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CADTH Reimbursement Recommendation

Aflibercept 8 mg/0.07 mL (Eylea HD)

Indication: For the treatment of neovascular (wet) age-related macular degeneration
Sponsor: Bayer Inc.
Final recommendation: Reimburse with conditions

Summary

What Is the CADTH Reimbursement Recommendation for Eylea HD?

CADTH recommends that Eylea HD should be reimbursed by public drug plans for the treatment of neovascular (wet) age-related macular degeneration (nAMD) if certain conditions are met.

Which Patients Are Eligible for Coverage?

Eylea HD should only be reimbursed for adults who have not previously been treated with an anti–vascular endothelial growth factor (VEGF) drug for their nAMD, have a baseline best-corrected visual acuity score between 78 to 24 letters based on the Early Treatment Diabetic Retinopathy Study (ETDRS) scoring system, more than 50% of the newly formed abnormal blood vessels originate from the choroid layer of the eye, and imaging shows there is fluid buildup affecting the centre of the eye.

What Are the Conditions for Reimbursement?

Eylea HD should only be reimbursed if it is prescribed by an ophthalmologist with experience managing nAMD, it is not used in combination with other anti-VEGF drugs, and the cost of Eylea HD is not more than the least costly anti-VEGF drug covered by the public drug plans for the treatment of nAMD. Eylea HD should only be authorized for reimbursement for 12 months the first time it is used. Eylea HD should not continue to be reimbursed if injections need to be given more frequently than every 12 weeks or if the patient's vision worsens by at least 5 letters due to their nAMD persisting or worsening and their central retina thickens by greater than 25 µm, new abnormal blood vessels form, or there is bleeding in the part of the eye responsible for central vision.

Why Did CADTH Make This Recommendation?

- One randomized controlled trial demonstrated that Eylea HD is no worse (but no better) than Eylea in improving or maintaining clearness or sharpness of vision in patients with nAMD who had not previously been treated with another anti-VEGF drug.
- Patients expressed a need for new treatments for nAMD that require fewer injections. Eylea HD administered every 12 or 16 weeks was no worse (but not better) than Eylea administered every 8 weeks in treating nAMD. However, there is not enough evidence to prove that using Eylea HD results in fewer injections than Eylea in real-world clinical practice.
- Based on CADTH's assessment of the health economic evidence, Eylea HD does not represent good value to the health care system at the public

Summary

list price. The committee determined there is not enough evidence to justify a greater cost for Eylea HD compared with other anti-VEGF drugs covered by the public drug plans for patients with nAMD.

- Based on public list prices, Eylea HD may decrease costs for the public drug plans; however, the extent of any savings realized will depend on the frequency of injections.

Additional Information

What Is nAMD?

nAMD is an eye disease in which there is a leakage of blood and fluids from abnormal blood vessels formed under the central retina, which causes damage to the retina and irreversible loss of central vision. It is estimated that nAMD affects more than 150,000 people in Canada.

Unmet Needs in nAMD

Patients with nAMD expressed a need for new treatments for nAMD that are safe, effective, and require fewer injections.

How Much Does Eylea HD Cost?

Treatment with Eylea HD is expected to cost between $6,250 to $10,000 per patient in the first year of use depending on how many injections are required (between 5 and 8 injections). In subsequent years, the annual cost per patient is expected to be between $5,000 to $8,750 (based on 4 to 7 injections per year).

Recommendation

The Canadian Drug Expert Committee (CDEC) recommends that aflibercept 8 mg/0.07 mL be reimbursed for the treatment of neovascular (wet) age-related macular degeneration (nAMD) only if the conditions listed in Table 1 are met.

Rationale for the Recommendation

One randomized, double-blind, active-controlled, phase III trial (PULSAR, N = 1,009) demonstrated that aflibercept 8 mg every 12 weeks and every 16 weeks was noninferior to aflibercept 2 mg every 8 weeks in improving best-corrected visual acuity (BCVA) from baseline over 48 weeks of treatment in adult patients with treatment-naive nAMD. The difference between treatment arms in the least squares (LS) mean change (improvement) from baseline to week 48 was −0.97 letters (95% confidence interval [CI], −2.87 to 0.92 letters) for aflibercept 8 mg every 12 weeks versus 2 mg every 8 weeks (noninferiority P = 0.0009; superiority P = 0.8437) and −1.14 letters (95% CI, −2.97 to 0.69 letters) for 8 mg every 16 weeks versus 2 mg every 8 weeks (noninferiority P = 0.0011, superiority P = 0.8884). In the absence of direct comparative evidence versus other currently available treatments for nAMD, results from a network meta-analysis that compared aflibercept 8 mg to other anti–vascular endothelial growth factor (VEGF) treatments for nAMD suggested uncertainty about which treatment might be favoured for visual acuity outcomes because point estimates were near the null with wide credible intervals.

