CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

aflibercept (Eylea HD)

(Bayer Inc.)

Indication: Treatment of diabetic macular edema (DME)

March 1, 2024

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813-00
Brand name (generic)	Eylea HD (aflibercept 8mg/0.07ml)
Indication(s)	Diabetic macular edema
Organization	Fighting Blindness Canada, The Canadian Council of the Blind, CNIB, Diabetes Canada, Vision Loss Rehabilitation Canada, International Federation of Ageing
Contact information[a]	Name: Larissa Moniz, Director Research and Mission Programs, [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 are pleased that CADTH has recommended reimbursing Eylea HD for DME. We feel that it's important for patients to have access to treatment choice and strongly advocate to have as many safe and effective treatments available as possible.

Based on results from clinical trials, this drug holds promise to reduce the frequency of injections for patients with DME which could have significant impact on patients' quality of life, reducing burden of appointments, anxiety, and side-effects. Reducing treatment frequency may also increase compliance and relieve strain on the health care system.

However, the reimbursement conditions outlined by CADTH in the draft recommendation appear to limit access to this treatment and therefore may limit its utility for patients. We did not feel there was a clear rational for the three conditions discussed below and they do not appear to be consistent with recommendations for other recently approved anti-VEGF medications or with patient experience. We would welcome CADTH providing more rational and reconsidering the following:

1) **Renewal of reimbursement is dependent on at least 15 letter improvement (Reimbursement condition 3)**

The rationale for this reimbursement condition was not clearly articulated in the draft recommendation and does not appear consistent with recommendations for other anti-VEGF drugs. It is not clear why this treatment specifically has this reimbursement condition.

Reviewing clinical trial and real-world experience data (for this treatment and other anti-VEGF drugs), a 15-letter improvement appears to be at the upper end of what a patient may experience after starting an anti-VEGF drug. This condition may disqualify patients who seek treatment earlier when they have less vision loss (e.g. less than 15 letters lost). Finally, from a patient perspective a gain of 5 or 10 letters can be very meaningful allowing individuals to continue doing daily tasks, reading, and even driving. As such the CADTH recommendation does not appear to take patient experience into account when setting this reimbursement condition.

We support realistic success metrics, including discontinuation of drug use in the absence of efficacy. However, without CADTH providing further rationale about this condition, we feel that the current recommendation may force many patients who are successfully responding to Eylea HD and are benefiting from a reduced treatment frequency to switch to other potentially less efficacious or more frequent treatments.

2) **Injection frequency must reach at least 12 weeks following 3 loading doses (Reimbursement condition 7).**

We agree that the overall treatment goal of this treatment should be to increase treatment interval to 12 or 16 weeks as successfully achieved in the majority of clinical trial participants. We also agree that from a public payer perspective it is appropriate to utilize the lowest cost drug that achieves the same treatment frequency and vision outcomes.

However, the rationale for this reimbursement condition was not clearly articulated in the draft recommendation and does not appear consistent with recommendations for other recently approved anti-VEGF drugs which also aimed for a longer treatment interval. As currently recommended, we are concerned that this may limit patient choice and reduce the likelihood that a patient is prescribed a drug that could reduce treatment frequency.

Based on current practice, many clinicians are more comfortable increasing interval dose in a stepwise manner. As comfort with an increased treatment intervals grows, this stepwise increase may not be necessary. However, forcing a jump from a 4 to 12-week treatment interval could discourage clinicians from starting patients on this treatment.

We also encourage CADTH to consider patients for whom this treatment increases treatment interval significantly but who can't achieve a 12-week interval. We are concerned that this reimbursement condition may disproportionately disadvantage those patients who have the highest treatment burden and are in most need of new treatment options. For example, a patient who can only achieve 4–6-week interval on older anti-VEGF may not achieve a 12-week interval even with this treatment but may achieve for example an 8- or 10-week interval. We believe this could still be a significant reduction in treatment frequency and large benefit to patients, their caregivers and the health system.

Overall, we believe that treatment choice should be guided by both clinician and patient input and feel that this reimbursement condition is not in line with a patient centered approach.

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?
We thank the committee for considering stakeholder input but do not feel that the impact of treatment burden on patients was fully considered in their conditions for reimbursement. The burden of travel, side effects and anxiety on patients and their wider care circle is significant. Treatments that reduce the number of injections patients need to receive would have direct impact on quality of life and may also increase treatment compliance and outcomes. We encourage the committee to consider the patient experience when reviewing current reimbursement conditions.

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. As outlined in question #1, we do not believe that the rationale for some of the reimbursement conditions was clearly laid out.		

[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	*Larissa Moniz*
Position	*Director, Research and Mission Programs*
Date	*22-02-2024*
☒	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	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813-000-000 Stakeholder Feedback on Draft Recommendation
Brand name (generic)	aflibercept 8mg/0.07mL
Indication(s)	Diabetic macular edema
Organization	Apex Eye Institute
Contact information[a]	Name: Mostafa Hanout

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.

I disagree with linking renewal of drug reimbursement at 6 months to achieving 15 letters of gain. This is clearly unrealistic and is never required, nor necessarily expected when using any of the existing anti-VEGF drugs. Further, this condition is contradictory to item 1.3 of the CADTH criteria itself which indicates the visual acuity range for DME patients between 20/32 to 20/320 Snellen. There is a ceiling effect for DME patients with 20/32 vision to achieve 15 letters gain since they are 10 letters away from 20/20.

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 refer to my explanation in the previous question.

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.
Reasons are clearly stated, but do not justify the recommendation.

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.
Implementation issues have been clearly articulated. However, they are not adequately addressed as I explained above in my response to 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.
Although reimbursement conditions are clearly stated, the rationale does not stand argument.

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

Appendix 2. Conflict of Interest Declarations for Clinician Groups

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- 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	*Mostafa Hanout, MD, MSc*
Position	*Ophthalmologist, Medical and Surgical Retina Consultant*
Date	*Please add the date form was completed (29-02-2024)*
☒	**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	*Justin French, MD, FRCSC*
Position	*Ophthalmologist, Medical and Surgical Retina Consultant*
Date	*Please add the date form was completed (29-02-2024)*
☒	**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	*Joe Wijay, MD, FRCSC*
Position	*Chief Ophthalmologist*
Date	*Please add the date form was completed (29-02-2024)*
☒	**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	*Aneesh Ratnam, MD*
Position	*Ophthalmologist*
Date	*Please add the date form was completed (29-02-2024)*
☒	**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	*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	☐	☐	☐	☐

J.H. WHELAN, M.D.
Box 13, 8-10 Rowan St.
St. John's, NF A1B 2X3
[redacted]

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813
Brand name (generic)	EYLEA HD (AFLIBERCEPT
Indication(s)	DIABETIC MACULAR EDEMA
Organization	ATLANTIC CORE RETINA CONSULTANTS
Contact information[a]	Name: JAMES H WHELAN

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.

DISAGREE WITH RECOMMENDATION #3 -
VA gain of 15 letters is unreasonable and will improved

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?

VA gain should be 5-10 letters minimum

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.

VA UE and limited support from literature

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

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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* JAMES N. WHELAN	
Position	*Please state currently held position* RETINA SURGEON	
Date	*Please add the date form was completed (DD-MM-YYYY)* 28/07/2024	
☐	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. Destiny Physicians		

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

Appendix 2. Conflict of Interest Declarations for Clinician Groups

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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. LITERATURE REVIEW AND CHART R		
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 – JOANNA FLYNN • Clinician 2 – CHRISTOPHER SPERMAN • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name* CHRISTOPHER SPERMAN
Position	*Please state currently held position* MEDICAL RETINA
Date	*Please add the date form was completed (DD-MM-YYYY)* 28/06/2024
☑	**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.
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 BAYER	☑	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name* ANNA FLYNN
Position	*Please state currently held position* RETINA SURGEON
Date	*Please add the date form was completed (DD-MM-YYYY)* 08/07/2024
☑	**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 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	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813-000
Brand name (generic)	Eylea HD
Indication(s)	Treatment of diabetic macular edema
Organization	Canadian Ophthalmological Society
Contact information[a]	Name: Dr. Phil Hooper

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.

Reimbursement condition 2:
"The maximum duration of initial authorization is six months".

The treatment of diabetic macular oedema in clinical practice requires treatment duration in excess of six months in a substantial minority of patients to achieve maximal benefit. A six month window will not allow adequate time for a decision to be made in these patients, and has not been validated in clinical trials.

Reimbursement condition 3:
"For renewal after initial authorization, patients must achieve at least 15 letters improvement in BCVA at 6 months compared with baseline (pre-treatment)"

ETDRS acuity testing is not performed routinely in clinical practice and use of this criteria is not relevant to the vision testing in routine use. More importantly, the ability of an eye to gain vision with treatment is directly related to the entry vision at the time of treatment initiation. Given the accumulated clinical experience with first generation anti-VEGF agents, patients are referred and treated with acuities that do not allow this level of improvement to occur. Use of this arbitrary cut off will disadvantage many of the patients who demonstrate significant anatomic benefit on OCT, yet do not show this level of vision change. This has not been a criterion for continued use of existing anti-VEGF drugs which are the comparator agents for this drug in clinical trials.

Reimbursement condition 4:
"Aflibercept 8mg should be discontinued upon any of the following:
4.1. Reduction in BCVA in the treated eye to less than 15 letters (absolute) on 2 consecutive visits in the treated eye, attributed to DME in the absence of other pathology.
4.2 Reduction in BCVA of 30 letters or more compared to either baseline and/or best recorded level since baseline.
4.3. Evidence of deterioration of the lesion morphology despite optimum treatment over 3 consecutive visits"

A decline in visual acuity is not a validated reason to discontinue therapy with anti-VEGF agents in diabetes. Many other factors affect vision in clinical practice and vision may deteriorate irrespective of the degree of control of macular edema.

Reimbursement condition 7:
"Injections should not be given more frequently than every 12 weeks after the first 3 consecutive doses."

In clinical practice, there is significant variability in the response to anti-VEGF agents. In clinical trials there is a need to minimize variability in dosing to facilitate comparison, however in clinical practice it is not possible to adhere to a rigid interval and achieve maximal benefit for individual patients. This variability of response has been demonstrated in longitudinal studies in clinical settings.

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.

- Concerns raised about maximum duration of initial authorization, renewal criteria, discontinuation criteria, and injection frequency
- Clarification on rationale behind committee's recommendations and specific evidence used to support conditions
- Document should explain evidence, clinical considerations, and stakeholder input informing reimbursement conditions
- Insights needed on potential implications of conditions on patient access, treatment duration, and clinical outcomes
- Concerns about relevance and impact of conditions on clinical practice and patient outcomes
- Provide rationale for inclusion of specific criteria, such as ETDRS acuity testing and rigid injection intervals in reimbursement conditions

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.

  On page 9, it is mentioned that clinical experts consulted by CADTH provided advice on potential implementation issues raised by the drug programs. However, the specific details

regarding these implementation issues and the advice provided are not explicitly outlined in the document.

- The responses to questions from the drug programs regarding implementation issues are presented in Table 2, but the document does not provide a comprehensive analysis or synthesis of these responses. This lack of detailed analysis means issues are not clearly articulated.
- The document includes stakeholder perspectives from patient and clinician groups, which highlight the impact of DME on daily lives and the unmet need for efficacious and durable treatments. However, the document does not explicitly connect these perspectives to the potential implementation challenges or provide a clear discussion of how the identified implementation issues could impact patient access and treatment outcomes.
- The document does not offer a detailed discussion of the potential barriers to treatment access, such as travel burdens for patients living in rural communities and vulnerable populations, which could impact the implementation of Aflibercept 8 mg in clinical practice.

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.

Please see “Stakeholder agreement with the draft recommendation” Question 1.

[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		
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	*Phil Hooper*
Position	*President, Board of Directors, Canadian Ophthalmological Society*
Date	*Please add the date form was completed (18-11-2023) (attached at end of document)*
☒	**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	*Mona Harrisi Dagher*
Position	*President Elect, Board of Directors, Canadian Ophthalmological Society*
Date	*Please add the date form was completed (18-11-2023) (attached at end of document)*
☒	**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	*Briar Sexton*
Position	*Treasurer, Board of Directors, Canadian Ophthalmological Society*
Date	*Please add the date form was completed (04-12-2023) (attached at end of document)*
☒	**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	*Cynthia Qian*
Position	*Chair of Continuing Professional Development, Board of Directors,*
Date	*Please add the date form was completed (30-11-2023) (attached at end of document)*
☒	**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 (consulting relationship)	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*David Plemel*
Position	*Secretary, Board of Directors, Canadian Ophthalmological Society*
Date	*Please add the date form was completed (18-11-2023) (attached at end of form)*
☒	**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	*Setareh Ziai*
Position	*YO Liason, Board of Directors, Canadian Ophthalmological Society*
Date	*Please add the date form was completed (07-12-2023) (attached at end of form)*

☒	**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	*Vivian Hill*
Position	*Chair on Advocacy, Board of Directors, Canadian Ophthalmological Society*
Date	*Please add the date form was completed (21-12-2023) (attached at end of form)*
☒	**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	☐	☐	☐	☐

Director Consent and Acknowledgement

TO: The Canadian Ophthalmological Society /Société canadienne d'ophtalmologie (the "**COS**").

