CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

INCLISIRAN (Leqvio)

(Novartis Pharmaceuticals Canada Inc.)

Indication ASCVD: as an adjunct to lifestyle changes, including diet, to further reduce low-density lipoprotein cholesterol (LDL-C) level in adults with Non-familial hypercholesterolemia with atherosclerotic cardiovascular disease who are on maximally tolerated dose of a statin, with or without other LDL-C -lowering therapies

Indication HeFH: as an adjunct to lifestyle changes, including diet, to further reduce low-density lipoprotein cholesterol (LDL-C) level in adults with Heterozygous familial hypercholesterolemia (HeFH) who are on maximally tolerated dose of a statin, with or without other LDL-C -lowering therapies

April 8, 2024

Disclaimer: The views expressed in this submission are those of the submitting organization or individual. As such, they are independent of CADTH and do not necessarily represent or reflect the view of CADTH. No endorsement by CADTH is intended or should be inferred.

By filing with CADTH, the submitting organization or individual agrees to the full disclosure of the information. CADTH does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter’s responsibility to ensure no identifying personal information or personal health information is included in the submission. The name of the submitting stakeholder group and all conflicts of interest information from individuals who contributed to the content are included in the posted submission.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791
Brand name (generic)	Leqvio (Inclisiran)
Indication(s)	nonfamilial Hypercholesterolemia and Atherosclerotic Cardiovascular Disease
Organization	Canadian Heart Patient Alliance (CHPA)
Contact information[a]	Name: Durhane Wong-Rieger

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

The Canadian Heart Patient Alliance expressed strong disagreement with CEDAC's original "do not reimburse" recommendation in 2022, but we felt that the company provided the evidence from two phase III, double-blind randomized controlled trials and showing, as acknowledged by CADTH, "a statistically significant improvement compared with placebo in lowering LDL-C levels in adult patients with nFH with ASCVD who were receiving a maximally tolerated dose of a statin or who were statin intolerant." These were the data requested by CEDEC as part of their initial negative recommendations that more than adequately addressed the concerns with the draft recommendation. In addition, CEDEC confirmed that "long-term efficacy and safety of inclisiran" requiring further review, could be addressed by evidence from two ongoing studies … to provide further evidence regarding the efficacy and safety of inclisiran in preventing pertinent clinical outcomes." However, CEDEC goes on to discount these studies because the analysis was "post-hoc" and the extension studies lacked a comparator group.

These objections totally miss the severe and deadly nature of the condition, the lack of alternative therapies, and the overall effectiveness of Leqvio in lowering LDL-C levels and the concomitant impact of reducing cardiovascular risks and events. It is not only unnecessary and unreasonable to expect and to conduct long-term randomized (controlled) trials to demonstrate the link between LDL-C levels and CV events, it is dangerous and unethical. The relationship has been overwhelmingly documented for many years across many years and many categories of patients.

More recent evidence confirm the benefit of Leqvio in with ASCVD not responsive to maximally-tolerated statin therapy in real-world setting. There is no scientific or clinical reason that these findings should not be extrapolated to nFH ASCVD patients. Moreover, we are informed by the company that they will not be doing follow-up studies specifically with nFH ASCVD patients; the population too small to generate data that can be analyzed with traditional statistics. Nevertheless, it would be valuable and entirely feasible to provide access to Leqvio to Canadian patients and monitor their response. All patients are enrolled with specialists and all follow a managed regimen including regular testing and plasma replacement, as necessary.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

As reported in our response to the original recommendation, the CHPA does not feel that CADTH has taken care to consider the patient input, especially with regard to the impact on quality of life CEDEC discounts impact on quality of life, citing lack of QoL scalar evidence submitted. We contend that the patients' own reports of the impact on QoL and their experience are important evidence that has not been taken seriously. We are very disappointed because we have seen CEDEC recognition of patient reports in other submissions and are dismayed that this acceptance is exhibited here.

The patients using or seeking access to Leqvio were clear that they were not adequately managed not only on statins, plasma exchange, and, importantly PCSK-9 inhibitors, despite the opinion from CEDEC that there is no evidence switching would be more efficacious.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒

If not, please provide details regarding the information that requires clarification.

The reasons do not make sense; the rationale behind the recommendations are absolutely not justified, even when compared to other recommendations, especially for rare conditions and other small patient populations with serious unmet needs.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

If not, please provide details regarding the information that requires clarification.

While the CEDEC does not detail implementation issues, they are clearly ignoring the fact that all of these patients are registered, carefully monitored in terms of current therapies and the impact, and followed even across centres. There can be no concern that inappropriate usage would be prescribed. There is no doubt that patients will be carefully monitored to ensure that the drug works as it should and any adverse effects are identified immediately and interventions are provided.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification.
Not applicable

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Durhane Wong-Rieger*
Position	*Chair*
Date	*08/04/2024*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Sanofi	☐	☐	☒	☐
Ultragenyx	☐	☐	☒	☐
Novartis	☐	☐	☒	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
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- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	**SR0791-000**
Brand name (generic)	**Leqvio**
Indication(s)	**Primary hypercholesterolemia**
Organization	HeartLife
Contact information[a]	Name: Marc Bains

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

It has come to our attention that (CADTH) recently recommended that Leqvio (Inclisiran) should not be reimbursed due to insufficient evidence regarding its long-term reduction in mortality and hospitalization rates. While we respect the rigorous evaluation process undertaken by CADTH, we believe this decision overlooks several crucial aspects of patient care and well-being that merit further consideration.

Impact on Quality of Life
Leqvio is not just another medication; it's a beacon of hope for many patients struggling with the disease who have not responded well to other treatments. The prospect of a twice-yearly injection not only offers a novel therapeutic approach but significantly enhances the quality of life for patients. It allows for greater freedom and flexibility, reducing the daily burden of medication management, which is a significant consideration for those juggling multiple prescriptions.

Reduction in Pill Burden
The innovative dosing regimen of Leqvio significantly reduces the pill burden on patients. This aspect cannot be overstated, as the simplification of treatment protocols directly correlates with improved adherence and outcomes. For many patients, the transition from daily oral medications to a bi-annual injection can dramatically improve compliance, a crucial factor in managing chronic conditions.

Improvement in Day-to-Day Activities

Our members have expressed that the potential for improved day-to-day functioning with Leqvio is significant. The ease of treatment and the reduction in side effects associated with traditional therapies can enable a more active and fulfilling lifestyle, aspects that are often overshadowed by clinical metrics but are paramount from a patient perspective.

HeartLife was able to get unique and valuable insight from the patient partners on the medication. Excerpts from the interviews are below:

Patient Partner # 4- *I experienced a significant improvement in my overall well-being. My doctor confirmed that the results were much better, and I now enjoy a better quality of life without any side effects. It's worth noting that I only qualified for*

this new drug due to participating in a study. The drug has shown remarkable effectiveness, with a 75% reduction in ldl numbers. I firmly believe that this medication has the potential to save lives, and it should be covered and made accessible to those who need it.

Patient Partner# 2- *The objective was to lower cholesterol levels, but not much more could be achieved through statins. Due to intolerance towards statins, experiencing undesirable side effects, my quality of life was adversely affected. However, finding an alternative solution allowed for better tolerance and fewer side effects, ultimately leading to reaching the target cholesterol levels. Nevertheless, the medication proved to be very expensive, making it unaffordable without coverage. The burden of paying out of pocket would have been substantial. Luckily, my doctor enrolled me in a special program. But I know this not available to all Canadians.*

Patient Partner # 5 - *Initially, there were concerns and hesitation due to a family history of cardiovascular issues. With a dad who passed away and a brother who underwent multiple open-heart surgeries at the age of 70, it was important to find a solution. The cost of the medication, at $6,000 per year I think, was steep, especially without any coverage. I have special coverage through a study. I started the medication on April 20th and being on the medication for 8 weeks, there have been significant positive changes. Within just 6 weeks, cholesterol levels improved remarkably. I haven't felt this good in years. The ease of the injection and absence of pill burden made the treatment process more manageable. Moreover, there has been a significant improvement in my mental well-being. Prior to starting inclisiran, maximum dosages of other medications failed to provide the desired results, leading to a sense of going to nowhere. The family doctor was happy to hear about these positive improvements.*

In light of these considerations, we kindly urge CADTH to re-evaluate its recommendation on Leqvio, taking into account the broader implications on patient well-being, adherence to treatment, and overall quality of life. The value of a medication should not be measured solely by its impact on mortality and hospitalization rates but also by its ability to improve the daily lives of those it seeks to treat.

We are more than willing to provide additional data, patient testimonials, and other relevant information to support our case. We believe a collaborative approach can lead to a more comprehensive understanding of Leqvio's potential benefits and its role in improving patient care

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

If not, what aspects are missing from the draft recommendation? Please see above.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

If not, please provide details regarding the information that requires clarification. I cannot see additional information on the following:

Relevant comparators
Considerations for initiation of therapy
Considerations for continuation or renewal of therapy

Considerations for discontinuation of therapy		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒
If not, please provide details regarding the information that requires clarification. Not Applicable.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

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A. Patient Group Information	
Name	*Marc Bains*
Position	*Co-Founder*
Date	*24-04-2024*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

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  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
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Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	**SR0791-000**
Brand name (generic)	**inclisiran**
Indication(s)	**Primary hypercholesterolemia**
Organization	HeartLife Foundation
Contact information[a]	Name:Marc Bains

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

Yes, we agree with the committee's recommendation, as it will significantly support patients by providing access to necessary treatments. While we advocate for the removal of all restrictions for heart failure treatments, we acknowledge that the need for additional data is critical to ensure patient safety and treatment efficacy. This balanced approach aligns with our commitment to patient-centered care.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐

If not, what aspects are missing from the draft recommendation?

Yes, it is clear that CADTH has thoroughly considered our stakeholder input. The incorporation of quality of life indicators, which are crucial to patients, reflects a comprehensive evaluation process. This attention to patient-reported outcomes ensures that the recommendations not only address clinical efficacy but also the real-world impact on patients' daily lives.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

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A. Patient Group Information	
Name	*Marc Bains*
Position	*Co-Founder*
Date	*July 30, 2024*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Name of the drug and Indication(s)	Inclisiran (Leqvio) as an adjunct to lifestyle changes, including diet, to further reduce low-density lipoprotein cholesterol (LDL-C) level in adults with Heterozygous familial hypercholesterolemia (HeFH) who are on maximally tolerated dose of a statin, with or without other LDL-C -lowering therapies
Organization Providing Feedback	FWG

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.		
Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	☐
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	X
	No requested revisions	☐

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
Please provide details regarding the information that requires clarification. Clarification is required to explain the rationale for the negative recommendation given that a positive recommendation was issued for Repatha for HeFH based on similar evidence.
b) Reimbursement conditions and related reasons

Version: 1.0
Publication Date: TBC
Report Length: 2 Pages

Single

Technology

Please provide details regarding the information that requires clarification.
c) Implementation guidance
Please provide high-level details regarding the information that requires clarification. You can provide specific comments in the draft recommendation found in the next section. Additional implementation questions can be raised here.

Outstanding Implementation Issues

In the event of a positive draft recommendation, drug programs can request further implementation support from CADTH on topics that cannot be addressed in the reimbursement review (e.g., concerning other drugs, without sufficient evidence to support a recommendation, etc.). Note that outstanding implementation questions can also be posed to the expert committee in Feedback section 4c.

Algorithm and implementation questions
1. Please specify sequencing questions or issues that should be addressed by CADTH (oncology only)
1. 2.
2. Please specify other implementation questions or issues that should be addressed by CADTH
1. 2.
Support strategy
3. Do you have any preferences or suggestions on how CADTH should address these issues?
May include implementation advice panel, evidence review, provisional algorithm (oncology), etc.

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-001
Name of the drug and Indication(s)	Inclisiran (Leqvio) as an adjunct to lifestyle changes, including diet, to further reduce low-density lipoprotein cholesterol (LDL-C) level in adults with Non-familial hypercholesterolemia with atherosclerotic cardiovascular disease who are on maximally tolerated dose of a statin, with or without other LDL-C -lowering therapies
Organization Providing Feedback	FWG

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.		
Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	☐
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	☐
	No requested revisions	X

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
Please provide details regarding the information that requires clarification.
b) Reimbursement conditions and related reasons
Please provide details regarding the information that requires clarification.

Version: 1.0
Publication Date: TBC
Report Length: 2 Pages

Single

Technology

c) Implementation guidance
Please provide high-level details regarding the information that requires clarification. You can provide specific comments in the draft recommendation found in the next section. Additional implementation questions can be raised here.

Outstanding Implementation Issues

In the event of a positive draft recommendation, drug programs can request further implementation support from CADTH on topics that cannot be addressed in the reimbursement review (e.g., concerning other drugs, without sufficient evidence to support a recommendation, etc.). Note that outstanding implementation questions can also be posed to the expert committee in Feedback section 4c.

Algorithm and implementation questions
1. Please specify sequencing questions or issues that should be addressed by CADTH (oncology only)
1. 2.
2. Please specify other implementation questions or issues that should be addressed by CADTH
1. 2.
Support strategy
3. Do you have any preferences or suggestions on how CADTH should address these issues?
May include implementation advice panel, evidence review, provisional algorithm (oncology), etc.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Instructions for Stakeholders

This template is for eligible stakeholders to provide feedback and comments on draft reimbursement recommendations. Draft recommendations are available for feedback for 10 business days.

CADTH will only consider feedback received from eligible stakeholders, including the sponsor, patient groups, clinician groups, and the participating drug programs. Individuals interested in providing feedback should contact the relevant patient and clinician organizations. This template may also be used by eligible industry stakeholders to provide feedback on draft recommendations from the non-sponsored review process (i.e., any current or future Drug Identification Number [DIN] holders for the drug under review).

The sponsor may use this form to provide general feedback on the draft recommendation if they are not filing a request for reconsideration. If the sponsor is filing a request for reconsideration, they must complete the reconsideration template and should not complete this template.

All submitted feedback must be disclosable and will be posted on the CADTH website.

If you have questions, please email requests@cadth.ca with the complete details of your question(s).

Before Completing the Template:

Please review the following documents to ensure an understanding of CADTH's procedures:

- Procedures for CADTH Reimbursement Reviews
- Procedures for Non-sponsored Reimbursement Reviews
- CADTH Pharmaceutical Review Updates for any applicable information.

Completing the Template:

Feedback should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated and specific reference must be made to the section of the recommendation document under discussion (i.e., page number, section title, and paragraph).

Comments should be restricted to the content of the draft recommendation and should not contain any language that could be considered disrespectful, inflammatory or could be found to violate applicable defamation law.

Feedback must be based on the information that was considered by the expert committee in making the draft recommendation. No new evidence will be considered at this part of the review process.

Feedback must not exceed 3 pages in length, using a minimum 11-point font on 8.5″ by 11″ paper. If comments exceed 3 pages, the feedback will not be accepted by CADTH. References may be provided separately; however, these cannot be related to new evidence.

Patient groups must complete Appendix 1.

Clinician groups must complete Appendix 2.

Filing the Completed Template:

The feedback must be provided in Microsoft Word format by using the *Submit* link next to the drug on the Open Calls page. In order to ensure fairness in CADTH's procedures, all stakeholder feedback must be received by the deadline posted on the CADTH website.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000 Stakeholder Feedback on Draft Recommendation
Brand name (generic)	Inclisiran
Indication(s)	Heterozygous Familial Hypercholesterolemia
Organization	CCS Dyslipidemia Guidelines Committee
Contact information[a]	Name: George Thanassoulis

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

We disagree with the recommendation not to reimburse inclisiran for patients with heterozygous Familial Hypercholesterolemia (HeFH). HeFH is a rare genetic condition characterized by a reduction in clearance of LDL-C due to mutations in the LDL receptor (or other related genes). The impaired clearance of LDL-C leads to lifelong elevations in plasma LDL-C which leads to early and aggressive atherosclerosis and ultimately cardiovascular events such as myocardial infarction, stroke and peripheral artery disease. In HeFH, the severity of the disease is directly proportional to the severity of the impairment in LDL-C clearance and therefore HeFH (and other genetic disorders of LDL clearance) have provided strong evidence that LDL-C is causal for atherosclerotic cardiovascular disease. Given the low prevalence of HeFH, it is difficult to perform large outcome trials in this patient population. Therefore, for a genetic disorder such as HeFH, where there remains a major unmet need for further lipid-lowering, randomized trial evidence of reductions in cardiovascular outcomes are not necessary to prove efficacy and that LDL-C lowering itself should be sufficient.

Furthermore, given the mechanism of action of inclisiran, which is to block PCSK9 production, inclisiran directly ameliorates (at least partially) the genetic defect in HeFH, by increasing the number of LDL receptors on the cell surface and promoting LDL clearance. Inclisiran leads to clinically significant reductions in LDL-C, which normalizes plasma LDL-C levels in the majority of HeFH patients (on statins). Therefore, by directly addressing the fundamental mechanism in HeFH, and by providing substantial LDL-C lowering in this population, inclisiran provides an important therapeutic option for individuals with this life-threatening genetic disorder.

Finally, we are concerned that the CADTH draft decision will lead to health care inequities in Canada, given that after reviewing the same data, The Institut National d'Excellence en Santé et en Services Sociaux (INESSS) in the province of Quebec made a positive recommendation. INESSS recognized the clinical relevance, utility and value of inclisiran for patients with HeFH.

Commented [JG1]: Correct clinically

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

If not, what aspects are missing from the draft recommendation? It is not clear how the stakeholder input factored into the decision reached.		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	
Position	
Date	
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • John Mancini • Priya Manjoo • Milan Gupta • David Lau • John Sievenpiper • Daniel Ngui • Alexander Leung • Gordon Francis • Paul Poirier		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*George Thanassoulis*
Position	*Professor of Medicine, Cardiologist. McGill University*

Date	*03-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Amgen	☐	☐	☒	☐
Novartis	☐	☐	☒	☐
Sanofi	☐	☒	☐	☐
HLS	☐	☒	☐	☐
New Amsterdam	☒	☐	☐	☐
Novo-Nordisk	☒	☐	☐	☐

New or Updated Declaration for Clinician 2

Name	*Ruth McPherson*
Position	*Professor of Medicine, Division of Cardiology, Univ Ottawa Heart Institute*
Date	*06/04/2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Amgen (grants, honoraria)	☐	☐	☒	☐
Novartis (grants, honoraria)	☐	☐	☒	☐
New Amsterdam	☒	☐	☐	☐

New or Updated Declaration for Clinician 3

Name	*Jean Gregoire*
Position	*Associate Professor, Université de Montréal, Interventional Cardiologist, Institut de Cardiologie de Montréal*
Date	*06/04/2024*

☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Amgen	☐	☐	☒	☐
HLS	☐	☐	☒	☐
Mantra	☐	☒	☐	☐
Novartis	☐	☐	☒	☐
New Amsterdam	☒	☐	☐	☐
Novonordisk	☐	☒	☐	☐
Sanofi	☐	☒	☐	☐

New or Updated Declaration for Clinician 4

Name	*Robert Hegele MD*
Position	*Distinguished Professor of Medicine and Biochemistry, Western University, London ON*
Date	*Please add the date form was completed 06-04-2024*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Amgen	☐	☐	☒	☐
Akcea/Ionis	☐	☐	☒	☐
Arrowhead	☐	☒	☐	☐
HLS Therapeutics	☐	☒	☐	☐
Medison	☐	☒	☐	☐
Novartis	☐	☐	☒	☐
Regeneron	☐	☒	☐	☐
Sanofi	☐	☒	☐	☐
Ultragenyx	☐	☒	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Glen J. Pearson, BSc, BScPhm, PharmD, FCSHP, FCSC*
Position	*Professor of Medicine (Cardiology)* *Co-Director, Advanced Heart Failure and Transplant Clinic* *Chair, Health Research Ethics Board (HREB- Biomedical Panel)* *Faculty of Medicine & Dentistry* *University of Alberta; Department of Medicine, Division of Cardiology* *Mazankowski Alberta Heart Institute*
Date	*April 6, 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Amgen	☒	☐	☐	☐
HLS Therapeutics	☒	☐	☐	☐
Novartis	☐	☒	☐	☐
Trimedic Therapeutics	☒	☐	☐	☐

Name	*Gordon A. Francis MD, FRCPC*
Position	*Professor of Medicine (Endocrinology and Metabolism)* *Healthy Heart Program Prevention Clinic, Centre for Heart Lung Innovation* *University of British Columbia*
Date	*April 6, 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
No conflicts to declare				

Name	*Patrick Couture MD, FRCPC, PhD*
Position	*Professor of Medicine (Internal Medicine)* *Lipid Research Centre, Université Laval, Québec*
Date	*April 7, 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
INESSS	X			

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Leqvio (inclisiran)
Indication(s)	Primary Hypercholesterolemia
Organization	Corcare Inc
Contact information[a]	Joe Ricci MD FRCPS

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

The committee's recommendation made recommendations with regards the approval for the use of inclisiran for ASCVD prevention and Familial Hyperlipidemia.

As stakeholders, we support the principle that approval of medication related to ASCVD secondary prevention should be supported by peer reviewed evidence for improvement in cardiovascular outcomes. The stakeholders are in support of this recommendation.

As Stakeholders, we are concerned with the recommendation related to Familial hyperlipidemia. In the context of the impact of LDL lowering by inclisiran in the FH population. In the context of FH for currently approved therapies, the value of LDL lowering, and safety data have been sufficient criteria for approval. CVOT outcome data involving a comparator LDL Lowering therapy for FH has not been a requirement for current agents including previously approved PSK9 inhibitors.

We appreciate the opportunity to present our thoughts on this important issue. It would be our pleasure to contribute in future in any manner of value to the process

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

If not, what aspects are missing from the draft recommendation?

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*NOT APPLICABLE*
Position	
Date	
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Not Applicable*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Boehringer Ingelheim	☐	☒	☐	☐
Pfizer	☐	☒	☐	☐
Novartis	☐	☒	☐	☐
NovoNordisk		☒		
Jansen		☒		

New or Updated Declaration for Clinician 2	
Name	*Brad Sarak*
Position	*Member, Corcare Inc*
Date	*2024-04-03*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Pfizer	☒	☐	☐	☐
Novartis	☒	☐	☐	☐
Boehringer Ingelheim	☒	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**

Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5

Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Amgen	X	☐	☐	☐
HLS	X	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr. Christopher Hayes*
Position	*Cardiologist at the Manitoba Clinic*
Date	*Please add the date form was completed (03-04-2024*
x	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Amgen	X	☐	☐	☐
HLS	X	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
    - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
    - Please note that declarations are required for each clinician that contributed to the input.
    - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
    - Please add more tables as needed (copy and paste).
    - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	X
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	X
	Yes	☐
If yes, please detail the help and who provided it.		

B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	X
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr Christopher Parr*
Position	*Cardiologist at the Manitoba Clinic*
Date	*Please add the date form was completed (03-04-2024*
X	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Appendix 1. Conflict of Interest Declarations for Patient Groups

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- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Manitoba Clinic Cardiology Dr. Scott-Herridge*
Position	*Cardiologists*
Date	*Please add the date form was completed (03-04-2024*
X	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	X
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	X
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	X
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Amgen	X	☐	☐	☐
HLS	X	☐	☐	☐
Add or remove rows as required		☐	☐	☐

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisiran
Indication(s)	HeFH
Organization	Manitoba Clinic
Contact information[a]	Name:Dr. Joel Scott-Herridge

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	X
Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.		