Patients expressed a need for new treatments for nAMD that, as well as being effective and safe, require fewer injections. In the PULSAR trial, the between-group difference between aflibercept 2 mg every 8 weeks and aflibercept 8 mg every 12 weeks in the mean number of active injections through week 48 was −0.9 injections (95% CI, [redacted] injections) and the difference between aflibercept 2 mg every 8 weeks and aflibercept 8 mg every 16 weeks was −1.8 injections (95% CI, [redacted] injections). However, this evidence was uncertain given the lack of statistical testing for this outcome, the risk of bias due to missing data, and the potential difference in number of injections driven by the trial protocol compared to clinical practice. There were no indirect comparisons versus other anti-VEGF drugs used to treat nAMD provided for injection frequency aside from naive (visual) comparison of pairwise meta-analyses for each regimen.

Due to limitations in the comparative efficacy evidence from the sponsor's indirect treatment comparison, it was not possible to estimate the incremental cost-effectiveness of aflibercept 8 mg relative to any other comparator treatment. At the sponsor-submitted price for aflibercept 8 mg and publicly listed prices for other comparator regimens, aflibercept had higher drug acquisition costs than bevacizumab and lower drug acquisition costs than all other comparators reimbursed for the treatment of nAMD. Therefore, aflibercept 8 mg should be negotiated so that it does not exceed the drug program cost of the least costly comparator reimbursed for the treatment of nAMD.

Table 1: Reimbursement Conditions and Reasons

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. Adults with nAMD who meet all the following criteria: 1.1. treatment naive to anti-VEGF drugs for nAMD 1.2. BCVA ETDRS letter score of 78 to 24 (Snellen equivalent of 20/32 to 20/320) 1.3. total area of CNV comprises > 50% of total lesion area in the eye 1.4. presence of IRF and/or SRF affecting the central subfield on OCT.	The PULSAR trial showed that aflibercept 8 mg was effective in adult patients with treatment-naive active CNV lesions secondary to nAMD (> 50% of the total lesion area), BCVA ETDRS letter scores of 78 to 24 (Snellen equivalent of 20/32 to 20/320), and with IRF and/or SRF affecting the central subfield on OCT. The PULSAR trial excluded patients who had any prior treatment with an anti-VEGF drug for nAMD and there was no evidence submitted supporting the use of this drug in patients who are treatment experienced.	Aflibercept 8 mg could be initiated in a similar manner to other anti-VEGF drugs for nAMD as per the reimbursement criteria for each public drug plan.
2. The maximum duration of initial authorization is 12 months.	This is to help ensure that aflibercept 8 mg is used in patients who benefit from treatment.	—
Discontinuation		
3. Aflibercept 8 mg should be discontinued upon any of the following occurring: 3.1. the patient is unable to be maintained on a 12-week or greater interval between injections based on the physician's judgment of visual and anatomic outcomes 3.2. the patient meets these 2 conditions: 3.2.1. > 5-letter loss in BCVA compared to baseline (pretreatment) baseline due to persistent or worsening AMD 3.2.2. > 25 µm increase in CRT compared to baseline (pretreatment) or new-onset foveal neovascularization or foveal hemorrhage.	This is to ensure that aflibercept 8 mg is being used in patients who are benefiting from treatment. Patients and clinicians expressed a need for drugs that have longer treatment intervals and thus require fewer injections. In the PULSAR trial, treatment intervals in the aflibercept 8 mg every 12 weeks arm or the every 16 weeks arm could be shortened if there was a > 5-letter loss in BCVA from week 12 BCVA due to persistent or worsening AMD and a > 25 µm increase in CRT from week 12 or new-onset foveal neovascularization or foveal hemorrhage.	Aflibercept 8 mg could be discontinued in a similar manner to other anti-VEGF drugs for nAMD as per the reimbursement criteria for each public drug plan.