Consent to Serve:

1. I hereby ratify and confirm my consent to act as a director of the COS (a "**Director**") effective as of the date of my election or appointment as a director (the "**Director Consent**"). The Director Consent shall continue in effect from year to year so long as I remain on the board of directors of the COS (the "**Board**"), but if I resign or am removed from the Board, the Director Consent shall cease to have effect from the effective date of such resignation or removal.

2. I further ratify and confirm my consent to any one or more of the directors of the COS from time to time participating in meetings of the Board or committees of the Board of the COS by means of such telephone, electronic or other communications facilities as permit all persons participating in the meeting to communicate adequately with each other simultaneously and instantaneously, such consent to continue in effect unless revoked by an instrument in writing delivered to the COS.

3. I hereby agree to advise the COS by a notice in writing delivered to the COS of any change in my place of residence forthwith after such change.

Acknowledgement re Fiduciary Obligations:

4. I acknowledge and agree that as a Director of the COS I have a fiduciary obligation to the COS to act honestly and in good faith with a view to the best interests of the COS and that this duty includes, but is not limited to the following:

    a. I have a duty of confidentiality to the COS, which requires me to hold all non-public information belonging to the COS or provided to me by the COS confidential unless such information is approved for disclosure by resolution of the Board. This obligation extends to all matters discussed at meetings of the Board and all information provided to me by the COS in any form, including but not limited to oral, written or electronic form. I specifically acknowledge that this obligation will be ongoing after I am no longer a Director of the COS in respect of any information I receive while I am a Director.

    b. I have a duty of loyalty to the COS, which duty includes a prohibition on public criticism of Board decisions, whether or not I personally agree with such decision.

c. I am required to be familiar with, and govern myself in accordance with, the Articles of Continuance and By-laws of the COS.

Conflict of Interest Disclosure:

5. I acknowledge that:

   a. For the protection of both the Directors of the COS and the COS itself, the Board of has adopted a policy whereby each Director on the Board is required to make an annual disclosure regarding conflicts of interest.

   b. For the purposes of such disclosure, a conflict of interest defined as: a situation where there could exist the perception or risk that the judgment of a Director, or the fiduciary duty of such Director to the COS, could be influenced or appear to be influenced by: (i) their personal interests or the personal interests of their friends, family or business associates; (ii) the interests of another entity in which they are involved, interested or to which they owe an obligation; or (iii) any interest or relationship that is outside of the COS.

   c. I have completed the Conflict of Interest Disclosure Form attached hereto as Schedule "A" and the information thereon is complete and accurate as of the date hereof. I will notify the COS if the information provided on this form is no longer accurate or if I engage in additional activities that could result in an actual or perceived conflict of interest within the meaning of the COS Conflict of Interest Policy

   d. I have read the COS Conflict of Interest Policy attached hereto as Schedule "B" and I hereby agree to comply with its requirements.

DATED the 04 day of December, in the year 2023.

Briar Sexton

Name: Briar Sexton (print name)

4-1854 W 1st Ave, Vancouver, BC, V6J 1G5

Insert address on line above.

Schedule "A": Conflict of Interest Disclosure Form

Please check one of the following boxes and, if making disclosure hereunder, complete the table below:

☒ **I do not have any conflicts of interest or potential conflicts of interest to report.** BS **_____ (initial)**

OR

☐ **I have the following affiliations, interests or relationships to report: _____ (initial)**

Interest/Affiliation/Relationship	Company/Organization	Details
Business relationship or contract		
Participation in clinical trial		
Employment/honoraria/consulting fees/in-kind compensation		
Investments (stock options, etc)		
Membership on an advisory panel, committee, or board of directors		
Grant/research support		
Other financial or material interest		

*In contemplating the nature of the relationships that should be disclosed, Directors should be cognizant of the requirements of the Royal College of Physicians and Surgeons of Canada ("**RCPSC**") as to continuing professional development, which require disclosure of relationships with commercial entities such as a pharmaceutical organizations, medical device companies or communications firms. Although these requirements do not necessarily apply to Directors of the COS in their role as Directors, disclosure of any potential conflicts is a best practice and disclosure in accordance with the RCPSC requirements is recommended.

Signature: Briar Sexton

I certify and confirm that the information herein is accurate.

Name: Briar Sexton

Position: Board Member

Date: 12/04/2023

Schedule "B": COS Conflict of Interest Policy

1. What is a Conflict of Interest?

Directors should be aware that conflicts of interest will arise from time to time and that the existence of a conflict is not an indication of wrong-doing on the behalf of the director in conflict. The key concern in regards to conflicts of interest is how such conflicts are addressed and whether or not they are disclosed. Where a conflict of interest exists and is not disclosed this is a violation of the fiduciary obligations of a director to the corporation.

A conflict of interest is defined somewhat broadly at common law, as there are many situations where a director could find themselves in a situation of conflict. At common law a conflict of interest is a situation where there could exist the perception or risk that the judgment of an individual, or the fiduciary duty of such individual to the corporation, could be influenced or appear to be influenced by:

1.1 their personal interests or the personal interests of their friends, family or business associates;
1.2 the interests of another entity in which they are involved, interested or to which they owe an obligation;
1.3 any interest or relationship that is outside of the corporation.

In addition to the common law definition of conflict of interest above, the *Canada Not-for-Profit Corporations Act* (the "**Act**") sets out certain situations where a director will be in conflict, conflict and the required disclosure in respect of same, as follows:

> **141.** (1) A director or an officer of a corporation shall disclose to the corporation, in writing or by requesting to have it entered in the minutes of meetings of directors or of committees of directors, the nature and extent of any interest that the director or officer has in a material contract or material transaction, whether made or proposed, with the corporation, if the director or officer
>
> (*a*) is a party to the contract or transaction;
>
> (*b*) is a director or an officer, or an individual acting in a similar capacity, of a party to the contract or transaction; or
>
> (*c*) has a material interest in a party to the contract or transaction.

Note that a conflict of interest exists whether or not the individual believes that they will not be swayed by the competing interest because a conflict of interest does not only involve situations where an individual is influenced, but also scenarios where there is the **perception** of influence or a conflict.

2. What should a Director do if they suspect or know that they are in conflict?

a) Disclose the Conflict:

Both the common law and the Act require that a director in conflict disclose the conflict on the earlier of (a) when the subject of the conflict is first discussed; or (b) as soon as the director becomes aware of the conflict.

This obligation to disclose is an ongoing obligation, meaning: if the issue is not the subject of a conflict when initially discussed, but later becomes the subject of a conflict, the director is required to disclose the conflict immediately upon the occurrence thereof.

For the protection of the director in conflict, the best practice is for the director to declare the conflict and request that the conflict be entered into the minutes of any meeting when the issue involving the conflict is discussed. Where the issue is discussed at multiple meetings, this declaration and insertion in the minutes should take place at each such meeting.

b) Abstain from Voting on the Issue involving the Conflict:

Where the conflict is a conflict within the meaning of Article 141 of the Act, the director in conflict is required to abstain from voting on the issue. Where the conflict is not addressed by the Act, the common law requires that a director abstain from voting on the issue.

c) Avoid the Perception of Influencing the Issue:

Although not required by law, where a conflict is serious in nature, a director may wish to step-out of a meeting where the issue is being discussed in order to avoid the perception of impropriety. The fact that a director in conflict has stepped out of the meeting should be recorded in the minutes of meeting.

Further, a director in conflict should avoid discussing the issue of the conflict with other board members or employees/staff of the corporation to avoid the perception of attempting to influence the outcome of the issue.

3. What if a Director Serves on the Board of another Organization?

Where an individual is a director of another corporation that may have competing or different interests from those of the COS, such director may find themselves in conflict as to issues discussed at one or both board tables. The fact that the director is a director of both organizations does nothing to derogate from the obligations of a director to the either entity. Directors have a fiduciary duty to all the corporations they serve as directors.

The same rules as to conflict of interest apply where the conflict is between the two corporations a director serves, even if the corporations are friendly, related or linked. The courts have held that a director ‘cannot serve two masters’ and if the interests of two corporations of which a

person is a director conflict on a particular matter, the director must recuse herself or himself for participating on both boards on the issue concerned.

Director Consent and Acknowledgement

TO: The Canadian Ophthalmological Society /Société canadienne d'ophtalmologie (the "**COS**").

Consent to Serve:

1. I hereby ratify and confirm my consent to act as a director of the COS (a "**Director**") effective as of the date of my election or appointment as a director (the "**Director Consent**"). The Director Consent shall continue in effect from year to year so long as I remain on the board of directors of the COS (the "**Board**"), but if I resign or am removed from the Board, the Director Consent shall cease to have effect from the effective date of such resignation or removal.

2. I further ratify and confirm my consent to any one or more of the directors of the COS from time to time participating in meetings of the Board or committees of the Board of the COS by means of such telephone, electronic or other communications facilities as permit all persons participating in the meeting to communicate adequately with each other simultaneously and instantaneously, such consent to continue in effect unless revoked by an instrument in writing delivered to the COS.

3. I hereby agree to advise the COS by a notice in writing delivered to the COS of any change in my place of residence forthwith after such change.

Acknowledgement re Fiduciary Obligations:

4. I acknowledge and agree that as a Director of the COS I have a fiduciary obligation to the COS to act honestly and in good faith with a view to the best interests of the COS and that this duty includes, but is not limited to the following:

    a. I have a duty of confidentiality to the COS, which requires me to hold all non-public information belonging to the COS or provided to me by the COS confidential unless such information is approved for disclosure by resolution of the Board. This obligation extends to all matters discussed at meetings of the Board and all information provided to me by the COS in any form, including but not limited to oral, written or electronic form. I specifically acknowledge that this obligation will be ongoing after I am no longer a Director of the COS in respect of any information I receive while I am a Director.

    b. I have a duty of loyalty to the COS, which duty includes a prohibition on public criticism of Board decisions, whether or not I personally agree with such decision.

c. I am required to be familiar with, and govern myself in accordance with, the Articles of Continuance and By-laws of the COS.

Conflict of Interest Disclosure:

5. I acknowledge that:

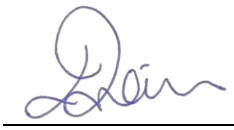
   a. For the protection of both the Directors of the COS and the COS itself, the Board of has adopted a policy whereby each Director on the Board is required to make an annual disclosure regarding conflicts of interest.

   b. For the purposes of such disclosure, a conflict of interest defined as: a situation where there could exist the perception or risk that the judgment of a Director, or the fiduciary duty of such Director to the COS, could be influenced or appear to be influenced by: (i) their personal interests or the personal interests of their friends, family or business associates; (ii) the interests of another entity in which they are involved, interested or to which they owe an obligation; or (iii) any interest or relationship that is outside of the COS.

   c. I have completed the Conflict of Interest Disclosure Form attached hereto as Schedule "A" and the information thereon is complete and accurate as of the date hereof. I will notify the COS if the information provided on this form is no longer accurate or if I engage in additional activities that could result in an actual or perceived conflict of interest within the meaning of the COS Conflict of Interest Policy

   d. I have read the COS Conflict of Interest Policy attached hereto as Schedule "B" and I hereby agree to comply with its requirements.

DATED the __30_____ day of __November_____,in the year _2023____.



Name: _Cynthia Qian_____ (print name)

2000 Drummond, Apt 1206
Montreal, QC
H3G 2X1

Insert address on line above.

Schedule "A": Conflict of Interest Disclosure Form

Please check one of the following boxes and, if making disclosure hereunder, complete the table below:

☐ **I do not have any conflicts of interest or potential conflicts of interest to report. _____ (initial)**

OR

☒ **I have the following affiliations, interests or relationships to report: CQ _____ (initial)**

Interest/Affiliation/Relationship	Company/Organization	Details
Business relationship or contract		
Participation in clinical trial		
Employment/honoraria/consulting fees/in-kind compensation	Abbvie, Bayer, Boehringer Inge	Consulting
Investments (stock options, etc)		
Membership on an advisory panel, committee, or board of directors	FBC, CRS	Pan-canadian inherited diseases s
Grant/research support	FBC, CRF, Paul Fournier Founda	
Other financial or material interest		

*In contemplating the nature of the relationships that should be disclosed, Directors should be cognizant of the requirements of the Royal College of Physicians and Surgeons of Canada ("**RCPSC**") as to continuing professional development, which require disclosure of relationships with commercial entities such as a pharmaceutical organizations, medical device companies or communications firms. Although these requirements do not necessarily apply to Directors of the COS in their role as Directors, disclosure of any potential conflicts is a best practice and disclosure in accordance with the RCPSC requirements is recommended.

