ODPRN ONTARIO DRUG POLICY RESEARCH NETWORK

Drug Class Review: Inhaled corticosteroids (ICS) + long-acting beta-agonists (LABA) combination products for treatment of chronic obstructive pulmonary disease (COPD)

Comprehensive Research Plan: Pharmacoeconomics Unit

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30 Bond Street, Toronto ON, M5B 1W8 www.odprn.ca info@odprn.ca

Study Questions:	1. What is the current evidence for the cost-effectiveness of ICS in combination with LABA for chronic treatment of COPD compared to single or combination therapies incorporating LABA, LAMA and ICS? 2. Based on a de novo economic model, what is the cost-effectiveness of ICS in combination with LABA for chronic treatment of COPD compared to single and combination therapies incorporating LABA, LAMA and ICS? 3. What is the economic impact of alternatives policies for reimbursing ICS in combination with LABA for chronic treatment of COPD?
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 ICS in combination with LABA for chronic treatment of COPD compared to single or combination therapies incorporating LABA, LAMA and ICS. A search of the medical literature will be conducted 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. Two reviewers will first review the abstracts of studies identified by the initial literature search literature searches 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. Focus will be on the strength and quality of evidence addressing the cost-effectiveness of ICS in combination with LABA compared to single or combination therapies incorporating LABA, LAMA and ICS at different stages of disease severity.

De novo Economic Evaluation

We will develop a de novo economic model to assess the cost effectiveness of alternative reimbursement strategies for ICS in combination with LABA compared the current strategy. The economic model will build on previous analyses. We will construct a Markov model which will model disease progression combined with rates of exacerbations and death. Natural history data relating to disease progression will be combined with treatment effectiveness and adverse event data from the clinical review conducted as part of this class review. Costs and utilities associated with disease severity, treatment related adverse events and exacerbations 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 Economic Assessment

The focus for this component of the proposal is to develop an applied, policy-oriented economic model which will help facilitate the reimbursement decision. Focus will be on identifying the optimal reimbursement criteria through considering both budget impact and clinical effectiveness as criteria with a focus on reimbursement strategies not just interventions. Analysis will identify the budget impact of alternative approaches to the current reimbursement status of ICS in combination with LABA (i.e. coverage of single products but not combination products). This will be achieved through a three stage process.

1. Forecasting of expenditure for COPD drug therapies the next three years
   We will obtain data on current usage of ICS, LABA and LAMA both as single and combination therapies for the treatment of chronic COPD 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). We will first standardize drug costs to the current year drug costs.
   We will use time series analyses to forecast the drug costs for the next three years adopting three approaches: simple linear interpolation (naïve approach), linear regression and logistic regression. For regression methods we will include the number of COPD products available on the formulary as a potential independent variable to assess the impact of market expansion.

	2. Identification of candidate reimbursement strategies The second stage will involve identifying alternative approaches to reimbursement of ICS combination with LABA. This will rely heavily on strategies identified during the scoping assessment along with further consultation with OPDP. Strategies could include coverage of combination therapies either as general benefit or more restricted access. Strategies could be general – applied to all combination therapies – or specific – targeted at specific combinations. 3. Assessment of budget impact of candidate strategies Using the techniques adopted in step 1 we will forecast the budget expenditure on COPD treatments for each alternative reimbursement strategy. Results will be presented in terms of budget impact and cost effectiveness using the de novo economic model.
Deliverables	We will provide a written report detaining methods adopted, results, discussion and summary policy recommendations. The report will comprise a two page executive summary followed by a detailed technical report. In addition, we will provide a fully executable excel based reimbursement economic model.
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 commencement. Both of these components are timed to coincide with the completion of the clinical review. The reimbursement based economic modelling will be completed between 12 and 16 weeks to allow delivery of an aligned final report at 16 weeks. Any reanalysis and a revised final report will be available 4 weeks after receipt of stakeholder reviews.