Reimbursement condition	Reason	Implementation guidance
Prescribing		
4. The patient should be under the care of an ophthalmologist with experience in managing nAMD.	This is to ensure that aflibercept 8 mg is prescribed for appropriate patients and administered by a trained ophthalmologist.	Aflibercept 8 mg could be prescribed in a similar manner to other anti-VEGF drugs for nAMD as per the reimbursement criteria for each public drug plan.
5. Aflibercept 8 mg should not be prescribed in combination with other anti-VEGF drugs.	There was no submitted evidence to support combination use of anti-VEGF drugs.	—
Pricing		
6. Aflibercept 8 mg should be negotiated so that it does not exceed the drug program cost of treatment with the least costly anti-VEGF reimbursed for the treatment of nAMD.	Results from an NMA that compared aflibercept 8 mg to other anti-VEGF treatments for nAMD suggested uncertainty about which treatment might be favoured for efficacy outcomes (visual acuity) because point estimates were near the null with wide credible intervals. As such, there is insufficient evidence to justify a cost premium for aflibercept 8 mg over the least expensive anti-VEGF reimbursed for nAMD.	—

AMD = age-related macular degeneration; BCVA = best-corrected visual acuity; CNV = choroidal neovascularization; CRT = central retinal thickness; IRF = intraretinal fluid; NMA = network meta-analysis; nAMD = neovascular (wet) age-related macular degeneration; OCT = optical coherence tomography; SRF = subretinal fluid; VEGF = vascular endothelial growth factor.

Discussion Points

- The sponsor requested a reconsideration of the initial draft recommendation to reimburse aflibercept 8 mg with conditions for the treatment of nAMD. The sponsor requested revisions to the initiation, renewal, and prescribing conditions for reimbursement. There were 3 issues outlined by the sponsor in the request for reconsideration that were discussed by CDEC. The sponsor requested that CDEC reconsider eligibility for initiating treatment in patients who are treatment experienced with anti-VEGF drugs for nAMD, the renewal condition regarding the required letters gained in BCVA at 6 months, and the prescribing condition that specified injections should not be given more frequently than every 12 weeks after the first 3 doses.
- The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) assessment of selected outcomes from the PULSAR trial's evidence concluded with high certainty that aflibercept 8 mg every 12 weeks or 8 mg every 16 weeks demonstrates noninferiority (but not superiority) to aflibercept 2 mg every 8 weeks in terms of the change (improvement) in BCVA from baseline over 48 weeks of treatment among adult patients with treatment-naive nAMD. Moderate certainty evidence showed that aflibercept 8 mg every 12 weeks or 8 mg every 16 weeks likely results in little to no difference in important outcomes such as the proportion of patients gaining 15 or more letters in BCVA and vision-related quality of life compared with aflibercept 2 mg every 8 weeks. Moderate

certainty evidence suggests aflibercept 8 mg every 12 weeks or 8 mg every 16 weeks likely results in little to no difference in the risk of ocular serious adverse events (SAEs) at 60 weeks compared with aflibercept 2 mg every 8 weeks.

- CDEC noted that frequency of injections was identified as an important outcome to both patients and clinicians because it potentially has implications for burden of treatment, AEs, and vision-related quality of life. The evidence from the PULSAR trial suggests that aflibercept 8 mg every 16 weeks may reduce the frequency of injections at 48 weeks. However, these results are associated with low certainty as per the GRADE assessment because of risk of bias due to missing outcome data as well as indirectness due to the number of injections being driven by the trial protocol. Furthermore, CDEC noted the decreased frequency of injections observed in the PULSAR trial may not be realized in clinical practice in Canada because the PULSAR trial's protocol-specified dosing interval of every 8 weeks for the aflibercept 2 mg arm was not aligned with the treat-and-extend protocol commonly used with aflibercept 2 mg in clinical practice.
- At the reconsideration meeting, CDEC further discussed patients' need for new treatments that require fewer injections (i.e., extend treatment intervals) and the frequency of injections when using aflibercept 8 mg. In the PULSAR trial, patients were randomized to receive aflibercept 2 mg administered every 8 weeks, aflibercept 8 mg administered every 12 weeks, or aflibercept 8 mg administered every 16 weeks (each after 3 initial monthly doses). Treatment intervals could be shortened in the PULSAR trial if there was a greater than 5 letter loss in BCVA from week 12 BCVA due to persistent or worsening AMD and/or greater than 25 µm increase in central retinal thickness (CRT) from week 12 or new-onset foveal neovascularization or foveal hemorrhage. CDEC noted that in the PULSAR trial, the majority of patients in the aflibercept 8 mg treatment arms (79.4% and 76.6% of patients in the aflibercept 8 mg every 12 weeks and every 16 weeks arms, respectively) maintained their randomized treatment interval at week 48. CDEC also noted that the product monograph recommends that aflibercept 8 mg be administered by intravitreal injection every month (4 weeks ± 1 week) for the first 3 consecutive doses, followed by 8 mg every 8 to 16 weeks (± 1 week) based on the physician's judgment of visual and anatomic outcomes. In addition, CDEC acknowledged that clinicians may want to use a treat-and-extend approach with this product, similar to how other anti-VEGF therapies are prescribed. However, CDEC also discussed that administering aflibercept 8 mg more frequently than every 12 weeks after the first 3 consecutive doses would be a similar frequency of injections to other anti-VEGF therapies that are currently reimbursed by the public drug plans (including aflibercept 2 mg) and therefore would not meet patients' need for treatments that require fewer injections.
- At the initial meeting, CDEC noted 2 gaps in the submitted evidence. First, the limitations of the indirect treatment comparison precluded CDEC from drawing conclusions regarding the efficacy of aflibercept 8 mg every 12 weeks or every 16 weeks compared to other anti-VEGF drugs. Second, CDEC noted that the PULSAR trial enrolled patients with treatment-naive nAMD; therefore, the comparative efficacy and harms of aflibercept 8 mg versus other anti-VEGF drugs in patients with previous anti-VEGF experience is a gap in the submitted evidence. At the reconsideration meeting,

