CADTH

CADTH Reimbursement Review

Patient Input

inclisiran (TBC)

(Novartis Pharmaceuticals Canada Inc.)

Indication: Primary hypercholesterolemia

CADTH received patient input from:
Canadian Heart Patient Alliance (CHPA)
HeartLife Foundation

April 9, 2021

Disclaimer: The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations.

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 personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

CADTH

CADTH Reimbursement Review Patient Input Template

Name of the Drug and Indication	**Inclisiran (Leqvio) for Familial Hypercholesterolemia and Atherosclerotic Cardiovascular Disease**
Name of the Patient Group	**Canadian Heart Patient Alliance (CHPA)**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

The Canadian Heart Patient Alliance (CHPA) is a patient-led nonprofit umbrella organization of patients, families, health professionals and supporters dedicated to reducing cardiovascular disease and preventing early death due to cholesterol and other risk factors. Our focus is high cholesterol and other lipids, due to genetic and non-genetic factors, as the leading under-diagnosed and under-treated cause of cardiovascular disease and early death. The Canadian Heart Patient Alliance is working toward the day when no Canadian will suffer reduced quality of life, life-altering event, or early death due to high cholesterol and other lipids.

The Canadian Heart Patient Alliance is the successor the FH Canada Patient Network and collaborates with FH Canada, Heart Healthy Prevention Program St. Paul's Hospital, and Lipid Genetics Clinic at LHSC-University Hospital. Internationally, CHPA engages with the FH Foundation (USA), Heart UK, and FH Europe.

The FH Canada Patient Network receives organizational and administrative support from the Institute for Optimizing Health Outcomes, a nonprofit organization guided by the vision of optimizing health outcomes for all individuals regardless of their health condition.

Website: http://www.heartpatientalliance.ca/

2. Information Gathering

This submission represents the summarized input of 262 individual respondents, 254 from the web-based Survey Monkey questionnaire. The survey was available only in English. reflecting the language of the CPHA and St. Paul's contact list. While there are individual and family members of CPHA residing in Quebec (about 5%), all previous correspondence and in-person events that have included Quebec residents have been conducted in English. There was a 95% completion rate of the questionnaire with an average response time of 13.5 minutes. An additional 8 individual interviews were conducted by two researchers by telephone or zoom call, with six calls in English and 2 in French.

The questionnaire was made available on Survey Monkey from March 18 - April 3, 2021.

The "call for participation" was sent out through the CPHA mailing list and BC St. Paul's Hospital Healthy Heart Program FH patient list. In addition, requests for participation were distributed through social media and also through FH Foundation Facebook page and social media requests from Heart UK - The Cholesterol Charity. Outreach was also made through two clinician researchers involved in extension clinical trials with inclisiran but it is not clear how many respondents were recruited through that route.

The survey was directed to patients and families affected by "high lipids" and in the introductory paragraph described the target respondent as individuals or family members with heterozygous familial hypercholesterolemia (HeFH) and atherosclerotic cardiovascular disease (ASCVD), which were the target patient populations for inclisiran. However, the drop-down respondent self-identification menu also included homozygous FH, not-familial FH, undiagnosed with family history of FH, other lipid disorders (dyslipidemia, hyperlipidemia, high triglycerides), and other.

Overall, 51% of survey respondents identified self or family member as affected with HeFH, 4% with HoFH, 9% with symptoms but not diagnosed with FH, 5% with family history of FH, 6% with ASCVD, 7% with other lipid disorders, and 13% indicating they were waiting diagnosis, unsure, or multiple indications.

The mean age of the patients (not respondents) was 59 years and the median age was 61 years. The oldest person referenced was 97 years old and the youngest was 22 years old. Overall, 18% were over 70 years of age, 32% between 61 and 70 years old, 26% between 51 and 60 years old, 14% between 41 and 50 years old, and 10% under 40 years old. This information is significant, indicating that some patients are being diagnosed and treated, if appropriate, early, pre-symptomatic, and pre-cardiovascular events.

About 95% identified themselves as residing in Canada, with 61% in BC, 19% in Ontario, 8% in Quebec, 3% in Alberta, and 4% in Manitoba, Saskatchewan and the Yukon. The remaining 5% identified as residing in the UK, EU country, USA, Mexico, and Iran.