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	X
If not, what aspects are missing from the draft recommendation?		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	
	No	X
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	X
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	X
If not, please provide details regarding the information that requires clarification. No other publically funded medication has required outcome data for HeFH indications		

[a] CADTH may contact this person if comments require clarification.

Feedback must not exceed 3 pages in length, using a minimum 11-point font on 8.5″ by 11″ paper. If comments exceed 3 pages, the feedback will not be accepted by CADTH. References may be provided separately; however, these cannot be related to new evidence.

Patient groups must complete Appendix 1.

Clinician groups must complete Appendix 2.

Filing the Completed Template:

The feedback must be provided in Microsoft Word format by using the *Submit* link next to the drug on the Open Calls page. In order to ensure fairness in CADTH's procedures, all stakeholder feedback must be received by the deadline posted on the CADTH website.

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Instructions for Stakeholders

This template is for eligible stakeholders to provide feedback and comments on draft reimbursement recommendations. Draft recommendations are available for feedback for 10 business days.

CADTH will only consider feedback received from eligible stakeholders, including the sponsor, patient groups, clinician groups, and the participating drug programs. Individuals interested in providing feedback should contact the relevant patient and clinician organizations. This template may also be used by eligible industry stakeholders to provide feedback on draft recommendations from the non-sponsored review process (i.e., any current or future Drug Identification Number [DIN] holders for the drug under review).

The sponsor may use this form to provide general feedback on the draft recommendation if they are not filing a request for reconsideration. If the sponsor is filing a request for reconsideration, they must complete the reconsideration template and should not complete this template.

All submitted feedback must be disclosable and will be posted on the CADTH website.

If you have questions, please email requests@cadth.ca with the complete details of your question(s).

Before Completing the Template:

Please review the following documents to ensure an understanding of CADTH's procedures:

- Procedures for CADTH Reimbursement Reviews
- Procedures for Non-sponsored Reimbursement Reviews
- CADTH Pharmaceutical Review Updates for any applicable information.

Completing the Template:

Feedback should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated and specific reference must be made to the section of the recommendation document under discussion (i.e., page number, section title, and paragraph).

Comments should be restricted to the content of the draft recommendation and should not contain any language that could be considered disrespectful, inflammatory or could be found to violate applicable defamation law.

Feedback must be based on the information that was considered by the expert committee in making the draft recommendation. No new evidence will be considered at this part of the review process.

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Instructions for Stakeholders

This template is for eligible stakeholders to provide feedback and comments on draft reimbursement recommendations. Draft recommendations are available for feedback for 10 business days.

CADTH will only consider feedback received from eligible stakeholders, including the sponsor, patient groups, clinician groups, and the participating drug programs. Individuals interested in providing feedback should contact the relevant patient and clinician organizations. This template may also be used by eligible industry stakeholders to provide feedback on draft recommendations from the non-sponsored review process (i.e., any current or future Drug Identification Number [DIN] holders for the drug under review).

The sponsor may use this form to provide general feedback on the draft recommendation if they are not filing a request for reconsideration. If the sponsor is filing a request for reconsideration, they must complete the reconsideration template and should not complete this template.

All submitted feedback must be disclosable and will be posted on the CADTH website.

If you have questions, please email requests@cadth.ca with the complete details of your question(s).

Before Completing the Template:

Please review the following documents to ensure an understanding of CADTH's procedures:

- Procedures for CADTH Reimbursement Reviews
- Procedures for Non-sponsored Reimbursement Reviews
- CADTH Pharmaceutical Review Updates for any applicable information.

Completing the Template:

Feedback should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated and specific reference must be made to the section of the recommendation document under discussion (i.e., page number, section title, and paragraph).

Comments should be restricted to the content of the draft recommendation and should not contain any language that could be considered disrespectful, inflammatory or could be found to violate applicable defamation law.

Feedback must be based on the information that was considered by the expert committee in making the draft recommendation. No new evidence will be considered at this part of the review process.

Feedback must not exceed 3 pages in length, using a minimum 11-point font on 8.5″ by 11″ paper. If comments exceed 3 pages, the feedback will not be accepted by CADTH. References may be provided separately; however, these cannot be related to new evidence.

Patient groups must complete Appendix 1.

Clinician groups must complete Appendix 2.

Filing the Completed Template:

The feedback must be provided in Microsoft Word format by using the *Submit* link next to the drug on the Open Calls page. In order to ensure fairness in CADTH's procedures, all stakeholder feedback must be received by the deadline posted on the CADTH website.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisiran
Indication(s)	Primary Hypercholesterolemia
Organization	Civic Heart Centre
Contact information[a]	Name: Saeed Darvish-Kazem

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	x ☐

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

I disagree with the recommendation reached by the CADTH CDEC stating that Inclisiran should not be reimbursed to further reduce low-density lipoprotein cholesterol (LDL-C) level in adults with HeFH or nHF with ASCVD who are on a maximally tolerated dose of statin, with or without other LDL-C lowering therapies. Inclisiran is Health Canada approved for this indication based on evidence from the ORION trials. There include large phase 3 clinical trials that have demonstrated the safety, tolerability and efficacy in this patient population for this very indication.

Multiple studies have demonstrated the clinical benefits of lowering LDL-C irrespective of pathway

In my practice, I manage a patient population that includes a high amount of high risk cardiovascular patients including FH an HeFH patients, South Asian patients with increased risk of CV disease and recurrent events. Despite aggressive risk factor modification, dietary and lifestyle medicine, high dose statin and ezetimibe therapy, over 20% of my patients do not achieve LDL targets set by the Canadian Cardiovascular Society. Previous PCSK9i therapy has required injections every 2-4 weeks and has predictably led to low uptake due to poor patient compliance. Having an option for a therapy that is given every 6 months has significantly improved patient willingness to stay on therapy and be compliant with their treatment regimen.

Alternative PCSK9i therapy has very low penetration amongst patients (<1-5% of eligible patients are on therapy) and traditionally, it has been exceedingly challenging to get patients on therapy despite having appropriate indications. Despite a need for treatment options outside of high-potency statin therapy, or in patients intolerant of statin therapy, we face challenges to get patients to agree to take an injectable subcutaneous therapy every 2-4 weeks. This barrier is eliminated by having an option that is taken every 6 months, which has significantly improved compliance and the initial barriers / resistance that patients demonstrate when having discussions about therapy.

While there is no direct comparison between Inclisiran and other PCKS9i therapy, having this on the market as an available therapeutic option would be a positive for patients and improve overall market price competition between manufacturers of this drug class.		
Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	x
If not, what aspects are missing from the draft recommendation? I have not previously participated in stakeholder input to CADTH		
Clarity of the draft recommendation		
3. **Are the reasons for the recommendation clearly stated?**	Yes	x
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. **Have the implementation issues been clearly articulated and adequately addressed in the recommendation?**	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification. N/A		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification. N/A		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	
Position	
Date	
x	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	x

	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	
	Yes	☐
If yes, please detail the help and who provided it.		
C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	
	Yes	☐
D. New or Updated Conflict of Interest Declaration		
3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.		

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
	☐		☐	☐
		☐	☐	☐
	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. **Did you receive help from outside your clinician group to complete this submission?**	No	x
	Yes	☐
If yes, please detail the help and who provided it.		
3. **Did you receive help from outside your clinician group to collect or analyze any information used in this submission?**	No	x
	Yes	☐
If yes, please detail the help and who provided it.		

B. Previously Disclosed Conflict of Interest		
4. **Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.**	No	X
	Yes	

If yes, please list the clinicians who contributed input and whose declarations have not changed:

- Clinician 1
- Clinician 2
- *Add additional (as required)*

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Saeed Darvish-Kazem*
Position	*Cardiologist, William Osler Health System, Assistant Clinical Professor, McMaster University*
Date	*25-03-2024*
☐x	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☐	X☐	☐	☐
Amgen	☐x	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	Karan Bami
Position	*Cardiologist, William Osler Health System*
Date	*25-03-2024*
x☐ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.	

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	
Position	
Date	
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	
Position	

Date	
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

New or Updated Declaration for Clinician 5

Name	
Position	
Date	
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisiran
Indication(s)	Hyperlipidemia
Organization	Main Street Health Center
Contact information[a]	Name: Dr George Zimakas

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Collectively as a group, we do not support the committee's recommendation not to reimburse Inclisiran.
HeFH patients are at exceptionally high cardiovascular risk. This genetic disease reduces clearance of LDL-C from the bloodstream, which has a direct consequence in the development of atherosclerosis, placing these patients at high risk of a cardiovascular event early in life. More treatment options are needed to address the unmet needs of these high CV risk HeFH patients. Inclisiran has proven to significantly lower LDL-C, thus helping patients successfully achieve the recommended therapeutic thresholds set out by the Canadian Cardiovascular Society. Achieving these thresholds in our HeFH patients is no easy feat and having more therapeutic options to choose from is essential. Based on our clinical experience, one of the key assets of Inclisiran is the 6-month dosing regimen. Not only does this assist patients with their compliance but it also reduces medication burden. It has been our experience that patients prefer this dosing option as it has minimal impact on their lifestyle.
It is important to note that there has never been a medication class (statin, ezetimibe, monoclonal antibodies PCSK9 inhibitors) that has proven in a randomized control trial to reduce cardiovascular morbidity and mortality in the HeFH patient population, nor is there any plans to conduct these trials. Therefore, to cite insufficient evidence for Inclisiran to demonstrate this benefit in cardiovascular events, death and all-cause mortality as reason to deny access to this therapy is unreasonable. Especially considering CADTH has previously issued positive recommendations for the monoclonal antibodies PCSK9 inhibitors in the HeFH population without these CV outcome trials. We strongly feel that having more treatment options available to address the unmet needs of our HeFH patients is imperative and Inclisiran is an essential tool to addressing these needs.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐

Not applicable - Our group did not previously provide stakeholder input to CADTH on this matter.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒

No, we feel the reasons advising not to reimburse Inclisiran were not clearly stated. It is unclear why the monoclonal antibodies PCSK9 inhibitors were provided with a positive recommendation from CADTH for reimbursement without CV outcome trials, however Inclisiran was not issued a positive recommendation based on this lack of evidence. More importantly, it further limits our treatment

options to effectively manage these high CV risk HeFH patients and removes access to a medication we have seen demonstrate effective results for our patients.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
Not applicable		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
Not applicable		

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
    - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
    - Please note that declarations are required for each clinician that contributed to the input.
    - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
    - Please add more tables as needed (copy and paste).
    - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr George Zimakas*
Position	*Medical Director*
Date	*03-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Novartis	☒	☐	☐	☐
Amgen	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr Aman Mangat*
Position	*Associate Physician, Internal Medicine*
Date	*03-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000

New or Updated Declaration for Clinician 3	
Name	*Simon Boulis*
Position	*Lead Pharmacist*
Date	*03-04-2024*

☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000

New or Updated Declaration for Clinician 4

Name	*Dr Robert Werhun*
Position	*Associate Physician, Respirology and Internal Medicine*
Date	*03-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	inclisiran
Indication(s)	hypercholesterolemia
Organization	N/A
Contact information[a]	Name: Dr. Jorin LindenSmith

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒
This medication fills an important void in the treatment of this condition, for a small but morbid patient population with dyslipidemia far above their accepted cardiovascular targets, which is clearly linked to adverse outcomes. I have several patients currently using this medication which is well tolerated and effective and there have been no other options for them to date.		

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒
N/A		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
N/A		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
N/A		

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Jorin LindenSmith*
Position	*General Internal Medicine specialist, Dartmouth General Hospital*
Date	*29 March 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Jason Yung*
Position	*Cardiologist, Dartmouth General Hospital*
Date	*29 March 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Leqvio
Indication(s)	Primary Hypercholesterolemia
Organization	Markham Health Plex Medical Centre
Contact information[a]	Name: Dr. Basel Bari

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

- The Orion 9 study was not powered to look at CV outcomes and this was not the intent of the trial. The intent of the trial was to show a robust and effective LDL lowering in the FH population who are at high risk of ultimately developing CV disease in their lifetime.
- This initial submission of this novel agent that reduces PCSK9 production with a very convenient dosing regime of every 6 months is similar to the initial submission of both presently available PCSK9 inhibitors. Both of these initially only showed data with respect to profound LDL lowering in a similar FH population, WITHOUT CV endpoints. The magnitude of LDL lowering, seen in the ORION 9 trials for inclisiran is similar to that seen in both PCSK9i trial that received a positive recommendation after their initial submission.
- Meta-analysis of all trials of LDL lowering agents has demonstrated that there is a linear relationship between LDL lowering and CV outcomes. The CV outcome trial, Orion 4, for inclisiran is ongoing and the results of this will be available in the coming years. Therefore, we feel it is unfair to give a negative recommendation to this agent at this point given that it has similar magnitude of LDL lowering to agents that received a positive recommendation prior to any CV outcome data.
- It is known in studies of any therapy that increasing dosing frequency decreases compliance and can have effects on outcomes including mortality and hospitalization. Patients generally reject injection therapies initially and one of the factors that may increase acceptance is a convenient injection schedule such as with inclisiran which is given every 6 months. Another factor that will improve compliance and QoL with inclisiran in comparison to the present PCSK9 inhibitors is that inclisiran is injected by the HCP to ensure compliance. When a patient is given the responsibility of injecting a PCSK9 inhibitor on their own every two weeks there is a potential for noncompliance and also wastage of medication that is publicly and privately reimbursed by payers. We have seen this in clinical practice where patients or family members have brought in unused PCSK9i pens which would have cost payors significant amounts of expenditure. With inclisiran it is ensured that the patient receives the dose and wastage of publicly reimbursed medication is minimised because a HCP has actually administered the medication dose.

- Although there are no HRQoL data our experience thus far in patients that have been initiated on inclisiran and more so those that have been switched from bi weekly PCSK9 injections is that these patients are much more satisfied with a 6 monthly injection that controls their LDL levels to acceptable targets than an injection that they have to self administer every two weeks		
Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒
Did not give previous feedback?		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
- They are clearly stated but the initial rational statement lists CV outcomes for the Orion 9 trial however, CV endpoints were not an outcome of this trial. The primary outcome was LDL lowering and safety in the FH patient population.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
NA		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
NA		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Basel Bari*
Position	*Medical Director Markham Health Plex Medical Centre*
Date	*25-03-24*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Alanna De Fry*
Position	*NP*
Date	*25-03-24*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Suganya Thaveswaran*
Position	*RPN*
Date	*25-03-24*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Viral Vyas*
Position	*Clinic Pharmacist*
Date	*25-03-24*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisiran
Indication(s)	Heterozygous Familial Hypercholesterolemia
Organization	University of Alberta-Mazankowski Alberta Heart Institute
Contact information[a]	Name: PAOLO RAGGI, MD

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	x

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

1. There is a large unmet need. Patients with HeFH are at very high risk of CV events due to an extreme elevation in LDL. LDL is the sole agent responsible for the increased risk of atherosclerosis in these patients and there is a paucity of effective treatments to lower **this mediator of disease**. LDL is not a surrogate marker; instead it is the sole agent responsible for the development of atherosclerosis in HeFH.

2. Many therapies in history have been approved because they reduced a marker of risk: systolic blood pressure for anti-hypertensive agents; phosphate for phosphorus binders in CKD etc. LDL lowering for HeFH is an obvious and necessary goal of any effective therapy. Inclisiran IS INDEED effective at lowering the one and only marker of risk in HeFH: LDL!

3. There is a failure to achieve targets with existing oral therapies. Statins and ezetimibe are helpful, but help attain a safe LDL level in a minority of patients. While these agents are helpful, they fail to address the pathophysiology of HeFH since they do not directly affect the life and function of the LDL-receptor. Therefore, PCSK9 antagonists (monoclonal antibodies and siRNA agents like inclisiran), play a MAJOR role in achieving low and safe LDL levels. The denial of this obvious fact seems specious at a minimum. PCS9i's have an indication for LDL lowering in HeFH and have NO outcome trials in HeFH. Hence the refusal to approve inclisiran on this basis of a lack of randomized outcome trials (effectively impossible to perform due the rarity of the disease) appears unjustified.

4. There has been a failure of PCSK9 monoclonal antibodies to achieve meaningful penetration. This may have been due to several factors. Among others: cost of therapy and inconvenience of drug administration. Inclisiran may secure superior patient compliance based on the twice yearly dosing and its administration by a healthcare professional.

5. Inclisiran is not the first siRNA agent released on the market. Indeed several other drugs use this safe and effective mechanism of action. Since it has amply been demonstrated that reducing LDL via inhibition of PCSK9 is safe and effective, and since siRNAs therapies ARE effective and safe, the denial of approval of inclisiran based on the fact the "mechanism of action is novel and not proven to

be safe" is incorrect and appears to be a convenient expedient.		
Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	x
	No	
If not, what aspects are missing from the draft recommendation?		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	x
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation? N/A	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation? N/A	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	
Position	
Date	
x	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
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- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	x
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	x
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 Paolo Raggi, MD • Clinician 2 Kevin Baineyz, MD • Clinician 3 Robert Welsh, MD • Clinician 4 Gabor Gyenes, MD (added; see below) • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*

☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2

Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3

Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range

	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Gabor Gyenes, MD*
Position	*Professor of Medicine-University of Alberta*
Date	*Please add the date form was completed 08-04-2024*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Novartis	x	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisiran
Indication(s)	Primary Hypercholesterolemia
Organization	One Heart Care
Contact information[a]	Name: Sumeet Gandhi

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

Many studies have demonstrated the benefit of lowering LDL-C irrespective of pathway. Many patients are not adherent or compliant with other therapies that other LDL-C. With Leqvio, the benefits of twice a year injections will alleviate this problem. The landmark trials for Leqvio have shown significant decreased in LDL-C levels. Lowering the LDL-C will most definitely result in strong outcomes for patients at risk.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

If not, what aspects are missing from the draft recommendation?

I have not submitted this previously.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification.

NA

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification.

NA

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Sumeet Gandhi*
Position	*Cardiologist*
Date	*April 4, 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Jennifer Meloche*
Position	*Cardiology*
Date	*April 4, 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR091000
Brand name (generic)	Inclisiran
Indication(s)	Primary hypercholesterolemia
Organization	Cardiology services group, Belleville Ontario
Contact information[a]	Name: PETER HOLLETT

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

1. Many requested Comparative clinical trials and familial hypercholesterolemia, but no such Comparison of studies have been completed in the past. This seems somewhat onerous to request.
2. The Dyslipidemia guideline committee has recommended guidelines for familial hypercholesterolemia, and this is an option. It should be considered.
3. Safety profile has been evaluated, and twice yearly dosing offers increased compliance.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

Know. We have not provided a recommendation to this Committee previously.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

See question 1.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☒
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis, Related to Entresto.	☒	☐	☐	☐
Bayer, Related to Jardiance	☒	☐	☐	☐
No talks related to lipids in the last 2 years	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr. Mike Courtland*
Position	*Partner*
Date	*April 5, 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
None.	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Leqvio (Inclisiran)
Indication(s)	As an adjunct to lifestyle changes, including diet, to further reduce low density lipoprotein cholesterol (LDL-C) level in adults who are on maximally tolerated dose of a statin, with or without other LDL-C lowering therapies, and who have heterozygous familial hypercholesterolemia (HeFH).
Organization	North York General
Contact information[a]	Name: Bruce Lubelsky

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

The ORION trials have shown to substantially reduce LDL-C levels in FH and ASCVD patients. It has been well established that LDL lowering is pivotal in the prevention and modification of CV disease. Furthermore, to date, the lipid hypothesis has been supported regardless of what modality is utilized. FH patients are notoriously difficult to bring to LDL target. Many of these patients are quiet young when first brought to medical attention and adherence and compliance to lipid reduction therapy is difficult. Despite our best intentions even with treatment with PCSK9i administered as little as once or twice a month, compliance still remains a large issue. My personal experience with a product like Inclisiran circumvents this issue. PCSK9is have been administered to provide a safe and significant LDL reduction despite lacking the necessary endpoint data. I do not see any reason why Inclisiran should not be included in this population of patients.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

This is my first time submitting into CADTH, therefore the stakeholder was not considered in this case.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒

No, I do not believe the recommendation can be equally applied to ASCVD and FH patients for the reasons stated above in question 1.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

NA

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒

NA

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration				
3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Bruce Lubelsky*
Position	*Staff cardiologist NYGH*
Date	*03-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Servier Canada	☒	☐	☐	☐
Bayer	☒	☐	☐	☐
Novartis	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Ravi Bajaj*
Position	*Staff cardiologist at NYGH*
Date	*03-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	
Brand name (generic)	Inclisiran
Indication(s)	HeFH
Organization	Lipid Clinic McMaster University and Hamilton Health Sciences
Contact information[a]	Name: Guillaume Pare

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

We acknowledge the recent recommendation against the reimbursement of inclisiran for the treatment of adults with Heterozygous familial hypercholesterolemia (HeFH), yet we must respectfully dissent. In our clinical practice, we serve a substantial cohort of HeFH patients, notably young individuals who are frequently on the move (e.g. for academic pursuits) making the bi-annual dosing schedule of inclisiran highly practical. The advised non-reimbursement jeopardizes effective treatment for these individuals, even as early intervention for LDL cholesterol lowering is universally recognized as critical for averting long-term cardiovascular events.

The ORION-9 trial has solidly established inclisiran's efficacy, evidencing a 50% reduction in LDL cholesterol levels in HeFH patients. Recent open-label extension data only fortify the case for inclisiran's safety profile. It is also important to consider the ethical and logistical impediments in demonstrating reductions in cardiovascular morbidity and mortality in this group. Conducting a trial that requires HeFH patients to receive a placebo is not only ethically questionable but also pragmatically challenging due to the rarity of correctly diagnosed HeFH cases necessary for a statistically significant outcome-driven trial.

Moreover, the argument against reimbursement based on the absence of health-related quality of life (HRQoL) data overlooks the fact that the prevention of atherosclerotic cardiovascular disease (ASCVD) events inherently indicates an HRQoL benefit — a benefit that is negated if prevention fails. Our clinic's experience with young HeFH patients suffering from their first ASCVD event in their third or fourth decade of life underscores the devastating impact on their quality of life and provides a compelling argument for proactive ASCVD prevention, in which inclisiran should play a role. The inclusion of inclisiran in our therapeutic arsenal for HeFH patients aligns with the lifestyle of many younger and older HeFH patients, and has the potential to transform outcomes positively by making treatment more practical for these individuals.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

The practical benefit of inclisiran versus other PCSK9i, in the context of clear indication for aggressive LDLc lowering in the HeFH patient population.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Guillaume Pare • Marie Pigeyre •		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Instructions for Stakeholders

This template is for eligible stakeholders to provide feedback and comments on draft reimbursement recommendations. Draft recommendations are available for feedback for 10 business days.

CADTH will only consider feedback received from eligible stakeholders, including the sponsor, patient groups, clinician groups, and the participating drug programs. Individuals interested in providing feedback should contact the relevant patient and clinician organizations. This template may also be used by eligible industry stakeholders to provide feedback on draft recommendations from the non-sponsored review process (i.e., any current or future Drug Identification Number [DIN] holders for the drug under review).