Signature: 

I certify and confirm that the information herein is accurate.

Name: Cynthia Qian

Position: CPD Council Chair

Date: 2023-11-18

Schedule "B": COS Conflict of Interest Policy

1. What is a Conflict of Interest?

Directors should be aware that conflicts of interest will arise from time to time and that the existence of a conflict is not an indication of wrong-doing on the behalf of the director in conflict. The key concern in regards to conflicts of interest is how such conflicts are addressed and whether or not they are disclosed. Where a conflict of interest exists and is not disclosed this is a violation of the fiduciary obligations of a director to the corporation.

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1.1 their personal interests or the personal interests of their friends, family or business associates;
1.2 the interests of another entity in which they are involved, interested or to which they owe an obligation;
1.3 any interest or relationship that is outside of the corporation.

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>
> (*a*) is a party to the contract or transaction;
>
> (*b*) is a director or an officer, or an individual acting in a similar capacity, of a party to the contract or transaction; or
>
> (*c*) has a material interest in a party to the contract or transaction.

Note that a conflict of interest exists whether or not the individual believes that they will not be swayed by the competing interest because a conflict of interest does not only involve situations where an individual is influenced, but also scenarios where there is the **perception** of influence or a conflict.

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For the protection of the director in conflict, the best practice is for the director to declare the conflict and request that the conflict be entered into the minutes of any meeting when the issue involving the conflict is discussed. Where the issue is discussed at multiple meetings, this declaration and insertion in the minutes should take place at each such meeting.

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Where the conflict is a conflict within the meaning of Article 141 of the Act, the director in conflict is required to abstain from voting on the issue. Where the conflict is not addressed by the Act, the common law requires that a director abstain from voting on the issue.

c) Avoid the Perception of Influencing the Issue:

Although not required by law, where a conflict is serious in nature, a director may wish to step-out of a meeting where the issue is being discussed in order to avoid the perception of impropriety. The fact that a director in conflict has stepped out of the meeting should be recorded in the minutes of meeting.

Further, a director in conflict should avoid discussing the issue of the conflict with other board members or employees/staff of the corporation to avoid the perception of attempting to influence the outcome of the issue.

3. What if a Director Serves on the Board of another Organization?

Where an individual is a director of another corporation that may have competing or different interests from those of the COS, such director may find themselves in conflict as to issues discussed at one or both board tables. The fact that the director is a director of both organizations does nothing to derogate from the obligations of a director to the either entity. Directors have a fiduciary duty to all the corporations they serve as directors.

The same rules as to conflict of interest apply where the conflict is between the two corporations a director serves, even if the corporations are friendly, related or linked. The courts have held that a director ‘cannot serve two masters’ and if the interests of two corporations of which a

person is a director conflict on a particular matter, the director must recuse herself or himself for participating on both boards on the issue concerned.

Director Consent and Acknowledgement

TO: The Canadian Ophthalmological Society /Société canadienne d'ophtalmologie (the "**COS**").

Consent to Serve:

1. I hereby ratify and confirm my consent to act as a director of the COS (a "**Director**") effective as of the date of my election or appointment as a director (the "**Director Consent**"). The Director Consent shall continue in effect from year to year so long as I remain on the board of directors of the COS (the "**Board**"), but if I resign or am removed from the Board, the Director Consent shall cease to have effect from the effective date of such resignation or removal.

2. I further ratify and confirm my consent to any one or more of the directors of the COS from time to time participating in meetings of the Board or committees of the Board of the COS by means of such telephone, electronic or other communications facilities as permit all persons participating in the meeting to communicate adequately with each other simultaneously and instantaneously, such consent to continue in effect unless revoked by an instrument in writing delivered to the COS.

3. I hereby agree to advise the COS by a notice in writing delivered to the COS of any change in my place of residence forthwith after such change.

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4. I acknowledge and agree that as a Director of the COS I have a fiduciary obligation to the COS to act honestly and in good faith with a view to the best interests of the COS and that this duty includes, but is not limited to the following:

    a. I have a duty of confidentiality to the COS, which requires me to hold all non-public information belonging to the COS or provided to me by the COS confidential unless such information is approved for disclosure by resolution of the Board. This obligation extends to all matters discussed at meetings of the Board and all information provided to me by the COS in any form, including but not limited to oral, written or electronic form. I specifically acknowledge that this obligation will be ongoing after I am no longer a Director of the COS in respect of any information I receive while I am a Director.

    b. I have a duty of loyalty to the COS, which duty includes a prohibition on public criticism of Board decisions, whether or not I personally agree with such decision.

c. I am required to be familiar with, and govern myself in accordance with, the Articles of Continuance and By-laws of the COS.

Conflict of Interest Disclosure:

5. I acknowledge that:

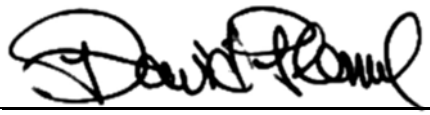
   a. For the protection of both the Directors of the COS and the COS itself, the Board of has adopted a policy whereby each Director on the Board is required to make an annual disclosure regarding conflicts of interest.

   b. For the purposes of such disclosure, a conflict of interest defined as: a situation where there could exist the perception or risk that the judgment of a Director, or the fiduciary duty of such Director to the COS, could be influenced or appear to be influenced by: (i) their personal interests or the personal interests of their friends, family or business associates; (ii) the interests of another entity in which they are involved, interested or to which they owe an obligation; or (iii) any interest or relationship that is outside of the COS.

   c. I have completed the Conflict of Interest Disclosure Form attached hereto as Schedule "A" and the information thereon is complete and accurate as of the date hereof. I will notify the COS if the information provided on this form is no longer accurate or if I engage in additional activities that could result in an actual or perceived conflict of interest within the meaning of the COS Conflict of Interest Policy

   d. I have read the COS Conflict of Interest Policy attached hereto as Schedule "B" and I hereby agree to comply with its requirements.

DATED the 18 day of November, in the year 2023.



Name: David Plemel (print name)

#609, 520 Talbot St. London ON N6A 6K4

Insert address on line above.

Schedule "A": Conflict of Interest Disclosure Form

Please check one of the following boxes and, if making disclosure hereunder, complete the table below:

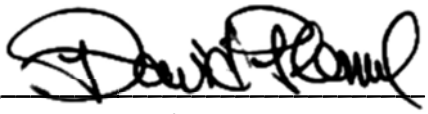
☒ **I do not have any conflicts of interest or potential conflicts of interest to report.** DP **_____ (initial)**

OR

☐ **I have the following affiliations, interests or relationships to report: _____ (initial)**

Interest/Affiliation/Relationship	Company/Organization	Details
Business relationship or contract		
Participation in clinical trial		
Employment/honoraria/consulting fees/in-kind compensation		
Investments (stock options, etc)		
Membership on an advisory panel, committee, or board of directors		
Grant/research support		
Other financial or material interest		

*In contemplating the nature of the relationships that should be disclosed, Directors should be cognizant of the requirements of the Royal College of Physicians and Surgeons of Canada ("**RCPSC**") as to continuing professional development, which require disclosure of relationships with commercial entities such as a pharmaceutical organizations, medical device companies or communications firms. Although these requirements do not necessarily apply to Directors of the COS in their role as Directors, disclosure of any potential conflicts is a best practice and disclosure in accordance with the RCPSC requirements is recommended.

Signature: 

I certify and confirm that the information herein is accurate.

Name: David Plemel

Position: Secretary

Date: November 18, 2023

Schedule "B": COS Conflict of Interest Policy

1. What is a Conflict of Interest?

Directors should be aware that conflicts of interest will arise from time to time and that the existence of a conflict is not an indication of wrong-doing on the behalf of the director in conflict. The key concern in regards to conflicts of interest is how such conflicts are addressed and whether or not they are disclosed. Where a conflict of interest exists and is not disclosed this is a violation of the fiduciary obligations of a director to the corporation.

A conflict of interest is defined somewhat broadly at common law, as there are many situations where a director could find themselves in a situation of conflict. At common law a conflict of interest is a situation where there could exist the perception or risk that the judgment of an individual, or the fiduciary duty of such individual to the corporation, could be influenced or appear to be influenced by:

1.1 their personal interests or the personal interests of their friends, family or business associates;
1.2 the interests of another entity in which they are involved, interested or to which they owe an obligation;
1.3 any interest or relationship that is outside of the corporation.

In addition to the common law definition of conflict of interest above, the *Canada Not-for-Profit Corporations Act* (the "**Act**") sets out certain situations where a director will be in conflict, conflict and the required disclosure in respect of same, as follows:

> **141.** (1) A director or an officer of a corporation shall disclose to the corporation, in writing or by requesting to have it entered in the minutes of meetings of directors or of committees of directors, the nature and extent of any interest that the director or officer has in a material contract or material transaction, whether made or proposed, with the corporation, if the director or officer
>
> (*a*) is a party to the contract or transaction;
>
> (*b*) is a director or an officer, or an individual acting in a similar capacity, of a party to the contract or transaction; or
>
> (*c*) has a material interest in a party to the contract or transaction.

Note that a conflict of interest exists whether or not the individual believes that they will not be swayed by the competing interest because a conflict of interest does not only involve situations where an individual is influenced, but also scenarios where there is the **perception** of influence or a conflict.

2. What should a Director do if they suspect or know that they are in conflict?

a) Disclose the Conflict:

Both the common law and the Act require that a director in conflict disclose the conflict on the earlier of (a) when the subject of the conflict is first discussed; or (b) as soon as the director becomes aware of the conflict.

This obligation to disclose is an ongoing obligation, meaning: if the issue is not the subject of a conflict when initially discussed, but later becomes the subject of a conflict, the director is required to disclose the conflict immediately upon the occurrence thereof.

For the protection of the director in conflict, the best practice is for the director to declare the conflict and request that the conflict be entered into the minutes of any meeting when the issue involving the conflict is discussed. Where the issue is discussed at multiple meetings, this declaration and insertion in the minutes should take place at each such meeting.

b) Abstain from Voting on the Issue involving the Conflict:

Where the conflict is a conflict within the meaning of Article 141 of the Act, the director in conflict is required to abstain from voting on the issue. Where the conflict is not addressed by the Act, the common law requires that a director abstain from voting on the issue.

c) Avoid the Perception of Influencing the Issue:

Although not required by law, where a conflict is serious in nature, a director may wish to step-out of a meeting where the issue is being discussed in order to avoid the perception of impropriety. The fact that a director in conflict has stepped out of the meeting should be recorded in the minutes of meeting.

Further, a director in conflict should avoid discussing the issue of the conflict with other board members or employees/staff of the corporation to avoid the perception of attempting to influence the outcome of the issue.

3. What if a Director Serves on the Board of another Organization?

Where an individual is a director of another corporation that may have competing or different interests from those of the COS, such director may find themselves in conflict as to issues discussed at one or both board tables. The fact that the director is a director of both organizations does nothing to derogate from the obligations of a director to the either entity. Directors have a fiduciary duty to all the corporations they serve as directors.

The same rules as to conflict of interest apply where the conflict is between the two corporations a director serves, even if the corporations are friendly, related or linked. The courts have held that a director ‘cannot serve two masters’ and if the interests of two corporations of which a

person is a director conflict on a particular matter, the director must recuse herself or himself for participating on both boards on the issue concerned.

Director Consent and Acknowledgement

TO: The Canadian Ophthalmological Society /Société canadienne d'ophtalmologie (the "**COS**").

Consent to Serve:

1. I hereby ratify and confirm my consent to act as a director of the COS (a "**Director**") effective as of the date of my election or appointment as a director (the "**Director Consent**"). The Director Consent shall continue in effect from year to year so long as I remain on the board of directors of the COS (the "**Board**"), but if I resign or am removed from the Board, the Director Consent shall cease to have effect from the effective date of such resignation or removal.

2. I further ratify and confirm my consent to any one or more of the directors of the COS from time to time participating in meetings of the Board or committees of the Board of the COS by means of such telephone, electronic or other communications facilities as permit all persons participating in the meeting to communicate adequately with each other simultaneously and instantaneously, such consent to continue in effect unless revoked by an instrument in writing delivered to the COS.

3. I hereby agree to advise the COS by a notice in writing delivered to the COS of any change in my place of residence forthwith after such change.