3. Disease Experience

Participants were asked, in an open-ended question, to … "Describe, in your own words, how living with high cholesterol or high lipids or cardiovascular disease has affected you currently or in the past. Has your condition affected your work, school, social and/or family life?

However, to put their responses in context, it is important to know that 95% said they had received or were still receiving treatment for their condition. About 80% are being managed in a cardiovascular program and most receive regular follow up care by a specialist or their family physician. In brief, these respondents are probably better managed than most patients with high cholesterol and present a very different profile than the 2015 survey done with respect to PCSK9 inhibitors Repatha and Praluent. Overall, about 90% reported their LDL cholesterol level was well managed while about 10% said they were not regularly within target.

The open-ended responses of living with high cholesterol were categorized under six non-exclusive themes: cholesterol management, lifestyle impact, cardiovascular events, treatments, stress/anxiety, and family impact. This summary reports tendencies rather than frequencies since this is neither a representative or random sample.

SYMPTOMS: About one-fourth reported regular physical symptoms related to their lipid condition, some minor and some significant, including headaches (like icy picks), chest pains, muscle pains in legs and ankles, shortness of breath, xanthomas (under the skin in wrists, ankles, or elsewhere), weakness, fatigue, muscle loss, and neuropathy. "My only physical experience living with high cholesterol is that my liver feels congested at times, which has me feeling tired and sluggish." "I have no symptoms of this disease other than edema in my right ankle which is now always sore and swells with much standing or walking."

MANAGING CHOLESTEROL: About one-fifth also indicated that managing their cholesterol level and keeping it at target was an on-going challenge. "Spent 15 years trying to bring my cholesterol down with diet and exercise with little success and living in fear of having a stroke or heart attack." "After long years of being on a strict cholesterol-free diet is too hard to maintain.-consuming too much medicine has side effects (even if not stated in the prescription notice) such as feeling muscle pain even during little physical

activities or work. For that reason, I cannot have a full-time job - traditional drugs (in my case) are not effective: LDL level still high even with Crestor 40 and Ezetrol 10 plus all other drugs."

LIFESTYLE IMPACT: About one-fifth said that their high cholesterol/lipid condition had little or no effect on their quality of life. Many reported that they had changed their diet and exercise. "It has not affected my life -- to my knowledge. My diet and exercise were good prior to finding out that my arteries were clogged." "The condition never affected my work, school or social life. It affected my family life by altering our diet." "I am an active person, cycling 180 km per week, playing tennis 3x week, and walking or hiking on other days.my cholesterol levels has not affected my daily live." Some even said they and their family had adopted healthier habits as a result of their condition.

However, some responses indicated that patients were not always aware of the impact of high cholesterol, in part, because they were well managed on treatment and did not experience daily symptoms. "Day to day high cholesterol has not adversely affected me except my doctor is very concerned and we have tried various treatments, the statins did bring my levels into a safe region but slowly over many years attacked the joints and had to quit."

CARDIOVASCULAR EVENTS: Three-fourths of the FH patients reported having had at least one cardiovascular intervention, that is, heart attack, stroke, angioplasty, bypass surgery, and/or stent insertion. Many have had multiple events requiring multiple interventions. Many expressed anxieties about the "unpredictability" of a cardiovascular event and potential severe consequences.

PSYCHOLOGICAL AND FAMILY IMPACT: Most respondents feel positive about their daily life and have accepted or adapted to living with high cholesterol, including those who have experienced a cardiovascular event or have stents. The two most frequently mentioned sources of anxiety were (1) future uncertainty of the medications not working or the risk of a cardiovascular event and (2) the impact on their children, whether diagnosed or at risk. "It is a relatively symptom free genetic disorder. My only concerns have been related to life expectancy due to the increased risk of heart failure or stroke. I am also concerned with my 2 young children and whether they will develop the condition as they grow older." "It has made me worry about the long-term effects of being on statins. It makes me worry about passing this on to my children." "Living with FH … am 38 … diagnosed at 25. …in the back of my mind I am always thinking 'are the statins working? will they stop working one day? how bad are the side effects really? Am I going to die young?' And more recently 'are my kids going to have FH?' I'm really excited that there may be a new drug coming. Especially because my Mother has FH and the statins don't work for her anymore."