The sponsor may use this form to provide general feedback on the draft recommendation if they are not filing a request for reconsideration. If the sponsor is filing a request for reconsideration, they must complete the reconsideration template and should not complete this template.

All submitted feedback must be disclosable and will be posted on the CADTH website.

If you have questions, please email requests@cadth.ca with the complete details of your question(s).

Before Completing the Template:

Please review the following documents to ensure an understanding of CADTH's procedures:

- Procedures for CADTH Reimbursement Reviews
- Procedures for Non-sponsored Reimbursement Reviews
- CADTH Pharmaceutical Review Updates for any applicable information.

Completing the Template:

Feedback should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated and specific reference must be made to the section of the recommendation document under discussion (i.e., page number, section title, and paragraph).

Comments should be restricted to the content of the draft recommendation and should not contain any language that could be considered disrespectful, inflammatory or could be found to violate applicable defamation law.

Feedback must be based on the information that was considered by the expert committee in making the draft recommendation. No new evidence will be considered at this part of the review process.

Feedback must not exceed 3 pages in length, using a minimum 11-point font on 8.5″ by 11″ paper. If comments exceed 3 pages, the feedback will not be accepted by CADTH. References may be provided separately; however, these cannot be related to new evidence.

Patient groups must complete Appendix 1.

Clinician groups must complete Appendix 2.

Filing the Completed Template:

The feedback must be provided in Microsoft Word format by using the *Submit* link next to the drug on the Open Calls page. In order to ensure fairness in CADTH's procedures, all stakeholder feedback must be received by the deadline posted on the CADTH website.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	inclisiran
Indication(s)	Primary hypercholesterolemia
Organization	Durham Care Clinic
Contact information[a]	Name: Rishi Handa

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	X

Lack of CV Outcomes Trials in HeFH Population

CADTH's decision to reject Leqvio reimbursement based on insufficient evidence of cardiovascular (CV) benefit disregards the absence of CV outcomes trials for approved therapies in patients with Heterozygous familial hypercholesterolemia (HeFH). Historically, no CV outcomes trials have been conducted for lipid medications in the HeFH population. The primary goal in treating HeFH patients is to reduce LDL cholesterol. The correlation between reducing LDL cholesterol and reducing CV outcomes is well-established in cardiovascular risk management. Orion 9, while not designed to assess CV outcomes, demonstrated a significant reduction in LDL-C levels compared to placebo, aligning with the established treatment objective for HeFH patients.

Challenges in LDL-C Management in HeFH

Patients with HeFH inherently face challenges in reaching guideline-recommended LDL-C thresholds due to their genetic predisposition for elevated LDL-C levels. Leqvio's mechanism of action directly targets this genetic defect by increasing the clearance of LDL-C, thereby reducing LDL-C levels and mitigating cardiovascular risk in this population. The Orion 9 trial confirmed a statistically significant improvement in lowering LDL-C levels in adult HeFH patients, underscoring the importance of additional LDL-C reduction strategies beyond standard therapies. Leqvio, indicated as an adjunct to maximally tolerated statin therapy, addresses this unmet need by further reducing LDL-C levels. CADTH's past positive recommendations for mAb PCSK9 inhibitors in HeFH without CV outcomes trials further support the validity of this approach.

Compliance and Patient Preference with Twice-Yearly Dosing

Leqvio's unique twice-yearly dosing regimen offers significant advantages in terms of patient compliance and convenience. By reducing the frequency of injections, Leqvio improves adherence to medication, essential for long-term management of HeFH. Moreover, given that HeFH is an asymptomatic risk factor, the impact of Leqvio on health-related quality of life may be less relevant compared to its efficacy in reducing LDL-C and potential long-term cardiovascular benefits.

Limiting access to Leqvio

There are several negative impacts by limiting access to Leqvio to only patients with private insurance. Access to healthcare should not be determined by financial status. By restricting Leqvio to patients

with private insurance, individuals without such coverage are unfairly disadvantaged. This creates a disparity in healthcare access based on socioeconomic status, exacerbating existing health inequities. Patients without private insurance may face significant financial barriers to accessing Leqvio. Without public reimbursement, the cost of Leqvio could be prohibitively expensive for many individuals, leading to financial strain or forcing them to forgo treatment altogether. For patients with HeFH who do not have private insurance, the lack of access to Leqvio means they have fewer treatment options available to effectively manage their condition. This limitation could result in suboptimal LDL-C control and increased cardiovascular risk, ultimately compromising their health outcomes. HeFH is a genetic disorder that affects a considerable number of individuals worldwide. By restricting access to Leqvio only to private patients, there is a missed opportunity to address a significant public health issue. Broader access to Leqvio could potentially benefit a larger population of individuals with HeFH, leading to improved health outcomes and reduced healthcare burden in the long term.

In conclusion, CADTH's rejection of Leqvio reimbursement fails to consider the unique challenges of managing HeFH, the genetic basis of the condition, and the potential benefits of novel therapies like Leqvio. By addressing LDL-C levels and offering improved compliance and patient preference, Leqvio represents a valuable addition to the treatment armamentarium for HeFH patients. Limiting access to Leqvio to only private patients exacerbates health inequalities, hampers efforts to effectively manage HeFH on a broader scale, and fails to address the significant public health impact of this genetic disorder. Achieving equitable access to innovative therapies like Leqvio is essential for promoting health equity and improving outcomes for all individuals affected by HeFH. Therefore, we urge CADTH to reconsider its decision and provide access to this innovative therapy for patients in need.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	X
We have never provided any previous information to CADTH		
Clarity of the draft recommendation		
3. **Are the reasons for the recommendation clearly stated?**	Yes	X
	No	☐
As per the information provided above, we do not agree with the recommendation.		
4. **Have the implementation issues been clearly articulated and adequately addressed in the recommendation?**	Yes	☐
	No	☐
NA		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
NA		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information			
Name	*Please state full name*		
Position	*Please state currently held position*		
Date	*Please add the date form was completed (DD-MM-YYYY)*		
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.		
B. Assistance with Providing Feedback			
1. Did you receive help from outside your patient group to complete your feedback?		No	☐
		Yes	☐
If yes, please detail the help and who provided it.			
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?		No	☐
		Yes	☐
If yes, please detail the help and who provided it.			
C. Previously Disclosed Conflict of Interest			
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.		No	☐
		Yes	☐
D. New or Updated Conflict of Interest Declaration			
3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.			

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
    - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
    - Please note that declarations are required for each clinician that contributed to the input.
    - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
    - Please add more tables as needed (copy and paste).
    - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	X
	Yes	☐
NA		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	X
	Yes	☐
NA		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	X
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Rishi Handa*
Position	*Director of Medicine, Durham Care Clinic*
Date	*27-MAR-2024*
X	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Khalid Bhatti*
Position	*Director of Pharmacy, Durham Care Pharmacy*
Date	*27-MAR-2024*
X	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Damian Wijeyesinghe*
Position	*Assistant Clinical Professor Queens University, DEPT of FAMILY MED*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000 Stakeholder Feedback on Draft Recommendation
Brand name (generic)	Inclisiran
Indication(s)	Heterozygous Familial Hypercholesterolemia (HeFH)
Organization	TotalCardiology
Contact information[a]	Name: Dr. Patrick Ma

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

FH is one of the most common yet underdiagnosed genetic diseases. Patients with HeFH have higher LDL-C levels making it harder to get to guideline recommended thresholds. They are also at higher risk cardiovascular events. In addition, many patients stop their LDL-C reduction medications and thus are non-compliant. By doing so, they are still at high risk for events. Despite the fact CDEC recognizes that Leqvio's bi-annual dosing regimen may provide patients with a more manageable administration schedule, they concluded that there is no data that demonstrates the impact on Leqvio on quality of life. Data alone cannot determine quality of life. It is our experience, when presenting the medication options of Leqvio or a PCSK9 monoclonal antibody to patients, invariably they have all chosen Leqvio due to the bi-annual dosing regimen.

Secondly, CDEC's recommendation was based off their interpretation of insufficient evidence to assess the clinical benefit of inclisiran in terms of reducing the risk of cardiovascular events, cardiovascular death, or all-cause mortality. However, there are no CV outcomes trials for approved HeFH therapies. CADTH previously issued positive recommendations for Repatha and Praluent in the same HeFH population without CV outcomes trials. It is unfortunate the same recommendation was not given to Leqvio. There is a direct relationship between income and accessibility to medial treatment and by restricting patients' options only further widens the gap between patients.

In our opinion, Leqvio is an almost ideal PCSK9 inhibitor. Given its bi-annual dosing, we know they are taking the drug leading to limited compliance issues. We know that these patients are getting the medication that they need most.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐

If not, what aspects are missing from the draft recommendation?

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒

CDEC's recommendation is based off their interpretation of insufficient evidence to asses the clinical benefit of inclisiran in terms of reducing the risk of cardiovascular events, cardiovascular death, or all-cause mortality. However, there are no CV outcomes trails for approved HeFH therapies. CADTH

previously issued positive recommendations for Repatha and Praluent in the same HeFH population without CV outcomes trials.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
Not applicable		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
Not applicable		

[a] CADTH may contact this person if comments require clarification.

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Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
No. We are cardiologists with decades of experience treating patients with ASCVD and HeFH. We have been involved in clinical research and Dr. Patrick Ma was also involved in the preliminary research with PCSK9 inhibitors.		
B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐

If yes, please list the clinicians who contributed input and whose declarations have not changed:

- Clinician 1
- Clinician 2
- *Add additional (as required)*

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Patrick TS Ma*
Position	*Cardiologist*
Date	*05-08-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
HLS Therapeutics	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr. Neil Filipchuk*
Position	*Cardiologist*
Date	*05-08-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3

Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4

Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5

Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	
Brand name (generic)	Inclisiran
Indication(s)	Hypercholesterolemia
Organization	Dr. Rabih Nour MD Clinic
Contact information[a]	Name: Dr. Rabih Nour

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

There are many reasons as to why we don't agree with this recommendation which will significantly impact our patient's lives especially their quality of life.

- Patient compliance – Leqvio provides FH patients with two injections a year, this significantly improves their compliance, the FH patient population is at the highest risk and need to be as compliant as possible with their medication to reduce their risk of further events. This has been directly noticed with our use of Leqvio with our patients
- Patient convenience – Leqvio provides FH patients with the convenience necessary to remain adherent to keeping their LDL as low as possible – this has been directly noticed with our use of Leqvio with our patients
- Decrease in side effects – patients who have been using Leqvio have experienced a decrease in side effects due to less doses being need, this improves their quality of life and allows them to remain compliant with taking the medication – these high risk patients need to remain compliant
- We have received much better acceptance to start and continue therapy from patients when this option has been given to them – access to this medication for as many of these high risk patients is paramount
- This patient population (FH patients) are younger and more at risk for refusing therapy if multiple doses a month is their only option. These patients are at risk of worse disease and the anticipation of more events to occur is likely if refusal of other therapies with much higher dosing schedules

Having this option available to as many FH patients within our practice as possible will continue to give them better quality of life and reduce their CV events

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

If not, what aspects are missing from the draft recommendation?

See points above

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒

There is no CVOT data published for FH patients. No trial has been conducted nor is there any planned in the future because of the unique nature of this patient population		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
N/A		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
N/A		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Rabih Nour*
Position	*Endocrinologist*
Date	*26-03-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novo	☒	☐	☐	☐
Amgen	☒	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Rovene Marogi*
Position	*Nurse Practitioner*
Date	*26-03-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisiran
Indication(s)	FH
Organization	Heart Care and IMCare
Contact information[a]	Name: Rishi Bhargava, [redacted]

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

If not, what aspects are missing from the draft recommendation?

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification.
NA

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification.

NA

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	
Position	
Date	
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 Rishi Bhargava, MD, FACC • Clinician 2 Rakesh Bhargava, MD • Clinician 3 Mukesh Bhargava, MD		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr Rishi Bhargava, Heart Care and IMCare*
Position	*Cardiologist, Director of Heart Care Lipid Clinic; Chair, Pharmacy and Therapeutics NHH*
Date	*03-29-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Rakesh Bhargava*
Position	*Director, Heart Care Canada*
Date	*03/29/2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Mukesh Bhargava*
Position	*Director, IMCare, Chief of Staff, Northumberland Hills Hospital*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	N/A	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-001 Leqvio Resubmission
Brand name (generic)	Leqvio (inclisiran)
Indication(s)	HeFH
Organization	Victoria Lipid Clinic Society including Dr Harvey Pat Marshall, Dr Gordon Hoag, Dr Richard Bebb, Dr MaryLyn Fyfe, Dr Michael Chen
Contact information[a]	Name: Dr. Gordon Hoag, MD, PhD, FRCPC, Victoria Lipid Clinic Society, [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

The requirement for an outcome trial in this patient population is not rationale. The standard is that a 1 mmol reduction in LDL-C results in a 20% relative risk reduction in cardiovascular outcomes. In this inherited population there is no outcome trials with any previous medication. It appears the submitted data confirms the LDL-C reduction in the HeFH population which correlates with our clinical experience of inclisiran.

Your second paragraph in the recommendation focused on quality of life. Our experience with patients is that QoL is not negatively impacted. The patient benefits are multiple including patient travel, patient compliance and patient receptivity. Our patient follow up occurs with every injection which has confirmed the patient experience. We have some patients with experience up to 1 year that confirms the virtual absence of any adverse effects.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐

If not, what aspects are missing from the draft recommendation?

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification.

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☐
	Yes	☐
No. We are experts in the field with decades of experience on HeFH in patients and their families as well as all atherosclerosis management. We have been partnering with patients to improve their care through a mix of life style (diet and exercise and weight management) and medications since the 1990's. We also have been involved in clinical research in the field for decades. We have read the response from CADTH ourselves and judged it against our extensive clinical and research experience.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
We did not participate in the original submission and have no conflict of interest to declare.		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Instructions for Stakeholders

This template is for eligible stakeholders to provide feedback and comments on draft reimbursement recommendations. Draft recommendations are available for feedback for 10 business days.

CADTH will only consider feedback received from eligible stakeholders, including the sponsor, patient groups, clinician groups, and the participating drug programs. Individuals interested in providing feedback should contact the relevant patient and clinician organizations. This template may also be used by eligible industry stakeholders to provide feedback on draft recommendations from the non-sponsored review process (i.e., any current or future Drug Identification Number [DIN] holders for the drug under review).

The sponsor may use this form to provide general feedback on the draft recommendation if they are not filing a request for reconsideration. If the sponsor is filing a request for reconsideration, they must complete the reconsideration template and should not complete this template.

All submitted feedback must be disclosable and will be posted on the CADTH website.

If you have questions, please email requests@cadth.ca with the complete details of your question(s).

Before Completing the Template:

Please review the following documents to ensure an understanding of CADTH's procedures:

- Procedures for CADTH Reimbursement Reviews
- Procedures for Non-sponsored Reimbursement Reviews
- CADTH Pharmaceutical Review Updates for any applicable information.

Completing the Template:

Feedback should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated and specific reference must be made to the section of the recommendation document under discussion (i.e., page number, section title, and paragraph).

Comments should be restricted to the content of the draft recommendation and should not contain any language that could be considered disrespectful, inflammatory or could be found to violate applicable defamation law.

Feedback must be based on the information that was considered by the expert committee in making the draft recommendation. No new evidence will be considered at this part of the review process.

Feedback must not exceed 3 pages in length, using a minimum 11-point font on 8.5″ by 11″ paper. If comments exceed 3 pages, the feedback will not be accepted by CADTH. References may be provided separately; however, these cannot be related to new evidence.

Patient groups must complete Appendix 1.

Clinician groups must complete Appendix 2.

Filing the Completed Template:

The feedback must be provided in Microsoft Word format by using the *Submit* link next to the drug on the Open Calls page. In order to ensure fairness in CADTH's procedures, all stakeholder feedback must be received by the deadline posted on the CADTH website.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	LEQVIO (Inclisiran)
Indication(s)	High Risk cardiovascular Patient with lipidopathy
Organization	Dr V Sluzar Medicine Professional Corporation
Contact information[a]	Dr Vladimir Sluzar [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	X
Limiting patient access to LU for this drug, will only Delay the lowering of their Risk of coronary events & hospitalization & morbidity and mortality. Predessors in this field Werę approved without the data which you Insist must be present, but we MD"s utilize these medications b/c of the well accepted lipid hypothesis, meaning the Lower the LDL , the getter patient outcomes.		
S		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	x☐
All the Orion trial showed consistent LDL lowering with Inclisiran ie. The LDL hypothesis. This is my first Opportunity to submit to your Committee.		
Clarity of the draft recommendation		
3. **Are the reasons for the recommendation clearly stated?**	Yes	☐
	No	X
The insistence on outcomes data is inconsistent with available Clinical evidence for efficacy in HeFH, but this Lack is present in molecules already approved by you		
4. **Have the implementation issues been clearly articulated and adequately addressed in the recommendation?**	Yes	☐
	No	X
N/a		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	X
N/a		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
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- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	X
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	X
	Yes	☐
If yes, please detail the help and who provided it.		

B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	X
	Yes	☐
Didn't participate well		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr Vladimir Sluzar*
Position	*Clinical Cardiologist*
Date	*02 04 2024*

X	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis Canada	X	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2

Name	*Dr John Jovanovic*
Position	*Clinical Cardiologist*
Date	*02 04 2024*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
N/a	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3

Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*

☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*

☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	
Brand name (generic)	Inclisiran
Indication(s)	Hypercholesterolemia
Organization	Dr. Rabih Nour MD Clinic
Contact information[a]	Name: Dr. Rabih Nour

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

There are many reasons as to why we don't agree with this recommendation which will significantly impact our patient's lives especially their quality of life.

- Patient compliance – Leqvio provides FH patients with two injections a year, this significantly improves their compliance, the FH patient population is at the highest risk and need to be as compliant as possible with their medication to reduce their risk of further events. This has been directly noticed with our use of Leqvio with our patients
- Patient convenience – Leqvio provides FH patients with the convenience necessary to remain adherent to keeping their LDL as low as possible – this has been directly noticed with our use of Leqvio with our patients
- Decrease in side effects – patients who have been using Leqvio have experienced a decrease in side effects due to less doses being need, this improves their quality of life and allows them to remain compliant with taking the medication – these high risk patients need to remain compliant
- We have received much better acceptance to start and continue therapy from patients when this option has been given to them – access to this medication for as many of these high risk patients is paramount
- This patient population (FH patients) are younger and more at risk for refusing therapy if multiple doses a month is their only option. These patients are at risk of worse disease and the anticipation of more events to occur is likely if refusal of other therapies with much higher dosing schedules

Having this option available to as many FH patients within our practice as possible will continue to give them better quality of life and reduce their CV events

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

If not, what aspects are missing from the draft recommendation?

See points above

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒

There is no CVOT data published for FH patients. No trial has been conducted nor is there any planned in the future because of the unique nature of this patient population		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes No	☐ ☐
N/A		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes No	☐ ☐
N/A		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
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- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Rabih Nour*
Position	*Endocrinologist*
Date	*26-03-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novo	☒	☐	☐	☐
Amgen	☒	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Rovene Marogi*
Position	*Nurse Practitioner*
Date	*26-03-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisiran
Indication(s)	As an adjunct to lifestyle changes, including diet, to further reduce low-density lipoprotein cholesterol (LDL-C) level in adults with the following conditions who are on maximally tolerated dose of a statin, with or without other LDL-C lowering therapies.
Organization	Circulate Cardiac and Vascular Care
Contact information[a]	Name: Dr Joseph Berlingieri

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

We do not agree with the committee's recommendation advising not to reimburse Inclisiran. No currently used medication (statins, ezetimibe, PCSKP mAbs) is ever been shown in a randomized controlled trial to reduce cardiovascular morbidity specifically in patients with HeFH, nor are there trials ever planned to be conducted. Therefore, it is unreasonable to deny access to Inclisiran based on this lack of evidence in this patient population when other therapies such as the PCSK9 mAbs have been garnered such access.
HeFH patients are a very high cardiovascular risk patient population, with a 220-fold risk of developing CAD and 50% of these patients having a cardiovascular event by the age of 50. These patients have significantly higher LDL-C levels and therefore it is much harder to reach the CCS guideline recommended thresholds. Inclisiran has clearly demonstrated its effectiveness in lowering LDL-C and would serve as a valuable tool in achieving and surpassing these threshold for HeFH patients. Given that these patients are at such high CV risk, having more therapeutic options is essential to addressing the unmet needs of HeFH patients within our clinical practice. Compliance is an ongoing battle that we clinicians face each day with our patients and having a medication that can be administered on a twice-yearly basis significantly reducing the medication burden on patients and also assists with better adherence to treatment. Based on clinical usage with Inclisiran, it has been our experience that our patients prefer the option of twice-yearly dosing to every 2 weeks or monthly with PCSK9 mAbs.
Lastly, we disagree with the rationale that Inclisiran not be reimbursed due to no data on health-related quality of life (HRQoL). This metric is not relevant for a class of medication whose sole purpose is to treat the asymptomatic risk factor of hypercholesterolemia.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

Not applicable – Our group did not previously provide stakeholder input to CADTH on this matter.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☐

	No	☒
The rationale that cardiovascular outcome trials would be required to support a recommendation to reimburse Inclisiran for patients with HeFH is unclear and unsubstantiated given no evidence has ever been provided in this patient population and it is unlikely to ever occur. It ignores the day-to-day challenges that clinicians face when striving to effectively manage these high risk patients and restricts access to an effective treatment option.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
Not applicable.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
Not applicable.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
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- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr Joseph Berlingieri*
Position	*Medical Director*
Date	*02-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis, HLS, Bayer	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr Hisham Dokanish*
Position	*Medical Director*
Date	*02-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis, HLS, Bayer	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Dr William Nisker*
Position	*Medical Director*
Date	*02-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis, HLS, Bayer	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Leqvio (Inclisiran)
Indication(s)	HeFH
Organization	McMaster university – Secondary cardiovascular prevention Clinic
Contact information[a]	Name:Dr Vikas Sardana

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

"…..Differences in percentage change in LDL-C from baseline to day 510 was -49.52 (95% confidence interval [CI], -55.04 to -43.99, P<0.0001). However, clinically relevant cardiovascular-related morbidity and mortality outcomes were exploratory, and thetrial was not powered to detect statistical significance for these outcomes" –

Benefit of LDL lowering in patients with familial hypercholesterolemia cannot be overstressed for this I will quote the update of UK Simone Broome registry

"..these data confirm the benefit of statin treatment in reducing CHD mortality in patients with a clinical diagnosis of FH, but suggest that, despite recent European and UK guidelines recommending the use of potent statins to lower LDL-C, FH patients with pre-existing CHD, and a proportion of women with FH, may not be treated adequately. Because of their high CHD risk, patients with FH cannot be recruited into a randomised-controlled trial of placebo versus lipid lowering therapy, but long-term follow-up registers such as used here, and the Familial Hypercholesterolaemia Studies Collaboration can provide valuable data to examine the utility of statin treatment"

Coronary heart disease mortality in treated familial
hypercholesterolaemia: Update of the UK Simon Broome FH register
S.E. Humphries a, et al, on behalf of the Simon Broome Familial Hyperlipidaemia Register Group

As it is unethical in all probability to do a randomised controlled trial of placebo vs inclisiran, we would have to look at long term data from such registries to see LDL lowering benefits.
Similar permissions have been given to other PCSK9 inhibitors(Repatha, Praluent)
The ease of administration of Inclisiran, once in 6 months as well as safety demonstrated by real world data makes it an attractive choice for the patients, which they should not be denied.
Our concern is with patients with Familial hypercholesterolemia getting access to an excellent medication that would definitely reduce their risk for future Cardiovascular events.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
If not, what aspects are missing from the draft recommendation?		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
	Yes	☒

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	No	☐
If not, please provide details regarding the information that requires clarification.		

