Pharmacological Treatments for Type II Heparin-Induced Thrombocytopenia: Clinical Effectiveness
Authors: Kelsey Seal, Nina Frey


Acknowledgments:

Disclaimer: The information in this document is intended to help Canadian health care decision-makers, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. While patients and others may access this document, the document is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose. The information in this document should not be used as a substitute for professional medical advice or as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process. The Canadian Agency for Drugs and Technologies in Health (CADTH) does not endorse any information, drugs, therapies, treatments, products, processes, or services.

While care has been taken to ensure that the information prepared by CADTH in this document is accurate, complete, and up-to-date as at the applicable date the material was first published by CADTH, CADTH does not make any guarantees to that effect. CADTH does not guarantee and is not responsible for the quality, currency, propriety, accuracy, or reasonableness of any statements, information, or conclusions contained in any third-party materials used in preparing this document. The views and opinions of third parties published in this document do not necessarily state or reflect those of CADTH.

CADTH is not responsible for any errors, omissions, injury, loss, or damage arising from or relating to the use (or misuse) of any information, statements, or conclusions contained in or implied by the contents of this document or any of the source materials.

This document may contain links to third-party websites. CADTH does not have control over the content of such sites. Use of third-party sites is governed by the third-party website owners’ own terms and conditions set out for such sites. CADTH does not make any guarantee with respect to any information contained on such third-party sites and CADTH is not responsible for any injury, loss, or damage suffered as a result of using such third-party sites. CADTH has no responsibility for the collection, use, and disclosure of personal information by third-party sites.

Subject to the aforementioned limitations, the views expressed herein are those of CADTH and do not necessarily represent the views of Canada’s federal, provincial, or territorial governments or any third party supplier of information.

This document is prepared and intended for use in the context of the Canadian health care system. The use of this document outside of Canada is done so at the user’s own risk.

This disclaimer and any questions or matters of any nature arising from or relating to the content or use (or misuse) of this document will be governed by and interpreted in accordance with the laws of the Province of Ontario and the laws of Canada applicable therein, and all proceedings shall be subject to the exclusive jurisdiction of the courts of the Province of Ontario, Canada.

The copyright and other intellectual property rights in this document are owned by CADTH and its licensors. These rights are protected by the Canadian Copyright Act and other national and international laws and agreements. Users are permitted to make copies of this document for non-commercial purposes only, provided it is not modified when reproduced and appropriate credit is given to CADTH and its licensors.

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada’s health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada’s federal, provincial, and territorial governments, with the exception of Quebec.
Research Questions

1. What is the clinical effectiveness the use of fondaparinux to treat patients with type II heparin-induced thrombocytopenia?

2. What is the clinical effectiveness the use of direct oral anticoagulants to treat patients with type II heparin-induced thrombocytopenia?

Key Findings

One systematic review and eight non-randomized studies were identified regarding the clinical effectiveness of fondaparinux and/or direct oral anticoagulants to treat patients with type II heparin-induced thrombocytopenia.

Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials and non-randomized studies. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between Jan 1, 2012 and April 4, 2017. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Patients with type II heparin-induced thrombocytopenia</th>
</tr>
</thead>
</table>
| Intervention | Q1: Fondaparinux  
               Q2: Direct oral anticoagulants (DOACs) |
| Comparator | Q1-2: No comparator;  
               Any comparator |
| Outcomes | Q1-2: Clinical effectiveness, safety |
| Study Designs | Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies |
Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials and non-randomized studies.

One systematic review and eight non-randomized studies were identified regarding the clinical effectiveness of fondaparinux and/or direct oral anticoagulants to treat patients with type II heparin-induced thrombocytopenia. No relevant health technology assessments or randomized controlled studies were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

One systematic review and eight non-randomized studies (NRS) were identified regarding the clinical effectiveness of fondaparinux and/or direct oral anticoagulants to treat patients with heparin-induced thrombocytopenia (HIT).

One systematic review and five NRS reported on the clinical effectiveness regarding the use of fondaparinux to treat patients with heparin-induced thrombocytopenia. Results from the systematic review indicated that the majority of cases (86%) improved clinically after being treated with fondaparinux. The authors also concluded that the risk of thrombosis and bleeding with fondaparinux use in cardiac surgery patients with HIT are low and largely comparable to outcomes reported in the literature with other interventions. The authors from one non-randomized study observed that fondaparinux was similar in efficacy and safety when compared to direct thrombin inhibitors for the treatment of suspected HIT. In another NRS, results indicated that fondaparinux may be a safe treatment option for patients with a left ventricular assist device who are suspected of HIT. Fondaparinux appeared to be a good alternative to heparin in postoperative cardiac surgery patients in one NRS, while another NRS examined patients with isolated HIT who were treated prophylactically with fondaparinux in patients with subarachnoid hemorrhage. The authors of another study did not observe any difference in incidence of new thromboses, incidence or hemorrhage, or hospice/death when compared to a control group, but patients who were treated with fondaparinux had fewer poor treatment related effects. The authors of another identified NRS observed that fondaparinux was well tolerated and safe as prophylaxis and as therapy in patients with acute, suspected, or antecedent HIT.

Two NRS examined the clinical effectiveness regarding the use of fondaparinux and direct oral anticoagulants. The authors from one study observed that fondaparinux had similar efficacy and safety as argatroban and danaparoid in patients with suspected HIT. The other study compared fondaparinux with argatroban, lepirudin, and danaparoid, with results indicating that the efficacy and safety of fondaparinux for HIT treatment needs to be studied further.

One NRS reported on the clinical effectiveness regarding the use of direct oral anticoagulants to treat patients with type II heparin-induced thrombocytopenia. The authors observed that, in patients with HIT, argatroban followed by administration of a new oral anticoagulants is safe and effective to prevent of thrombosis and normalize platelet count.
It is important to note that most of the studies identified in this report did not specify the whether patients had type I or II heparin-induced thrombocytopenia.

**References Summarized**

**Health Technology Assessments**

No literature identified.

**Systematic Reviews and Meta-analyses**


**Randomized Controlled Trials**

No literature identified.

**Non-Randomized Studies**


Appendix — Further Information

Previous CADTH Reports

   https://www.cadth.ca/pharmacological-options-patients-type-ii-heparin-induced-thrombocytopenia-clinical-effectiveness

Non-Randomized Studies

Alternate Interventions

   PubMed: PM23461610

Case Series

   PubMed: PM23167229

Review Articles

   PubMed: PM28301915

   PubMed: PM27102287

   PubMed: PM26695419

   PubMed: PM25855702

   PubMed: PM24861800