Acknowledgement re Fiduciary Obligations:

4. I acknowledge and agree that as a Director of the COS I have a fiduciary obligation to the COS to act honestly and in good faith with a view to the best interests of the COS and that this duty includes, but is not limited to the following:

    a. I have a duty of confidentiality to the COS, which requires me to hold all non-public information belonging to the COS or provided to me by the COS confidential unless such information is approved for disclosure by resolution of the Board. This obligation extends to all matters discussed at meetings of the Board and all information provided to me by the COS in any form, including but not limited to oral, written or electronic form. I specifically acknowledge that this obligation will be ongoing after I am no longer a Director of the COS in respect of any information I receive while I am a Director.

    b. I have a duty of loyalty to the COS, which duty includes a prohibition on public criticism of Board decisions, whether or not I personally agree with such decision.

c. I am required to be familiar with, and govern myself in accordance with, the Articles of Continuance and By-laws of the COS.

Conflict of Interest Disclosure:

5. I acknowledge that:

   a. For the protection of both the Directors of the COS and the COS itself, the Board of has adopted a policy whereby each Director on the Board is required to make an annual disclosure regarding conflicts of interest.

   b. For the purposes of such disclosure, a conflict of interest defined as: a situation where there could exist the perception or risk that the judgment of a Director, or the fiduciary duty of such Director to the COS, could be influenced or appear to be influenced by: (i) their personal interests or the personal interests of their friends, family or business associates; (ii) the interests of another entity in which they are involved, interested or to which they owe an obligation; or (iii) any interest or relationship that is outside of the COS.

   c. I have completed the Conflict of Interest Disclosure Form attached hereto as Schedule "A" and the information thereon is complete and accurate as of the date hereof. I will notify the COS if the information provided on this form is no longer accurate or if I engage in additional activities that could result in an actual or perceived conflict of interest within the meaning of the COS Conflict of Interest Policy

   d. I have read the COS Conflict of Interest Policy attached hereto as Schedule "B" and I hereby agree to comply with its requirements.

DATED the 18 day of November, in the year 2023.

Name: Mona Harissi Dagher (print name)

5955 ave Wilderton PH 10C, Mtl Qc

Insert address on line above.

Schedule "A": Conflict of Interest Disclosure Form

Please check one of the following boxes and, if making disclosure hereunder, complete the table below:

☒ **I do not have any conflicts of interest or potential conflicts of interest to report.** MHD **_____ (initial)**

OR

☐ **I have the following affiliations, interests or relationships to report: _____ (initial)**

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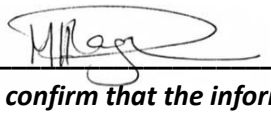
Signature: 

I certify and confirm that the information herein is accurate.

Name: Mona Harissi Dagher

Position: Chair Annual Meeting

Date: 18 November 2023

Schedule "B": COS Conflict of Interest Policy

1. What is a Conflict of Interest?

Directors should be aware that conflicts of interest will arise from time to time and that the existence of a conflict is not an indication of wrong-doing on the behalf of the director in conflict. The key concern in regards to conflicts of interest is how such conflicts are addressed and whether or not they are disclosed. Where a conflict of interest exists and is not disclosed this is a violation of the fiduciary obligations of a director to the corporation.

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>
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The same rules as to conflict of interest apply where the conflict is between the two corporations a director serves, even if the corporations are friendly, related or linked. The courts have held that a director ‘cannot serve two masters’ and if the interests of two corporations of which a

person is a director conflict on a particular matter, the director must recuse herself or himself for participating on both boards on the issue concerned.

Director Consent and Acknowledgement

TO: The Canadian Ophthalmological Society /Société canadienne d'ophtalmologie (the "**COS**").

Consent to Serve:

1. I hereby ratify and confirm my consent to act as a director of the COS (a "**Director**") effective as of the date of my election or appointment as a director (the "**Director Consent**"). The Director Consent shall continue in effect from year to year so long as I remain on the board of directors of the COS (the "**Board**"), but if I resign or am removed from the Board, the Director Consent shall cease to have effect from the effective date of such resignation or removal.

2. I further ratify and confirm my consent to any one or more of the directors of the COS from time to time participating in meetings of the Board or committees of the Board of the COS by means of such telephone, electronic or other communications facilities as permit all persons participating in the meeting to communicate adequately with each other simultaneously and instantaneously, such consent to continue in effect unless revoked by an instrument in writing delivered to the COS.

3. I hereby agree to advise the COS by a notice in writing delivered to the COS of any change in my place of residence forthwith after such change.

Acknowledgement re Fiduciary Obligations:

4. I acknowledge and agree that as a Director of the COS I have a fiduciary obligation to the COS to act honestly and in good faith with a view to the best interests of the COS and that this duty includes, but is not limited to the following:

    a. I have a duty of confidentiality to the COS, which requires me to hold all non-public information belonging to the COS or provided to me by the COS confidential unless such information is approved for disclosure by resolution of the Board. This obligation extends to all matters discussed at meetings of the Board and all information provided to me by the COS in any form, including but not limited to oral, written or electronic form. I specifically acknowledge that this obligation will be ongoing after I am no longer a Director of the COS in respect of any information I receive while I am a Director.

    b. I have a duty of loyalty to the COS, which duty includes a prohibition on public criticism of Board decisions, whether or not I personally agree with such decision.

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Conflict of Interest Disclosure:

5. I acknowledge that:

   a. For the protection of both the Directors of the COS and the COS itself, the Board of has adopted a policy whereby each Director on the Board is required to make an annual disclosure regarding conflicts of interest.

   b. For the purposes of such disclosure, a conflict of interest defined as: a situation where there could exist the perception or risk that the judgment of a Director, or the fiduciary duty of such Director to the COS, could be influenced or appear to be influenced by: (i) their personal interests or the personal interests of their friends, family or business associates; (ii) the interests of another entity in which they are involved, interested or to which they owe an obligation; or (iii) any interest or relationship that is outside of the COS.

   c. I have completed the Conflict of Interest Disclosure Form attached hereto as Schedule "A" and the information thereon is complete and accurate as of the date hereof. I will notify the COS if the information provided on this form is no longer accurate or if I engage in additional activities that could result in an actual or perceived conflict of interest within the meaning of the COS Conflict of Interest Policy

   d. I have read the COS Conflict of Interest Policy attached hereto as Schedule "B" and I hereby agree to comply with its requirements.

DATED the 18 day of November, in the year 2023

Philip HOOPER

Name: PHooper (print name)

320 Grosvenor Street London Ont

Insert address on line above.

Schedule "A": Conflict of Interest Disclosure Form

Please check one of the following boxes and, if making disclosure hereunder, complete the table below:

☑ **I do not have any conflicts of interest or potential conflicts of interest to report.** PH **(initial)**

OR

☐ **I have the following affiliations, interests or relationships to report: _____ (initial)**

Interest/Affiliation/Relationship	Company/Organization	Details
Business relationship or contract		
Participation in clinical trial		
Employment/honoraria/consulting fees/in-kind compensation		
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*In contemplating the nature of the relationships that should be disclosed, Directors should be cognizant of the requirements of the Royal College of Physicians and Surgeons of Canada ("**RCPSC**") as to continuing professional development, which require disclosure of relationships with commercial entities such as a pharmaceutical organizations, medical device companies or communications firms. Although these requirements do not necessarily apply to Directors of the COS in their role as Directors, disclosure of any potential conflicts is a best practice and disclosure in accordance with the RCPSC requirements is recommended.

Signature: _____

I certify and confirm that the information herein is accurate.

Name: Philip HOOPER

Position: President COS-SCO

Date: Nov 18 2023

Director Consent and Acknowledgement

TO: The Canadian Ophthalmological Society /Société canadienne d'ophtalmologie (the "**COS**").

Consent to Serve:

1. I hereby ratify and confirm my consent to act as a director of the COS (a "**Director**") effective as of the date of my election or appointment as a director (the "**Director Consent**"). The Director Consent shall continue in effect from year to year so long as I remain on the board of directors of the COS (the "**Board**"), but if I resign or am removed from the Board, the Director Consent shall cease to have effect from the effective date of such resignation or removal.

2. I further ratify and confirm my consent to any one or more of the directors of the COS from time to time participating in meetings of the Board or committees of the Board of the COS by means of such telephone, electronic or other communications facilities as permit all persons participating in the meeting to communicate adequately with each other simultaneously and instantaneously, such consent to continue in effect unless revoked by an instrument in writing delivered to the COS.

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Acknowledgement re Fiduciary Obligations:

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    a. I have a duty of confidentiality to the COS, which requires me to hold all non-public information belonging to the COS or provided to me by the COS confidential unless such information is approved for disclosure by resolution of the Board. This obligation extends to all matters discussed at meetings of the Board and all information provided to me by the COS in any form, including but not limited to oral, written or electronic form. I specifically acknowledge that this obligation will be ongoing after I am no longer a Director of the COS in respect of any information I receive while I am a Director.

    b. I have a duty of loyalty to the COS, which duty includes a prohibition on public criticism of Board decisions, whether or not I personally agree with such decision.

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   d. I have read the COS Conflict of Interest Policy attached hereto as Schedule "B" and I hereby agree to comply with its requirements.

DATED the 7th day of December, in the year 2023

Name: Setareh Ziai (print name)

Eye Institute - 501 Smyth Rd
Ottawa, ON
K1H 8L6

Insert address on line above.

Schedule "A": Conflict of Interest Disclosure Form

Please check one of the following boxes and, if making disclosure hereunder, complete the table below:

☑ **I do not have any conflicts of interest or potential conflicts of interest to report.** SS **(initial)**

OR

☐ **I have the following affiliations, interests or relationships to report: _____ (initial)**

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Participation in clinical trial		
Employment/honoraria/consulting fees/in-kind compensation		
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Membership on an advisory panel, committee, or board of directors		
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Signature: _____

I certify and confirm that the information herein is accurate.

Name: Setareh Zia

Position: VO Liaison

Date: Dec 7 / 2023

Director Consent and Acknowledgement

TO: The Canadian Ophthalmological Society /Société canadienne d'ophtalmologie (the "**COS**").

Consent to Serve:

1. I hereby ratify and confirm my consent to act as a director of the COS (a "**Director**") effective as of the date of my election or appointment as a director (the "**Director Consent**"). The Director Consent shall continue in effect from year to year so long as I remain on the board of directors of the COS (the "**Board**"), but if I resign or am removed from the Board, the Director Consent shall cease to have effect from the effective date of such resignation or removal.

2. I further ratify and confirm my consent to any one or more of the directors of the COS from time to time participating in meetings of the Board or committees of the Board of the COS by means of such telephone, electronic or other communications facilities as permit all persons participating in the meeting to communicate adequately with each other simultaneously and instantaneously, such consent to continue in effect unless revoked by an instrument in writing delivered to the COS.

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   d. I have read the COS Conflict of Interest Policy attached hereto as Schedule "B" and I hereby agree to comply with its requirements.

DATED the 21 day of December, in the year 2023.

Name: Vivian Hill (print name)

Insert address on line above.

Schedule "A": Conflict of Interest Disclosure Form

Please check one of the following boxes and, if making disclosure hereunder, complete the table below:

☑ **I do not have any conflicts of interest or potential conflicts of interest to report.** _____ **(initial)**

OR

☐ **I have the following affiliations, interests or relationships to report:** _____ **(initial)**

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Signature: _____

I certify and confirm that the information herein is accurate.

Name: Vivian Hill

Position: Director - Advocacy Chair

Date: 2023/

Schedule "B": COS Conflict of Interest Policy

1. What is a Conflict of Interest?

Directors should be aware that conflicts of interest will arise from time to time and that the existence of a conflict is not an indication of wrong-doing on the behalf of the director in conflict. The key concern in regards to conflicts of interest is how such conflicts are addressed and whether or not they are disclosed. Where a conflict of interest exists and is not disclosed this is a violation of the fiduciary obligations of a director to the corporation.

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1.3 any interest or relationship that is outside of the corporation.

In addition to the common law definition of conflict of interest above, the *Canada Not-for-Profit Corporations Act* (the "**Act**") sets out certain situations where a director will be in conflict, conflict and the required disclosure in respect of same, as follows:

> **141.** (1) A director or an officer of a corporation shall disclose to the corporation, in writing or by requesting to have it entered in the minutes of meetings of directors or of committees of directors, the nature and extent of any interest that the director or officer has in a material contract or material transaction, whether made or proposed, with the corporation, if the director or officer
>
> (*a*) is a party to the contract or transaction;
>
> (*b*) is a director or an officer, or an individual acting in a similar capacity, of a party to the contract or transaction; or
>
> (*c*) has a material interest in a party to the contract or transaction.

Note that a conflict of interest exists whether or not the individual believes that they will not be swayed by the competing interest because a conflict of interest does not only involve situations where an individual is influenced, but also scenarios where there is the **perception** of influence or a conflict.

2. What should a Director do if they suspect or know that they are in conflict?

a) Disclose the Conflict:

Both the common law and the Act require that a director in conflict disclose the conflict on the earlier of (a) when the subject of the conflict is first discussed; or (b) as soon as the director becomes aware of the conflict.