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
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- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
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- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
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  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr Vikas Sardana,MD*
Position	*Fellow Preventive cardiology*
Date	*02-0402024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
None	☐	☐	☐	☐
None	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	Frketich Cassandra
Position	*Nurse Practitioner*
Date	*02-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
None	☐	☐	☐	☐
None	☐	☐	☐	☐
None	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	inclisiran
Indication(s)	Heterozygous familial hypercholesterolemia (HeFH), or Non-familial hypercholesterolemia with atherosclerotic cardiovascular disease
Organization	PACE Cardiology
Contact information[a]	Name: Dr. Yaariv Khaykin, [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.
We concur that the current data on the clinical efficacy of Inclisiran remains inconclusive. However, it is noteworthy that extensive research spanning several decades, involving statin therapies in tens of thousands of patients, has established a direct link between LDL reduction and improved clinical outcomes. We assert that there is ample evidence to suggest that Inclisiran, when combined with statin therapy, can achieve further LDL reduction, reaching therapeutic levels in patients who are otherwise challenging to treat. Additionally, it is well-documented that adherence to statin therapy is suboptimal, with approximately 50% of patients discontinuing their medication within one year. Lipid-lowering medications are particularly notorious for poor long-term adherence. In this context, Inclisiran presents a uniquely superior solution, given its dosing regimen and the innovative approach of administration by healthcare professionals, thereby ensuring higher compliance rates. This advantage positions Inclisiran as a more effective option compared to existing treatments in the market.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

If not, what aspects are missing from the draft recommendation?
The recommendation does not consider are feedback and does not explicitly state that LDL lowering would be expected to correspond to improved clinical outcomes and that adherence/compliance is important in ensuring that clinical outcomes expected based on clinical trial data are actually achieved in real world patients.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Yaariv Khaykin*
Position	*Cardiologist*
Date	*Please add the date form was completed (07-04-2024)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**

New or Updated Declaration for Clinician 2	
Name	*Yana Shamiss*
Position	*Pharmacist*
Date	*Please add the date form was completed (07-04-2024)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**

New or Updated Declaration for Clinician 3	
Name	*Bernice Tsang*
Position	*Cardiologist*
Date	*Please add the date form was completed (07-04-2024)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000 Stakeholder Feedback on Draft Recommendation
Brand name (generic)	Inclisiran
Indication(s)	Primary hypercholesterolemia
Organization	Diabetes Heart Research Centre
Contact information[a]	Name: Dr. Luis Noronha

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

In particular, there are two primary reasons that we disagree with the recommendation: Since LDL-C is the primary factor influencing CV risk in the HeFH population, all initial clinical studies including with statins and PCK9 inhibitors have been designed with LDL lowering as initial target in this high-risk population. Data specifically pertaining to Inclisiran that have been released thus far demonstrate a noteworthy reduction in LDL, with a margin of significance that is on par with high potency LDL-C lowering therapies like PCSK-9 inhibitors and statins. This means that it is in line with all earlier treatments intended to lower LDL-C. Furthermore, although other PCSK9 inhibitors are approved for coverage for heFH, no dedicated CVOT trials in these patients have been conducted to my knowledge and the same standards should be applied to Inclisiran.

Secondly, more tools are needed by clinicians to manage patients with elevated LDL-C. Moreover, CDEC comments that there are no CV risk reduction studies or comparison trials with PCSK-9 inhibitors to support treating LDL-C reduction with Inclisiran rather than PCSK-9 inhibitors. We concur with this statement, but in the actual Canadian context, there has been low and suboptimal use of PCSK-9 inhibitors leading to suboptimal reach of optimal recommended LDL levels. For a variety of reasons, it is difficult to start patients on current PCSK9 inhibitors even when access to PCSK-9 inhibitors is available. There, there remains an unmet need for lipid reduction strategies.

As clinical experts we recommend using inclisiran to treat high risk HeFH patients who require additional LDL lowering prior to the availability of the cardiovascular outcomes trial, given the overwhelming body of evidence establishing a consistent relationship between reduction in LDL cholesterol and reductions in MACE. While the completion of the CV outcomes trials is important, the use of inclisiran should not be rejected given the magnitude of the unmet medical need.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

Not applicable.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
	Yes	☐

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	No	☐
N/A		

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
N/A		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
• *N/A*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Luis Noronha*
Position	*Medical Director*
Date	*04 Apr 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.	

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Novartis	☒	☐	☐	☐
Amgen	☒	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Sylvia Mikhail*
Position	*Clinical Pharmacist*
Date	*04 Apr 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791 - 000
Brand name (generic)	Leqvio
Indication(s)	Primary Hypercholesterolemia
Organization	Family Medicine Clinic
Contact information[a]	Name: Dr. G Jee

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

1. Reducing of injection burden by 80% is big advantage and significant. Twice a year dosing is big advantage and very convenient for patients and long-term care.
2. Canadian Cardiovascular guidelines recommend developing alternative therapies for FH. Inclisiran meets that criteria.
3. Requirement for comparative clinical trials is impractical. This has not been required for other similar medications approved by CDEC.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

N/A

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

The recommendations didn't adequately address my concerns in question 1.

1. Reducing of injection burden by 80% is big advantage and significant. Twice a year dosing is big advantage and very convenient for patients and long-term care.
2. Canadian Cardiovascular guidelines recommend developing alternative therapies for FH. Inclisiran meets that criteria.
3. Requirement for comparative clinical trials is impractical. This has not been required for other similar medications approved by CDEC.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐

N/A

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
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- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information			
CADTH project number			
Brand name (generic)	Leqvio (inclisiran)		
Indication(s)			
Organization			
Contact information[a]	Name: Karen Chu		
Stakeholder agreement with the draft recommendation			
1. Does the stakeholder agree with the committee's recommendation.		Yes	☐
		No	☒
Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale. patients prefer the 2x a year vs every two weeks and many patients don't like to self inject Leqvio will help ensure compliance- since it is HCP injected you and the patient knows that their LDL-C is controlled & patient does not need to self-inject. Pt can pick up their other prescriptions at the pharmacy when they are receiving their Inclisiran shot. the CDEC committee agree that lowering LDL-C improves outcomes and agree that the exploratory endpoints are trending in the right direction . So with many patients not being able to access the PCSK9i's, Inclisiran could be that option. Monoclonal antibody PCSK9i's are always in the bloodstream while Inclisiran is only systemic for 48 hours therefore reducing the chance of drug/drug interaction and adverse events.			
Expert committee consideration of the stakeholder input			
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?		Yes	☐
		No	☒
As stated above, Leqvio is 2x/year injection and will improve patient's quality of life and compliance 2x/year injection is more convenient to the patient that 2x/month or 1/month. Having a HCP inject the medication while the patient is at the pharmacy also helps with compliance. I don't think there needs to be a study to show this.			
Clarity of the draft recommendation			
3. Are the reasons for the recommendation clearly stated?		Yes	☐
		No	☒
N/A			
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?		Yes	☐
		No	☒
N/A			
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?		Yes	☐
		No	☐

N/A

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name: Karen Chu*
Position	*Please state currently held position: Cardiologist, Kamloops*
Date	*Please add the date form was completed (DD-MM-YYYY): April 5, 2024*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☒
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisriran
Indication(s)	As an adjunct to lifestyle changes, including diet, to further reduce low-density lipoprotein cholesterol (LDL-C) level in adults with the following conditions who are on maximally tolerated dose of a statin, with or without other LDL-C -lowering therapies: Heterozygous familial hypercholesterolemia (HeFH), or Non-familial hypercholesterolemia with atherosclerotic cardiovascular disease
Organization	Cambridge PREVENT Clinic & Secondary Cardiac Rehab
Contact information[a]	Name: Dr. A. Shekar Pandey

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

We respectfully disagree with the Committee's recommendation. As a group of health care providers at the regional cardiac rehabilitation and cardiovascular prevention program serving the Waterloo-Wellington Region with a service catchment of over 750,000 persons, we manage patients with hypercholesterolemia on a daily basis, We feel that the recommendation to deny reimbursement for Inclisiran is inappropriate for the following reasons:

• There is a great unmet need for LDL cholesterol lowering in patients with Heterozygous Familial Hypercholesterolemia (HeFH) for the following reasons:

1. Statin therapy is the corner stone of management in these but does not achieve adequate LDL reduction in a large percentage of HeFH patients and has poor adherence. Other add on therapies beyond statin have low efficacy (ezetimibe), or lack of access or have high cost (PCSK9 monoclonal antibodies).
2. Inclisiran has the potential to address many of these issues and provide a much-needed new option for patients who require additional LDL lowering beyond statins.
3. We disagree with the rationale to not reimburse inclisiran on the basis that "clinically relevant cardiovascular-related morbidity and mortality outcomes were exploratory outcomes and the trials were not powered to detect statistical significance" The primary goal in treating these HeFH patients is a reduction in LDL cholesterol, and the relationship between reducing LDL cholesterol and reducing cardiovascular morbidity has been established categorically with various therapeutic interventions both lifestyle based, surgical or pharmacological therapies. Furthermore, the mechanism by which inclisiran acts to increase the expression of LDL receptors by inhibiting PCSK9 has already been shown to reduce cardiovascular morbidity in large clinical trials of other agents that act through this same pathway (i.e., PCSK9 monoclonal antibodies). While demonstrating the magnitude of the reduction in cardiovascular morbidity with inclisiran will be important, and will be established by the ongoing ORION-4 trial, we strongly disagree with denying high-risk patients access to this therapy until those results are available since there is a large unmet need for intervention in reducing LDL in HeFH patients. These patients are at high cardiovascular risk and delays in therapy risks progression of atherosclerotic disease and occurrence of potentially avoidable adverse cardiovascular events.

.• From our perspective as clinical experts in this area, we would recommend using inclisiran to treat high risk patients who require additional LDL lowering prior to the availability of the

cardiovascular outcomes trial, given the overwhelming body of evidence establishing a consistent, log-linear relationship between reduction in LDL cholesterol and reductions in the occurrence of major adverse cardiac events(1)

• The rationale to not reimburse inclisiran for patients with HeFH is particularly troublesome. No currently used drug (statins, ezetimibe, PCSK9 mAb) has been shown in a randomized controlled trial to reduce cardiovascular morbidity specifically in patients with HeFH, and it is extremely unlikely that such a trial would ever be conducted due to the logistical challenges of performing a large clinical trial in patients with a rare genetic conduction, as well as the lack of clinical equipoise about the need to aggressively lower LDL cholesterol in these patients. Indeed, we are a clinical research site and we along with most clinical experts, we suspect, would consider it unethical to conduct such a trial. The Committee's rationale therefore sets a bar of evidence that will never be reached for this group of HeFH patients, and in so doing would deny them access to much needed new therapies.

• Lastly, we disagree with the Committee's rationale that inclisran not be reimbursed because "no health-related quality of life (HRQoL) data was included".. HRQoL does not appear to be relevant for a medication whose purpose is to treat an asymptomatic risk factor (hypercholesterolemia). By the time this condition causes symptoms that could be prevented, an adverse cardiovascular event would have had to occur. Since it is unlikely a clinical trial will ever be conducted to assess the reduction of adverse cardiovascular events as noted above, HRQoL data will also be unavailable in the future. Treating and lowering LDL in the asymptomatic state is the corner stone of management for HeFH patients.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to, CADTH?	Yes	☐
	No	☒

In our last submission, our group had emphasized the unmet need for therapies in the HeFH patients and the potential benefits of Inclisriran to this patient population. This input does not appear to have been adequately addressed in the decision of CADTH.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒

The rationale for denying coverage to the HeFH population in particular is not at all clear to us in the final decision of CADTH to deny coverage for Inclisriran.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐

N/A

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐

N/A

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	\$0 to 5,000	**\$5,001 to 10,000**	**\$10,001 to 50,000**	**In Excess of \$50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. A. Shekhar Pandey*
Position	*Lead Cardiologist, Cambridge PREVENT Clinic*
Date	*Please add the date form was completed (30-03-24)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

THERE ARE NO NEW OR UPDATED CONFLICT OF INTERESTS FROM OUR PREVIOUS SUBMISSION.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000 Stakeholder Feedback on Draft Recommendation
Brand name (generic)	Leqvio
Indication(s)	inclisiran
Organization	Cardiology Associates of Niagara
Contact information[a]	Name: Dr. Adnan Hameed

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒
Historically, cardiovascular outcome data in familial hypercholesterolemia (FH) patients have been lacking, creating a gap in addressing this high-risk group. Introducing another treatment option for these patients seems logical. Due to their elevated LDL levels, achieving target levels is particularly challenging, necessitating additional therapeutic options. FH is a genetic disorder characterized by impaired LDL clearance, making Inclisiran's mechanism of action beneficial in enhancing LDL clearance for this patient population. Given the complexity of this demographic, often requiring multiple agents, expanding our therapeutic arsenal is warranted. The flexibility of this medication is particularly advantageous for a population known for low adherence, thanks to its attractive dosing regimen. Disagreement with the current recommendation underscores concerns about creating a two-tiered healthcare system, where access to therapies may be determined by financial resources, exacerbating disparities in care.		
Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
While the report acknowledges the numerous benefits associated with the therapy, it falls short of providing a positive endorsement. This is indeed a significant concern, as it leaves patients and healthcare providers in a state of uncertainty. The absence of a positive response in the report impacts patient access to a therapy that effectively reduces LDL. Further, the cited deficit in lack of health related quality of life data is hard to reconcile when there are no symptoms associated with elevated LDL.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
Not applicable.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
Not applicable.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Adnan Kazi Hameed • Marian Kotrec • Alexandra Bojcevski		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791000
Brand name (generic)	Inclisiran
Indication(s)	Primary hypercholesterolemia
Organization	DOC
Contact information[a]	Name: Vlad Ovchinnikov
Stakeholder agreement with the draft recommendation	

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

I am writing to appeal the recent decision regarding the assessment of Leqvio (inclisiran) based on the recommendations provided by the Canadian Drug Expert Committee (CDEC). As a healthcare professional deeply involved in the care of patients with familial hypercholesterolemia (FH) and atherosclerotic cardiovascular disease (ASCVD), I strongly believe that Leqvio offers significant clinical benefits that warrant its consideration for inclusion in treatment guidelines and reimbursement programs.

Firstly, I would like to emphasize that CDEC acknowledges the critical health need for patients who fail to reach LDL-C targets despite available treatments. This is particularly relevant for patients with FH and ASCVD, where reducing LDL-C levels is a paramount outcome in managing their conditions and reducing the risk of cardiovascular events.

CDEC's recognition of Leqvio's efficacy in reducing LDL-C levels in patients with FH and ASCVD is a crucial acknowledgment. However, I must express my concern regarding the committee's conclusion of insufficient evidence to assess Leqvio's clinical benefit in terms of reducing the risk of cardiovascular events, cardiovascular death, or all-cause mortality.

It's important to note that Leqvio represents a novel approach with its biannual dosing regimen, which not only enhances patient compliance but also offers a more manageable administration schedule. This convenience factor can significantly improve patient adherence to treatment, thereby potentially reducing the overall burden of cardiovascular disease.

Furthermore, while CDEC acknowledges the potential benefits of Leqvio's dosing regimen, they raised concerns about the lack of data demonstrating its impact on health-related quality of life (HRQoL). I would like to highlight the need for a more comprehensive assessment that considers not only clinical outcomes but also the holistic well-being and quality of life improvements that Leqvio may offer to patients.

In light of these points, I respectfully request CADTH to reconsider the assessment of Leqvio, taking into account its demonstrated efficacy in reducing LDL-C levels, the convenience of its biannual

dosing regimen, and the potential positive impact on patients' quality of life. A thorough review considering additional evidence and perspectives from healthcare providers and patients alike would contribute to a more informed and balanced decision regarding the inclusion of Leqvio in clinical practice guidelines and reimbursement programs.

Thank you for considering this appeal, and I remain available to provide any further information or clarification required to support this request.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐
Have not provided feedback in previous submission		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
Yes but we respectfully disagree based on the above discussion points		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification. N/A		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification. N/A		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

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- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Vladislav Ovchinnikov*
Position	*Please state currently held position*
Date	*27-03-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Jameel Razack*
Position	*Family medicine*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000 Stakeholder Feedback on Draft Recommendation
Brand name (generic)	Inclisiran
Indication(s)	Heterozygous Familial Hypercholesterolemia
Organization	Familial Hypercholesterolemia Canada
Contact information[a]	Name: Liam Brunham

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

We disagree with the recommendation not to reimburse inclisiran for patients with heterozygous Familial Hypercholestoerolemia (HeFH), and in particular with the rationale to not reimburse based on CDEC's conclusion that "there is no evidence that inclisiran reduces the risk of cardiovascular morbidity and mortality in the HeFH population." HeFH is a rare genetic condition, and conducting trials of sufficient duration and size to assess an effect on morbidity or mortality is not feasible nor desirable. No currently reimbursed therapy for treating HeFH has been studied in such a trial, and making this the bar for a positive recommendation has the effect of denying patients with HeFH access to new therapies on the basis of a level of evidence that is impossible to achieve.

HeFH is a condition of excessive low density lipoprotein cholesterol (LDL-C) caused in the majority of cases by mutations in the LDL receptor. At a very fundamental level, HeFH is characterized by reduced clearance of plasma LDL-C. By blocking production of PCSK9, inclisiran improves clearance of LDL-C which leads to clinically significant lowering of LDL-C, and therefore directly addresses the basic pathophysiologic mechanism of HeFH. Put differently, elevated LDL-C is the disease in HeFH, and therefore treatment is based entirely on reducing levels of LDL-C. We also disagree with CDEC's view that "extrapolation from other trials or to other populations based on LDL-C levels is not substantiated by current evidence" as this appears to misunderstand that for patients with HeFH lowering LDL-C is the goal of therapy, and extrapolation is not required.

We also note that previous agents that target PCSK9 were recommended by CADTH for reimbursement for the treatment of patients with familial hypercholesterolemia prior to the completion of pivotal cardiovascular outcome trials. Specifically a positive recommendation for evolocumab was issued in early 2016 prior to the publication of the FOURIER trial in March of 2017, and for alirocumab a positive recommendation was issued in the summer of 2016, prior to the publication of the ODYSSEY-Outcomes trial in 2018. In this light, the current draft recommendation regarding inclisiran appears to be both unfounded and inconsistent with previous CADTH decision. This type of inconsistency in decision making results in a very unpredictable and difficult environment for Canadian physicians to practice in.

Lastly, we are very concerned about the implications of the CADTH draft decision as it relates to equitable access to care across jurisdictions in Canada. In Quebec, INESS has issued a positive recommendation to reimburse inclisiran, based on review of the same data as reviewed by CADTH. We feel that these two bodies reaching different recommendations on the basis of the same evidence

creates a situation that is at odds with foundational principles of the Canadian Health of equity and portability.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒
If not, what aspects are missing from the draft recommendation? It is not clear how the stakeholder input factored into the decision reached.		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	
Position	
Date	
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Liam Brunham • Jacques Genest • George Thanassoulis • John Mancini • Iulia Iatan		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*

☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Leqvio (inclisiran)
Indication(s)	Heterozygous Familial Hypercholeseremia (HeFH)
Organization	North Shore Heart Centre
Contact information[a]	Name: John Vyselaar, MD, FRCPC,
Stakeholder agreement with the draft recommendation	

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

As cardiologists, we see serious atherosclerotic cardiovascular disease in "young" people every day. It changes not only the life of the patient but the lives of the people around them. We are responding today to your draft recommendations for heterozygous familial hypercholesteremia (HeFH), a genetic abnormality that cannot be meaningfully changed with diet and exercise.

My groups supports and participates in clinical research, but I feel we also must highlight the clinical realities that research rarely addresses. The mean age of HeFH is 43 years of age(1). Generally, these patients have young families and are in the most productive working years of their lives. A stroke or a myocardial infarction impacts these lives greatly. Some patients will die, some will recover and some will partially recover. This is however preventable through medications.

Low-density lipoproteins (LDL-C) are widely acknowledged as causative of atherosclerosis. We stand with the Canadian Cardiology Society statement that "Studies consistently show a 20%-22% relative risk reduction for each 1 mmol/L reduction in LDL-C>" (2). Outcomes for patients with HeFH are clearly linked to the compounding years at high levels of LDL-C. Although we would love to read a Cardiovascular Outcomes trial in patients with HeFH we want to highlight that one does not exist. There are trials that include some HeFH patients and they consistently fall in line with the 20%-22% relative risk reduction mentioned above.

The medication options available now are statins, ezetrol and PCSK9 inhibitors.

Statins work for many patients. We use them widely, but they are not always well tolerated, or sufficient for lipid lowering in FH patients.

Ezetrol produces only modest cholesterol lowering, and isn't effective enough for the vast majority of HeFH patients. Internationally it is not commonly used for HeFH treatment.

PCSK9's are extremely effective but come with their own challenges including self-injection and drug plan coverage.

We consider inclisiran as a PCSK9-related option with some unique differences:

1- Retail Pharmacy Injection. Some patients just can't bring themselves to inject themselves.
2- Twice a year dosing. Some patients prefer it for a variety of reasons.
3- Side effects that are clinically very rare in our experience.

Every patient is unique. Shared decision making requires options and Leqvio has been deemed a safe option by countless regulatory systems.

Thank you for reviewing this submission, and I hope this can be offered to patients.

1- Brunham et.al, atherosclerosis 277 (2018). 419-424

2- Pearson et al., 2021 Canadian Cardiovascular Society (CCS) Dyslipidemia Guidelines, Canadian Journal of Cardiology, 37, (2021) 1129-1150

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐

We did not provide previous stakeholder input.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification.

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. John Vyselaar, MD, FRCPC*
Position	*Head of Cardiology, Lion's Gate Hospital*
Date	*04-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Various Research but no financial payments related directly or indirectly to clinical use or recommendation of use thus $0 of influence	☒	☐	☐	☐
Add company name Novartis – PREVAIL trial	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**

Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Leqvio (inclisiran)
Indication(s)	Heterozygous familial hypercholesterolemia (HeFH) or non-familiam hypercholesterolemia with atherosclerotic cardiovascular disease
Organization	CardioPulmonary Services at the Boardwalk, Waterloo, Ontario
Contact information[a]	Name: Dr.Amelia Yip [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

As a group of cardiologists that practice in a large regional group practice, we have taken the proactive approach to have a focused secondary prevention lipid clinic. A significant proportion of these patients have been identified as having HeFH. We find that this at-risk group are especially vulnerable to issues of noncompliance. Whether it is the nature of a younger population or the lack of symptoms, there appears to be a greater inertia to obtain and stay on medical treatment. From our experiences, the availability of different treatment options helps to bring these patients' low-density lipoprotein cholesterol (LDL-C) level to target. Treatments that are more tailored to their needs help achieve this. Often, the infrequent dosage of inclisiran (every 6 months) comes out as the only option for these patients who tend not to be complaint to their medications.

