

Low molecular weight heparins (LMWH) for the prophylactic treatment of venous thromboembolism (VTE)

FINAL COMPREHENSIVE RESEARCH PLAN

September 28, 2015

Study Team: Pharmacoeconomic Unit

Research Questions

- RQ1a. What is the current evidence for the comparative cost-effectiveness of low-molecular weight heparins (LMWH), as compared with each other, warfarin, mechanical intervention, parenteral anticoagulation or placebo, for the *prevention* of deep vein thrombosis (DVT) or pulmonary embolism (PE) in patients with cancer?
- RQ1b. What is the current evidence for the comparative cost-effectiveness of LMWH, as compared with each other, warfarin, mechanical intervention, parenteral anticoagulation or placebo, for the *treatment* of deep vein thrombosis (DVT) or pulmonary embolism (PE) in patients with cancer?
- RQ2a. If necessary and feasible, based on a de novo economic model, what is the comparative cost-effectiveness of LMWH, as compared with each other, warfarin, mechanical intervention, parenteral anticoagulation or placebo, for the *prevention* of DVT or PE in patients with cancer?
- RQ2b. If necessary and feasible, based on a de novo economic model, what is the comparative cost-effectiveness of LMWH, as compared with each other, warfarin, mechanical intervention, parenteral anticoagulation or placebo, for the *treatment* of deep vein thrombosis (DVT) or pulmonary embolism (PE) in patients with cancer?
- RQ3a. What is the budget impact of alternative policies for reimbursing LMWH for the *prevention* of DVT or PE in patients with cancer?
- RQ3b. What is the budget impact of alternative policies for reimbursing LMWH for the *treatment* of DVT or PE in patients with cancer?
- RQ3c. If necessary and feasible, what is the impact of alternative policies for reimbursing LMWH for indications other than those listed above?
- RQ4a. If necessary and feasible, based on a de novo economic model, what is the cost-effectiveness of alternative policies for reimbursing LMWH for the *prevention* of DVT or PE in patients with cancer?
- RQ4b. If necessary and feasible, based on a de novo economic model, what is the cost-effectiveness of alternative policies for reimbursing LMWH for the *treatment* of DVT or PE in patients with cancer?

Methods

Systematic Review of Published Economic Evaluations

To address RQ1a and RQ1b, we will conduct a systematic review of the available literature on the cost-effectiveness of pharmacotherapy options for the treatment and prevention of deep vein thrombosis (DVT) or pulmonary embolism (PE) in patients with cancer. Therapeutic options will include warfarin, mechanical prophylaxis, parenteral anticoagulation or placebo.

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, 1980 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.

Emphasis will be placed on the strength and quality of evidence addressing the cost-effectiveness of LMWH (dalteparin, enoxaparin, nadroparin, tinzaparin), as compared with each other, warfarin, mechanical prophylaxis, parenteral anticoagulation or placebo, for the treatment of DVT or PE and prophylactic management of patients with cancer patients.

De novo Economic Evaluation

If necessary and feasible, we will develop one or two de novo economic models to assess the cost-effectiveness of alternative pharmacotherapies for the treatment and prevention of DVT or PE in patients with cancer.

The economic models will build on previous analyses. Disease progression within each patient group will be modeled using Markov modeling techniques. Natural history data relating to disease progression among cancer patients will be combined with treatment effectiveness data from the clinical review conducted as part of this class review.

Costs and utilities associated with disease progression within each patient group will be derived from the literature. Analysis will be conducted from the perspective of the Ministry of Health, and results will be presented as incremental cost per quality-adjusted life years (QALY) 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 LMWH for the treatment or prevention of DVT or PE in patients with cancer. This will be achieved through a two stage process.

1. Identification of candidate reimbursement strategies
 - The first stage will involve identifying alternative approaches to reimbursement. 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.

2. Assessment of budget impact of candidate scenarios
 - We will forecast the budget expenditure on LMWH for each alternative reimbursement strategy.

If necessary and feasible, the impact of alternative policies for reimbursing LMWH for indications other than those listed above will be assessed, using the approach described above. This will be determined in discussion with the research team at the initiation of the project.

Reimbursement-based Economic Evaluation

If a de novo economic model was developed for either indication, 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 and not just interventions. Analysis will identify the cost-effectiveness of alternative approaches to the current reimbursement status of pharmacotherapies for the treatment and prevention of DVT or PE in patients with cancer.

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 the initial 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.