This obligation to disclose is an ongoing obligation, meaning: if the issue is not the subject of a conflict when initially discussed, but later becomes the subject of a conflict, the director is required to disclose the conflict immediately upon the occurrence thereof.

For the protection of the director in conflict, the best practice is for the director to declare the conflict and request that the conflict be entered into the minutes of any meeting when the issue involving the conflict is discussed. Where the issue is discussed at multiple meetings, this declaration and insertion in the minutes should take place at each such meeting.

b) Abstain from Voting on the Issue involving the Conflict:

Where the conflict is a conflict within the meaning of Article 141 of the Act, the director in conflict is required to abstain from voting on the issue. Where the conflict is not addressed by the Act, the common law requires that a director abstain from voting on the issue.

c) Avoid the Perception of Influencing the Issue:

Although not required by law, where a conflict is serious in nature, a director may wish to step-out of a meeting where the issue is being discussed in order to avoid the perception of impropriety. The fact that a director in conflict has stepped out of the meeting should be recorded in the minutes of meeting.

Further, a director in conflict should avoid discussing the issue of the conflict with other board members or employees/staff of the corporation to avoid the perception of attempting to influence the outcome of the issue.

3. What if a Director Serves on the Board of another Organization?

Where an individual is a director of another corporation that may have competing or different interests from those of the COS, such director may find themselves in conflict as to issues discussed at one or both board tables. The fact that the director is a director of both organizations does nothing to derogate from the obligations of a director to the either entity. Directors have a fiduciary duty to all the corporations they serve as directors.

The same rules as to conflict of interest apply where the conflict is between the two corporations a director serves, even if the corporations are friendly, related or linked. The courts have held that a director 'cannot serve two masters' and if the interests of two corporations of which a

person is a director conflict on a particular matter, the director must recuse herself or himself for participating on both boards on the issue concerned.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813
Brand name (generic)	Eylea HD (Aflibercept 8 mg/0.07 mL)
Indication(s)	DME
Organization	Canadian Retina Society
Contact information[a]	Name: Varun Chaudhary, MD FRCSC

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

The CRS has concerns regarding the following reimbursement recommendations for Eylea HD as it pertains to treatment for patients with diabetic macular edema.

Reimbursement condition 2

"The maximum duration of initial authorization is 6 months".

CRS disagrees that a 6-month window is a validated end point to base clinical decision and reimbursement decisions on. Although much of the gain is typically seen early on with anti-VEGF treatment (typically first 5 injections), long term disease control and visual acuity maintenance is critical to optimize visual outcomes for Canadian patients living with DME. Since this 6-month window has never been tested or validated in clinical trials to base clinical decision making on, CRS is not supportive of this reimbursement condition as it can jeopardize long term vision status of Canadian patients. The reason provided states that this criteria will help ensure that Eylea HD is used in patients who "benefit" from treatment. Benefit from treatment in this chronic disease cannot be judged at an arbitrary 6-month time point. Multiple post hoc analysis including those form Protocol I demonstrate that over 50% of late responders to anti-VEGF treatment can continue to achieve benefit with on-going regular treatment. All patients, both early responders and late responders, should be given access to aflibercept 8mg to optimize long term outcomes.

Published in final edited form as:
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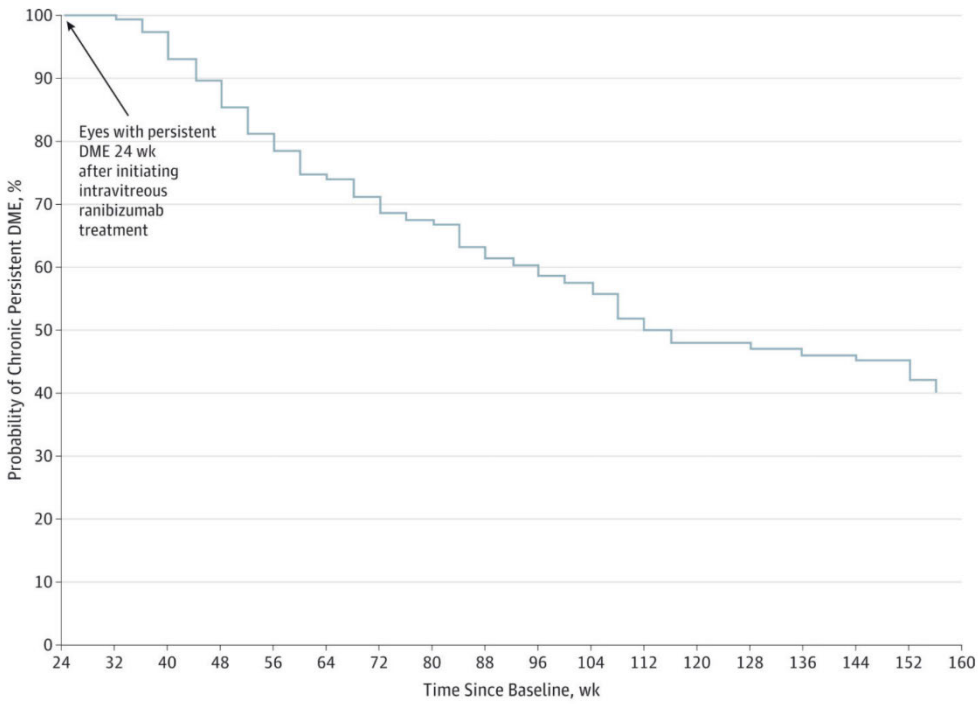
Persistent Macular Thickening After Ranibizumab Treatment for Diabetic Macular Edema With Vision Impairment

Susan B. Bressler, MD, **Allison R. Ayala, MS**, **Neil M. Bressler, MD**, **Michele Melia, ScM**, **Haijing Qin, MS**, **Frederick L. Ferris III, MD**, **Christina J. Flaxel, MD**, **Scott M. Friedman, MD**, **Adam R. Glassman, MS**, **Lee M. Jampol, MD**, **Michael E. Rauser, MD**, and **Diabetic Retinopathy Clinical Research Network**



Reimbursement condition 3

"For renewal after initial authorization, patients much achieve at least 15 letters improvement in BCVA at 6 months compared with baseline (pre-treatment)"

CRS disagrees that a minimum 15 letter improvement is an appropriate threshold to guide clinical decision making and on-going access to Canadian patients living with DME. The rationale states that "inadequate response" to treatment justifies this arbitrary cut-off. However, there is no validated definition of "inadequate response" in the field of DME. Moreover, the 6-month timepoint once again is an arbitrary, unvalidated cut off that has no merit as a clinical decision end point as it has never been tested in any clinical trial. Moreover, ETDRS VA is never tested in clinical practice. ETDRS VA is a research protocol that necessitates that patients are refracted every visit to achieve the best corrected visual acuity. This variable that has been suggested as the key decision-making point has little relevance to clinical practice as it is never tested in routine practice. Hence, mandating real world clinical decision making based on this variable is not in the best interest for Canadian patients.

As demonstrated below, Protocol T demonstrated persistent DME at 6 months in a large proportion of patients. However, ongoing treatment led to increasing anatomic and functional outcomes for all patients at 2 and 5 years. Overall, 30-65% of patients have persistent DME at week 24 in clinical trials and nearly 50% had persistent DME after 2 years of continuous treatment.

Anatomical Response

- Protocol T (persistent DME)
  - Week 12: 50.8, 72.9, 53.2% (Aflibercept,Bevacizumab,Ranibizumab)
  - Week 24: 31.6, 65.6, 41.5% (A,B,R)

Reimbursement condition 4

"Aflibercept 8mg should be discontinued in patient with"

CRS disagrees that decline in VA is a validated endpoint for discontinuing access to aflibercept 8mg for Canadian patients. This cut off has never been tested in clinical trials. This cut off is not an accepted decision point used by clinicians who manage this disease. Late response is common in DME management as stated above. Patients with DME may lose vision due to a whole host of factors (non DME related pathology or worsening of DME), however, discontinuing access to them based on vision loss criteria is not substantiated with any robust evidence.

Reimbursement condition 7

"Injections should not be given more frequently than every 12 weeks after the first 3 consecutive doses."

CRS disagrees with this condition. The explanatory PHOTON trial, similar to any other explanatory RCT, is not pragmatic by design and typically cannot be replicated in real world practice. The PHOTON trial did not employ a typical treat and extend or PRN paradigm which are commonly used paradigms in practice in Canada. The paradigm used in PHOTON has only been tested in one explanatory phase 3 trial and will not be widely replicated in clinical practice. Canadian physicians have extensive experience successfully implementing PRN or treat and extend paradigms to manage DME and the reimbursement criteria for aflibercept 8mg should not mandate a fixed extension interval for all patients after loading. Treating the "right" patient at the "right" time based on all clinical expertise.

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 above response.

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.
See above response.

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.
See above response.

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.
See above response.

[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: • Dr. Varun Chaudhary • Dr. Cynthia Qian • Dr. Amin Kherani • Dr. Bernard Hurley		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	Varun Chaudhary
Position	President, Canadian Retina Society
Date	27-02-2024
☒	**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	☐	☒	☐	☐
Roche	☐	☒	☐	☐
Novartis	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	Cynthia Qian
Position	Vice President, Canadian Retina Society
Date	27-02-2024
☒	**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**
Abbvie	☒	☐	☐	☐
Apellis	☒	☐	☐	☐
Boehringer Ingelheim	☒	☐	☐	☐
Bayer		X		
Novartis		X		
Roche		X		

New or Updated Declaration for Clinician 3	
Name	Dr. Amin Kherani
Position	Past President
Date	28-02-2024
☒	**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	☐	☒	☐	☐
Bausch + Lomb	☒	☐	☐	☐
Roche	☒	☐	☐	☐
Apellis		X		
Novartis	X			
Alcon	X			
Allergan	X			

New or Updated Declaration for Clinician 3	
Name	Dr. Bernard Hurley
Position	Director, Continuing Professional Development
Date	28-02-2024
☒	**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
Allergan	☒	☐	☐	☐
Novartis	☒	☐	☐	☐
Alcon	☒	☐	☐	☐
Bayer	X			
Roche	X			
Biogen	X			

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813
Brand name (generic)	Eylea HD (aflibercept)
Indication(s)	Diabetic Macular Edema
Organization	
Contact information[a]	Name: Kathy Cao

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 recommendations restricts use ONLY in naïve pts with AMD. An effective treatment should not be restricted to patients who have never tried any anti-VEGF agents before, given potential improvements in clinical efficacy. This would not have the patients' best interests in mind. Many patients currently on injections can benefit from potential longer treatment duration that Eylea 8mg can provide, which not only reduces treatment burden on the patient, but can also reduce provincial insurance costs given reduced dosing of treatment.

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?

Ability for ophthalmologists to provide the medication to patients already receiving anti-VEGF treatment

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.

Not at all. There is absolutely no reason given for restricting this medication to treatment naïve patients. All previous new anti-VEGF medications were allowed to be used in both treatment naïve and existing patients. This is the ONLY anti-VEGF medication on which this restriction has been placed. Simply because the clinical trials were done on treatment naïve patients does not justify restricting use to treatment naïve patients as all patients can benefit from this treatment.

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.

The implementation responses are very limited and not detailed enough. There is very little explicit information on the clinical rollout of the new treatment.		
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. The rationale given (ie. No reimbursement for treatment naïve patients or limiting to q12 week dosing) is not explained or justified. Both do not place patients' interests first. In order to continue treatment, AMD and DME patients need to have at least 15 ETDRS letters gain at 6 months compared to baseline. Why is this limited to 15 ETDRS letters? What about patients who have improvement, but less than that? There is no rationale given for this. ANY improvement in vision is valuable. How can we justify abandoning a treatment that provided improvement, and perhaps having to resort to a less effective medication (and losing this vision gain) simply because of lack of coverage?		

[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		
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	*Kathy Cao*
Position	*Ophthalmologist*
Date	*29-02-2024*
☒	**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	*Jessica Cao*
Position	*Ophthalmologist*
Date	*29-02-2024*
☒	**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 Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813
Brand name (generic)	Eylea HD
Indication(s)	Diabetic Macular Edema
Organization	Central Alberta Eye Surgery and Clearfield Eye Physicians and Surgeons
Contact information[a]	Name: Dr. Kaisra Esmail

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 requirement to gain three lines of vision at 6 months demonstrates a limited understanding of real life clinical outcomes. Patients with limited visual potential may never gain 3 lines of vision, but may still benefit from the medication by preventing further deterioration of vision and progression of disease. Other patients may only gain 1 or 2 lines of vision, which can still significantly increase a patient's quality of life, and may be the difference between driving or living independently. This can allow patients to continue contributing meaningfully to society and limit dependence on government assistance.

