CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

FARICIMAB (Vabysmo)

(Hoffmann-La Roche Ltd.)

Indication: For the treatment of Neovascular (wet) age-related macular degeneration (nAMD).

July 28, 2022

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0719-000
Brand name (generic)	VABYSMO (faricimab)
Indication(s)	For the treatment of Neovascular (wet) age -related macular degeneration (nAMD)
Organization	Canadian Retina Society (CRS)
Contact information[a]	Name: Varun Chaudhary [redacted]

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

General Comments

There is currently lack of any evidence around a biosimilar that has been tested head-to-head with faricimab to demonstrate equivalent efficacy, safety and durability. Hence, any comparison between faricimab and biosimilar is completely hypothetical and unsubstantiated.

Faricimab with its dual mode of action may have disease modifying effects that are different and potentially superior to anti-VEGF alone antibody. This area requires further evidence generation. Pre-planned extension studies from the pivotal trials will provide important information. Moreover, early signal with superior anatomic effects in matched head to head loading with current gold standard anti-VEGF agent suggests there might be an important and differential role for the dual mechanism of action for faricimab as an anti-Ang2 and anti-VEGF antibody.

CRS believes that there is robust evidence (with both high internal and external validity) generated in the large phase 3 AMD and DME programs for faricimab. These clinical programs provide strong evidence of clinically meaningful improvements in patient outcomes, drug durability and no new safety signals. In the Canadian treatment environment, where Treat & Extend is the predominant treatment paradigm used by clinicians, such evidence around durability and anatomic improvement has the potential to have a very meaningful impact on patient care by reducing treatment and monitoring burden for patients with nAMD and DME.

Moreover, since there is no evidence on head to head comparison for efficacy, durability or safety between faricimab and avastin, these comparisons are once again hypothetical and unsubstantiated.

Specific Comments

1. Page 3 – The appropriate "incremental cost-effectiveness ratio" should compare faricimab to the Health-Canada approved anti-VEGF agents currently available, i.e., ranibizumab, aflibercept, and brolucizumab. Comparing the cost-effectiveness of an on-label, licensed therapeutic to an off-label, unlicensed one is unhelpful for this discussion.
2. Table 1 (and elsewhere in the document) – Due to limitations in the design of phase II studies, the CRS does not recommend drawing conclusions from phase II data to develop recommendations, especially when data from phase III studies are available.
3. Sources of Information Used by the Committee – The CRS recommends that the "clinical specialist" used for future analyses be a certified Canadian retinal specialist.
4. Stakeholder Perspective, Clinician input – With regards to potential candidates for faricimab, the document includes a recommendation by the clinical expert, stating that "… patients with nAMD who have early and small (in size) neovascular lesions… are candidates." This implies that eyes with "later" or "larger" lesions would not be candidates. However, the phase III trials, TENAYA and LUCERNE, included lesion sizes up to nine disc areas, and there were no inclusion or exclusion criteria for "early/late" lesions. Therefore, this statement should be removed from the document.
5. Stakeholder perspective, Clinician input – The statement stating that "patients with very poor baseline visual acuity" should not be candidates for faricimab is vague as it does not specifically explain what is meant by "poor". The phase III trials included patients with ETDRS visual acuities of 20/32 - 20/320. Further, in clinical practice, Snellen visual acuities are more commonly performed than ETDRS visual acuities. As Snellen acuities may underestimate visual acuity, it may be inappropriate to exclude patients from faricimab due to baseline visual acuity criteria.
7. Page 10 (indirect comparisons) – The use of an indirect treatment comparison (ITC) may be unnecessary to include in the document as recently released 2-year data from the phase III trials provides high-quality data and information for the questions posed. In particular, the 2-year data showed that faricimab remained noninferior to aflibercept and that faricimab treated eyes achieved this with a median of 5 fewer injections when compared to the aflibercept group.
8. Economic evidence (table) – As noted above, comparing the cost of faricimab to bevacizumab may be an unfair comparison as bevacizumab is unlicensed and not approved by Health Canada for intraocular use. More relevant price comparisons would be to ranibizumab, aflibercept, and brolucizumab.

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 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	☐
Unchanged Declarations: • *Varun Chaudhary* • *Jason Noble* • *Cynthia Qian* • *Robert Gizicki*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Bernard Hurley*
Position	*CPD chair*
Date	*28-07-2022*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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

New or Updated Declaration for Clinician 2	
Name	*Wai Ching Lam*
Position	*Director, Advocacy*
Date	*28-07-2022*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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

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	SR0719
Name of the drug and Indication(s)	Faricimab (Vabysmo) for the treatment of neovascular (wet) age-related macular degeneration (nAMD)
Organization Providing Feedback	FWG

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

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

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

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	
Brand name (generic)	faricimab
Indication(s)	Macular degeneration, age-related
Organization	Fighting Blindness Canada, CNIB, Vision Loss Rehabilitation Canada, Canadian Council of the Blind
Contact information[a]	Larissa Moniz [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 agree that it's important for patients to have more treatment options. In particular, faricimab holds the promise of extending treatment intervals which has real positive implications for patients. Patients often find attending appointments challenging, putting a burden on other family members or friends to accompany them. Injections are also a source of pain and anxiety. New treatments that can reduce treatment burden will not only have a positive impact on patients emotional and financial well being but is likely to improve compliance and possibly overall outcomes.

It will be important as faricimab is used in the clinic to monitor real world outcomes in terms of interval of treatment (can the treatment be extended past 16 weeks?), outcomes and compliance to understand the true impact of this new 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?