4. Experiences With Currently Available Treatments

TREATMENTS: Respondents' perceptions of their treatments were drawn from the open-ended experiential question as well as two rating scales about 13 treatments that included drug therapies, diet, and apheresis as options. They were asked to rate, first, on the effectiveness of each therapy (five-option scale) and the experience of adverse effects (five-option scale).

Overall, the majority (90%) of these respondents appear to be well supervised by their clinic or physician and have had their medications adjusted, as needed. This is in contrast to our survey of six years ago when only 25% of respondents said they were doing well on their drug regimen (usually statins or statins with ezetimibe), either in terms of getting their LDL cholesterol to target levels or tolerating the side effects. Similarly, in contrast to previous surveys, these respondents with poorly controlled cholesterol did NOT mention that their clinician had challenged their adherence to the medication nor did their clinician disbelieve they experienced serious adverse effects to their medication (statins) that kept them from taking them as prescribed.

In this survey, about 95% of respondents reported they were prescribed a drug therapy regimen consisting of one or more drugs. Almost all those on treatment said that they were also following a low-fat diet and exercising. About 94% had taken or were currently taking statins. About 55% reported statins worked well or very well and only 18% said they had not worked in managing their cholesterol. However, about one-fourth reported they had experienced severe or very severe adverse effects.

About two-thirds of respondents had added an additional drug (often Ezetimibe) and about 40 - 50% had switched or added PCSK9 to their treatment regimen. Overall, 43% had experience with an injectable PCSK9, Repatha or Praluent. The responses were similar, with 83% (Repatha) and 79% (Praluent) reporting that these therapies worked well or very well; only 12% reported they did not work well. Between 83% (Repatha) and 95% (Praluent) of patients reported none or very few adverse effects with only 10% (Repatha) reporting some "severe" adverse effects.

"I also was not able to tolerate any form of statin, many were tired to little effect of sufficiently lowering my numbers nor could I tolerate the side effects of the statin. Being on Repatha, has been very efficient for me.

"I have high cholesterol but cannot take more than 10 mg vastatin since it gives me muscle pain. Vastatin also has other side effects such as dry mouth and I feel it is hard to treat and Biotin mouth wash does not help much. I am very careful with my diet and try to exercise as much as I can."

“While taking a specific statin drug, I experienced severe pain in my muscle tissue in various parts of my body. Laboratory results confirmed that my creatine kinase (CK) levels were dangerously high. The muscle pain from the statin was severe and caused me to have difficulty walking."

“I was one of the very early patients introduced to the injectable PCSK9 inhibitors … to be used in combination with statins. My cholesterol levels did retreat … but I again had an adverse reaction to the statin which resulted in muscle pain and a significantly high CK level. My body is able to tolerate the PCSK9 inhibiter but alone, it has not been successful.”

“At present, no drug alone or in combination has been successful in managing my cholesterol level and statins have caused severe side effects. The PCSK9 inhibiter, while tolerable without adverse side effects, has shown a small measurable decrease in cholesterol levels but not significant enough to be called successful.”

"Managed with statins for a while, but muscle cramping precluded that option. Repatha seems to work well." "I have been taking cholesterol medication for 25+ years. Have watched my diet and tried to exercise regularly. Presently on Repatha, and mostly low carbohydrate diet. Feel pretty good." "I am on Repatha and it has lowered my cholesterol. I am unsure of the damage with build up from age 25 to 59 when the drop occurred using the Repatha."

"My body does not tolerate the many statins I have used and causes significant elevations to my CK and liver levels. Hence, I have been taking PCSK9 along with low doses of Crestor, along with Ezetimibe to aggressively manage the LDL levels. These drug use over the years have caused many side effects such as muscle and joint pain, low libido, sleep problems, and headaches over the years. They have led to anxiety and depression. The physical symptoms have made it difficult to engage in regular sports, exercise and personal and intimate relationships in order to enjoy a high-quality life."