Limiting treatment intervals to 12 weeks after the first three monthly loading doses is not congruent with real life practice and would be harmful to patients. If a patient deteriorates during the 12 week interval, they need to be rescued with an additional injection to avoid potentially irreversible vision loss. In the clinical trial, patients were capable of being rescued with more frequent dosing whenever required, which is the minimum standard of care. Otherwise the trial would not have received ethics approval.

In order to continue providing the high standard of care expected of Canadian physicians, Ophthalmologists need the ability to tailor a patient's anti-VEGF treatment, and this includes switching effortlessly between anti-VEGF medications if there is inadequate response, removing restrictions on visual acuity outcomes, and being able to rescue a patient demonstrating deterioration with more frequent dosing.

No other anti-VEGF agent has ever had these restrictions placed on them when they were released. We strongly urge you to reconsider these recommendations.

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 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. **See 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. **See above**		
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. **See above**		

[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	*Kaisra Esmail*
Position	*Ophthalmologist with a medical retina practice*
Date	*29-02-2024*
☒	**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	*Nathan Carrell*
Position	*Ophthalmologist with medical retina practice*
Date	*29-02-2024*
☒	**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	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	○ SR0813
Brand name (generic)	EYLEA® HD (aflibercept injection)
Indication(s)	DME
Organization	EPSNB
Contact information	Name:Dr Ken Roberts

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

Our provincial section has an issue with a few points of the committees recommendations.

1) Only for treatment naiive patients - There is a wide landscape of possible injections for AMD currently, and it seems to be getting larger. Each medication, while similar, may offer benefits to specific patients. This may be lost in clinical trials with very strict criteria and often this has to be adjusted to real world conditions. EyleaHD also offers a longer treatment interval with the higher dose. This will reduce treatment burden on both patients and physicians. We would recommend that this medication be open to patients who may have had previous treatment with another anti-vegf, but are not meeting the clinical targets. a) patients who fail to extend beyond 4 weeks. b) patients who are dry at 4 weeks, but regress at 6 weeks.
2) No switching - Due to the chaning landscape of injections, it is important for physicians to have the ability to use a different product if necessary. While switching is not going to be a solution for all issues around AMD and injections, it remains a viable option for some patients in some clinical scenarios. We would not want to be limited in this area.

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	*☐

Real world data is often missing from clinical trials.

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	☐

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

[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	*DR Kenneth Roberts*
Position	*Consulting Ophthalmologist*
Date	*20-02-2024*
*☐	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	☐
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	*☐
	Yes	☐

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**
None	☐	☐	☐	☐
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	☐
3. 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		
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	☐
• Dr Vinicius Vanzan • Dr Robert Javidi • Dr Wei Wei Lee		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr Vinicius Vanzan*
Position	*Consultant Ophthalmologist*
Date	*20/02/2024*
*☐	**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 2	
Name	*Dr Wei Wei Lee*
Position	*Consultant Ophthalmologist*
Date	*20/02/2024*
*☐	**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	*Dr Robert Javidi*
Position	*Consultant Ophthalmologist*
Date	*20/02/2024*
*☒	**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 4	
Name	*Dr Simon Javidi*
Position	*Consultant Ophthalmologist*
Date	*20/02/2024*
*	**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 5	
Name	*Daniela Strauch*
Position	*Consultant Ophthalmologist*
Date	*20-02-2025*
*	**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**
None	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813-000-000
Brand name (generic)	Eylea HD (aflibercept 8 mg/0.07 mL)
Indication(s)	For the treatment of diabetic macular edema
Organization	Niagara Ophthalmologists
Contact information[a]	Name: Amber Sheikh, MD [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.

- *Reimbursement conditions 1.2-1.3 (page 4, table 1)* – These criteria are far too stringent to impose and should just be the presence of intraretinal or subretinal fluid as this is when treatment is indicated. Additionally, the need to document the specific measurements listed would add a major administrative burden for clinicians.
- *Reimbursement condition 2 (page 4, table 1)* – The duration of treatment should be based on physician discretion to promote optimal patient outcomes which will benefit the healthcare system overall (i.e. less indirect costs from undertreated/poorly treated disease); however, if a maximum duration of initial authorization must be applied it should be 12 months, not 6, as confounding factors can delay response.
- *Reimbursement condition 3 (page 4, table 1)* – We strongly disagree with requiring a 15 letter improvement for treatment renewal. Improvement is relative to each patient (e.g. some start with very poor vision and cannot obtain 2 line improvement; vision may continue to decline on treatment due to comorbidities like glaucoma or cataracts). This restriction does not include individualized patient features or confounding factors.
- *Reimbursement conditions 4.1-4.2 (page 4-5, table 1)* – We disagree with imposing these criteria for discontinuation as these measurements of vision can fluctuate (e.g. depending on patient mood/effort, whether feeling ill, transitioning from outside to inside). Vision should not be used as a solitary marker of treatment success – this is multifactorial and also includes patient quality of life and imaging results. This is a disease requiring considerable clinical judgment to decide the optimal approach for each patient (e.g. some respond better to certain treatments, injection interval frequency varies).
- *Reimbursement condition 7 (page 5, table 1)* – We disagree with this condition as injection interval is very patient-dependent; while every 12 weeks may work for some, others may require more frequent injections. Additionally, aflibercept 8 mg could offer cost savings to the healthcare system as a patient who may be receiving injections every 4 weeks on another anti-VEGF could possibly receive them less frequently (e.g. every 8 weeks) with aflibercept 8 mg.

Expert committee consideration of the stakeholder input		
	Yes	☒

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	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. While the reasons are clear in relation to the clinical trial, they do not reflect the real-world experience of clinicians.		
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. • *Relevant comparators (page 9, table 2)* – Brolucizumab should not be considered as a comparator due to risks of severe loss of vision from this treatment. • *Considerations for prescribing of therapy (page 11, table 2)* – Although faricimab is touted as a longer-acting treatment, real-world experience of our group and our colleagues does not reflect this.		
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 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. A medical writer recorded our feedback.		
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: • N/A		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Amber Sheikh*
Position	*Ophthalmologist Chief of Staff Ophthalmology Niagara Health System*
Date	*01-03-2024*
☒	**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**
Bayer	☐	☒	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Sarit Khimdas*
Position	*Ophthalmologist*
Date	*01-03-2024*
☒	**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**
Bayer	☐	☒	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813-000-000
Brand name (generic)	Eylea HD (aflibercept 8 mg/0.07 mL)
Indication(s)	For the treatment of diabetic macular edema
Organization	Northeastern Ontario Ophthalmology Group
Contact information[a]	Name: Stephen Kosar [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.

- **p. 4, Table 1, 1.3** – ETDRS is not used routinely in clinical practice as it requires special charts and lighting (used in academic/research scenarios only). It would therefore be impractical to impose upon ophthalmologists in private offices as a required measurement.
- **p. 4, Table 1, 2** – The initial authorization should be at least 12 months in order to determine if the treatment is working, especially if patients will only be permitted injections every 3 months (12 weeks) as in condition 7.
- **p. 4, Table 1, 3** – The 15 letter improvement in BCVA is much greater than observed in the clinical study and would be unachievable by the majority of patients. Additionally, disease usually affects both eyes and we will begin treatment on the "good eye" despite better vision. This eye will not be able to gain 3 lines of improvement based on its higher baseline level.
- **p.4-5, Table 1, 4.1-4.2** – Visual acuity is just one aspect of care, treatment success is multifaceted and not represented based on vision alone. Anatomy, angiography, contrast sensitivity, clinical experience, medical judgement and patient improvement in visual function/quality of life and quality of vision are important and not reflected in Snellen or BCVA. Any amount of improvement is valuable, even if just preservation (i.e. slowing of deterioration/decline).
- **p.5, Table 1, 7 –** While most patients will likely be able to receive aflibercept 8 mg every 12 weeks, some inevitably will require more frequent dosing intervals. To optimize patient care, physicians must maintain control over clinical decisions and should not be forced by dosing restrictions.

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 clinical study criteria have been applied verbatim and real-world clinical practices are not reflected in the draft recommendation. Patients in clinical trials are highly motivated to attend appointments, treatment-naïve and have dedicated nurse/injector teams; however, this does not reflect the reality of patient care, especially in Northeastern Ontario where retinal specialists are sparse and patients must travel long distances for care.

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. • **p. 9, Table 2, Relevant comparators** – Brolucizumab is not a relevant comparator as there are essentially no new patients on this treatment due to safety concerns. • **p. 10, Table 2, Considerations for discontinuation of therapy** – This statement contradicts above, and the numerous conditions proposed for aflibercept 8 mg but not other anti-VEGFs. This sets a poor precedent for all future biologics. • **p.11, Table 2, System and economic issues** – As biosimilars are relatively new in this space, their comparable efficacy has not yet been shown in a real-world setting. Thus it is too soon to assume biosimilars are a cost-saving measure if their efficacy does not pan out.		
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 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.
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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		
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. Medical writer to summarize our feedback.		
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: • Dr. Stephen Kosar • Dr. Alejandro Oliver		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 2	
Name	*Dr. Vanessa Ellies*
Position	*Ophthalmologist*
Date	*26-02-2024*
☒	**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	☒	☐	☐	☐
Roche	☒	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813-000-000
Brand name (generic)	Eylea HD (aflibercept 8 mg/0.07 mL)
Indication(s)	For the treatment of diabetic macular edema
Organization	Retina Division of The Ottawa Hospital
Contact information[a]	Name: John Adam McLaughlin [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) Condition 1.3 (pg. 4, Table 1): The range of 20/32-20/320 excludes patients with good vision who would benefit from early treatment as well as those with very poor vision (e.g. 20/400 or counting fingers) who are particularly in need of improvement.
2) Condition 2 (pg. 4, Table 1): 6 months is not a long enough length of time to determine if a treatment is efficacious.
3) Condition 3 (pg. 4, Table 1): Most studies for DME have shown an average improvement of 8-9 letters, thus only a small proportion of patients (e.g. 15-20%) would be able to achieve 15 letters. Additionally, a patient starting at 20/40 vision is not able to gain 3 lines of improvement and would be ineligible, yet these patients benefit the most from treatment.
4) Conditions 4.1-4.3 (pg. 4-5, Table 1): Vision may deteriorate over time, but we would not stop treatment entirely. These discontinuation criteria imply clinicians should stop anti-VEGF treatment, which would be a grave mistake. Additionally, declining vision may still occur with successful treatment – the treatment is just slowing the decline/deterioration, which is a major benefit for some patients. There are numerous clinical situations where vision loss/lesion morphology worsening would be temporary and ongoing treatment would be appropriate. For example, a new sub-retinal hemorrhage or RPE rip.
5) Condition 7 (pg. 5, Table 1): We disagree with the restriction of every 12 week injection intervals; This reflects the trial design only and not the real-world where patients may have more aggressive lesions that require treatment at more frequent intervals. Additionally, we want to preserve physician decision-making within the physician and patient relationship.

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?

While the draft recommendation summarizes our group's previous feedback well, the application of verbatim study criteria indicates the patient quality of life impact of fewer injections was not taken into consideration.

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. 1) Relevant comparators (pg. 9, Table 2): Use of brolucizumab is contentious given safety concerns. Faricimab has only recently become available for use in Ontario. Thus, as standard of care, aflibercept 2 mg is still the best comparator for 8 mg. 2) Considerations for prescribing of therapy (pg. 10-11, Table 2): Brolucizumab is not a fair comparator given its limited clinical use. While faricimab is suggested as a longer-acting treatment, extended duration has not borne out in our real-world experience. Additionally, we always need more treatment options. We would also prefer to switch a patient on aflibercept 2 mg to the 8 mg dose rather than faricimab to avoid potential emergence of adverse events. 3) System and economic issues (pg. 11, Table 2): Biosimilars of ranibizumab/aflibercept 2 mg do not work at the extended dosing intervals of aflibercept 8 mg and should therefore not be equivalent in cost. Aflibercept 8 mg should only be required to be equivalent in cost to the other long-acting option used, faricimab. Extended treatment intervals in all studies are arrived at after careful lengthening of the treatment interval. This is the same approach for all drugs and needs to be for 8 mg.		
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 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. We used a medical writer to record our discussion/feedback on the draft recommendation.		
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: • Dr. John Adam McLaughlin • Dr. David Maberley • Dr. Michael Dollin		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	Thomas Lee
Position	Assistant Professor
Date	*26-02-2024*
☒	**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**
Roche	☒	☐	☐	☐
Bayer	☒	☐	☐	☐
Apellis	☒	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813
Brand name (generic)	Aflibercept 8 mg (Eylea)
Indication(s)	DME
Organization	Dalhousie Univ.
Contact information[a]	Name: [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. The conditions + indications of use should mirror Faricimab.		