CDEC discussed whether reimbursement should be restricted to patients with nAMD naive to anti-VEGF therapy. CDEC acknowledged that the sponsor and clinicians were of the opinion that reimbursement of aflibercept 8 mg should not be restricted to patients who are anti-VEGF naive, and that patients who have previously received another anti-VEGF therapy for nAMD may want this treatment option. However, CDEC again noted that the PULSAR trial restricted enrolment to patients who were treatment naive to anti-VEGF drugs, therefore the committee had no evidence to support reimbursement in patients with nAMD who are treatment experienced. CDEC did not consider results from a trial conducted in patients with diabetic macular edema who were treatment experienced with anti-VEGF therapy to be generalizable to patients with nAMD who were treatment experienced because they are different patient populations.

- Regarding the pricing condition, CDEC discussed considerations regarding identifying the least costly comparator due to the potential introduction of biosimilars and off-label comparator use at the initial and reconsideration meetings. Biosimilars for aflibercept are currently under review by Health Canada, and so at the time of this review, the comparative cost and cost-effectiveness of aflibercept 8 mg relative to biosimilars of anti-VEGF drugs is unknown. Additionally, CDEC discussed that bevacizumab was the lowest cost comparator included in the review and noted that it is used off label, without an indication for the treatment of nAMD. CDEC recognized that drug plans may or may not consider bevacizumab a relevant comparator in their negotiations.
- At the reconsideration meeting, CDEC discussed whether achieving at least a 15-letter improvement in BCVA at 6 months compared with baseline should be a condition for renewal of reimbursement. CDEC included this renewal criterion in the initial draft recommendation based on a CADTH therapeutic review (2016) of anti-VEGF drugs for the treatment of retinal conditions that found that an inadequate response to treatment can be defined as not achieving any improvement in BCVA at 3 months or not achieving an improvement in BCVA at 6 months of at least 15 ETDRS letters compared with the baseline (pretreatment) BCVA. The clinical expert indicated this a high standard of clinical response that may not be achievable depending on patients' baseline BCVA due to a ceiling effect, and CDEC noted that the proportion of patients gaining 15 or more letters in BCVA at week 48 ranged from 20.7% to 22.1% in the PULSAR trial. Upon reconsideration, CDEC determined that it would be reasonable to revise the reimbursement criteria regarding renewal and discontinuation, and these revisions are reflected in Table 1.

Background

AMD is a progressive condition characterized by central vision loss due to aging. nAMD is a late-stage version of AMD affecting approximately 10% of patients, which accounts for 90% of severe vision loss in Canada. The overall prevalence of any AMD in Canada is estimated at 9% among adults aged 45 years and older, with approximately 10% of patients reportedly presenting with the neovascular form. AMD affects more than 2.5 million Canadians, with approximately 180,000 patients experiencing vision loss. Patients experience rapid vision loss with worsening of central vision (caused by scotoma) and/or distortion of

straight lines. If left untreated, nAMD produces scarring and irreversible vision loss. Prompt treatment is imperative because patients who experience treatment delay have lower chances of visual outcome improvement. Thus, patients with impaired visual acuity caused by progressive disease will experience difficulties with daily living, have an increased risk of falls, and are at higher risk of social dependence and premature admission to nursing homes.

The clinical expert consulted by CADTH indicated that intravitreal injections with anti-VEGF therapies have become the current standard of care for nAMD, including aflibercept 2 mg, ranibizumab, brolucizumab, and faricimab. Bevacizumab is an off-label treatment for this condition. Anti-VEGF therapies are recommended as the first-line treatment by guidelines from international ophthalmology societies including the Canadian Retina Society, American Academy of Ophthalmology, the European Retina Society, and the British Royal College of Ophthalmology. The clinical expert consulted by CADTH noted that there are different treatment strategies currently in practice for the management of nAMD including a fixed-dosing regimen, as-needed regimen, or treat-and-extend regimen.