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

A. Patient Group Information	
Name	*Larissa Moniz*
Position	*Director, Research and Mission Programs*
Date	*19-07-2022*
☒	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

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0719-000
Brand name (generic)	VABYSMO (faricimab)
Indication(s)	For the treatment of Neovascular (wet) age-related macular degeneration (nAMD)
Organization	Hoffmann-La Roche Ltd. (Roche)
Contact information[a]	[redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
Roche Canada agrees that the committee's recommendation is aligned with the evidence from the TENAYA and LUCERNE clinical trials. The population identified in the recommendation is reflective of the populations included in the trials and that of clinical practice.		

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
The recommendation reflects that the clinical and economic data submitted were considered as part of the assessment.		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
The reasons for the recommendation are clearly stated and are based on the clinical trial data.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
The implementation issues have been clearly articulated and adequately addressed in the recommendation.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
Overall, Roche acknowledges that the rationale provided in the reimbursement conditions and associated reasons are clearly stated. While Roche acknowledges that there is limited direct comparative evidence versus each individual anti-VEGF agent, the pivotal studies for faricimab (TENAYA and LUCERNE) were conducted versus the most relevant comparator (aflibercept) and demonstrated non-inferiority with respect to change from baseline in best-corrected visual acuity (BCVA) and a reduction in mean number of treatment injections.		

With respect to reimbursement condition #2 (Pricing) in Table 1 (Page 4), third sentence within the reason provided: *'Additionally, no definitive conclusion could be reached regarding whether faricimab is associated with fewer injections compared to other anti-VEGF agents'*, Roche acknowledges that at the time of this review, the studies were ongoing and data from the primary analysis at week 48 were only available (and as a result, submitted as part of the reimbursement package at the time). Within 48 weeks, faricimab-treated patients had achieved their dosing intervals with fewer injections on average, than those treated with aflibercept. As noted in the CADTH report, "the studies measured the proportion of patients in the faricimab arm on a Q8W, Q12W, and Q16W injection interval as a secondary outcome. The proportion of patients who received faricimab Q8W, Q12W, and Q16W at week 48 was 20.3%, 34.0% and 45.7%, respectively, in TENAYA, and 22.2%, 32.9%, and 44.9%, respectively, in LUCERNE."

With this considered, Roche would like to highlight that the two-year data (up to week 112), from the TENAYA and LUCERNE studies, was presented at the 2022 American Society of Retina Specialists (ASRS) Annual Scientific Meeting on July 14, 2022. Faricimab further demonstrated the efficacy, safety and durability over time, with fewer injections, while achieving comparable vision gains versus aflibercept. Moreover, patients treated with faricimab received a median number of 10 injections over the two years versus 15 injections for those treated with aflibercept, decreasing the number of injections over that time period. During the personalised treatment interval (PTI) phase of the trial from week 60 onwards, patients in the aflibercept arm received a median number of 6 injections, whereas patients in the faricimab arm (up to Q16W) only received half the number, i.e. 3 injections (Table 1). Hence, the proportions of patients in the TENAYA study on Q16W dosing increased from 45.7% at week 48 to 59% at week 112. Similarly, in LUCERNE the proportion of patients on Q16W dosing increased from 44.9% at week 48 to 66.9% at week 112 (Table 2).

Table 1. Median Number of Injections with Faricimab Up to Q16W Compared with Aflibercept Q8W through Week 112

Median number of injections	Faricimab (up to Q16W)	Aflibercept (Q8W)
Week 0 - 108	10	15
Week 60 - 108 (during PTI phase)	3	6

Results are based on a mixed model for repeated measures analysis in the ITT population (TENAYA: aflibercept Q8W, N = 337; faricimab up to Q16W, N = 334; LUCERNE: aflibercept Q8W, N = 327; faricimab up to Q16W, N = 331).Interval at week 112 is calculated using data recorded at week 108. ITT, intent-to-treat; Q8W, every 8 weeks; Q16W, every 16 weeks.

Table 2. At Week 112, >60% of Faricimab-treated Patients Achieved Q16W Dosing and ~80% Achieved ≥Q12W Dosing

	TENAYA - Week 48	TENAYA - Week 112	LUCERNE - Week 48	LUCERNE - Week 112
Q8W	20.3%	25.8%	22.2%	18.8%
Q12W	34.0%	15.1%	32.9%	14.3%
Q16W	45.7%	59.0%	44.9%	66.9%

Percentages are based on number of patients randomized to the faricimab arm who have not discontinued the study at that visit. Proportions for week 48 are based on the primary analysis. Treatment interval at a given visit is defined as the treatment interval decision followed at that visit. Interval at week 112 is calculated using data recorded at week 108. Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

Thus, the funding of faricimab is expected to result in significantly less injections and substantial cost savings to the publicly funded health care system over a three-year period, compared to currently available treatments.

In addition, Roche would like to highlight a real world evidence study also presented at ASRS 2022, titled the TRUCKEE study (non-Roche sponsored), which further corroborates the efficacy and safety of faricimab and its use in treatment-naïve patients as well as treatment-experienced patients. The TRUCKEE study is an ongoing, multi-site study looking at the efficacy and safety of faricimab in wet AMD in a real-world setting with a target population of treatment-naïve patients and patients requiring frequent injections due to persistent disease activity. In the study population with a total of 377 patients (421 eyes) treated with faricimab, more than half of the patients were previously treated with aflibercept (59.6%), followed by ranibizumab (14.3%), and brolucizumab (9.9%). About 6.6% were treatment-naïve. Based on this early experience and collection of real world evidence, faricimab is further showing efficacy and safety in both treatment-naïve patients and treatment-experienced patients.

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