PCS9 Inhibitors for Hyperlipidemia: Comparative Clinical Effectiveness
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**Acknowledgments:**

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**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 comparative clinical effectiveness of evolocumab versus alirocumab for the treatment of adults with heterozygous familial hyperlipidemia (HeFH) on maximally tolerated statin therapy who require additional lowering of low density lipoprotein cholesterol (LDL-C)?

2. What is the comparative clinical effectiveness of evolocumab versus alirocumab for the treatment of adults with clinical atherosclerotic cardiovascular disease (CVD) on maximally tolerated statin therapy who require additional lowering of low density lipoprotein cholesterol (LDL-C)?

Key Findings

Four systematic reviews, three systematic reviews with meta-analysis, and one non-randomized study were identified regarding PCSK-9 inhibitors for hyperlipidemia.

Methods

A limited literature search was conducted on key resources including PubMed, Medline, Embase, 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. No filters were applied to limit retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2012 and May 2, 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

| Population                | Q1: Adults with heterozygous familial hyperlipidemia (HeFH) on maximally tolerated statin therapy who require additional lowering of low density lipoprotein cholesterol (LDL-C)  
|                          | Q2: Adults with clinical atherosclerotic cardiovascular disease (CVD) on maximally tolerated statin therapy who require additional lowering of low density lipoprotein cholesterol (LDL-C) |
| Intervention             | Evolocumab |
| Comparator               | Alirocumab |
Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Clinical effectiveness, including:</th>
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<tbody>
<tr>
<td></td>
<td>• Mortality</td>
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<td>• Morbidity (cardiovascular-related; i.e., cardiovascular events, hospitalizations, minimally-invasive cardiovascular interventions [e.g., PCI])</td>
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<td>• Changes in LDL-C</td>
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<td>• Health related quality of life (HRQoL)</td>
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<td>• Health care resource utilization</td>
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<td>• Vascular imaging</td>
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<td>• Other laboratory parameters (i.e., Apo-B, LP-A, Non-HDL-C, TG, VLDL-C); Harms outcomes (e.g., adverse events, serious adverse events, withdrawal due to adverse events; notable harms include: immune reactions, injection site reactions, muscle symptoms, neurocognitive impairment, Hepatitis C, elevated liver enzymes)</td>
</tr>
</tbody>
</table>

| 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.

Four systematic reviews, three systematic reviews with meta-analysis, and one non-randomized study were identified regarding PCSK-9 inhibitors for hyperlipidemia. No relevant health technology assessments or randomized controlled trials were identified.

Additional references of potential interest are provided in the appendix.

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


Health Technology Assessments – Alternate Comparator


Systematic Reviews - No Differentiation of PCSK9 Inhibitors for Results


Review Articles


Additional References