Comprehensive Research Plan:

Cognitive enhancers for the treatment of Alzheimer's disease

Pharmacoeconomic Unit

February 10, 2015

ODPRN Drug Class Review Proposal: Pharmacoeconomics Unit

Study Title: Cognitive enhancers for the treatment of Alzheimer's disease

Research Questions

RQ1.   What is the current evidence for the cost-effectiveness of cognitive enhancers, as compared with placebo, other cognitive enhancers, or best supportive care, for the treatment of Alzheimer's disease (AD)?

RQ2.   Based on a de novo economic model, what is the cost-effectiveness of cognitive enhancers versus placebo, other cognitive enhancers, or best supportive care for the treatment of AD?

RQ3.   What is the budget impact of alternative policies for reimbursing cognitive enhancers versus placebo, other cognitive enhancers, or best supportive care for the treatment of AD?

RQ4.   Based on a de novo economic model, what is the cost-effectiveness of alternative policies for reimbursing cognitive enhancers versus placebo, other cognitive enhancers, or best supportive care for the treatment of AD?

Methods

Systematic Review of Published Economic Evaluations

To address RQ1 we will conduct a systematic review of the available literature on the cost-effectiveness of pharmacotherapies for the treatment of Alzheimer's disease (AD). Specifically, pharmacologic treatments will be limited to cognitive enhancers approved for use in Canada (donepezil, galantamine, rivastigmine, memantine), as compared with other cognitive enhancers, placebo and/or best supportive care.

A search of the medical literature will be conducted in MEDLINE (OVID interface, indexed, in-process and other non-indexed citations, 1946 onwards), EMBASE (OVID interface, 1947 onwards), NHS EED, and Tufts CEA registry in order to capture all relevant literature based on the NHS EED recommended search strategy. This literature search will be carried out by coupling a standard search strategy for identifying economic studies with the clinical search terms adopted by the clinical review. Moreover, a search of grey literature sources such as the CADTH and NICE websites, as well as hand-searching of reference lists of retrieved studies will supplement the electronic database search.

Two independent reviewers will screen the titles and abstracts of citations retrieved by the initial literature search, and potentially relevant full-text articles will be obtained and screened for inclusion in the economic appraisal by the same two reviewers. Any disagreements will be resolved by discussion or the involvement of a third reviewer.

Extracted studies will then be further reviewed with studies excluded for lack of context or for not being full economic evaluations.

Critical appraisal of economic evidence will entail identifying common methodological issues within included studies. Each study will be assessed through a three step process: initial assessment for validity,

assessment of study quality, and assessment of study's pertinence to the decision question. Comparators will include the cholinesterase inhibitor drug class (donepezil, galantamine and rivastigmine), memantine, placebo, and/or supportive care.

Emphasis will be placed on the strength and quality of evidence addressing the cost-effectiveness of cognitive enhancers versus placebo, other cognitive enhancers, or best supportive care in the treatment of AD.

De novo Economic Evaluation

We will develop a de novo economic model to assess the cost-effectiveness of alternative pharmacotherapies for the treatment of Alzheimer's disease (AD).

The economic model will build on previous analyses. We will construct a Markov model which will model disease progression. Natural history data relating to disease progression will be combined with treatment effectiveness data from the clinical review conducted as part of this class review. Specific data required will relate to the relative effect of therapies on cognition and function as well as MMSE Score, as measured by validated scales.

Costs and utilities associated with disease progression will be derived from the literature. Analysis will be conducted from the perspective of the Ministry of Health with results presented as incremental cost per quality adjusted life years gained. Detailed deterministic sensitivity analysis will be conducted along with Monte Carlo simulation methods to determine decision uncertainty.

Reimbursement Based Budget Impact Analysis

The aim of this portion of the pharmacoeconomic review is to develop a budget impact analysis that will facilitate the reimbursement decision-making process. Emphasis will be placed on identifying the budget impact of alternative approaches to the current reimbursement status of pharmacologic treatments for patients with AD. This will be achieved through a three stage process.

1. Forecasting of current expenditure for AD pharmacotherapies.

   We will obtain data on current usage of cognitive enhancers for treating AD from OPDP to allow identification of the number of claims, number of claimants, total costs, and drug unit costs in a given year (broken down quarterly).

2. Identification of candidate reimbursement strategies

   The second stage will involve identifying alternative approaches to reimbursement of combination therapies. This will rely heavily on strategies identified during the scoping assessment along with further consultation with OPDP. Reimbursement strategies could be general (applied to all products) or specific (targeted at specific products), and consideration may be given to the availability of generics and changes to EAP listing.

3. Assessment of budget impact of candidate scenarios

   Using the techniques adopted in step 1, we will forecast the budget expenditure on pharmacotherapies for the treatment of AD for each alternative reimbursement strategy.

Reimbursement Based Economic Evaluation

The aim of this component is to utilize data from the de novo economic model to allow identification of the optimal reimbursement criteria through considering cost-effectiveness as criteria with a focus on reimbursement strategies not just interventions. Analysis will identify the cost-effectiveness of alternative approaches to the current reimbursement status of cognitive enhancers for treating patients with AD.

Deliverables

We will provide a written report detailing methods adopted, results, discussion and summary policy recommendations. The report will comprise a two-page executive summary followed by a detailed technical report.

Timelines

Our work will commence on acceptance of this proposal. The review of economic evidence will be completed within 6 weeks of project onset. The de novo economic model will be developed and populated within 12 weeks of commencement, and forecasting of drug expenditures will be completed within the same time frame. Both of these components are scheduled to coincide with the completion of the clinical review. Moreover, reimbursement based economic modelling will be completed between 12 and 16 weeks to allow delivery of an aligned final report at 16 weeks. Reanalyses and revisions of the final report will be available 4 weeks after receipt of stakeholder reviews.