Aflibercept 8 mg/0.07 mL is indicated for the treatment of nAMD. Aflibercept is an anti-VEGF drug, which inhibits predominant signalling pathways responsible for angiogenesis and vascular leakage: VEGF-A and placental growth factor. The recommended dosage is administered by intravitreal injection every month (4 weeks ± 1 week) for the first 3 consecutive doses, followed by 8 mg/0.07 mL every 8 to 16 weeks (± 1 week) based on the physician's judgment of visual and anatomic outcomes.

Sources of Information Used by the Committee

To make its recommendation, the committee considered the following information:

- a review of 1 phase III randomized controlled trial in patients with nAMD and 1 sponsor-submitted indirect treatment comparison
- patients' perspectives gathered by 2 patient groups, Canadian Council of the Blind (CCB) and a joint input from Fighting Blindness Canada, the Canadian Council of the Blind, Vision Loss Rehabilitation Canada, and the International Federation on Ageing (IFA)
- input from public drug plans and cancer agencies that participate in the CADTH review process
- 1 of clinical specialist with expertise diagnosing and treating patients with nAMD
- input from 6 clinician groups, including the Southwestern Ontario Community Ophthalmologists, Toronto Retina Institute, the Canadian Retina Society, Retina Division of the Ottawa Hospital, the Northeastern Ontario Ophthalmology Group, and Toronto Ophthalmologists
- a review of the pharmacoeconomic model and report submitted by the sponsor
- information submitted as part of the sponsor's Request for Reconsideration (described subsequently)
- stakeholder feedback on the draft recommendation.

Stakeholder Perspectives

Patient Input

Input was received from the CCB and a joint input from Fighting Blindness Canada, the Canadian Council of the Blind, Vision Loss Rehabilitation Canada, and the IFA. They surveyed patients living with nAMD, including 337 people in Canada.

According to the patient groups, vision loss due to AMD has substantial and life-altering effects on patients' daily lives, manifesting as physical, psychological, and social impacts. Patients expressed they often relied on assistance from others to attend appointments and felt isolated or lonely. Patients worried about their condition worsening due to missed injection appointments. The patient groups noted that the burden associated with injection appointments increased when the appointments were frequent.

None of the patients surveyed had experience with the drug under review. Respondents indicated they were satisfied with their current therapies and expressed that it helped them avoid losing more eyesight. According to the patient groups, a treatment that is efficacious and reduces the number of visits to the ophthalmologist (i.e., a treatment that requires fewer injections) will undoubtedly lead to fewer missed appointments and improve outcomes.

Clinician Input

Input From the Clinical Expert Consulted by CADTH

The clinical expert indicated that the cost of travelling to medical appointments and the burden on family members for assistance are some of the obstacles that limit older adult patients with nAMD from having an optimal treatment outcome. Therefore, a drug or treatment program that allows for less frequent visits is an important option to improve patient compliance to fill this treatment gap. The clinical expert highlighted the newer emerging anti-VEGF agents, faricimab and brolucizumab, can extend the treatment interval to 12 weeks and even up to 16 weeks. However, the clinical expert reported that brolucizumab is associated with intraocular inflammation. Therefore, the clinical expert concluded a more durable treatment with high efficacy and without the increase of adverse side effects is an unmet need.

The clinical expert noted that the introduction of longer-acting therapy represents a treatment paradigm shift. The expert indicated that aflibercept 2 mg has been used for over 10 years and has a known safety profile. The clinical expert noted that aflibercept 8 mg could be considered as first-line treatment for nAMD. In addition, the clinical expert indicated that it could be considered as replacement therapy when the other anti-VEGF treatments are ineffective or for treatment of those patients who do not respond to the other anti-VEGF treatments.

The clinical expert consulted by CADTH noted that the outcome measures used in clinical practice align with those in the trial: visual acuity, optical coherence tomography (OCT) to assess intraretinal or subretinal fluid, central retinal thickness measurement, and fundus examination for retinal or subretinal hemorrhage. Following the initial monthly aflibercept 8 mg treatment for 3 months, the treatment interval can be extended to every 12 weeks and, subsequently, the interval can be adjusted by increments or reductions of 4 weeks for

the next treatment cycle. The clinical expert indicated the features of treatment failure are decreasing visual acuity, persistent or increased intraretinal or subretinal fluid, or development of new subretinal hemorrhage despite active treatment. The clinical expert noted the treatment with aflibercept 8 mg can be given in the clinic or hospital. The treatment should be provided by an ophthalmologist who is familiar with the diagnosis and management of retinal diseases including nAMD.

