Notice of Compliance with conditions (NOC/c) for memantine. As part of the NOC/c, Health Canada has requested that a RCT be performed to provide additional efficacy and safety data. The manufacturer’s Product Monograph reports numerically more patients with chest pain, dyspnea and heart failure, and includes warnings against use of memantine in patients with cardiac conditions and seizure disorders.