

Low Molecular Weight Heparin

Stakeholder Review: Comprehensive Research Plans

September 2015

GENERAL

Comment:

1. In the research outline for Treatment of symptomatic acute VTE in patients with cancer, the plan has search criteria for specific LMWH limited to Dalteparin only. Tinzaparin should also be included in the search criteria, as there is a substantial body of evidence to show its safety and efficacy in this patient population
2. Use of enoxaparin in prophylaxis for colorectal surgery, high risk abdominal surgery, gynecological and urological surgeries is indicated in the product monograph. Enoxaparin should be included in the review for the use in the prevention (prophylaxis) of VTE in patients with cancer as well as post-operative prophylaxis of VTE for patients undergoing hip or knee surgery (who cannot use warfarin)
3. Treatment of Deep Venous Thromboembolism (DVT) in non-cancer patients Clinical efficacy of enoxaparin is supported by studies and guidelines in this patient population for treatment of venous thromboembolism (VTE).
4. We ask that each of your Research Units include both nadroparin and fondaparinux in their analyses. Both products are cited widely and favourably in the literature, including in Clinical Practice Guidelines and pharmaco-economic analyses for a range of applications.

Response: *We will be including all LMWHs (i.e., dalteparin, enoxaparin, nadroparin, tinzaparin, fondaparinux) in the systematic review of the guidelines for each of the identified indications. As well, the pharmacoepidemiology team will be analyzing data for all LMWHs.*

Comment: It would be important to consider the role of LMWH for the treatment of not only acute deep vein thrombosis (DVT) or prevention of DVT, but also for Pulmonary Embolism (PE). Pulmonary embolism is indeed the consequence of a symptomatic or an asymptomatic DVT. Both of these clinical events, DVT and PE could be defined under the broader term Venous Thromboembolism (VTE).

Response: *The broader term “venous thromboembolism” will be used in the report when appropriate. In their review of guidelines, the systematic review team will provide summaries for DVT/PE or VTE, depending on how the guidelines are structured.*

Comment: Many pregnant women who previously experienced VTE, or at who are at risk of pre-eclampsia, often receive a LMWH as VTE prophylaxis. This could be an additional topic of interest to be included in this class review.

Response: *A review of guidelines will be conducted by the systematic review team for pregnant patients. As well, trends in prescribing for publicly-funded LMWHs in Ontario, including use in pregnant or lactating females (Limited Use code 187) will be reviewed by the pharmacoepidemiology team.*

Comment: It was recommended that the pediatric population be included as they are patients at risk of thromboembolism in certain diseases.

Response: *Due to the rapid review period as well as the limited use of LMWH in the pediatric population, we will be focusing our drug class review in the adult population.*

Qualitative Research Team

Comment: Many stakeholders will be recruited to have their experience of prescription and use of LMWH. In the draft Comprehensive Research Plan, specialists are listed as primary care physicians, hematologists, internal medicine physician, pharmacists and oncologists. We would like to suggest adding surgeons and emergency medicine physicians to this list because they are regularly prescribing anticoagulants.

Response: *Thank you for your comment. We have added emergency medicine physicians to our list of specialists.*

Identified stakeholders for the low molecular weight heparins review include primary care practitioner (PCP), pharmacists, hematologists, internal medicine, emergency medicine, and oncologists who are involved in the prescription and dispensing of low molecular weight heparins.

Systematic Review Unit

Comment: At present, the Systematic Review unit indicated that fondaparinux will be assessed only for post-operative prophylaxis of VTE in patients undergoing orthopaedic surgery of the lower limbs. Fondaparinux is also indicated for:

- Prophylaxis of VTE in general surgery, including cancer surgery
- Treatment of DVT and PE
- Management of ACS NSTEMI

Response: *Thank you for your input. While carrying out our review of guidelines, we will be considering all treatments and comparators. Limitations on LMWH and comparators in the original draft research plan (Table 1) have been removed to avoid confusion or exclusion of relevant drugs.*

Comment: We also ask that your Systematic Review Team include nadroparin in its review of agents for prophylaxis of DVT and PE in patients undergoing both general and orthopaedic surgery as this is also an indicated use.

Response: *Thank you for your input. While carrying out our review of guidelines, we will be considering all treatments and comparators. Limitations on LMWH and comparators in the original draft research plan (Table 1) have been removed to avoid confusion or exclusion of relevant drugs.*

Comment: We recommend inclusion of a specific category for the use of LMWH in the management of Acute Coronary Syndrome (ACS) as this is not presently included in the list of indications for review.

Response: *For this drug class review, we are focusing on the outpatient use of LMWH. Since patients with ACS are primarily managed as inpatients, we will not be including this indication in our review.*

Pharmacoeconomics Team

Comment: We ask that Aspen Pharmacare be considered in the pharmacoeconomic analysis. This is a new company in the Canadian market, and is in the process of re-evaluating its pricing of both nadroparin and fondaparinux. We anticipate bringing the pricing of both products in Ontario into line with other available LMWH over the coming months.

Response: *Thank you for your comment. We will consider all LMWH products in our pharmacoeconomic analysis, as they apply to the indications that we will be reviewing.*