Clinician Group Input

Southwestern Ontario Community Ophthalmologists, Toronto Retina Institute, the Canadian Retina Society, Retina Division of the Ottawa Hospital, the Northeastern Ontario Ophthalmology Group, Toronto Ophthalmologists provided input to this review.

Treatment goals highlighted for AMD were consistent across groups (i.e., to maintain vision while extending the duration between treatments to reduce the treatment burden). The clinician groups highlighted that although current treatments (anti-VEGFs) target the underlying disease mechanism, they are not curative, and the extent and duration of damage to the retina may affect their ability to achieve improvement. Therefore, there is a need for new treatments that are efficacious and durable, improve long-term visual outcomes, and maintain a favourable safety profile that minimizes the risk of ocular complications. They agreed that a treatment formulation designed and studied with an extended dosing interval would help address the high burden of repeated injections for patients, caregivers, ophthalmologists, and reduce backlogs in the health care system. One group added that a treatment that promotes fluid-free retina for longer durations will allow improved quality of life metrics that have been associated with vision loss secondary to nAMD. The clinician groups anticipate that aflibercept 8 mg will replace the aflibercept 2 mg formulation, establishing it as a new first-line treatment choice for AMD. The clinician groups inputs aligned with the input submitted by the clinical expert consulted for this review.

Drug Program Input

Input was obtained from the drug programs that participate in the CADTH reimbursement review process. The clinical expert consulted by CADTH provided advice on the potential implementation issues raised by the drug programs.

Table 2: Responses to Questions From the Drug Programs

Implementation issues	Response
Relevant comparators	
PULSAR is a phase III, multicentre, randomized, double-masked, active-controlled study that compared aflibercept high dose (8 mg) to aflibercept 2 mg for efficacy, safety, and tolerability and to determine if aflibercept 8 mg administered in 2 extended dosing regimens was noninferior to aflibercept 2 mg. There were no trials comparing aflibercept 8 mg with other anti-VEGF drugs (brolucizumab and faricimab) that can be administered at the same extended dosing interval.	This is a comment from the drug programs to inform CDEC deliberations.

Implementation issues	Response
Considerations for initiation of therapy	
Most provinces have retinal programs and therefore no published reimbursement criteria or the reimbursement criteria is not adjudicated against. Some provinces have initiation criteria that was developed by a working group and may be outdated. The inclusion criteria for the PULSAR trial are not consistent with existing drug plan criteria for nAMD. The ranibizumab recommendation is from 2008 with no initiation or discontinuation criteria. The aflibercept 2 mg recommendation is from 2014 and does not include initiation or discontinuation criteria. More recently, the brolucizumab recommendation includes wording from existing drug plan criteria (discontinuation criteria), and faricimab was to list in a similar manner to other anti-VEGF drugs.	The clinical expert consulted by CADTH advised that the initiation of treatment for patients diagnosed with nAMD, defined by the presence of retinal fluid (either intraretinal or subretinal) or hemorrhages, is warranted. In terms of discontinuing treatment, the clinical expert consulted by CADTH noted that several factors should be considered, such as the absence of a positive response in a patient after receiving the treatment for at least 3 interval injections, as well as a lack of improvement in retinal fluid or visual acuity. In such cases, the clinical expert suggested that it is advisable to contemplate switching or discontinuing the medication because it may not be delivering the intended benefits, while acknowledging that each injection carries inherent risks. Conversely, the clinical expert noted that patients at the end stages of the disease with extensive scarring are unlikely to derive significant benefits from anti-VEGF treatment. Therefore, this also warrants consideration in terms of treatment cessation.
Considerations for discontinuation of therapy	
The drug plans asked CDEC to consider consistency with discontinuation criteria associated with other drugs reviewed by CADTH in the same therapeutic space.	This is a comment from the drug programs to inform CDEC deliberations.
Considerations for prescribing of therapy	
The sponsor noted that aflibercept 8 mg meets an unmet need by having a dosing frequency of every 12 to 16 weeks. The recommended dosage of brolucizumab is 6 mg every 6 weeks for the first 5 doses then every 12 weeks. The recommended dosage of faricimab is 6 mg every 4 weeks for the first 4 doses then every 8, 12, or 16 weeks.	This is a comment from the drug programs to inform CDEC deliberations.
Does aflibercept 8 mg meet an unmet need given there are other products marketed with an extended dosing interval?	The clinical expert consulted by CADTH indicated that currently, there are 3 medications that offer extended dosing intervals: aflibercept 8 mg, faricimab, and brolucizumab. The clinical expert indicated that it is essential to note that brolucizumab has been associated with a higher frequency of intraocular inflammations and severe cases of hemorrhagic retinal vasculitis. These severe effects have the potential to cause significant vision loss, to the extent that some patients may even experience complete blindness as a result of complications arising from the treatment. The clinical expert noted that faricimab represents a relatively newer medication that can extend treatment intervals up to 12 weeks. Although it is not clear if the intention is to extend treatment to 16 weeks, this 16-week extension is the optimal treatment goal. This is noteworthy because even aflibercept 2 mg, in some cases, allows for extension up to 12 weeks when using a treat-and-extend protocol. The clinical expert noted that aflibercept 2 mg, with a history of over a decade in clinical use, demonstrated an appropriate safety profile. The clinical expert highlighted that the primary objective, as