In summary, most respondents reported they were not well managed on diet or nutritional supplements alone. However, about half of volunteered that they followed diet and exercise plans in addition to their drug therapies. Most had used statins, with about 55% reporting they worked well alone or in combination with another drug. Slightly more than 40% had used one of the PCSK9s, with about 80% of those reporting they worked well or very well to manage their cholesterol levels. Less than 10% indicated that none of the drug regimens were effective.

5. Improved Outcomes

The majority of respondents felt they were well managed on their current therapy but also expressed multiple concerns. These may be categorized as treatment schedule, side effects, and cost. “I want an “easier” treatment. When I was working, the two weeks turn around for injections was ok but now retired, my ability to travel is based on my injection schedule!” “I hope that there is more development of these types of drugs. I need this type of drug for the rest of my life. I am always concerned about long term side

effects, especially to my liver. And of course, the cost of the drug." "I'm having trouble tolerating Repatha as time goes on. My symptoms are fatigue and muscles aches and pains for about a week post injection." "Please make them more affordable for those who have no drug plan."

Few Canadian patients had previous experience with inclisiran (Leqvio) given the lack of initial clinical trials in Canada; however, there are some now enrolled in extension trials in a couple of Canadian sites. Overall, about 55% of respondents reported they knew little or nothing about the PCSK9s, Repatha and Praluent, while 40% knew much or very much. In contrast, 88% said they knew little or nothing about inclisiran (Leqvio) and only 10% knew much or very much.

Among those who did know, the response was mostly positive, as an alternative to statins or as an alternative to the biweekly injection of PCSK9s. When provided with minimal information (synthesized small interfering RNA (siRNA) molecule, which targets production of PCSK9 and can result in sustained reductions in low-density lipoprotein (LDL) cholesterol levels with biannual injection by a healthcare provider), many saw it as a favourable alternative to daily statins or biweekly PCSK9 injections. Those taking statins expressed hope it would be more effective in controlling cholesterol. For those on PCSK9s, the impact on quality of life was considered as the positive aspect.

"I hope this helps with my high cholesterol; it will be better for me to get an injection instead of a lot of pills." "I think it's amazing, especially with patients who may forget to take daily medication or need health care providers. Because I work as a pilot, the daily statins is more reliable, than 2-week injections. But bi-annual injections would be great since I won't have to remember to carry pills with me all the time between home and travel." "Hopefully it will reduce/manage cholesterol for folks like me who struggle to keep the levels where they should be, despite maximum statins, ezetimibe, healthy diet and exercise routines."

Additionally, several respondents expressed the hope that the cost of biannual injections would be less than biweekly injections. "I have no knowledge but would hope it would lower HdL dramatically without raising my glucose levels and without needing to inject myself. I would hope that this would be effective at a much lower cost than Repatha."

Some expressed caution based on the lack of evidence. "It effectively lowers LDL [but] we need to see outcome data with regards decrease HEART ATTACKS, strokes, cardiac death & total mortality." "I hope there is a drug that could keep us patients in the "normal" range. I also find an injection every two weeks impedes my ability to travel or be away when delivery is expected. It is not an easy drug to commit too. I would prefer to go back to a daily pill so I can make personal plans easier.

The survey also presented a number of paired "trade-off" decisions comparing a daily pill, bi-weekly self-injection, and biannual HCP injection. The results were as follows:

- 52% preferred a daily pill to bi-weekly self-injection if both worked equally well
- 76% preferred a bi-weekly injection over a pill if the injection worked better or had fewer side effects
- 35% preferred a daily pill to twice yearly injection if both worked equally well; 47% preferred the twice-yearly injection
- 81% would take a biannual injection with or without daily pill it were more effective
- 76% would prefer a biannual HCP injection over a biweekly self-injection if both worked equally well.

Overall, respondents clearly preferred the treatment modality that was most effective (with fewest side effects), whether pill or injection. When treatments are considered equally effective, there is a small preference for a daily pill over a bi-weekly self-injection but a preference for a biannual HCP injection over

the daily pill. Finally, respondents overwhelmingly preferred a biannual HCP injection to a bi-weekly self-injection (factor of 7 to 1).