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 Alan F. Graves MD • Clinician 2 John D. Dickinson MD, FRCSC • *Add additional (as required)* R. Rishi Gupta MD Arif Samad MD		

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	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813
Brand name (generic)	Eylea HD
Indication(s)	Diabetic Macular Edema
Organization	Retina Specialists of Vancouver Island Health Authority
Contact information[a]	Name: Dr. Rajinder Nirwan

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.

Limiting usage on treatment naive patients would exclude many patients who have inadequate response to older-generation anti-VEGF agents who would benefit from this new medication. Switching a patient from another agent to Eylea HD is being done in the "real world" and has shown to be effective.

Limiting treatment intervals to a minimum of 12 weeks would mean that if the patient is deteriorating in the meantime, they cannot be rescued with an additional injection. This would jeopardize patient vision and potentially lead to irreversible vision loss. Furthermore, within the actual clinical trial, the patients were capable of being rescued in clinical trial with more frequent dosing whenever required.

The requirement that patients must achieve a 3 line visual acuity gain is not well-thought out. Some patients start with relatively good vision, so there is a "ceiling" as to how much vision can be gained. Other patients present with severe disease and have limited visual potential and may never gain as much as 3 lines of vision, but they may still benefit from the medication in terms of preventing further deterioration of vision and progression of disease. It could also help patients maintain independence with driving and day-to-day if they are able to maintain 20/40 or better vision. In turn this can also save the health system financially through preventing disability support from the Government.

Finally, no other anti-VEGF agent has ever had these types of restrictions placed on them when they came to market. We won't be able to use the medication in the capacity that it could best benefit the patient.

We strongly urge you to reconsider these recommendations.

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 as no previous input was provided by our group.**		
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 see previous responses.**		
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. **Please see previous responses.**		
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. **Please see previous responses.**		

[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		
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	*Rajinder Nirwan*
Position	*Vitreoretinal surgeon (Medical and surgical retina) Victoria, BC*
Date	*25-02-2024*
☒	**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	☒	☐	☐	☐
Roche	☐	☒	☐	☐
Apellis	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Daniel Warder*
Position	*Vitreoretinal surgeon (Medical and surgical retina) Victoria, BC*
Date	*25-02-2024*
☒	**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	*Murray Erasmus*
Position	*Retina specialist in Victoria BC*
Date	*02-25-2024*
☒	**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	*Brett Williams*
Position	*Retina specialist in Duncan BC*

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**
None	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Jessica Ruzicki*
Position	*Vitreoretinal surgeon (Medical and surgical retina) Nanaimo, BC*
Date	*02-25-2024*
☒	**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 6	
Name	*Si Xi Zhao*
Position	*Vitreoretinal surgeon (Medical and surgical retina) Victoria, BC*
Date	*02-25-2024*
☒	**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 Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813
Brand name (generic)	Eylea HD (aflibercept 8 mg)
Indication(s)	Diabetic Macular Edema
Organization	Saskatchewan Health Authority
Contact information[a]	Name: Raymond Ko

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. Please see answer to Q5		
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? Did not submit previous 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. Recommendation is clearly stated, but the rationale is not aligned with clinical practice		
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. See previous		
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. *Renewal – criteria does not align to real-world clinical practice – a 15 letter improvement is NOT often realistic since many patients are treated earlier on in their disease spectrum; for example, a patient starting at 20/40 vision and achieves 20/25 vision will NOT have a 15 letter improvement but will have still achieved a meaningful and sustainable visual outcome and patient benefit. Also, the mean vision gain on existing anti-VEGF pivotal studies is less than 15 letters. *Reimbursement 7 – standard of care practice in Canada is using a treat and extend regimen to optimize and individualize care for each patient. Although 12 week intervals may be adequate for some patients, others may do well at 16+ weeks, while others may require treatment every 6-8 weeks. This latter group is the one that would benefit from this higher potency medication and should not be denied access due to a more frequent treatment interval.		

[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 Raymond Ko MD FRCSC MSC*
Position	*Ophthalmologist, Clinical associate professor, vitreoretinal surgeon*
Date	*27-02-2024*
☒	**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	☒	☐	☐	☐
Roche	☒	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr Kevin Colleaux MD FRCSC*
Position	*Associate clinical professor, Vitreoretinal surgeon*
Date	*28-02-2024*
☒	**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**
Roche	☒	☐	☐	☐
Bayer	☒	☐	☐	☐
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	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813-000-000
Brand name (generic)	Eylea HD (aflibercept 0.8 mg/0.07 mL)
Indication(s)	Diabetic macular edema
Organization	Scarborough Ophthalmologists
Contact information[a]	Name: David Assaad [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.

- p.4, Table 1, Condition 1.3 – The range of 20/32 to 20/320, although taken from the clinical trial is not reflective of the spectrum of patients in the real-world requiring treatment with anti-VEGF therapies like aflibercept. We often treat those who have better vision than this minimum (i.e. 20/32) to prevent vision loss, and there may be those with worse vision than 20/320 who could also benefit from aflibercept 8 mg.
- p.4, Table 1, Condition 3 – The benchmark of 15 letters improvement in the BCVA has never been achieved in pivotal clinical trials for DME. The improvement in the PHOTON trial specifically was only ~6-8 letters, thus 15 letters is an unachievable cut-off which will mean no patients would qualify. The enforcement of this cut-off will also impose major logistical barriers both in clinics and at the payer level. Additionally, vision alone is not an adequate endpoint and should instead include resolution of fluid and anatomy.
- p.4-5, Table 1, Conditions 4.1-4.3 – Discontinuation criteria should not be required as this removes clinical judgment and physician autonomy. If a patient is responding poorly or has disciform scars with no benefit to therapy, the clinician should ultimately make the decision to discontinue/modify treatment.
-p.5, Table 1, Condition 7 – We completely disagree with restricting injections to no more frequent than 12-week intervals, as this observation is categorically incorrect based on real-world experience. While many can extend to 12-week injection intervals, some cannot and applying this to all patients will result in undertreatment of some individuals. The injection frequency should be personalized based on OCT results, clinical response and anatomy.

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 rationale for use of high dose/8 mg aflibercept is lacking. Greater durability translates to fewer injections and less cost, fewer safety issues and improved quality of life. The significant cost savings to the healthcare system and impact on patient quality of life should be considered.

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.

While real-world insights should take precedence, the draft recommendation inconsistently applies criteria/observations of the PHOTON study design (e.g. inclusion criteria in conditions 1.1-1.3, but ignoring the proportion of patients who required injections every 8 weeks in condition 7).

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.

- p.9, Table 2, “Relevant comparators” – Brolucizumab is not used in clinical practice due to risks of intraocular inflammation and should not be considered. As aflibercept 2 mg is the standard of care with a well-established track record and the PHOTON study question was investigating a higher dose, aflibercept 2 mg was the most relevant comparator.
- p.11, Table 2, “Considerations for prescribing of therapy” – the question of whether aflibercept 8 mg meets an unmet need has not been adequately addressed; Brolucizumab should not be used as a comparator due to its infrequent use, and while faricimab has a longer duration, clinicians are always in need in additional options. We would also prefer to switch patients on aflibercept 2 mg in need of a longer dosing interval to the same molecule.
- p.11, Table 2, “System and economic issues” – Ranibizumab is the only biosimilar available currently, but this is an old molecule and is not comparable in terms of efficacy to aflibercept.

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 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.
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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		
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. Medical writer – captured our feedback.		
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: • N/A		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. David Assaad*
Position	*Physician*
Date	*26-02-2024*
☒	**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	☒	☐	☐	☐
Novartis	☒	☐	☐	☐
Roche	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Jason Kwok*
Position	*Ophthalmologist*
Date	*28-02-2024*
☒	**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	☒	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813-000-000
Brand name (generic)	Eylea HD (Aflibercept 8 mg/0.07 mL)
Indication(s)	For the treatment of diabetic macular edema
Organization	Southwestern Ontario Community Ophthalmologists
Contact information[a]	Name: Richard Weinstein [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.

Our group disagrees with reimbursement conditions, in which the Phase 3 clinical study criteria have been strictly, yet inconsistently, applied without considering real-world practices for treating DME. This therefore limits physician autonomy in decision-making for patients.

Specifics on these conditions are outlined below:

- Page 4, Table 1. Reimbursement Conditions and Reasons, Reimbursement Condition 1.2: CRT of ≥ 300 µm is an arbitrary and not clinically meaningful threshold. Additionally, this condition was not applied to other anti-VEGF. Furthermore, not all ophthalmologists have access to a Spectralis, so its less relevant to include as part of the condition.
- Page 4, Table 1. Reimbursement Conditions and Reasons, Reimbursement Condition 1.3: BCVA EDTRS is not accessible by all ophthalmologists – BCVA on a Snellen chart is the standard and should be used instead.
- Page 4, Table 1. Reimbursement Conditions and Reasons, Reimbursement Condition 2: The maximum duration of initial therapy suggested (i.e. 6 months) is not reflective of real-world practice. Most patients would receive treatment with an anti-VEGF for a year or more, and the clinical study had patients treated for 12-24 months. We would recommend this maximum duration of initial therapy be changed to 12 months.
- Page 4, Table 1. Reimbursement Conditions and Reasons, Reimbursement Condition 3: We disagree with the requirement for a 15 letter improvement in BCVA to renew as not every patient will reach this threshold as vision alone can be a poor indicator of treatment success. Improvement in anatomy and other indirect measures are more accurate indicators of an efficacious treatment than BCVA. These indirect indicators include the ability to see contrast, or metamorphopsia (i.e. waviness/warping). Additionally, even patients with what would be considered poor vision at the level of hand motion or count fingers can have significant quality of life deterioration if that limited vision is lost. We also note the need to record and submit criteria for renewal would be a major deterrent to physicians and costly to the healthcare system.
- Page 5, Table 1. Reimbursement Conditions and Reasons, Reimbursement Condition 4.2: In certain instances, a patient may experience a critical event (e.g. large macular hemorrhage) in which their vision decreases by more than 30 letters, but treatment should not be discontinued as this catastrophic change warrants swift intervention with a treatment such as aflibercept 8 mg. Therefore, this threshold for discontinuation does not reflect all patients who could benefit from aflibercept 8 mg.

- Page 5, Table 1. Reimbursement Conditions and Reasons, Reimbursement Condition 4.3: Ophthalmologists do not use lesion morphology to determine the need for treatment.
- Page 5, Table 1. Reimbursement Conditions and Reasons, Reimbursement Condition 7: In both the clinical trial and the real-world setting, many patients require injections more frequently than every 12 weeks, and for this reason we recommend omitting this condition entirely.
- Page 5, Table 1. Reimbursement Conditions and Reasons, Reimbursement Condition 8: A higher cost could be justified as a longer interval between injections would obviously result in fewer yearly injections and the associated decrease in direct (less physician appointments and diagnostic tests) costs to OHIP. The associated, but often overlooked, indirect cost related to patient and caregiver time and expense would also be decreased with fewer yearly injections.

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?

While this summarizes our group's feedback, the major potential impact on patient quality of life were not fairly reflected in the draft recommendation. The recommendations fail to mention the indirect cost of vision loss on the individual and on society. Individuals of working age that are no longer able to remain productive are estimated to cost the Canadian economy 4.4 billion dollars annually. Those beyond working age with low vision are 4x more likely to sustain hip fractures and in general are admitted to nursing homes an average of 3 years earlier than those without low vision. These costs should be taken into account.

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 for the recommendations are clearly stated, but please see our response to question 1 for the major issues with the reasons/rationale used in making the recommendations.

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.

- Page 10-11, Table 2. Responses to Questions from the Drug Programs, Considerations for prescribing of therapy, Left Column, Paragraph 2: We recommend the include dosing frequency ranges be clarified to say "up to" every 12 weeks/8, 12 or 16 weeks, for brolucizumab and faricimab, respectively.
- Page 11, Table 2. Responses to Questions from the Drug Programs, System and economic issues, Left Column, Paragraph 1: The direction of this budget impact should be considered (i.e. more or less costly?) – if considering indirect treatment costs, it would be a positive impact.