Implementation issues	Response
	dictated by the unmet need, is to extend treatment intervals and alleviate the treatment burden on both patients and clinicians.
System and economic issues	
Aflibercept 8 mg would have a significant budget impact on public drug plans. Biosimilars have already been marketed for ranibizumab. Biosimilars are anticipated for aflibercept 2 mg next year. Public drug plans have expressed concerns regarding brand manufacturers marketing an improved version of an existing originator drug to maintain market share and to extend a product's patent. There has been a significant increase in drug utilization in some jurisdictions for aflibercept 2 mg due to prescriber switching from ranibizumab. It is expected that this would occur with aflibercept 8 mg. Should the pricing recommendation for reimbursement recommend that aflibercept 8 mg be negotiated so that it provides cost savings to drug programs relative to the cost of currently funded anti-VEGF drugs for AMD?	Refer to pricing condition in Table 1.
Confidential pricing agreements exist for most anti-VEGF drugs. Based on current list price, aflibercept 8 mg is not a cost-effective treatment option.	This is a comment from the drug programs to inform CDEC deliberations.

AMD = age-related macular degeneration; CDEC = Canadian Drug Expert Committee; nAMD = neovascular age-related macular degeneration; VEGF = vascular endothelial growth factor.

Clinical Evidence

Systematic Review

Description of Studies

PULSAR (N = 1,009) was a phase III, multicentre (3 sites in Canada), double-blind, randomized, active-controlled noninferiority trial to demonstrate the efficacy and safety of aflibercept 8 mg every 12 weeks and aflibercept 8 mg every 16 weeks compared to aflibercept 2 mg every 8 weeks in adult patients with treatment-naive nAMD. The study included a screening period (up to 3 weeks) followed by a treatment period. Outcomes were assessed at the 48-week and 60-week time points of the treatment period. The primary outcome of PULSAR was the change from baseline in BCVA at 48 weeks. Secondary outcomes that were relevant to the review included the proportion of patients with no intraretinal fluid (IRF) and no subretinal fluid (SRF) at week 48, proportion of participants gaining at least 15 letters in BCVA from baseline at week 48, frequency of injection through week 48, change from baseline in National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25) total score at week 48, treatment-emergent adverse events (TEAEs), and SAEs through week 60.

The overall proportion of male and female participants was 45.5% and 54.5%, respectively. The median age was 75 years (range, 50 to 96 years), and the majority of participants were Asian (23.2%) or white (75.8%). Most patients had a baseline BCVA of 73 letters or less on ETDRS charts (86.2%).

Efficacy Results

Change From Baseline in BCVA at Week 48

The difference in LS mean change from baseline to week 48 was −0.97 letters (95% CI, −2.87 to 0.92 letters) for 8 mg every 12 weeks versus 2 mg every 8 weeks (noninferiority P = 0.0009; superiority P = 0.8437) and −1.14 letters (95% CI, −2.97 to 0.69 letters) for 8 mg every 16 weeks versus 2 mg every 8 weeks (noninferiority P = 0.0011, superiority P = 0.8884). Results of analysis of the PPS and sensitivity analyses using different missing data imputation approaches were consistent with those in the FAS. The differences in LS mean change from baseline to week 60 were −0.86 letters (95% CI, −2.57 to 0.84 letters; noninferiority P = 0.0002; superiority P = 0.8393) and −0.92 letters (95% CI, −2.51 to 0.66 letters; noninferiority P < 0.0001; superiority P = 0.8371) for the 8 mg every 12 weeks and 8 mg every 16 weeks arms, respectively, compared to the 2 mg every 8 weeks arm. The results of PPS for week 60 were consistent with those in the FAS.