The evidence that lower LDL-C reduces cardiovascular risks is proven beyond a doubt. And inclisiran has been found to be effective in lowering that, as seen in the ORION trials. Health Canada has approved inclisiran for this exact indication. It is the only drug in the PCSK9 pathway that uses small interfering RNA as its method of inhibition. Not providing reimbursement for inclisiran unfairly discriminates those who rely on this medication to lower LDL-C to the threshold needed to decrease cardiovascular events.

In addition, having inclisiran on the market would supply healthy competition for other PCSK9 pathway therapies and may lower the price points for these therapies as a group. The actual cost to each provincial program may very well be much lower having another option on the market.

The above salient points are the reasons we do not agree with the recommendation reached by the CADTH CDED to not reimburse for inclisiran as an option to further reduce LDL-C level in adults with HeFH who are on a maximally tolerated dose of statin, with or without other LDL-C lowering therapies. We strongly suggest the committee reconsider their decision.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐

If not, what aspects are missing from the draft recommendation?
N/A

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☐

	No	☒
If not, please provide details regarding the information that requires clarification. As a group, it did not appear to us the reasons to reject reimbursement for inclisiran were clear. In our opinion, the input from patient groups, clinicians and clinical groups were all in favour for potential usefulness of inclisiran yet funding was ultimately denied.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification. N/A		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification. N/A		

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
	No	☒

3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Amelia Yip*
Position	*Cardiologist*
Date	*01-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Amgen	☒	☐	☐	☐
Sanofi	☒	☐	☐	☐
EOCI	☒	☐	☐	☐
MD Analytics	☒	☐	☐	☐
Bayer	☒	☐	☐	☐
BI-Agence LIV	☒	☐	☐	☐
HLS	☒	☐	☐	☐
Fusion MD	☒	☐	☐	☐
Novonordisk	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Mohan Babapulle*
Position	*Cardiologist*
Date	*01-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
NONE	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Usha Manian*
Position	*Cardiolgist*
Date	*01-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
NONE	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Hahn Hoe Kim*
Position	*Cardiologist*
Date	*01-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
NONE	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	**SR0791-000**
Brand name (generic)	Incliseran
Indication(s)	Familial Hypercholesterolemia
Organization	TotalCardiology Rehabilitation
Contact information[a]	Name: Sandeep Aggarwal , [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Incliseran works in a similar way to evolocumab (through modulation of PSCK9) and has been shown to reduce LDL similarly to evolucumab in patients with Familial Hypercholesterolemia (FH). In the 2015 review of evolocumab CADTH only required LDL lowering and there was no data regarding reducing events (SR0441-000). There still is no hard data on reducing events with evolocumab in patients with FH and without cardiovascular disease. The main reason for this is that it takes a very long time in patients with FH to have events but we have good data that these patients do have increased vascular events and also that lowering their LDL reduces their risk of developing cardiovascular disease. It is illogical and inconsistent that CADTH would grant approval for evolocumab in 2015 and reject incliseran in 2024 with almost the same data.

Comparison of Evolucumab (which has CADTH approval for FH) and Inclideran:

Mechanism of action: Both drugs target PCSK9 in different ways. Evolocumab as an antibody and Incliseran as a silencing RNA.
Efficacy: Bother show similar efficacy in lowering LDL. Incliseran shows a 50% reduction, evolocumab shows a 60% reduction.
Cardiovascular outcomes: Neither drug has show a reduction in morbidity or mortality in FH patients without cardiovascular disease although in the Fourier trial (which included those with and without FH but with cardiovascular disease there was evidence of a MACE outcome benefit of 15% and in the Fourier OLE there is not Cardiovascular mortality benefit. Given that both drugs work on the same pathway and on the same protein it would be expected that incliseran should have similar effects in cardiovascular patients. Regardless the FH data in patients without cardiovascular disease is similar.
Drug deliver: Incliseran is twice yearly and given by a health care practitioner which will improve compliance.
Cost: It is known that incliseran is less costly than evolocumab and therefore should save health care dollars when implemented.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐

If not, what aspects are missing from the draft recommendation?

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*TotalCardiology Rehabilitation*
Position	*Medical Director, TotalCardiology Rehabilitation*
Date	*April 1, 2024*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☐	☐	☐	☒
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Sandeep Aggarwal • Grant Peters • Umair Iftikhar		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Sandeep Aggarwal*
Position	*TotalCardiology Rehabilitation*
Date	*April 1, 2025*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☐	☐	☐	☒
	☐	☐	☐	☐
	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Umair Iftikhar*
Position	*Physician, TotalCardiology Rehabilitation and Lipid Clini*
Date	*April 2, 2024*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☐	☐	☐	☒
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Grant Peters*
Position	*President and Cardiologist TotalCardiology*
Date	*April 2, 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☐	☐	☐	☒
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisiran
Indication(s)	Primary hypercholesterolemia
Organization	North York Cardiac Diagnostic Center
Contact information[a]	Name: Dr. Anup Gupta

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

I am writing to respectfully appeal the recent decision regarding the assessment of Leqvio (inclisiran) based on the recommendations presented by the Canadian Drug Expert Committee (CDEC). As a practicing physician specializing in the management of patients with familial hypercholesterolemia (FH) and atherosclerotic cardiovascular disease (ASCVD), I am compelled to advocate for the inclusion of Leqvio in treatment guidelines and reimbursement programs based on its significant clinical benefits.

I appreciate that CDEC recognizes the pressing health need for patients who struggle to achieve LDL-C targets despite available treatments. This is particularly critical for individuals with FH and ASCVD, where lowering LDL-C levels is a pivotal therapeutic goal for mitigating cardiovascular risks.

While CDEC acknowledges Leqvio's efficacy in reducing LDL-C levels in patients with FH and ASCVD, there remains a concern about the insufficient evidence to evaluate its clinical benefits regarding reducing the risk of cardiovascular events, cardiovascular death, or all-cause mortality. I urge reconsideration of this assessment in light of emerging data and the broader impact on patient outcomes.

One notable advantage of Leqvio is its biannual dosing regimen, which not only simplifies treatment adherence but also offers a more patient-friendly administration schedule. This aspect can significantly enhance patient compliance and contribute to better long-term outcomes in managing cardiovascular health.

Additionally, although CDEC noted the potential benefits of Leqvio's dosing regimen, concerns were raised about the lack of specific data demonstrating its impact on health-related quality of life (HRQoL). While clinical endpoints are crucial, it's equally important to consider the holistic well-being and quality of life improvements that Leqvio may provide to patients dealing with chronic cardiovascular conditions.

Therefore, I respectfully request CADTH to revisit the assessment of Leqvio, considering its proven efficacy in reducing LDL-C levels, the practicality of its dosing schedule, and the potential positive effects on patients' overall quality of life. A comprehensive review taking into account updated evidence and diverse healthcare perspectives will contribute to a more informed and equitable decision regarding the incorporation of Leqvio into clinical practice guidelines and reimbursement frameworks.

Thank you for your attention to this matter, and I am available to provide further information or participate in discussions to support this appeal.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐
NA		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
Yes, but we respectfully disagree with your recommendation.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
N/A		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
N/A		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr.Anup Gupta*
Position	*Cardiologist*
Date	*04-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Harshad Patel*
Position	*Clinical Pharmacist*
Date	*04-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	
Position	
Date	
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000 Stakeholder Feedback on Draft Recommendation
Brand name (generic)	inclisiran
Indication(s)	Primary hypercholesterolemia
Organization	Oakville Cardiologists
Contact information[a]	Name: Dr. Michael Heffernan

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

We respectfully disagree with the CADTH Canadian Drug Expert Committee (CDEC) recommendation that inclisiran not be reimbursed as an adjunct to lifestyle changes, including diet, to further reduce low-density lipoprotein cholesterol (LDL-C) level in adults with Heterozygous familial hypercholesterolemia (HeFH) who are on maximally tolerated dose of a statin, with or without other LDL-C -lowering therapies. There are numerous CDEC decision points with which we take exception.

Inclisiran was first approved by Health Canada in 2021 based on clinical trials that demonstrated its efficacy to safely lower LDL cholesterol. The refusal by CDEC for public reimbursement is in contrast to the approval of this important medication in 31 countries around the world. Perhaps most troubling is the fact that this decision by CDEC, based upon an analysis of the same data, is in direct contraindication of the approval that was granted to Canadians living in the province of Quebec by the Institut national d'excellence en santé et en services sociaux (INESSS) in 2021 for adults with heterozygous familial hypercholesterolemia (HeFH). As a result, this rather inexplicable decision from CDEC, unless changed, will establish a two tier system within the same country for the same condition for the same medication. Please know that this will not be something that we as clinicians will be able to explain to our patients.

The CDEC cited a lack of cardiovascular outcome data in ORION-9 as a significant reason to deny public reimbursement in patients with HeFH while recognizing that this trial established a meaningful reduction in LDL-C of 49.5%. There have been no cardiovascular outcome studies in this patient population to date with any of the medications we prescribe to reduce LDL-C (statins, ezetimibe, mAB PCSK9 inhibitors). The suggestion by CDEC that this is required for public reimbursement is a goal that will never be achieved nor was it ever required for any of the other LDL-C lowering medications. A clinical trial to assess an outcome such as MACE in this patient population would be seen as squarely unethical. This portion of the CDEC response is perplexing and concerning.

We disagree with the notion put forth by the CDEC that HRQoL is a significant factor in an asymptomatic patient population with hypercholesterolemia and that the lack of this data is an impediment to public reimbursement. There is no expectation that any dyslipidemia therapy in an asymptomatic patient to reduce a risk factor will result in a positive HRQoL.

Our group of clinicians also find it concerning that the CDEC has misgivings about the safety of a small interfering RNA based therapy. Health Canada did not share that concern and approved the medication for use in 2021. In addition, 91 other regulatory health agencies around the world did not share this

concern. To deny public reimbursement based upon the premise of a safety concern is not consistent with the regulatory approval of this medication globally.

Our enthusiasm for an additional publicly reimbursed PCSK9 inhibitor originates with the solid scientific background and has been fortified by our practical clinical experience with the molecule. Our group of cardiologists have treated over 150 patients with dyslipidemia including HeFH with inclisiran. Patients are thankful for the twice yearly injection (rather than q 2 weekly with a mAB PCSK9 inhibitor) and the touchpoint with a medical practitioner. This medication has proved to be a well-tolerated, effective option for the reduction of LDL-C in a patient population with exceeding high values that require a marked reduction from baseline. The reduction required is often not met by the currently available oral therapies and as such inclisiran has served an important role to close this care gap.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes ☐	No ☒

If not, what aspects are missing from the draft recommendation?

Our group has taken note of the numerous responses to the CDEC submitted by expert clinician groups across the country following the CDEC review and we are disheartened that the CDEC did not appear to heed any of the expert opinions from thought leaders in the nation.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes ☐	No ☐

If not, please provide details regarding the information that requires clarification.

N/A

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes ☐	No ☐

If not, please provide details regarding the information that requires clarification.

N/A

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes ☐	No ☐

If not, please provide details regarding the information that requires clarification.

N/A

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Dr. Michael Heffernan • Dr. Jan Orfi • Dr. Michelle Paikin • Dr. David McConachie • Dr. Sean Jedrzkiewicz • Dr. Vera Chiamvimonvat • Dr. Qin Li • Dr. Jeremy Paikin • Dr. Shy Amlani		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*

Date	*Please add the date form was completed*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration	
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.	
Company	**Check Appropriate Dollar Range**

	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	inclisiran
Indication(s)	Primary hypercholesterolemia
Organization	One Heart Care
Contact information[a]	Name:Dr Anil Gupta, Cardiologist
Stakeholder agreement with the draft recommendation	

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

We have generally accepted LDL as a surrogate marker for cardiovascular outcomes. Numerous studies and trials have clearly demonstrated the clear correlation with lowering LDL and reduced cardiovascular events. The most recent Canadian lipid guidelines suggests that there is no lower limit to LDL (in fact lower is better) and there is benefit as low as 0.5mmol/L, without safety concerns. In fact, all previous LDL lowering in Canada therapies (statins, ezetimibe and PCSK9i's) were approved based on their ability to lower LDL, before CV outcome trials were available.

In the ORION trials, Inclisiran significantly reduced LDL-C in patients not only with established atherosclerotic CV disease, but also in those with atherosclerotic disease equivalent. These studies included patients who were already on substantial, maximally tolerated, guideline-based therapy.

In the HeFH population specifically, CV disease occurs frequently and at a young age. Their lifetime risk for CV outcomes is very high. Elevated LDL is the main factor for developing cardiovascular disease and previous trials have targeted LDL-C. The published data shows that inclisiran significantly reduces LDL, as effectively at PCSK9i's. In the case of PCSK9i's, they have subsequently established a significant reduction in CV outcomes. At this stage, especially with Health Canada's previous approval of inclisiran, we have been using this therapy successfully. To conduct an outcomes trial in this very high risk patient population with a therapy that lowers LDL so effectively, and in patients with limited options, would be an injustice and will create limitations in providing them optimal care.

Despite the available therapies, there remains a significant gap in care. Clinicians and patients need more options to safely reduce LDL and improve compliance and adherence. Inclisiran offers this opportunity and gives the medical community (and public) more options. Inclisiran therapy has proven to be well tolerated and safe.

Our groups' recent experience, from our own evaluation and based on patient feedback, supports the opportunity to use a q6 months therapy, which is effective and safe, is highly welcomed.

Not having inclisiran available though public funding, is a major concern for us and our patients. It will create health inequity amongst patients who have private coverage compared to those who do not have private coverage, and cannot afford this important therapeutic option to reduce LDL and ultimately cardiovascular disease. In fact, we support the notion that getting Inclisiran to market would result in market competition and may lower the cost for these and other therapies.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐
N/A		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒
Please see answer #1		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
N/A		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
N/A		

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr Anil Gupta*
Position	*Cardiologist*
Date	*April 7, 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☒	☐	☐	☐
Amgen	☒	☐	☐	☐
BMS	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr Vineeta Ahooja*
Position	*Cardiologist, One Heart Care*
Date	*April 7, 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
HLS	☒	☐	☐	☐
Sanofi	☒	☐	☐	☐
Novo Nordisk	☒	☐	☐	☐

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisiran
Indication(s)	Leqvio
Organization	Western University, Division of Cardiology, Cardiac Rehabilitation and Secondary Prevention Program
Contact information[a]	Name: Drs. Neville Suskin, Robert McKelvie & Ashlay Huitema

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

The prevalence of HeFH in ASCVD patients have been reported at approximately 6% (https://doi.org/10.1161/CIRCULATIONAHA.119.044795). Consistent with these data, routine screening of new ASCVD patients at our CRSP program using the "FH Calculator" (within the CardioRisk App), reveals that patients with "probable HeFH" make up at least 6% (or approximately 60 patients per year) of our annual new patient cohort. Moreover, "probable HeFH" patients make up an even greater proportion of patients (approximately 20%) whom we cannot get below the LDL (or ApoB) thresholds for treatment intensification by the conclusion of our 6-month CRSP program. This is despite aggressive lifestyle and maximally tolerated dosed statin therapy. Even with our multi-disciplinary team, that includes nurses, a nurse practitioner and social work support, we cannot implement existing PCSK9-inhibitor therapy in most patients that do not have private insurance coverage, prior to the conclusion of our 6-month CRSP program. Thus, we respectfully recommend reconsideration by CDEC for approval of Inclisiran for re-imbursement in patients with HeFH and ASCVD.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

If not, what aspects are missing from the draft recommendation?

Approval for re-imbursement for the use of Inclisiran in patients with HeFH was denied, despite similar commentary regarding the level of evidence for lipid-lowering efficacy in HeFH cohorts with Inclisiran compared to the previously approved Alirocumab.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification.		
N/A		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
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  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisiran
Indication(s)	Leqvio
Organization	Western University, Division of Cardiology, Cardiac Rehabilitation and Secondary Prevention Program
Contact information[a]	Name: Drs. Neville Suskin, Robert McKelvie & Ashlay Huitema

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

The prevalence of HeFH in ASCVD patients have been reported at approximately 6% (https://doi.org/10.1161/CIRCULATIONAHA.119.044795). Consistent with these data, routine screening of new ASCVD patients at our CRSP program using the "FH Calculator" (within the CardioRisk App), reveals that patients with "probable HeFH" make up at least 6% (or approximately 60 patients per year) of our annual new patient cohort. Moreover, "probable HeFH" patients make up an even greater proportion of patients (approximately 20%) whom we cannot get below the LDL (or ApoB) thresholds for treatment intensification by the conclusion of our 6-month CRSP program. This is despite aggressive lifestyle and maximally tolerated dosed statin therapy. Even with our multi-disciplinary team, that includes nurses, a nurse practitioner and social work support, we cannot implement existing PCSK9-inhibitor therapy in most patients that do not have private insurance coverage, prior to the conclusion of our 6-month CRSP program. Thus, we respectfully recommend reconsideration by CDEC for approval of Inclisiran for re-imbursement in patients with HeFH and ASCVD.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

If not, what aspects are missing from the draft recommendation?

Approval for re-imbursement for the use of Inclisiran in patients with HeFH was denied, despite similar commentary regarding the level of evidence for lipid-lowering efficacy in HeFH cohorts with Inclisiran compared to the previously approved Alirocumab.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification. N/A		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

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- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration				
3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

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- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
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  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

RISHI **BHARGAVA, MD, FACC**
Cardiology & Internal Medicine, Heart Care Canada
A: 372 King Street West, Oshawa, L1J 2J9

www.heartcarecanada.com

March 29th 2024

To: Canadian Agency for Drugs and Technologies in Health (CADTH)

Subject: Negative Recommendation of Leqvio for Familial Hypercholesterolemia

Dear Members of CADTH,

I am writing to express my strong disagreement with the recent negative recommendation of Leqvio (inclisiran) for the treatment of familial hypercholesterolemia (FH). As the director of the lipid clinic at Heart Care, associate professor at Queen's University, and chair of pharmacy and therapeutics at Northumberland Hills Hospital, I believe it is crucial to advocate for the approval and accessibility of medications that can significantly benefit patients with cardiovascular conditions. I would like to emphasize that my views regarding the approval of Leqvio are shared by fellow physicians within our group, including Drs. Rakesh Bhargava and Mukesh Bhargava.

Firstly, I would like to highlight the inconsistency in CADTH's recommendation process. While existing PCSK9 pathway medications such as Repatha and Praluent lack comprehensive cardiovascular outcomes data, they have received positive recommendations from CADTH. It is perplexing that Leqvio, which shows promising efficacy in reducing LDL cholesterol levels and has demonstrated safety in clinical trials, is met with a negative stance despite being approved by regulatory bodies like the FDA and Health Canada.

Leqvio presents several advantages over existing monoclonal antibodies in the PCSK9 pathway, particularly in terms of patient experience and cost-effectiveness. Many patients find frequent injections burdensome and prefer treatments with minimal administration requirements. Leqvio offers a convenient dosing schedule, potentially improving adherence and therefore long-term outcomes. Moreover, the cost of monoclonal antibodies remains prohibitively high for many patients, placing a significant financial strain on healthcare systems and individuals alike.
Patients with genetic conditions such as FH should not be deprived of access to innovative therapies due to financial constraints. It is essential to ensure that medications like Leqvio are accessible and affordable for all patients, regardless of their insurance coverage or pre-existing conditions. Denying coverage for crucial treatments can exacerbate health disparities and compromise patient outcomes.

Additionally, introducing competition into the market for PCSK9 inhibitors can foster price competition and ultimately reduce the financial burden on healthcare systems. A broader range of treatment options gives patients and healthcare providers the flexibility to choose the most suitable therapy based on individual needs and preferences.

Furthermore, it is imperative to consider the needs of patients who experience intolerance or inadequate response to existing PCSK9 inhibitors. Having alternative treatment options like Leqvio is essential for optimizing patient care and addressing individualized treatment challenges.
In conclusion, I urge CADTH to reconsider its negative recommendation of Leqvio for the treatment of FH. The approval and accessibility of this innovative therapy have the potential to significantly improve outcomes for patients with high cardiovascular risk, particularly those with genetic lipid disorders. As healthcare professionals committed to advancing patient care, it is our responsibility to advocate for evidence-based treatments that prioritize patient well-being and health equity.
Thank you for your attention to this matter. I am available to provide further information or clarification as needed.

Sincerely,

Rishi Bhargava, MD, FACC
Co-Director, Heart Care Canada
Associate Professor, Queen's University
Chair of Pharmacy and Therapeutics, Northumberland Hills Hospital

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000 and SR0791-001
Brand name (generic)	Inclisiran
Indication(s)	Primary hypercholesterolemia
Organization	Service of cardiologie, CHU Dr-Georges-L-Dumont
Contact information[a]	Name: Dr Luc Cormier

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

In reference to SR0791-000 (heterozygous familial hypercholesterolemia – HeFH) :

- The provided data appears to include most of the clinical data available to the committee at the time of submission.
- However, the committee's recommendation for heterozygous familial hypercholesterolemia (HeFH) is based available studies to demonstrating reduction of LDL by a significant margin such as demonstrated in the ORION-9 trial. This outcome is standard primary outcome for this patient population. Furthermore, in 2015, CADTH has approved another drug (Evelocumab) for this same indication using the LDL-C reduction outcome, without requesting demonstration of CV outcome reduction, which in our opinion is not expected to be reasonably demonstrated in HeFH patients without previous CV events. As such, CADTH/CDEC uses a different criterion for Inclisiran compared to Evelocumab. Furthermore, in 2015, no data on morbidity and mortality or HRQoL was referenced by CADTH in 2015 for Evelocumab.
- The recommendation of Evelocumab by CADTH in 2015 was rightfully justified based on the data provided and referenced. We recommend inclisiran be evaluated with similar criteria, especially for HeFH.

In reference to project SR0791-001 (non-familial hypercholesterolemia with atherosclerotic cardiovascular disease) :

- Even if we disagree with the decision against recommendation for non-HeFH primary hypercholesterolemia (ASCVD patients), we understand the committee's rationale for this decision, while the ASCVD trial are ongoing (VICTORION-2 and ORION-4 trials).

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

- The most important missing element relates to the current canadian landscape in access to enhanced lipid therapy. Currently, there is clear evidence that PCSK-9 inhibitors such as Evelocumab and alirocumab have not provided comprehensive and broad access in Canada, especially in a province such as New Brunswick where our clinician's group received almost the totality of patient referrals. Restrictive access through public and private payers remains significant, and access to a new treatment option, with the guidance of CADTH through cost condition for reimbursement could certainly address the current unmet need.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☒

	No	☐
If not, please provide details regarding the information that requires clarification.		

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒
N/A		

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒
N/A		

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐

B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒

If yes, please list the clinicians who contributed input and whose declarations have not changed:

- Dr Luc Cormier
- Dr Michel D'Astous
- Dr Jean-François Baril
- Dre Rina Lee
- Dre Stéphanie Thébeau
- Dre Annaëlle Kaczmarek

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	**SR0791-000**
Brand name (generic)	Inclisiran
Indication(s)	Familial and non-familial hyperlipidemia
Organization	Edmonton Zone Cardiac Rehabilitation
Contact information[a]	Name: Gabor T Gyenes

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
I agree with it because it opens up availability to a lot more patients than the currently available, similar medications.		