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.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

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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		
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. We engaged a medical writer to record our group's discussion.		
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: • Dr. Murari Patodia		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	Dr. Jaspreet S Rayat
Position	Assistant Clinical Professor Adjunct, McMaster University, Co-Owner of Ocular Health Centre
Date	*23-02-2023*
☒	**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.
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	☒	☐	☐	☐
Novartis	☒	☐	☐	☐
Bausch + Lomb	☒	☐	☐	☐
Roche	☒	☐	☐	☐
Thea	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	Richard Weinstein, M.D
Position	*Ophthalmologist, Co-founder of Ocular Health Centre*
Date	*26-02-2024*
☒	**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

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Bayer	☒	☐	☐	☐
Novartis	☒	☐	☐	☐
Bausch + Lomb	☒	☐	☐	☐
Roche	☒	☐	☐	☐
Thea	☒	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813-000-000
Brand name (generic)	Eylea HD (aflibercept 8 mg/0.07 mL)
Indication(s)	For the treatment of diabetic macular edema
Organization	Toronto Ophthalmologists
Contact information[a]	Name: Peng Yan - [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. Condition 1.3 (p.4, Table 1): The majority, if not all, retina practices in Ontario employ more cursory measurements for visual acuity and do not check BCVA. Moreover, a rigorous measure of visual acuity by letters, using an EDTRS chart, is almost exclusively reserved for clinical trials, not a busy ophthalmic practice. As a result, outcome criteria using this measure is flawed and impractical. The primary measure used for treatment decisions is OCT-based change including reduction in SRF/IRF or macular volume. In some cases, even small changes in SRF/IRF can be significant for patient's visual acuity and quality of life, especially when the fluid cannot be reduced by their current treatment. Any rigid criteria based on BCVA will exclude a large number of patients with reversible central vision loss from benefiting from aflibercept 8 mg.
2. Condition 2 (p.4, Table 1): While by 6 months physicians would certainly intervene to modify management for lack of response, it does not, however, mean that a treatment isn't working; In fact, treatment may be effective in preventing further edema (swelling) or bleeding, but pre-existing bleed or swelling may take time to resolve especially in cases of chronic fluid. Therefore more than 6 months is required to truly determine if a treatment is efficacious.
3. Condition 3 (p.4, Table 1): This criterion is biased towards those with more severe disease and will exclude those who have better baseline vision (i.e. those with 20/40 vision do not have 15 letters to gain); however, aflibercept is a valuable tool in preventing vision loss in the earlier onset of disease. Additionally, BCVA letter gain does not reflect earlier anatomical improvements – This highlights the important concept that visual function (i.e. vision) follows anatomy.
4. Conditions 4.2-4.3 (p. 5, Table 1): Absolute deterioration in symptoms/anatomical morphology does not necessarily mean that a treatment is ineffective – this may reflect natural disease course. Anti-VEGF treatments help to prevent/slow further deterioration of the lesion, which is not reflected in these criteria.
5. Condition 7 (p. 5, Table 1): While the majority of patients in the clinical trial were able to extend to 12-week injection intervals, this was a controlled population in a strict clinical research environment. In the real-world, as observed with aflibercept 2 mg, ranibizumab etc., there are patients who will ultimately require injections every 4-8 weeks. As with other anti-VEGF, the injection interval should be at the physician discretion and not restricted to 12 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	☐
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. While the reasons for the recommendation are clear based on the study, we direct you to our responses to question 1 for why clinical study criteria cannot be extrapolated to the real-world setting.		
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. 1. Considerations for prescribing of therapy (Table 2, p.11): Regarding if aflibercept 8 mg meets an unmet need, brolucizumab is not a true comparator as it is not commonly used in practice due to safety concerns. Additionally, faricimab has not experienced the uptake expected given its long-acting effects and still has minimal usage.		
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 2. Conflict of Interest Declarations for Clinician Groups

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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		
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. We engaged a medical writer to record our feedback on the draft recommendations.		
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: • Dr. Peng Yan • Dr. Sohel Somani • Dr. Efrem Mandelcorn		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Brian Ballios*
Position	*Clinician-Scientist, Ophthalmologist*
Date	*28-02-2024*

☒	**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 Pharmaceuticals Canada Inc	☒	☐	☐	☐
Bayer Pharmaceuticals	☒	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr. Hannah Chiu*
Position	*Comprehensive ophthalmologist*
Date	*28-02-2024*
☒	**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	*Daniel Weisbrod*
Position	*Ophthalmologist – Medical Retina*
Date	*Please add the date form was completed (DD-MM-YYYY)28-02-2024*
☒	**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	☒	☐	☐	☐

Bayer	☒	☐	☐	☐
Roche	☒	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Alexander Kaplan*
Position	*Ophthalmologist – Medical Retina and Uveitis*
Date	*28-02-2024*
☒	**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	☒	☐	☐	☐
Roche	☒	☐	☐	☐
AbbVie	☒	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Panos Christakis*
Position	*Ophthalmologist – Medical Retina and Uveitis*
Date	*29-02-2024*
☒	**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	SR0813-000-000
Brand name (generic)	Eylea HD (aflibercept 8 mg/0.07 mL)
Indication(s)	For the treatment of diabetic macular edema (DME)
Organization	Toronto Retina Institute
Contact information[a]	Name: Keyvan Koushan - [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.

Our group strongly disagrees with the draft recommendation for reimbursement and question why so many restrictive conditions have been proposed for aflibercept 8 mg that do not apply to the other anti-VEGF treatments available. The increased durability of aflibercept 8 mg addresses a major challenge for both physicians and patients; fewer injections translate to greater patient safety and overall care.

Direct Feedback on Reimbursement Conditions

- **1.3 (Table 1, pg. 4):** Restricting treatment to only those with 20/32 to 20/320 vision is not reflective of our practice as we often treat those who have better vision to prevent vision loss. If a patient had 20/25 vision but required treatment based on other disease features, we would never hold off until their vision declined to this arbitrary cut-off of 20/32.
- **2 (Table 1, pg. 4):** 6 months for initial authorization is too short to see treatment benefit. 12 months or ideally no maximum duration is preferred.
- **3 (Table 1, pg. 4):** 15 letters is a very large and unrealistic improvement, which would cause considerable physician burden to measure for renewal. Many patients have significant impacts on their quality of life from smaller improvements in vision. Additionally, a person with relatively good vision (e.g. 20/32) at the onset of the treatment may never achieve a 15-letter improvement due to the ceiling effect. Furthermore, vision alone is not the best endpoint, as many patients benefit from treatment in other aspects such as quality of vision and colour perception.
- **4 (Table 1, pg. 4-5):** The decision to discontinue or modify treatment should be at the physician's discretion and not subject to the criteria outlined.
- **7 (Table 1, pg. 5):** Restricting to 12 weeks interval impedes a physician's ability to utilize a patient-tailored approach. While the study may have shown most patients could extend to 12 week intervals, not all did, and the study population is not real-world. Physicians should have the ultimate responsibility in clinical decision making for their patients and should not be restricted to an arbitrarily applied interval such as this.

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 appears to be only based on a literal interpretation of the clinical trial and not reflective of input from practicing retinal specialists. It is well known that clinical trials do not directly apply to clinical practice, and the draft recommendation is missing these key insights on the applicability of the trials.

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.

- **"Notably, there were no comparative trials conducted between aflibercept 8mg and other extended-interval anti-VEGF medications like brolucizumab-dbll and faricimab." (Table 2, pg. 9):** Both when the trials were designed and currently, aflibercept 2 mg was/is the standard of care. Faricimab is still not the preferred treatment for this disease. Additionally, brolucizumab should not be considered as a possible comparator as it is rarely used in clinical practice due to concerns of intraocular inflammation.
- **"Does aflibercept 8 mg meet an unmet need given there are other products marketed with an extended dosing interval?" (Table 2, pg. 11):** While faricimab likely has similar durability to aflibercept 8 mg, different treatments have variable efficacy between patients. We therefore would value access to an additional long-acting treatment to increase the likelihood of patient response. Additionally, if a patient has had previous success with aflibercept 2 mg but would benefit from a longer dosing interval, we would prefer to switch to the same molecule to reduce chance of new adverse events.

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 2. Conflict of Interest Declarations for Clinician Groups

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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		
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. We used the services of a medical writer to record our feedback.		
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: • Dr. Alan Berger • Dr. Keyvan Koushan		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Shaheer Aboobaker*
Position	Managing Partner, Toronto Retina Institute
Date	*24-02-2024*
☒	**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**
Roche	☐	☐	☒	☐
Bayer	☐	☒	☐	☐
Novartis	☒	☐	☐	☐
Teva	☒	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813-000-000
Brand name (generic)	Eylea HD (Aflibercept 8 mg/0.07 mL)
Indication(s)	For the treatment of diabetic macular edema
Organization	Waterloo Eye
Contact information[a]	Name: Manreet Alangh [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.

- 1.3 (p. 4, table 1): This vision range is too stringent; in the real-world there is more variability in the patients receiving treatment (e.g. includes those with both better and worse vision than the proposed cut-offs).
- 3 (p. 4, table 1): We strongly disagree with this condition as 15 letters improvement is an arbitrary cut-off. Patients with improvements of 14 letters would have considerable benefits yet not permitted to continue treatment based on this restriction. Additionally, those starting with better vision have less room to gain and would never reach 3 additional lines. This does not mean the treatment is not effective. Also, a clinically meaningful effect is not always only improvement; in patients with poor vision, a stabilization or prevention of vision deterioration via anti-VEGF treatment is very impactful.
- 4.1-4.2 (p.4-5, table 1): We disagree with these discontinuation criteria as vision can decrease due to other factors, independent of anti-VEGF treatment (e.g. glaucoma, cataracts). A patient may require anti-VEGF treatment for DME, but may be waiting 12 months for cataract surgery, in which case they would not be eligible to continue the much needed DME treatment. This is therefore a major barrier to care.
- 7 (p.5, table 1): We strongly disagree with limiting injections to 12 weeks as the shortest frequency; some patients may need injections more frequently than every 12 weeks based on their baseline disease level and there are others who may require increased injection frequency based on fluctuations in disease activity.

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.

The reasons for the recommendation are clear, but they do not reflect real-world/clinical practice.

Physicians use the treat and extend regimen, but these conditions are far too restrictive, prevent personalized care clear and limit physician freedom.		
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 implementation issues have been fairly well addressed, we wanted to highlight there is definitely an unmet need for a durable treatment like aflibercept 8 mg. Additionally, it should not be required to be priced similarly to a biosimilar as the higher cost of novel medicines is necessary to drive innovation.		
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 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. We used a medical writer to record our feedback on the draft recommendation.		
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: • N/A		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Manreet Alangh*
Position	*Ophthalmologist*
Date	*Feb 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**
Bayer	☐	☒	☐	☐
Novartis	☐	☒	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr. Nimesh Desai*
Position	*Ophthalmologist*
Date	*Feb 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**
None (no COI to declare)	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813 Eylea HD nAMD
Brand name (generic)	Aflibercept 8mg
Indication(s)	DME
Organization	West Coast Retina Consultants Inc.
Contact information[a]	Name: Bryon McKay, MD, [redacted] [redacted] 805 W Broadway #205, Vancouver, BC V5Z 1K1

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 Majority of the indications in the draft are appropriate based on the data provided. We do not agree with the limitation to treatment renewal for patients at 6 months requiring 15 letter gain or better.
Table 1, section 3:
For renewal at 6 months patients must have at least 15 letter gain:
This is very concerning – study patients are selected from very tight inclusion criteria – real-world clinical patients tend to present with variable pathology, 15 letter gain after only 6 months in treatment naïve patients with mild DME may be appropriate, however patients presenting later with larger pathology or greater CST may be slower to achieve such gains. Limiting them after only 6 months is very premature in terms of real-world outcomes. We would strongly suggest the committee suggest extending these strict criteria to at least 12 months to allow for real-world situations such as missed visits, illness or slow initial responders.

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?

We feel the guideline of Table 1 point 3 – renewal is too restrictive and will limit dosing for patients who may be responding but may have issues such as missed visits from illness leading to slower response, We strongly suggest a minimum of 12 months to allow for a more real-world application of this medication.

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. We feel the guideline of Table 1 point 3 – renewal is too restrictive and will limit dosing for patients who may be responding but may have issues such as missed visits from illness leading to slower response, We strongly suggest a minimum of 12 months to allow for a more real-world application of this medication.		

[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		
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 •		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Bryon Robert McKay*
Position	*Vitreoretinal Specialist, staff Ophthalmologist, Providence Health Care and University of British Columbia, Vancouver BC, Canada (MD, PhD, FRCSC, DRCPSC- Retina)*
Date	*Please add the date form was completed (20-FEB-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 – no payments in last 2 years	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Andrew Merkur*
Position	*Retina Specialist, Associate Professor, UBC, Vancouver Canada*
Date	*Please add the date form was completed (20-FEB-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	*Andrew Kirker*
Position	*Retina Specialist, Associate Professor, UBC, Vancouver Canada*
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**
N/A	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*David Albiani*
Position	*Retina Specialist, Associate Professor, UBC, Vancouver Canada*
Date	*Please add the date form was completed (20-FEB-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 5	
Name	*Kaivon Vaezi*
Position	*Retina Specialist, Associate Professor, UBC, Vancouver Canada*
Date	*Please add the date form was completed (20-FEB-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	☐	☐	☐	☐

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0813
Name of the drug and Indication(s)	Aflibercept (Eylea HD) for the treatment of diabetic macular edema (DME)
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.
b) Reimbursement conditions and related reasons
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. Implementation guidance for renewal criteria, similar to those outlined for initiation criteria, would be helpful.