6. Experience With Drug Review

Overall, we received feedback from 10 patients who had experience with inclisiran through clinical trials or early access program. Four resided in Canada and six in USA or UK. All were diagnosed with ASCVD or HeFH and reported they had been on maximum statin levels without achieving target cholesterol levels. All had received between four and six doses of inclisiran while continuing their statin regimen. All had experienced significant reduction in LDL levels and had experienced no adverse effects related to inclisiran.

For respondents, the most important impact was knowing that there was a treatment that could lower their cholesterol levels and keep them closer to target, thereby reducing the risk of further cardiovascular events. "I feel good that I am doing something to prevent further lipid build up and reduce risk of hardening of arteries." "I am a whole lot less concerned about my cholesterol and motivated to stick with my statins." "I feel a lot more optimistic and have a lot more energy. I've even changed my diet and started exercising; it's been good for the whole family." "I just hope it is affordable so it could be available to everyone who needs it."

7. Companion Diagnostic Test

Despite significant improvements in awareness and accessibility, HeFH is still undiagnosed and underdiagnosed. It would be important to increase testing not just to access PCSK9 inhibitors and inclisiran but to reduce risk of poorly managed high cholesterol.

8. Anything Else?

From our perspective as the patient organization supporting individuals and families with high cholesterol due to inherited and non-inherited factors, it was surprising and very gratifying to compare responses from this survey to those received six years ago when we were seeking feedback to submit to the assessment of PCKS9s. Six years ago, only 25% of respondents said they were able to keep their LDL cholesterol levels at desired levels. Among those not at target, about half said they had experienced challenges getting the statin dosage correct or access to a supplemental medication. About half complained of severe side effects that kept them from taking their statins as prescribed. Today, about 90% said they were maintaining their cholesterol levels within range. The big difference is that about 40% had been prescribed one of the PCSK9 inhibitors, with about 5% not remaining on therapy. While we realize these respondents do not represent the universe of Canadians living with high cholesterol, they give a clear picture of what can happen when patients receive an appropriate diagnosis, education, support, and the right medication.
it would be extremely beneficial to introduce an alternative therapy that would be available to those not well managed on current therapies, with immediate access to those not at target despite a maximum statin dosage

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

No.

2. Did you receive help from outside your patient group to collect or analyze data 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.

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			

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.

Name: Durhane Wong-Rieger
Position: Chair
Patient Group: Canadian Heart Patient Alliance
Date: 8 April 2021

CADTH

CADTH Reimbursement Review Patient Input Template

Name of the Drug and Indication	**inclisiran**
Name of the Patient Group	**HeartLife Foundation**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

Describe the purpose of your organization. Include a link to your website.

The HeartLife Foundation is a patient-driven charity whose mission is to transform the quality of life for people living with heart failure by engaging, educating, and empowering a global community to create lasting solutions and build healthier lives.

www.heartlife.ca

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

This submission has been completed by the executives of the HeartLife Foundation and represents discussions held by HeartLife with our members across Canada. Our members include both patients a living with heart failure and their family caregivers.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

The Health consequences and impact of Atherosclerotic Cardiovascular Disease (ASCVD) including outcomes such as Myocardial Infarctions, Ischemic Stroke, Coronary Artery disease including unstable angina, for patients, their caregivers, and the health system are very well documented.

One of the key modifiable risk factors for the serious disease consequences of ASCVD is adequate control of blood lipids, specifically LDL-Cholesterol (LDL-C).

The prevalence and incidence of cardiovascular disease (CVD) in this country is well known burden. ASCVD is considered by health systems in Canada and around the world as a major non-infectious pandemic. The negative effects of ASCVD on caused to Canadian families and to our health system are significant. More needs to be done to address CVD and improve health outcomes for patients.

The number of people that suffer serious health consequences caused by ASCVD, heart attack and ischemic strokes, and the number of people that ultimately die from the effects of CVD is immense. Risk factors for ASCVD need to be address as aggressively as possible with the tools and interventions that are available. One of these interventions, and the product under review, is one of these valuable interventions that should be widely available for Canadians.