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
If not, what aspects are missing from the draft recommendation?		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Gabor T Gyenes*
Position	*Edmonton Zone Director of Cardiac Rehabilitation*
Date	*Please add the date form was completed (28-03-2024)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Leqvio (inclisiran)
Indication(s)	Heterozygous familial hypercholesterolemia
Organization	Riverside Cardiology and Diagnostic Imaging
Contact information[a]	Name: Peter Mitoff, [redacted]

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

As physician stakeholders at Riverside Cardiology, representing a large community Cardiology practice in the West End of Toronto, we are writing to express our objection to the draft recommendation issued by CADTH regarding the reimbursement of inclisiran.

We believe that inclisiran represents a pivotal advancement in the management of hypercholesterolemia and cardiovascular risk reduction, and its exclusion from reimbursement would limit our ability to provide optimal care to our patients with Heterozygous Familial Hypercholesterolemia (HeFH), patients at very high risk of premature atherosclerotic cardiovascular events.

The landmark ORION clinical trial program unequivocally demonstrates the efficacy, safety, and clinical benefits of inclisiran in patients with hypercholesterolemia. The ORION trials have consistently shown that inclisiran achieves significant and sustained reductions in LDL-C levels on top of background therapy of statins and ezetimibe.

While CV outcome trial data for inclisiran are pending, there is already substantial evidence from numerous observational studies, randomized controlled trials and meta-analyses that prove the association between lower LDL-C levels and decreased risk of cardiovascular events. Given the similar mechanism of action of other drugs in this class, there is no biologically plausible reason to believe that the observed reduction in cardiovascular outcomes would be different with inclisiran. Furthermore, to our knowledge, there have been no CV outcome trials specifically in patients with HeFH, which has not excluded other drugs with a similar mechanism being approved for this condition.

Of particular importance is the innovative dosing regimen of inclisiran, which requires only twice-yearly subcutaneous injections. This extended dosing interval stands in contrast to monoclonal antibody PCSK9 inhibitors, which necessitate more frequent administration. This unique dosing schedule not only enhances

patient convenience and compliance but also alleviates the burden associated with frequent injections, thereby improving treatment adherence, patient satisfaction and long-term outcomes. We have received very favourable feedback from our patients regarding this dosing regimen.

Finally, we worry that the decision to not reimburse inclisiran will further exacerbate inequalities in health care by excluding patients without financial means or private coverage required to access it.

As frontline healthcare providers, we are acutely aware of the substantial impact of hypercholesterolemia on cardiovascular health and the urgent need for effective therapeutic interventions. Inclisiran represents a significant advancement in this regard, offering a novel approach to LDL-C reduction that addresses the limitations of existing therapies and holds the promise of improving patient outcomes.

Given the compelling evidence from the ORION trials and the unique benefits of inclisiran's twice-yearly dosing schedule, we strongly urge CADTH to reconsider its draft recommendation and acknowledge the clinical value of inclisiran in the management of HeFH. Access to inclisiran is important for ensuring that patients with HeFH at high risk of cardiovascular events receive optimal care and achieve meaningful reductions in their cardiovascular risk.

Thank you for considering our perspective.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒
N/A		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
Please refer to 1		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
N/A		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
N/A		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Peter Mitoff*
Position	*Cardiologist, Riverside Cardiology*
Date	*04-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
None	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Ronnen Maze*
Position	*Cardiologist, Riverside Cardiology*
Date	*08-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
None	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Giridhar Logsetty*
Position	*Cardiologist, Riverside Cardiology*
Date	*08-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☒	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Richard Choi*
Position	*Cardiologist, Riverside Cardiology*
Date	*08-04-2024*

☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Novartis	☒	☐	☐	☐

New or Updated Declaration for Clinician 5

Name	*Mark Fisher*
Position	*Cardiologist, Riverside Cardiology*
Date	*08-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Pfizer	☒	☐	☐	☐

Michael C. Hartleib, MD, FRCPC
CARDIOLOGIST
Michael C. Hartleib Medicine Professional Corporation

THE KAWARTHA CARDIOLOGY CLINIC

To Whom It May Concern:

RE CADTH Inclisirin Reimbursement Review

CADTH Project number: SR0791-000 Stakeholder Feedback on Draft Recommendation
Generic Drug Name: Inclisiran
Indication: LDL Lowering
Name of Clinician Group: Kawartha Cardiology Clinic
Author of Submission: Dr. Michael C Hartleib

We are writing this letter out of concern for recent CADTH review recommending that inclisiran not be reimbursed for patients with established vascular disease or HeFH. In particular, we are concerned with the recommendation as it applies to those patients with HeFH.

The Kawartha Cardiology Clinic provides care to patients in Peterborough and the entire north-east cluster of the Central East LHIN in Ontario. Currently there are 7 cardiologists working at the clinic. This document reflects the collected responses and opinions of the physicians identified herein. www.kawarthacardiology.com

LDL lowering remains the cornerstone of risk reduction for patients with vascular disease. We have efficacious therapies (eg statins, ezetimibe, evolocumab, alirocumab) that are broadly used in Canada. Current guidelines recommend that high-risk patients should receive additional aggressive therapy for and LDL>1.8.

Despite currently available therapies, due to intolerance or non-adherance up to 50% of high-risk patients in Canada are not able to achieve currently identified treatment targets, which leaves them at substantially increased risk for recurrent events.[2,3] It should be noted that many jurisdictions have treatment targets that are substantially more aggressive than Canadian targets.[4] There is an acute need for an agent that successfully lowers LDL, is well tolerated, and geared to optimization of adherence.

It has been established that LDL-C lowering, primarily although not exclusively, via upregulation of LDL receptor expression leads to substantial risk reduction This has been demonstrated in several non-statin based pharmacologic approaches such as

ezetimibe, PCSK9 inhibitors, as well as non-pharmacologic mechanisms such as ileal bypass.[1,2] Therapies that have demonstrated efficacy in special patient populations (eg PCSK9 and FH) have been approved despite a paucity of outcomes data. While the longer term outcome studies assessing inclisiran are ongoing, retrospective review of patient level data from early trials have demonstrated a reduction in vascular events consistent with the LDL hypothesis.[5] Accordingly, the demonstrated safety and efficacy of inclisiran in sustained lowering of LDL, associated with a risk reduction that is consistent with the LDL hypothesis is, in our opinion, sufficient to warrant availability of another important option for high-risk patients who are not able to meet treatment targets with currently available therapy.

We are particularly concerned about the recommendation as it applies to patients with HeFH. These patients are at very high risk of developing end stage vascular disease with an almost 50% risk of non-fatal vascular events by the age of 50-60. Various organizations recommend lipid lowering therapy in patients with HeFH (eg ACC/AHA, CCS). These societies recommend treatment with statins, ezetimibe, PCSK9 therapy, and reference lipoprotein apheresis. Notably, these approaches lower LDL levels by a variety of different physiologic pathways: what is common is LDL reduction. Importantly, these recommendations are not based on long term randomized studies in patients with HeFH, although this strategy has demonstrated significant benefit in observational studies and is now standard of care for these patients. As patients with HeFH are at extremely high risk, and LDL lowering is accepted practice, it is not ethically reasonable to demand a large long term RCT of lipid lowering in these patients. Two other PCSK9 agents (the monoclonal antibodies evolocumab and alirocumab) have been approved for use in patients with HeFH in the absence of a large RCT and outcome data. Although there were initial concerns raised about the long-term safety of inclisiran, at this stage inclisiran has accumulated a similar body of evidence comparable to monoclonal antibodies, when they were approved for use by CADTH, demonstrating sustained efficacy and safety.[5] Accordingly, the recommendation that inclisiran not be reimbursed pending long term safety and efficacy studies in this group of patients appears contrary to current evidence and guideline recommendations, and contradictory to previous recommendations made by CADTH for other lipid lowering therapies. These recommendations, particularly in patients with HeFH, are therefore not based on current evidence, a nuanced understanding of the management of our highest risk patients, particularly those with HeFH, shortsighted, contradictory and impede access to a safe, well tolerated and efficacious therapy for our highest risk patients.

As has been identified many patients are completely or partially intolerant of currently available lipid lowering strategies or struggle with adherence. We personally have accumulated over 2 years of clinical experience with inclisiran. The experience of our patients has been uniformly positive with patient comments such as "***Finally, something I don't have to worry about, and I know I am protected***" and "***That's it?*** (post injection). ***That was nothing, to think all this time this is what I have been waiting***

for…thank you!". Our patients appreciate the ease of use, and the long-term efficacy and as clinicians and patients we value the sustained and significant LDL lowering and mechanism of action which resolves concerns associated with adherence.

Having multiple therapies available will only increase the clinician's ability to optimally treat high risk patients with significant societal impact related to lowering of first events, recurrent events, as well as mortality.

With the above in mind, we formally request that the committee reconsider their decision such that this unique and necessary therapy can be made available to clinicians and high-risk patients in Canada.

Sincerely,

Michael C Hartleib, MD, MSc, FRCPC
Chief and Director of Medicine, Peterborough Regional Health Centre
Director, Kawartha Cardiology Clinical Trials
Peterborough Regional Health Centre
Kawartha Cardiology Clinic
327 Charlotte Street, Suite 204
Peterborough, Ontario, K9J 0B2

On Behalf of:

Dr. William Hughes

Dr. Katie Doucet

Dr. Karen Wagner

Dr. John Reesor

Dr. Rachelle Krause

Dr. Andrew Kelly

April 07, 2024

To Whom It May Concern:

RE: Inclisiran

The recent decision by CADTH regarding the utilization of inclisiran in both patients with HeFH and ASCVD was disappointing. While the recommendation for using this innovative drug in individuals with ASCVD was not unexpected, the extension of this decision to include those with HeFH was very surprising.

Why it is important to consider reversing CADTH's decision on use of inclisiran in HeFH lies in the fundamental distinction between these patients and the broader spectrum of individuals with ASCVD. Notably, individuals with HeFH are exposed to life-long elevated LDL-C levels that underlie a very high risk of vascular events which may lead to premature mortality. Fortunately, empirical evidence shows that intensive reduction of LDL-C levels through efficacious therapies can substantially reduce cardiovascular events and thus normalize life expectancy in these patients. A key point in realizing this objective is to initiate effective interventions at an early age. In HeFH patients, the availability of therapeutic alternatives, particularly those capable of significantly reducing LDL-C levels and potentially enhancing adherence, represent a potent and appealing tool to prolong the lives of individuals with HeFH. Inclisiran lowers LDL-C markedly and its low frequency of administration make it an attractive option for use in those with HeFH.

The efficacy of LDL-C reduction through targeting PCSK9 in saving lives has been demonstrated in pivotal outcome trials such as FOURIER and ODYSSEY. Prior to the completion of these Major Adverse Cardiovascular Events (MACE) trials in the population with ASCVD, CADTH approved the use of alirocumab and evolocumab in HeFH knowing the abilities of these antibodies to lower LDL-C. A similar approach should be applied to make available the use of inclisiran for HeFH patients.

In our specialized clinic dedicated to the management of FH patients, treatments to achieve guideline-recommended LDL-C thresholds frequently require use of multiple agents with distinct mechanisms of action. Consequently, access to an innovative therapeutic agent that adds to the current available LDL-C lowering options is extremely valuable. The integration of inclisiran into our treatment protocols has been welcomed by both our clinical staff and patients, as it holds promise in addressing the urgent therapeutic need of this unique group of patients.

Sincerely,

Norman CW Wong, MD, FRCPC and
Henry J. Duff, MD, Ph.D., FRCPC
Professors of Medicine
3330 Hospital Dr. NW,
Calgary, AB
T2N-4N1

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Leqvio (Inclisiran)
Indication(s)	As an adjunct to lifestyle changes, including diet, to further reduce low-density lipoprotein cholesterol (LDL-C) level in adults with the following conditions who are on maximally tolerated dose of a statin, with or without other LDL-C -lowering therapies: Heterozygous familial hypercholesterolemia (HeFH), or Non-familial hypercholesterolemia with atherosclerotic cardiovascular disease
Organization	Queen Elizabeth II Health Sciences Centre – Interventional cardiologists
Contact information[a]	Name: Dr Wael Sumaya – [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

1) Cardiovascular disease is the second biggest killer in Canada. Dyslipidemia is the core pathophysiology driving ischemic heart disease. In Canada, there is clear evidence for need for better preventative therapies. In Alberta, a study including ~26000 MI patients found that ~64% were not achieving guideline-recommended level prior to their event. After their MI, at least 30% were not achieving their LDL target. (Reference Scory T et al. JACC 2020, 75 (11_supplement_1). Another study in Ontario including nearly 48000 who had their first PCI between Oct 2011 and Sep 2014, 48% did not have lipids checked within 6 months of PCI and in those who had it checked, only nearly have had LDL levels above target. The study demonstrated clear relationship between achieved LDL levels and major cardiovascular events. (Reference Sud M et al. JACC 2020; 76:1440-1450).
   Having inclisiran as a treatment option for clinicians to consider, we believe, will enable us to achieve treatment targets in greater proportions of patients. This in part is likely to improve outcomes. The trials that the committee have considered, clearly show inclisiran's effectiveness at reducing LDL levels by at least 50% in various conditions including HeFH, FH and ASCVD. Meta-analysis of these different trials showed inclisiran to reduce major cardiovascular events by 25% during treatment period (Reference: Ray K et al. EHJ 2022; 00-1-10). Reassuringly, inclisiran appears very safe with the safety profile almost identical to the placebo group.

2) Anecdotally, patients seem to prefer the bi-annual treatment that inclisiran offers. Compliance, missing doses do not appear to be an issue.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐

If not, what aspects are missing from the draft recommendation?
Not applicable

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.
Although they are clearly stated, we do believe there is enough evidence supporing having inclisiran as a treatment option to address an unmet clinical need discussed above.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification.
Not applicable.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐

If not, please provide details regarding the information that requires clarification.

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
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- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Wael Sumaya*
Position	*Interventional Cardiologist*
Date	*28-03-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Novartis	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Ali Hillani*
Position	*Interventional Cardiologist*
Date	*28-03-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
ACIST	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Wan Cheol Kim*
Position	*Interventional Cardiologist*
Date	*28-03-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Tony Haddad*
Position	*Interventional Cardiology Fellow*
Date	*28-03-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Osama Elkhateeb*
Position	*Interventional Cardiologist*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Abbott	☒	☐	☐	☐
Medtronic	☒	☐	☐	☐
Boston Scientific	☒	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisiran
Indication(s)	Primary hypercholesterolemia
Organization	Cape Breton Regional Hospital Cardiology
Contact information[a]	Name: Brian J. (B.J.) Grechuk, MN NP, A-GNP-C

<table>
<tr><th colspan="3">Stakeholder agreement with the draft recommendation</th></tr>
<tr><td rowspan="2">1. Does the stakeholder agree with the committee's recommendation.</td><td>Yes</td><td>☐</td></tr>
<tr><td>No</td><td>☒</td></tr>
<tr><td colspan="3">Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

We disagree as other PCSK9 inhibiting agents have been funded, there is obvious benefit and risk reduction with improvements in LDL</td></tr>
<tr><th colspan="3">Expert committee consideration of the stakeholder input</th></tr>
<tr><td rowspan="2">2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?</td><td>Yes</td><td>☐</td></tr>
<tr><td>No</td><td>☒</td></tr>
<tr><td colspan="3">If not, what aspects are missing from the draft recommendation?

Please refer to the considerations/comments listed within this form.</td></tr>
<tr><th colspan="3">Clarity of the draft recommendation</th></tr>
<tr><td rowspan="2">3. Are the reasons for the recommendation clearly stated?</td><td>Yes</td><td>☐</td></tr>
<tr><td>No</td><td>☒</td></tr>
<tr><td colspan="3">If not, please provide details regarding the information that requires clarification.

With the known, and evidence-informed benefit of LDL/lipid reduction in reducing cardiovascular risk – and in this case especially in young individuals (FH), denying funding to an efficacious lipid lowering agent is not in the best interests of this patient cohort.</td></tr>
<tr><td rowspan="2">4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?</td><td>Yes</td><td>☒</td></tr>
<tr><td>No</td><td>☐</td></tr>
<tr><td colspan="3">If not, please provide details regarding the information that requires clarification.</td></tr>
<tr><td rowspan="2">5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?</td><td>Yes</td><td>☐</td></tr>
<tr><td>No</td><td>☒</td></tr>
<tr><td colspan="3">If not, please provide details regarding the information that requires clarification.

Inclisiran has been reimbursed (for the same indication) in other countries. This patient cohort/population is relatively small, thus the cost of reimbursement would also be relatively small.</td></tr>
</table>

Where this is an only twice yearly injection, there is an obvious improvement in quality of life and reduction in medication burden.

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Brian J. Grechuk – Cape Breton Regional Hospital Cardiology*
Position	*Nurse Practitioner*
Date	*26-03-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Chris Browner – Cape Breton Regional Hospital Cardiology*
Position	*Nurse Practitioner*
Date	*26-03-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☒	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Dr. Paul Morrison – Cape Breton Regional Hospital Cardiology*
Position	*Physician*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☒	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Dr Dongsheng Gao – Cape Breton Regional Hospital Cardiology*
Position	*Physician*
Date	*26-03-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☒	☐	☐	☐

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisiran
Indication(s)	Primary Hypercholesterolemia
Organization	Heart Health Institute
Contact information[a]	Name: Dr. Andrew Yadegari

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

The decision by CADTH to deny reimbursement for Leqvio overlooks critical aspects of managing Heterozygous familial hypercholesterolemia (HeFH) and the potential benefits of this innovative therapy. Managing LDL-C levels in HeFH patients presents unique challenges due to their genetic predisposition for elevated cholesterol. Leqvio's mechanism of action directly targets this genetic defect, offering a promising solution by enhancing LDL-C clearance. The statistically significant improvement in LDL-C reduction observed in adult HeFH patients during the Orion 9 trial underscores the importance of additional LDL-C reduction strategies beyond standard therapies. By serving as an adjunct to maximally tolerated statin therapy, Leqvio fills an unmet need in HeFH management.

While there may be a lack of cardiovascular outcomes trials specifically in the HeFH population, it's essential to recognize the broader context of lipid medication efficacy in reducing cardiovascular risk. Historically, the primary focus in treating HeFH patients has been on lowering LDL cholesterol, a goal Leqvio effectively addresses. The Orion 9 trial, while not designed to assess cardiovascular outcomes, demonstrated significant LDL-C reduction compared to placebo, aligning with established treatment objectives for HeFH.

The twice-yearly dosing regimen of Leqvio presents significant advantages in terms of patient compliance and convenience. Simplifying the treatment regimen can enhance adherence, crucial for achieving long-term benefits in HeFH management. Despite limited data on quality of life outcomes, the consistent reduction in LDL-C demonstrated in trials like Orion 9 underscores the importance of this novel treatment option in addressing the needs of patients with HeFH.

Only allowing private patients to get Leqvio creates unfair healthcare access based on wealth, deepening health disparities. Patients without private insurance face barriers to accessing Leqvio, limiting their treatment choices and potentially worsening their health outcomes. By not providing broader access to Leqvio, there's a missed chance to address a significant public health concern, impacting a larger population affected by HeFH.

CADTH's decision fails to account for the unique challenges of managing HeFH and the potential benefits of innovative therapies like Leqvio. By effectively addressing LDL-C levels and offering improved compliance and patient preference, Leqvio represents a valuable addition to HeFH treatment options. However, limiting access to Leqvio solely to private patients exacerbates

healthcare disparities, hindering equitable treatment and potentially worsening health outcomes for those without private insurance. It's imperative for CADTH to reconsider its decision and provide access to this promising therapy for all patients in need.		
Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐
NA		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
The reasons are clear, but we disagree with the recommendation for the above stated reasons.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
NA		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
NA		

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
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  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Andrew Yadegari*
Position	*Interventional and General Cardiology*
Date	*28-03-24*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr. Jason Burstein*
Position	*Interventional and General Cardiology*
Date	*28-03-24*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Dr. Natalie Ho*
Position	*Cardiologist*
Date	*28-03-24*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Dr. Kibar Yared*
Position	*Cardiologist*
Date	*28-03-24*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Dr. Ram Vijayaraghavan*
Position	*Interventional Cardiology*
Date	*28-03-24*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 6	
Name	*Dr. Raymon Yan*
Position	*Cardiologist*
Date	*28-03-24*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	inclisiran
Indication(s)	Primary Hypercholesterolemia
Organization	Horizon Health Network, The Moncton Hospital
Contact information[a]	Name: Rochelle Johnston, Cardiology Pharmacist

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

- HeFH patients do not have evidence-based options for CV event reduction due to lack of high-quality clinical trials in this patient group (i.e. treatments typically used for lowering LDL and reducing CV risk – HMG coA reductase inhibitors, ezetimibe, PCSK9-inhibitors – CV endpoint trials specifically for HeFH have not yet been conducted)
- HeFH patients are at an exceptionally high risk for CV events (both primary and secondary) and require aggressive risk factor reduction in the form of LDL lowering with pharmacotherapy. HeFH patients with excessively high LDL levels are unlikely to achieve target, evidence-based, LDL thresholds (as recommended in the Canadian Cardiovascular Society 2021 Dyslipidemia - Can J Cardiol 2021;37:1129-50) with oral agents alone and often require additional parenteral therapy.
- PCSK9-inhibitors (alirocumab/evolocumab) are self-administered biweekly, but many patients have difficulty with compliance to this regimen and/or self-administration. Many HeFH patients will benefit from improved compliance with less frequent dosing regimens of this medication, which will greatly assist in success & reduction in CV events due to excess LDL exposure.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐

If not, what aspects are missing from the draft recommendation?

N/A

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

	Yes	☐

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	No	☐
If not, please provide details regarding the information that requires clarification. N/A		

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification. N/A		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Rochelle Johnston*
Position	*Pharmacist (Cardiology)*
Date	*04-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Ronald Bourgeois*
Position	*Cardiologist*
Date	*04-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☒	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*

Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	
Brand name (generic)	Inclisiran
Indication(s)	Hypercholesterolemia
Organization	St. Thomas Elgin General Hopsital (STEGH)
Contact information[a]	Name: Dr. Phil Andros

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	X

- By not giving a positive recommendation CADTH is creating an even larger gap in patient access to PCSK9 inhibitors, this is a crucial part of treatment for FH patients where risk of multiple events is high
- The only patients that will have access to this medication are patients who have private insurance thus limiting a large amount of patients specifically in our geographic catchment area
- Patients of all socioeconomic status deserve to have access to the latest advances in cholesterol lowering medications on the market, not just the ones with the means to do so
- There are no CVOT outcomes for FH patients, why would it be expected that Leqvio provide this type of data in order to get a positive recommendation. This negative recommendation sets a bar that will never be able to be reached therefore setting inequalities for patients who need access
- Although there are alternative PCSK9is available, compliance has been an issue with our patients due to high frequency of administration. The ability for them to have Leqvio instead would ensure compliance is less cumbersome for specifically FH patients and most importantly can reduce the incidence of hospital readmission for MACE.
- We have noticed with our patients that they experience an improved quality of life in part because of the significantly reduced doses of the drug. More importantly because of the success of the pronounced lipid lower effect with Leqvio, they are less anxious about the potential for experiencing future CV events which in turn improves their overall quality of life and mental health. This in turn enables patients to become even more proactive in partaking in healthy lifestyle modifications

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	X

Please see points above

Clarity of the draft recommendation		
3. **Are the reasons for the recommendation clearly stated?**	Yes	☐

	No	X

No, we do not agree. There is no CVOT data that has been published for this patient population, nor is there any future trial planned. Therefore we feel this recommendation is not appropriate.

