Comprehensive Research Plan:

Treatment of Chronic Hepatitis B

Pharmacoeconomic Unit

November 7, 2014

ODPRN Drug Class Review:

Pharmacotherapies in the Treatment of Hepatitis B

Summary Pharmacoeconomic Proposal

Research Questions

RQ1.   What is the current evidence for the cost-effectiveness of pharmacotherapies in the treatment of Hepatitis B?

RQ2.   Based on a de novo economic model, what is the cost-effectiveness of pharmacotherapies in the treatment of Hepatitis B?

RQ3.   What is the budget impact of alternative policies for reimbursing pharmacotherapies in the treatment of Hepatitis B?

RQ4.   Based on the de novo economic model, what is the cost effectiveness of alternative policies for reimbursing pharmacotherapies in the treatment of Hepatitis B?

Methods

RQ1   Systematic Review of Published Economic Evaluations

We will conduct a review of the available literature on the cost-effectiveness of pharmacotherapies in the treatment of Hepatitis B.

RQ2   De Novo Economic Model

We will develop a new economic model assessing the cost effectiveness of pharmacotherapies in the treatment of Hepatitis B.

RQ3   Reimbursement Based Budget Impact Analysis

We will develop a model which will identify the budget impact of alternative policies relating to pharmacotherapies in the treatment of Hepatitis B. Analysis will identify the change in the forecasted drug budget for the next three years associated with different reimbursement policies and will be discussed in conjunction with any impact on clinical effectiveness.

RQ4   Reimbursement Based Economic Evaluation

We will use the results from the de novo economic model to identify the cost effectiveness of the alternative policies relating to pharmacotherapies in the treatment of Hepatitis B, as identified in RQ3.

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.

ODPRN Drug Class Review:

Pharmacotherapies in the Treatment of Hepatitis B

Detailed Pharmacoeconomic Proposal

Research Questions

RQ1. What is the current evidence for the cost-effectiveness of pharmacotherapies in the treatment of Hepatitis B?

RQ2. Based on a de novo economic model, what is the cost-effectiveness of pharmacotherapies in the treatment of Hepatitis B?

RQ3. What is the budget impact of alternative policies for reimbursing pharmacotherapies in the treatment of Hepatitis B?

RQ4. Based on the de novo economic model, what is the cost effectiveness of alternative policies for reimbursing pharmacotherapies in the treatment of Hepatitis B?

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 in the treatment of Hepatitis B. Therapies will be limited to privately and publically-funded treatment prescriptions dispensed in Canada; standard interferon, pegylated interferon, lamivudine, adefovir, entecavir, telbivudine and tenofovir. Focus will be on the cost effectiveness of treatments as both first and second line therapies.

A search of literature from 1948 to present in Medline (indexed, in-process and other non-indexed), Embase, NHS EED and Tufts CEA registry will be conducted in order to capture all relevant literature based on the NHS EED recommended search strategy. A standard search strategy for identification of economic studies will be linked to the clinical search terms adopted by the clinical review. In addition, the reference lists of retrieved studies will be hand searched and any additional studies identified by stakeholders will be considered for inclusion.

Two reviewers will first review the abstracts of studies identified by the initial literature search in order to identify potential articles for inclusion within the critical appraisal. Any disagreements will be resolved through consensus with erring on the side of caution through inclusion.

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

The critical review will identify common methodological issues within studies. Each study will be assessed through a three step process: initial assessment for validity, assessment of study quality, assessment of study's pertinence to the decision question. Comparators will include standard interferon, pegylated interferon, lamivudine, adefovir, entecavir, telbivudine and tenofovir. Adefovir, entecavir, telbivudine and tenofovir will be evaluated as both second line therapies based on current OPDP listing status as well as first line therapies. Where relevant, generic costs will be incorporated.

Focus will be on the strength and quality of evidence addressing the cost-effectiveness of pharmacotherapies in the treatment of Hepatitis B.

De novo Economic Evaluation

We will develop a de novo economic model to assess the cost effectiveness of alternative pharmacotherapies in the treatment of Hepatitis B.

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 virologic response (undetectable levels of HBV DNA); biochemical response (normal ALT levels) and the absence of HBeAg or HBsAg detection.

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 focus for this component of the proposal is to develop a budget impact analysis which will help facilitate the reimbursement decision. Focus will be on identifying the budget impact of alternative approaches to the current reimbursement status of pharmacotherapies in the treatment of Hepatitis B. This will be achieved through a three stage process:

1. Forecasting of current expenditure for pharmacotherapies for Hepatitis B

    We will obtain data on current usage of pharmacotherapies in the treatment of Hepatitis B 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. Strategies could be general – applied to all products– or specific – targeted at specific products. Consideration of the availability of generics and changes to EAP listing may be considered.

3. Assessment of budget impact of candidate strategies

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

<u>Reimbursement Based Economic Evaluation</u>

The focus for this component of the proposal 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 pharmacotherapies in the treatment of Hepatitis B.

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

On acceptance of this proposal, work will commence. The review of economic evaluations will be completed within 6 weeks of the commencement. The de novo economic model will be developed and populated within 12 weeks of commencement. The forecasting of drug expenditures will be completed within 12 weeks of receipt of OPDP expenditure data. Both of these components are timed to coincide with the completion of the clinical review. The reimbursement based economic modelling will be completed four weeks after receipt of the companion systematic review scheduled for 12 weeks, to allow timely delivery of an aligned final report. Any reanalyses and a revised final report will be available 4 weeks after receipt of stakeholder reviews.