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

There is a magnitude of published evidence and current authoritative clinical guidelines issued by multiple national expert advisory bodies around the world, clearly indicated that controlling LDL-C will reduce patients' risk for ASCVD and related health consequences. In the phase 3 Trial to Evaluate the Effect of Inclisiran Treatment on Low Density Lipoprotein Cholesterol in Subjects With Heterozygous Familial Hypercholesterolemia (ORION-9), Inclisiran for Participants With Atherosclerotic Cardiovascular Disease and Elevated Low-density Lipoprotein Cholesterol (ORION-10), and Inclisiran for Subjects With ASCVD or ASCVD-Risk Equivalents and Elevated Low-density Lipoprotein Cholesterol (ORION-11) trials, inclisiran demonstrated LDL-C lowering in patients with heterozygous FH or with, or at high risk of, atherosclerotic CVD.[1]

Currently available treatments for LDL-C include fibrates, statins, ezetimibe, and PCSK9 inhibitors to name a few. Apart from PCSK(inhibitors, the inability of some patients to achieve goal LDL-C levels with other currently available therapies is well documented. A large proportion of the population treated with statins cannot achieve goal LDL-C levels.

[1] Raal FJ, Kallend D, Ray KK, et al. Inclisiran for the treatment of heterozygous familial hypercholesterolemia. N Engl J Med 2020;382:1520-30. And Ray KK, Wright RS, Kallend D, et al. Two phase 3 trials of inclisiran in patients with elevated LDL cholesterol. N Engl J Med 2020;382:1507-19.

In addition, patient adherence to currently available and publicly reimbursed therapeutic options is recognized as poor. PCSK9 inhibitory therapies are highly effective and have been recommended by CADTH for public reimbursement. Unfortunately, public reimbursement for PCSK9 in Canada is limited, and access for patients with uncontrolled LDL-C is highly restricted by provincial health benefit program reimbursement criteria. All this leading to limited access and a reduction in quality of life.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

The outcome that Canadians deserve, is the ability to reduce the long-term ASCVD health consequences in high-risk patients caused by uncontrolled or poorly managed LDL-C levels. Based on the information we have reviewed to date, it is apparent that Inclisiran is highly effective at lowering LDL-C and would an appropriate intervention for high-risk ASCVD patients whose LDL-C levels cannot be controlled by diet and statins alone. Early results from clinical trials suggest that if inclisiran is given to 300,000 patients annually, it could help prevent 55,000 heart attacks and strokes, and has the potential of saving 30,000 lives in the next 10 years.[2]

Furthermore, the merits of a twice-yearly dosage schedule will reduce pill burden and make it significantly easier for patients to take this drug, resulting in greater adherence and improved LDL-C control. This may result in lowering the incidence of important ASCVD health outcomes such as ischemic stroke and ultimately improving the quality of lives for people living with ASCVD.

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies' patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

Unfortunately, none of the individuals who took part in the discussion had experience with the drug under review. That being said, a number of our members have experience, both successfully and unsuccessfully, controlling their LDL-C with diet, statins, or other oral medications and understand the challenges in achieving a target LDL-C level. Many members also expressed significant interest in reducing the number of pills taking and moving towards a twice a year medication.

[2] https://www.gov.uk/government/news/new-heart-disease-drug-to-be-made-available-for-nhs-patients

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

Not Applicable.

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

We have reviewed publicly available documents related to the agreement the manufacturer has made with the UK National Health Service (NHS) to develop a program to address ASCVD through improved LDL-C control and feel a similar program would be beneficial in Canada.

We are hopeful that CADTH's evaluation of Inclisiran results in a positive recommendation.

9. References

Raal FJ, Kallend D, Ray KK, et al. Inclisiran for the treatment of heterozygous familial hypercholesterolemia. N Engl J Med 2020;382:1520-30.

Ray KK, Wright RS, Kallend D, et al. Two phase 3 trials of inclisiran in patients with elevated LDL cholesterol. N Engl J Med 2020;382:1507-19.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.
    a. No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.
    a. 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.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Astra Zeneca				x
Boehringer Inglehiem				x
Novartis			x	
Servier		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.

Name: Marc Bains
Position: Co-Founder
Patient Group: HeartLife Foundation
Date: April 7, 2021