4. **Have the implementation issues been clearly articulated and adequately addressed in the recommendation?**	Yes	☐
	No	☐

N/A

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐

N/A

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**

Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	X
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	X
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	X
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Dr. Phil Andros • Dr. Waleed Chehade • Dr. Martin Cieslak		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*

Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2

Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range

	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Instructions for Stakeholders

This template is for eligible stakeholders to provide feedback and comments on draft reimbursement recommendations. Draft recommendations are available for feedback for 10 business days.

CADTH will only consider feedback received from eligible stakeholders, including the sponsor, patient groups, clinician groups, and the participating drug programs. Individuals interested in providing feedback should contact the relevant patient and clinician organizations. This template may also be used by eligible industry stakeholders to provide feedback on draft recommendations from the non-sponsored review process (i.e., any current or future Drug Identification Number [DIN] holders for the drug under review).

The sponsor may use this form to provide general feedback on the draft recommendation if they are not filing a request for reconsideration. If the sponsor is filing a request for reconsideration, they must complete the reconsideration template and should not complete this template.

All submitted feedback must be disclosable and will be posted on the CADTH website.

If you have questions, please email requests@cadth.ca with the complete details of your question(s).

Before Completing the Template:

Please review the following documents to ensure an understanding of CADTH's procedures:

- Procedures for CADTH Reimbursement Reviews
- Procedures for Non-sponsored Reimbursement Reviews
- CADTH Pharmaceutical Review Updates for any applicable information.

Completing the Template:

Feedback should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated and specific reference must be made to the section of the recommendation document under discussion (i.e., page number, section title, and paragraph).

Comments should be restricted to the content of the draft recommendation and should not contain any language that could be considered disrespectful, inflammatory or could be found to violate applicable defamation law.

Feedback must be based on the information that was considered by the expert committee in making the draft recommendation. No new evidence will be considered at this part of the review process.

Feedback must not exceed 3 pages in length, using a minimum 11-point font on 8.5″ by 11″ paper. If comments exceed 3 pages, the feedback will not be accepted by CADTH. References may be provided separately; however, these cannot be related to new evidence.

Patient groups must complete Appendix 1.

Clinician groups must complete Appendix 2.

Filing the Completed Template:

The feedback must be provided in Microsoft Word format by using the *Submit* link next to the drug on the Open Calls page. In order to ensure fairness in CADTH's procedures, all stakeholder feedback must be received by the deadline posted on the CADTH website.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791 - 001
Brand name (generic)	Leqvio(inclisiran)
Indication(s)	Heterozygous FH. (HeFH)
Organization	North Shore Lipid Clinic and Internal Medicine
Contact information[a]	Dr. Naveen Sandhu, 200-101 W16th St, North Vancouver, BC

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	X

As physicians that manage Familial Hypercholesteremia we recommend that the draft recommendation change. We feel that provinces should reimburse inclisiran. Releasing a draft version for clinician input is a smart feature as it allows input on features that don't show up in publications. It also shows that CADTH is an organization that listens to clinicians' needs.

Limiting choice for patients is detrimental to outcomes in asymptomatic conditions like HeFH. Educating the patient on their condition is the start of the conversation but when they choose their own path forward they are more likely to comply with the decision. Inclisiran offers an additional option with its twice yearly dosing and has the potential advantage of improving patient adherence to therapy.

Heterozygous FH patients experience the effects of atherosclerosis relatively young. Genetics causing high levels of cholesterol for an entire life means that plaque buildup happens much sooner than average, thereby, increasing risk of peripheral vascular disease, myocardial infarction and strokes in 40 to 50 year old patients. Most importantly, we know the risk can be minimized through existing treatments. Reimbursing inclisiran would allow access to another option for these high risk patients especially in whom twice yearly dosing would improve adherence and, thus, long term outcomes, and at similar medications costs.

In conclusion, untreated HeFH patients often have a negative health event at a young age with dramatic consequences for their whole family. This is well documented in the literature but the literature cannot document the human decisions needed to manage to Canadian and International standards. Inclisiran allows for an additional option for our high risk patients based on their individual profile at similar cost to other already reimbursed alternatives.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐

Our group did not realize there was a previous opportunity to input.

Clarity of the draft recommendation		
3. **Are the reasons for the recommendation clearly stated?**	Yes	x
	No	☐

The reasons are clearly stated but seem to extrapolate the need for mortality data in ASCVD to familial Hypercholesteremia which is not an accepted standard for HeFH management.

4. **Have the implementation issues been clearly articulated and adequately addressed in the recommendation?**	Yes	☐
	No	☐
Implementation is not an issue for inclisiran.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	x
No. They don't list any reimbursement conditions. This draft limits inclisiran as an option for patients in need of unique options.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
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- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	X
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	X
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
Not applicable since we did not submit an earlier recommendation.		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr Naveen Sandhu*
Position	*Lipid Specialist and General Internal Medicine*
Date	*04-04-2024*
×	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. We have nothing meaningful to declare.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	Dr. Adam Chruscicki
Position	Lipid Specialist and General Internal Medicine
Date	*04-04-2024*
×	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

We have nothing meaningful to declare.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Dr. Takashi Bourchier*
Position	*General Internal Medicine*
Date	*04-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

We have nothing meaningful to declare.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000 Stakeholder Feedback on Draft Recommendation
Brand name (generic)	Inclisiran
Indication(s)	Heterozygous Familial Hypercholesterolemia (HeFH)
Organization	Edmonton Cardiology Consultants
Contact information[a]	Name: Dr. Debraj Das

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

To the knowledge of our team, there is no hard endpoint data/outcomes, available for the HeFH, patient population. In the HeFH population, there has not been any outcome trial to attach with any other previous medications.
The rationale for utilization within this high risk population, 1 mmol/L reduction in LDL-C is demonstrated to result in a 20% RRR in cardiovascular outcomes. This is very important within a high risk group that has challenges to reach CCS recommended LDL-C target. The current Inclisiran research has demonstrated significant impact on LDL-C, within this population. This correlates with our clinical experience in this patient population as well. By definition, this patient population presents with higher LDL-C levels, it is more challenging to reach the appropriate CCS recommended threshold.

There are multiple benefits to the patient when considering this treatment option. The ECC care team directly oversees each patient's injection and we currently have patients with experience >1yr. Our team can confirm the absence of any adverse side effects. To date, only a couple minor injection site reactions have been observed. Patients are very pleased with the frequency of dose administration and this has had a direct impact on compliance. The patients are aware that they must meet with our team to administer this medication every 6 months, which helps to ensure compliance and LDL-C remains at the acceptable target.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐

If not, what aspects are missing from the draft recommendation?

Not applicable – did not submit previous stakeholder input

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name: Dr. Debraj Das*
Position	*Please state currently held position : Clinical Cardiologist*
Date	*Please add the date form was completed (DD-MM-YYYY): 04-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name: Amgen	☒	☐	☐	☐
Add company name : Novartis	☒	☐	☐	☐
Add company name: Novo Nordisk	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name: Dr. Micha Dorsch*
Position	*Please state currently held position: Clinical Cardiologist*
Date	*Please add the date form was completed (DD-MM-YYYY): 04-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name: Amgen	☒	☐	☐	☐
Add company name: Novartis	☒	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name: Dr. Neil Brass*
Position	*Please state currently held position: Clinical Cardiologist, President: Edmonton Cardiology Consultants*
Date	*Please add the date form was completed (DD-MM-YYYY) 04-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐

Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name: Dr. Sudheer Sharma*
Position	*Please state currently held position: Clinical Cardiologist*
Date	*Please add the date form was completed (DD-MM-YYYY) 04-04-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name: Amgen	☒	☐	☐	☐
Add company name: Novartis	☒	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-000
Brand name (generic)	Inclisiran
Indication(s)	Primary hypercholesterolemia
Organization	Novartis
Contact information[a]	Christopher Fordyce, MD, MHS, Msc 2775 Laurel St – 9th Floor Vancouver, BC V6N 3V5

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation. Yes ☐ No ☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

LDL is the one the strongest surrogate markers in CV medicine, and inclisiran has consistently been shown to lower LDL in an HeFH population with good safety data. There is an urgent need to develop more therapies in this space, including among patients who have challenges with compliance.

For example, 30% of patients with MI do not achieve guideline recommended LDL levels often due to cost and access. Many of these patients are young with HeFH.

Patients really feel that the q6 month injections are very convenient, and this dosing regimen can actually reduce disparities in care for those living in more remote communities, such as indigenous communities in Northern BC.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH? Yes ☐ No ☒

If not, what aspects are missing from the draft recommendation?

N/A

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated? Yes ☐ No ☒

If not, please provide details regarding the information that requires clarification.

Please refer to Answer #1.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒
If not, please provide details regarding the information that requires clarification. N/A		

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒
If not, please provide details regarding the information that requires clarification. N/A		

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Christopher Fordyce, MD, MHS, MSc*
Position	Associate Professor, UBC Division of Cardiology, and Director and attending physician, VGH Cardiac Intensive Care Unit
Date	*08-04-2024*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Bayer	☒	☐	☐	☐
Novo Nordisk	☐	☒	☐	☐
Boehringer Ingelheim	☐	☒	☐	☐
Sanofi	☐	☒	☐	☐
Novartis	☒	☐	☐	☐
New Amsterdam	☒	☐	☐	☐
HLS Therapeutics	☒	☐	☐	☐

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: **SR0791-000**
Generic Drug Name (Brand Name): **Inclisiran (Leqvio)**
Indication: **As per the Health Canada approved indication, for primary hypercholesterolemia (Heterozygous familial hypercholesterolemia (HeFH)**
Name of Clinician Group: **University of Toronto faculty and clinicians at St Michael's Hospital who are actively involved in the treatment of patients with heterozygous familial hypercholesterolemia (HeFH)**
Author of Submission: **Dr. Shaun G. Goodman**

1. About Your Clinician Group

We are Faculty at the University of Toronto (https://www.utoronto.ca/about-u-of-t) and clinicians at St Michael's Hospital, Unity Health Toronto (https://unityhealth.to/locations/st-michaels-hospital/) who are actively involved in the treatment of patients with heterozygous familial hypercholesterolemia (HeFH) with and without atherosclerotic cardiovascular disease (ASCVD) in order to lower their blood levels of atherogenic lipoproteins (including low-density lipoprotein-cholesterol [LDL-C]) in order reduce their risk of developing ASCVD and/or experiencing a (recurrent) cardiovascular vascular event.

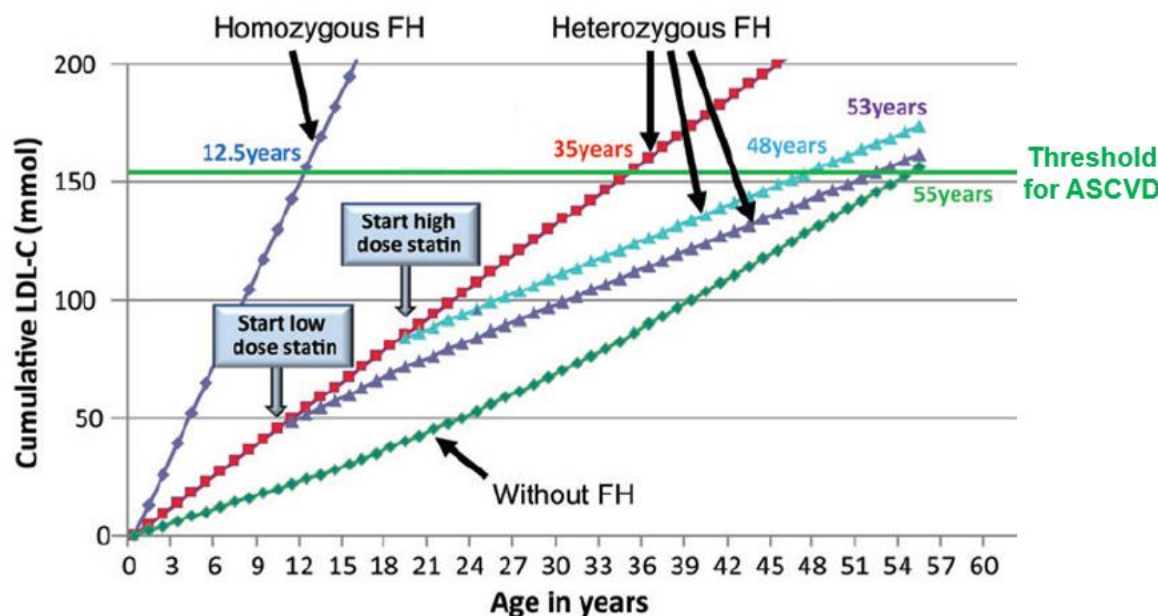
2. Information Gathering

This submission is based on published data, including Canadian Cardiovascular Society (CCS) Guidelines and Positions Statements, and our clinical experience.

3. Current Treatments and Treatment Goals

ASCVD remains a major cause of morbidity and mortality in Canada and lowering and optimizing LDL-C is an essential component of our risk reduction strategies. HeFH is the most common monogenic disorder causing premature ASCVD, affecting 1 in 250 individuals worldwide (Akioyamen et al *BMJ Open* 2017;7:e016461), including an estimated 145,000 Canadians (Brunham et al *Can J Cardiol* 2018;34:1553-63). HeFH causes elevated LDL-C levels across a person's lifespan. Prompt recognition and initiation of therapy with statins in youth or young adulthood has been shown to lower LDL-C levels, markedly decrease the risk of ASCVD, and normalize life expectancy (Nordestgaard et al *Eur Heart J* 2013;34:3478-90).

The concept of a cumulative LDL-C (**Figure below**) illustrates the importance of early treatment (Nordestgaard et al *Eur Heart J* 2013;34:3478-90). For an individual with heterozygous FH, this LDL-C burden is reached by age 35 years if untreated, by age 48 years if treated since age 18, and by age 53 years if treated since age 10 years. The cumulative LDL cholesterol burden of a 55-year-old person without FH is typically 160 mmol, a burden sufficient for ASCVD to develop.



While there is no randomized clinical trial evidence supporting a specific LDL-C goal, a reasonable therapeutic goal for primary prevention in adults with HeFH is to reach a threshold of LDL-C<2.5 mmol/L (Nordestgaard et al *Eur Heart J* 2013;34:3478-90; Brunham et al *Can J Cardiol* 2018;34:1553-63). In patients with HeFH with established ASCVD, the CCS dyslipidemia guideline currently recommends a threshold of LDL-C<1.8 mmol/L, apolipoprotein B<0.70 g/L, or non-high-density lipoprotein-cholesterol (HDL-C)<2.4 mmol/L (Pearson et al *Can J Cardiol* 2021;37:1129-50).

Since LDL-C elevation over time is a causal factor for the development of ASCVD, it is essential to lower LDL-C (and other atherogenic lipoproteins) as a diagnosis of HeFH is made and to maintain LDL-C below threshold for an individual's lifetime. While health behaviour modification (e.g., healthy diet, physical activity, smoking cessation) is an initial step in the management of patients with elevated LDL-C levels, it is important to recognize that HeFH patients will also require pharmacological therapy. Randomized controlled trials on the reduction in CV events with the use of any lipid-lowering agent for FH do not exist (Brunham et al *Can J Cardiol* 2018;34:1553-63) nor, to the best of our knowledge, are any currently underway. Despite limited evidentiary basis, statins are the initial drug class of choice for HeFH, on the basis of landmark trials in the non-FH population that have shown that statins are the best treatment available for lowering LDL-C in patients with increased ASCVD risk. Further, an observational study from the Dutch screening program for FH revealed that treatment with moderate- or high-intensity statins conferred a 44% relative risk reduction in ASCVD and mortality, compared with patients who did not use statins (Versmissen et al *BMJ* 2008;337:a2423).

The addition of adjunctive agents is recommended on an individualized basis to reach the desired LDL-C levels. In patients with HeFH in whom the target LDL-C level cannot be achieved with statin monotherapy, or when high doses of statins are not tolerated because of adverse effects, the combination of a lower dose of statin with ezetimibe can be an alternative. However, since the LDL-C-lowering effect of ezetimibe is modest (e.g., 14% relative LDL-C lowering vs. placebo when added to high-intensity statins [atorvastatin 40-80 mg/day or rosuvastatin 20-40 mg/day; Lee et al Cardiol Res 2021;12:98-108]), additional therapy is often required.

The monoclonal antibodies to proprotein convertase subtilisin/kexin type 9 (PCSK9), alirocumab (75 or 150 mg subcutaneously every 2 weeks) and evolocumab (140 mg subcutaneously every 2 weeks) are approved by Health Canada and received a recommendation to list on provincial formularies by CADTH based on LDL-C lowering (50%-60% relative from baseline) and a safety profile similar to

that of placebo in HeFH patients (Kastelein et al *Eur Heart J* 2015;36:2996-3003; Hovingh et al *J Clin Lipidol* 2017;11:1448-57). Further, these treatments have been shown in large CV outcome studies of ASCVD patients—but with relatively few recognized HeFH patients included--to significantly reduce the risk of CV morbidity and mortality, with excellent safety and tolerability profiles (Sabatine et al *N Engl J Med* 2017;376:1713-22; Schwartz G et al *N Engl J Med* 2018;379:2097-107).

Inclisiran is a small interfering RNA (siRNA) drug that in phase 3 trials was shown to reduce LDL-C levels by about 50% with a safety profile that is similar to the PCSK9 monoclonal antibodies (the only treatment emergent adverse event more frequently seen with inclisiran vs. placebo being a small increase in local injection site reactions, none of which were severe or persistent) (*Wright et al. J Am Coll Cardiol. 2021;77:1182*). A dedicated trial in HeFH patients included 482 adults receiving four subcutaneous injections of inclisiran sodium (300 mg) or matching placebo over a 1.5 year period and demonstrated a 44%-48% relative difference in LDL-C lowering, with robust reductions in LDL-C levels in all genotypes of FH (Raal et al *N Engl J Med* 2020;382:1520-30). Adverse events and serious adverse events were similar in the inclisiran and placebo groups. While the primary outcome in all of these phase III trials (including patients with HeFH, ASCVD, or ASCVD risk-equivalent on maximally tolerated statin-therapy) was LDL-C lowering, and none were powered to assess clinical outcomes, a prespecified exploratory analysis of CV outcomes demonstrated that inclisiran significantly reduced the composite of major adverse CV events (CV death, cardiac arrest, non-fatal myocardial infarction, and stroke [OR (95% CI): 0.74 (0.58–0.94)]) at 1.5 years (Ray et al *Eur Heart J* 2023; 44, 129–38). Further, when added to statin therapy, twice-yearly (after an initial dose and another at three months) inclisiran consistently reduced LDL-C (78% achieved LDL-C goal) in an open-label extension study (including HeFH patients) in which patients were followed up for between one and four years (mean exposure of 3.7 years, longest exposure of 6.8 years)(Wright et al *Eur Heart J* 2023 [late-breaking clinical science abstract]).

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Attainment of guideline-recommended lipid targets in patients with HeFH is particularly critical since, relative to individuals with comparably high levels of LDL-C, individuals with pathogenic FH-causing mutations are at particularly increased risk of developing ASCVD and associated CV events, reflecting the lifelong cumulative exposure to toxic levels of circulating LDL-C (Razek et al *Can J Cardiol* 2018;34:1004-9). Further, while the prevalence of HeFH in Canada has been estimated to be 145,000 Canadians (Brunham et al *Can J Cardiol* 2018;34:1553-63), the proportion of diagnosed patients not achieving LDL-C goals is uncertain. Indeed, limited real-world Canadian data is available to describe the current unmet treatment needs for HeFH patients. In a prospective provincial registry of patients with FH (British Columbia FH Registry [BC FH Registry]), <35% of patients achieved a ≥50% reduction in LDL-C, and <10% achieved an LDL-C<2 mmol/L (Brunham et al *Can J Cardiol* 2017;33:385-92).

The suboptimal achievement of LDL-C targets may be attributed to multiple factors including insufficient LDL-C lowering with statins and ezetimibe (particularly in HeFH patients), statin-associated side effects, suboptimal medication adherence, and treatment inertia. In addition, some patients will decline the use of monoclonal antibody PCSK9 inhibitors because they are self-administered subcutaneous injections every 2-4 weeks. Over the years, individual cases of suboptimal LDL-C lowering or complete intolerance to both monoclonal agents are increasingly recognized. The availability of an additional PCKS9 inhibitor treatment option with improved access and less frequent administration would be a most welcome addition and would help to get the LDL-C of these high risk HeFH patients to below threshold values. This would, in turn, significantly reduce major adverse cardiovascular events (MACE), including myocardial (re-)infarction, ischemic stroke, the need for coronary revascularization (percutaneous coronary intervention/stenting and coronary artery bypass surgery), and cardiovascular death.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

The BC FH Registry analysis noted above was based on data collected from 2012-15, prior to the approval in Canada of PCSK9 inhibitors for the treatment of HeFH (Razek et al *Can J Cardiol* 2018;34:1004-9). A subsequent 2016-17 publication reported that, among 275 patients with a clinical diagnosis of FH, 48 had started using a monoclonal antibody PCSK9 inhibitor; the reduction in LDL-

C was significantly greater in patients receiving a PCSK9 inhibitor compared with those who did not receive one (1.85 mmol/L vs 3.23 mmol/L; p<0.001). Further, among patients receiving a PCSK9 inhibitor, 85% achieved a ≥50% reduction in LDL-C or LDL-C<2 mmol/L, compared with 50% of patients not receiving a PCSK9 inhibitor (p<0.001).

Although this subcutaneously administered drug (by healthcare providers instead of patient self-administration) is cleared from the blood stream within 48 hours, it has a prolonged action in the liver where it decreases the synthesis of naturally made PCSK9, allowing for infrequent dosing (injections every 6 months after the initial and 3-month dose). Two large CV outcome studies (n=33,000 patients with ASCVD) have completed enrolment and in the longer term follow-up phase; while major adverse CV event information won't be available sooner than 2026,

Thus, inclisiran would provide an additional treatment option that requires less frequent dosing which may lead to better medication adherence and perhaps greater accessibility than the monoclonal antibody PCSK9 inhibitors. As there are a relatively finite number of FH patients in Canada, CATH listing of inclisiran would not increase provincial costs as the monoclonal antibody PCSK9 inhibitors are already generally reimbursed. In fact, there could potentially be some cost savings realized provincially as inclisiran is less expensive than the monoclonal antibody PCKS9 inhibitors after the first year of treatment.

It is important to note that all other LDL-C-lowering drugs, including the monoclonal antibody PCSK9 inhibitors, have been approved by Health Canada (and listed by CADTH) based on the efficacy and safety of LDL-C lowering alone in patients with HeFH; as noted above, there are no randomized clinical trials in this population providing CV outcome data.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

As per the CCS Position Statement on Familial Hypercholesterolemia: Update 2018 (Brunham et al *Can J Cardiol* 2018;34:1553-63) and the CCS Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adults (Pearson et al *Can J Cardiol* 2021;37:1129-1150), HeFH patients who cannot achieve therapeutic LDL-C targets on maximally tolerated statins and ezetimibe should receive PCSK9 inhibitors. Further, HeFH patients with ASCVD are identified as a specific group of secondary prevention patients shown to derive similar relative, but greater absolute, benefit from PCSK9 inhibition (Pearson et al *Can J Cardiol* 2021;37:1129-1150).

Inclisiran could also be considered for individuals who are intolerant to the PCSK9 monoclonal antibodies, those with learning disabilities (e.g. attention deficit/hyperactivity disorder), and patients who are uncomfortable with or cannot self-inject.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

The maximum LDL-C lowering of inclisiran is typically achieved by about 90 days. As with other lipid-lowering drugs, treatment efficacy is monitored by measuring LDL-C, typically every 6 to 12 months. As noted above, sustained lowering of LDL-C is required to reduce the risk in HeFH patients of developing ASCVD and for premature CV events.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

None; LDL-C-lowering therapy to achieve guideline-recommended threshold will be required for an HeFH patient's lifetime.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

The specific indication (As an adjunct to lifestyle changes, including diet, to further reduce LDL-C level in adults who are on maximally tolerated dose of a statin, with or without other LDL-C -lowering therapies, and who have HeFH), simple dosing regimen of inclisiran,

and straightforward safety and tolerability profile should allow for the drug to be prescribed by either primary care or specialist physicians. However, it is acknowledged that the initial diagnosis of HeFH may be supported by referral to a specialist.

6. Additional Information

None

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   No

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Shaun G. Goodman

Position: Professor of Medicine, University of Toronto; Associate Head, Division of Cardiology, St. Michael's Hospital-Unity Health Toronto; Adjunct Professor of Medicine, University of Alberta

Date: 02-04-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis			X (for consulting and Executive Steering Committee activities in the VICTORION-2 PREVENT trial of inclisiran vs. placebo)	

Declaration for Clinician 2

Name: Lawrence A. Leiter

Position: Professor of Medicine and Nutritional Sciences, University of Toronto; Director, Lipid Clinic, St. Michael's Hospital-Unity Health Toronto

Date: 02-04-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis			X (for providing CME, consulting and Steering Committee activities in the LACAN LOWERS LDL-C study (inclisiran vs placebo post ACS)	

Declaration for Clinician 3

Name: Alice Y. Y. Cheng

Position: Associate Professor of Medicine, University of Toronto; Endocrinologist, St. Michael's Hospital-Unity Health Toronto and Trillium Health Partners,

Date: 04-04-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 3

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis	X ($0)			

Declaration for Clinician 4

Name: Subodh Verma

Position: Professor of Surgery, and Pharmacology and Toxicology; Cardiac Surgeon, St. Michael's Hospital-Unity Health Toronto; Canada Research Chair in Cardiovascular Surgery, University of Toronto

Date: 05-06-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 4: Conflict of Interest Declaration for Clinician 4

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis		X		

Declaration for Clinician 5

Name: Cynthia T. Luk

Position: Assistant Professor of Medicine, University of Toronto; Endocrinologist, St. Michael's Hospital-Unity Health Toronto

Date: 05-04-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 5

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis	X			

Declaration for Clinician 6

Name: Dominic S. Ng

Position: Associate Professor of Medicine, Physiology and Laboratory Medicine and Pathobiology, University of Toronto; Endocrinologist, St. Michael's Hospital-Unity Health Toronto

Date: 05-04-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 6: Conflict of Interest Declaration for Clinician 6

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis	X			

Declaration for Clinician 7

Name: Beth L. Abramson

Position: Associate Professor of Medicine, University of Toronto; Cardiologist, St. Michael's Hospital-Unity Health Toronto

Date: 05-04-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 7: Conflict of Interest Declaration for Clinician 7

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis		X For Advisory Boards and speaker for Educational Programs		

Declaration for Clinician 8

Name: John L. Sievenpiper

Position: Professor of Nutritional Sciences and Medicine, University of Toronto; Staff Physician, Division of Endocrinology and Metabolism, St. Michael's Hospital-Unity Health Toronto

Date: 04-04-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 8: Conflict of Interest Declaration for Clinician 8

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis	X ($0)			

Declaration for Clinician 9

Name: Kim A. Connelly

Position: Professor of Medicine and Physiology, University of Toronto; Division Head of Cardiology, St. Michael's Hospital-Unity Health Toronto; Executive Director of Keenan Research Center for Biomedical Science, Li Ka Shing Knowledge Institute, St. Michael's Hospital

Date: 05-04-2023

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 9: Conflict of Interest Declaration for Clinician 9

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis	X ($0)			

March 27, 2024

Dear Sir/Madame:

I respectfully disagree with the draft CADTH recommendation regarding inclisiran for the HeFH population. While the CADTH review is technically correct regarding mortality and quality of life results, there appears to be no acknowledgment of expert practitioner input nor any understanding of the historical imperative of allowing HeFH patients access to safe LDL-C lowering drugs given the difficulty in undertaking mortality trials in patients with lifelong, genetic dyslipidemias, including the ethical barriers involved in contemplating such trials. Mortality data has not been required for the other classes of LDL-C lowering drugs routinely used in patients with HeFH such as statins, ezetimibe and existing PCSK9 inhibitors. Indeed, early introduction of statins in patients with HeFH, even without mortality data, led to a significant improvement in the natural history of such patients with respect to overall reduction in cardiovascular risk and events. All safe LDL-C lowering drugs to date have been associated with a reduction over the long term in cardiovascular risk and events. CADTH is implying a new threshold of evidence which is not congruent with practice in this field either in Canada or internationally. I believe also that the safety data have been under-appreciated by the CADTH review. While the CADTH recommendation quotes the patient groups as asking for mortality benefits, this is an unreasonable requirement by them and is not an appropriate reason for CADTH to demand the same. In summary, inclisiran is a safe and effective LDL-C lowering intervention which would be a useful adjunct to lifestyle interventions and existing interventions that are not adequately reducing LDL-C to guideline-sanctioned levels.

Sincerely,

G. B. John Mancini, MD, FRCPC

University of British Columbia

Perceived COI: Honoraria for medical education talks, advisory board discussions and grants for research projects from Novartis, Esperion, Merck, AstraZeneca, Pfizer, HLS Therapeutics.

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	
Brand name (generic)	Leqvio (inclisiran)
Indication(s)	
Organization	
Contact information[a]	Name: Karen Chu

Stakeholder agreement with the draft recommendation

1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

patients prefer the 2x a year vs every two weeks and many patients don't like to self inject
Leqvio will help ensure compliance- since it is HCP injected you and the patient knows that their LDL-C is controlled & patient does not need to self-inject. Pt can pick up their other prescriptions at the pharmacy when they are receiving their Inclisiran shot.

the CDEC committee agree that lowering LDL-C improves outcomes and agree that the exploratory endpoints are trending in the right direction . So with many patients not being able to access the PCSK9i's, Inclisiran could be that option.

Monoclonal antibody PCSK9i's are always in the bloodstream while Inclisiran is only systemic for 48 hours therefore reducing the chance of drug/drug interaction and adverse events.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

As stated above, Leqvio is 2x/year injection and will improve patient's quality of life and compliance 2x/year injection is more convenient to the patient that 2x/month or 1/month. Having a HCP inject the medication while the patient is at the pharmacy also helps with compliance. I don't think there needs to be a study to show this.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒

N/A

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

N/A

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐

N/A

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name: Karen Chu*
Position	*Please state currently held position: Cardiologist, Kamloops*
Date	*Please add the date form was completed (DD-MM-YYYY): April 5, 2024*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☒
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0791-001
Brand name (generic)	Inclisiran
Indication(s)	As an adjunct to lifestyle changes, including diet, to further reduce low-density lipoprotein cholesterol (LDL-C) level in adults who are on maximally tolerated dose of a statin, with or without other LDL-C -lowering therapies, and who have non-familial hypercholesterolemia (nFH) with atherosclerotic cardiovascular disease (ASCVD).
Organization	Novartis Pharmaceuticals Canada Inc.
Contact information[a]	[redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

1. **The CDEC draft recommendation not to reimburse is inconsistent with prior CDEC recommendations for hypercholesterolemia.**

CDEC notes in its Rationale for the Recommendation (p.3, second paragraph in section), *"…there is insufficient evidence to assess the clinical benefit of inclisiran in terms of reducing the risk of cardiovascular events, cardiovascular death, or all-cause mortality"*. This is inconsistent with past recommendations for hypercholesterolemia drugs and inconsistent with the new evidence presented for MACE outcomes pooled in the ORION-10 and -11 studies.

CDEC previously recommended that alirocumab be reimbursed for patients with HeFH or with clinical ASCVD.[1] The evidence at the time of this recommendation notably did not include the ODYSSEY OUTCOMES trial which was 2 years away from its primary completion date at the time of the CDEC review. Therefore, CDEC clearly determined that LDL-C data was sufficient to recommend alirocumab for reimbursement in the ASCVD population, and CDEC is not following the standard established in this disease area by stipulating that CV outcomes data are required for reimbursement of hypercholesterolemia drugs.

CDEC noted in its rationale: "*A key limitation to the pooled analysis of MACE was that it was conducted post hoc and included exploratory outcomes, as noted above. These limitations precluded CDEC from determining whether inclisiran reduces the risk of cardiovascular morbidity and mortality.*" (p.4 first bullet point of Discussion Points). Novartis accepts that these are limitations with this analysis,[3] as there are for any post-hoc analysis, but highlight that these results are highly consistent with the primary outcome findings of significantly reduced LDL-C, and are consistent with the extremely well-established causal link between LDL-C and CV events. As such, the effective and safe LDL-C reduction together with the causal link between LDL-C and CV events should be sufficient to recommend inclisiran for reimbursement in the ASCVD population as for other therapies that target PCSK9 pathways.[4]

Therefore, CDEC did not act consistently or equitably by recommending against the reimbursement of inclisiran compared with past reviews for PCSK9 inhibitors (evolocumab and alirocumab) which target the same PCSK9 protein and were recommended for conditional reimbursement upon reduced price.

2. **The CDEC draft recommendation not to reimburse does not consider the causal relationship between LDL-C and cardiovascular outcomes and is inconsistent with the approach to surrogate outcomes in other disease areas.**

CDEC notes in its second Discussion Point, "*While CDEC recognized that that there is a health need for patients who do not reach LDL-C targets despite available treatments and that reducing LDL-C levels is an important outcome in patients with ASCVD, it was noted that while for many treatments there is evidence that lowering LDL-C levels correlates with a reduction in risk of cardiovascular events, extrapolation from other trials or to other populations based on LDL-C levels is not substantiated by current evidence.*" (p.4 second paragraph Discussion Point)

CDEC regularly accepts drugs on the basis of surrogate evidence of improving cardiovascular outcomes. For example, CDEC recommended reimbursement for Veltassa (patiromer) to treat adult patients with chronic kidney disease who have hyperkalemia and who are receiving renin-angiotensin-aldosterone system inhibitor therapy.[5] Notably, CDEC cited: *"…There is no evidence that patiromer improves patient relevant outcomes, such as survival, cardiovascular, and renal outcomes; prevents hospitalization or emergency department visits; or improves health-related quality of life*"[5] In diabetes, HbA1c is a well-known validated surrogate endpoint that can predict long-term outcomes in trials of six months to one year.[6] Indeed, both HbA1c and LDL-C are cited by the FDA as validated surrogate markers for diabetic complications, and cardiovascular outcomes, respectively.[6] Accordingly, CDEC routinely recommends approval for diabetes drugs on the basis of HbA1c efficacy, with no evidence that medication improve long-term micro- or macro-vascular complications. For example, Adlyxine was approved despite no evidence that it was superior to standard of care in reducing micro- or macro-vascular complications.[7; 8]

As noted by the consensus statement from the European Atherosclerosis Society Consensus Panel, "*LDL is not merely a biomarker of increased risk but a causal factor in the pathophysiology of ASCVD*".[9] The correlation between LDL-C reduction and reduction in CV outcomes is extremely well-established for statin therapies by the Cholesterol Treatment Trialists (CTT) meta-analyses.[10] As the concentration of LDL-C increases, the risk of atherosclerotic events increases in a dose-dependent manner.[11] Multiple studies and reviews show that LDL-C and other apoB-containing lipoproteins cause the initiation and progression of ASCVD.[12] A large number of meta-analyses have investigated the effects of LDL-C lowering with statins across populations and within specific population subgroups.[10; 13-24] In a meta-analysis of individual-participant data from 26 statin trials including almost 170,000 individuals, treatment with a statin was associated with a log-linear 22% proportional reduction in the risk of major CV events per mmol/L reduction in LDL-C over a median of 5 years treatment. In the statin trials, the yearly event rate observed in each randomized treatment arm was strongly and linearly associated with the absolute LDL-C level achieved.[24]

Building on this evidence, recent placebo-controlled clinical trials have shown that non-statin LDL-C lowering therapies, such as ezetimibe[25] or PCSK9 inhibitors,[26; 27] also reduce the risk of CV events. These trials showed that lowering LDL-C with non-statin therapies reduced the risk of major CV events by the same amount as statins per mmol/L reduction in LDL-C, after adjusting for the duration of the studies.[28] Recent analyses have also shown that the relationship between LDL-C reduction and CV outcomes benefit extends to very low levels of LDL-C, without attenuation of the relationship at lower levels.[29; 30] Another meta-analysis of more than 50 randomized trials, involving more than 350,000 patients and 50,000 major CV events compared the effect of therapies that lower LDL-C by eight different mechanisms. Nearly all therapies evaluated (including statins, fibrates, niacin, bile resins, diet, and ileal bypass surgery) were associated with a similar (20–25%) relative reduction in the risk of CV events per mmol/L reduction in LDL-C.[31]

These data led to worldwide clinical guidelines to emphasize reduction in LDL-C levels with incremental use of lipid-lowering therapies due to their effectiveness and safety, even at low LDL-C levels. For example, the most recent 2021 Canadian Cardiovascular Society (CCS) Dyslipidemia Guidelines state "*The totality of evidence from observational, pathophysiological, epidemiological, Mendelian randomization studies and RCT's of lipid lowering therapies indicate a causal relationship between LDL-C (as well as non-HDL-C and ApoB) and ASCVD and show that lower concentrations of plasma LDL-C levels are associated with a lower risk of ASCVD events extending to very low LDL-C concentrations (< 0.5 mmol/L)*".[32]

The post-hoc analysis presented in this re-submission are completely consistent with this paradigm, as the combined ORION-10 and -11 trial data demonstrate a reduction in MACE events,[3] which is fully in line with the hypothesis that inclisiran, by reducing LDL-C, will reduce CV events. While post-hoc analyses are always subject to limitations, this evidence strongly aligns with the totality of the evidence that LDL-C is causally linked to reductions in CV events. This position is also supported by the patient and physician groups surveyed by CADTH. For example, "*The patient groups stated that patients seek a safe, tolerable and effective treatment that can minimize the long-term health consequences by effectively managing LDL-C levels below the recommended threshold.*" (p. 7, second paragraph in Patient Input) The clinician group surveyed also cited LDL-C as a primary outcome of importance "*The clinician groups agreed that the major issues with managing hypercholesterolemia, whether it be in HeFH or nFH patients with ASCVD, are adherence (as well as intolerance) and lack of accessibility of drug therapies, and that the main outcomes of interest are reduction in lipid parameters (LDL-C, non-HDL-C and ApoB) at 6 months initially and then assessed annually thereafter.*" (p 7 Clinician group input, 2nd paragraph in section). On this basis, reimbursement should have been granted given that inclisiran potently reduces LDL-C for patients with ASCVD.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification: N/A		

[a] CADTH may contact this person if comments require clarification.

References

1. CADTH Common Drug Review (2015). *Common Drug Review Pharmacoeconomic Review Report: Alirocumab (Praluent)*. Available online at: https://www.cadth.ca/sites/default/files/cdr/pharmacoeconomic/SR0469_Praluent_PE_Report.pdf. Accessed: March 22, 2024.
2. CADTH Common Drug Review (2015). *Common Drug Review Pharmacoeconomic Review Report: Evolocumab (Repatha)*. Available online at: https://www.cadth.ca/sites/default/files/cdr/pharmacoeconomic/SR0441_Repatha_PE_Report.pdf. Accessed: March 22, 2024.
3. Ray KK, Raal FJ, Kallend DG, Jaros MJ, Koenig W et al. (2022) Inclisiran and cardiovascular events: a patient-level analysis of phase III trials. *Eur Heart J* 44(2) (2): 129-138.
4. INESSS (2021). LEQVIO: Hypercholestérolémie familiale hétérozygote et maladie cardiovasculaire athéroscléreuse.
5. CADTH (2021). *CADTH Reimbursement Recommendation: Patiromer (Veltassa)*. Available online at: https://cadth.ca/sites/default/files/attachments/2021-06/CADTH_reimbursement_recommendation_patiromer_%28veltassa%29.pdf. Accessed: March 22, 2024.
6. FDA (2020). *BEST (Biomarkers, EndpointS, and other Tools) Resource: Validated Surrogate Endpoint*. Available online at: https://www.ncbi.nlm.nih.gov/books/NBK453484/. Accessed: March 22, 2024.
7. CADTH (2019). *CADTH Canadian Drug Expert Committee Recommendation: Lixisenatide (Adlyxine — Sanofi-aventis Canada Inc.)*. Available online at: https://cadth.ca/sites/default/files/cdr/complete/SR0520_Adlyxine_complete_Nov-23-17.pdf. Accessed: March 22, 2024.
8. CADTH (2021). *CADTH Reimbursement Recommendation: Semaglutide (Rybelsus)*. Available online at: https://www.cadth.ca/sites/default/files/attachments/2021-06/CADTH_reimbursement_recommendation_semaglutide_%28rybelsus%29.pdf. Accessed: March 22, 2024.
9. Ference BA, Ginsberg HN, Graham I, Ray KK, Packard CJ et al. (2017) Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J* 38 (32): 2459-2472.
10. Cholesterol Treatment Trialists C, Mihaylova B, Emberson J, Blackwell L, Keech A et al. (2012) The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. *Lancet* 380 (9841): 581-590.
11. Goldstein JL, Brown MS (2015) A century of cholesterol and coronaries: from plaques to genes to statins. *Cell* 161 (1): 161-172.
12. Ference BA, Graham I, Tokgozoglu L, Catapano AL (2018) Impact of lipids on cardiovascular health: JACC health promotion series. *Journal of the American College of Cardiology* 72 (10): 1141-1156.
13. Cholesterol Treatment Trialists C, Baigent C, Blackwell L, Emberson J, Holland LE et al. (2010) Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet* 376 (9753): 1670-1681.

14. Cholesterol Treatment Trialists C, Fulcher J, O'Connell R, Voysey M, Emberson J et al. (2015) Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials. *Lancet* 385 (9976): 1397-1405.
15. Baigent C, Keech A, Kearney PM, Blackwell L, Buck G et al. (2005) Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet* 366 (9493): 1267-1278.
16. Cholesterol Treatment Trialists C, Herrington WG, Emberson J, Mihaylova B, Blackwell L et al. (2016) Impact of renal function on the effects of LDL cholesterol lowering with statin-based regimens: a meta-analysis of individual participant data from 28 randomised trials. *Lancet Diabetes Endocrinol* 4 (10): 829-839.
17. Genser B, Marz W (2006) Low density lipoprotein cholesterol, statins and cardiovascular events: a meta-analysis. *Clin Res Cardiol* 95 (8): 393-404.
18. Gould AL, Rossouw JE, Santanello NC, Heyse JF, Furberg CD (1995) Cholesterol reduction yields clinical benefit. A new look at old data. *Circulation* 91 (8): 2274-2282.
19. Gould AL, Rossouw JE, Santanello NC, Heyse JF, Furberg CD (1998) Cholesterol reduction yields clinical benefit: impact of statin trials. *Circulation* 97 (10): 946-952.
20. LaRosa JC, He J, Vupputuri S (1999) Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials. *JAMA* 282 (24): 2340-2346.
21. Mills EJ, Rachlis B, Wu P, Devereaux PJ, Arora P et al. (2008) Primary prevention of cardiovascular mortality and events with statin treatments: a network meta-analysis involving more than 65,000 patients. *J Am Coll Cardiol* 52 (22): 1769-1781.
22. Mills EJ, Wu P, Chong G, Ghement I, Singh S et al. (2011) Efficacy and safety of statin treatment for cardiovascular disease: a network meta-analysis of 170,255 patients from 76 randomized trials. *QJM* 104 (2): 109-124.
23. Ray KK, Seshasai SR, Erqou S, Sever P, Jukema JW et al. (2010) Statins and all-cause mortality in high-risk primary prevention: a meta-analysis of 11 randomized controlled trials involving 65,229 participants. *Arch Intern Med* 170 (12): 1024-1031.
24. Taylor F, Huffman MD, Macedo AF, Moore TH, Burke M et al. (2013) Statins for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev* (1): CD004816.
25. Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA et al. (2015) Ezetimibe added to statin therapy after acute coronary syndromes. *New England Journal of Medicine* 372 (25): 2387-2397.
26. Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD et al. (2017) Evolocumab and clinical outcomes in patients with cardiovascular disease. *New England Journal of Medicine* 376 (18): 1713-1722.
27. Schwartz GG, Steg PG, Szarek M, Bhatt DL, Bittner VA et al. (2018) Alirocumab and cardiovascular outcomes after acute coronary syndrome. *New England Journal of Medicine* 379 (22): 2097-2107.
28. Ference BA, Cannon CP, Landmesser U, Lüscher TF, Catapano AL et al. (2018) Reduction of low density lipoprotein-cholesterol and cardiovascular events with proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitors and statins: an analysis of FOURIER, SPIRE, and the Cholesterol Treatment Trialists Collaboration. *European heart journal* 39 (27): 2540-2545.
29. Boekholdt SM, Arsenault BJ, Mora S, Pedersen TR, LaRosa JC et al. (2012) Association of LDL cholesterol, non-HDL cholesterol, and apolipoprotein B levels with risk of

cardiovascular events among patients treated with statins: a meta-analysis. *JAMA* 307 (12): 1302-1309.
30. Giugliano RP, Pedersen TR, Park J-G, De Ferrari GM, Gaciong ZA et al. (2017) Clinical efficacy and safety of achieving very low LDL-cholesterol concentrations with the PCSK9 inhibitor evolocumab: a prespecified secondary analysis of the FOURIER trial. *The Lancet* 390 (10106): 1962-1971.
31. Silverman MG, Ference BA, Im K, Wiviott SD, Giugliano RP et al. (2016) Association between lowering LDL-C and cardiovascular risk reduction among different therapeutic interventions: a systematic review and meta-analysis. *JAMA* 316 (12): 1289-1297.
32. Pearson GJ, Thanassoulis G, Anderson TJ, Barry AR, Couture P et al. (2021) 2021 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult. *Can J Cardiol*