Proportion of Patients Gaining 15 or More ETDRS Letters at Week 48

The between-group difference in the proportion of patients gaining 15 or more letters in BCVA from baseline to week 48 was −1.75% (95% CI, −7.78% to 4.29%; P = 0.5704) for aflibercept 8 mg every 12 weeks versus 2 mg every 8 weeks and −0.94% (95% CI, −7.00% to 5.12%; P = 0.7611) for aflibercept 8 mg every 16 weeks versus 2 mg every 8 weeks based on last observation carried forward in the FAS. The observed findings were maintained at week 60.

Presence of IRF or SRF at Week 48

At week 48, 71.1% and 66.8% of patients in the aflibercept 8 mg every 12 weeks and aflibercept 8 mg every 16 weeks arms, respectively, had no retinal fluid (no intraretinal fluid [IRF] and no subretinal fluid [SRF]) compared with 59.4% in the aflibercept 2 mg every 8 weeks. This resulted in a difference in the proportion of patients with no IRF and SRF in the central subfield of 11.72% (95% CI, 4.52% to 18.92%; P = 0.0001) for 8 mg every 12 weeks versus 2 mg every 8 weeks and 7.45% (95% CI, 0.14% to 14.76%; P = 0.0051) 8 mg every 16 weeks versus 2 mg every 8 weeks, based on last observation carried forward in the FAS. The observed findings were maintained at week 60.

Frequency of Injections

At week 48, 251 (79.4%) and 239 (76.6%) of completers in the aflibercept 8 mg every 12 weeks and 8 mg every 16 weeks arms, respectively, maintained their randomized treatment interval. This resulted in mean numbers of active injections through week 48 of 6.1 and 5.2 in the aflibercept 8 mg every 12 weeks and 8 mg every 16 weeks arms, respectively, compared to 6.9 in the aflibercept 2 mg every 8 weeks arm. Treatment group difference between 2 mg every 8 weeks aflibercept 8 mg every 12 weeks and aflibercept 2 mg every 8 weeks was −0.9 injections (95% CI, [redacted] injections) and the difference between aflibercept 2 mg every 8 weeks and aflibercept 8 mg every 16 weeks and aflibercept 2 mg every 8 week was −1.8 [redacted] injections.

At week 60, the mean number of injections was 8.8 (SD = [redacted]), 7.1 (SD = [redacted]), and 6.2 (SD = [redacted]) for the aflibercept 2 mg every 8 weeks, 8 mg every 12 weeks, and 8 mg every 16 weeks groups, respectively.

NEI VFQ-25

LS mean changes from baseline were observed in all arms at week 48, ranging from 3.35 (SE= [redacted]) in the aflibercept 8 mg every 16 weeks arm to 4.22 (SE = [redacted]) in the aflibercept 2 mg every 8 weeks arm. The difference in the LS mean change from baseline using the mixed model for repeated measurements (MMRM) in the FAS were −0.72 [redacted] for 8 mg every 12 weeks versus 2 mg every 8 weeks and −0.87 [redacted] for both 8 mg every 12 weeks and 8 mg every 16 weeks versus 2 mg every 8 weeks. The results were consistent at week 60.

Harms Results

Patients in the trial reported at least 1 ocular TEAE with similar proportions across the treatment arms (45% in the aflibercept 2 mg every 8 weeks arm, 42.4% in the aflibercept 8 mg every 12 weeks, and 42.3% in the aflibercept 8 mg every 16 weeks). The most common ocular TEAEs in all treatment arms were reduced visual acuity (6.3% in the aflibercept 2 mg every 8 weeks arm, 3.9% in the aflibercept 8 mg every 12 weeks arm, and 5.9% in the aflibercept 8 mg every 16 weeks arm), cataract (3.9%, 4.8%, and 4.4%), retinal hemorrhage (4.5%, 3.6%, and 3.8%, respectively). The proportion of patients with non-ocular TEAE were 59.8%, 59.4%, 61.2% in the aflibercept 2 mg every 8 weeks, the aflibercept 8 mg every 12 weeks, and the aflibercept 8 mg every 16 weeks arms, respectively. At least 1 treatment-emergent SAE was reported in 1.2% of patients in the aflibercept 2 mg every 8 weeks arm, and 2.1% of patients in each of the aflibercept 8 mg every 12 weeks and every 16 weeks arms. Retinal hemorrhage and retinal detachment were the most common SAE in the treatment groups with same percentage (0.3%, 0.6%, and 0.6% in the aflibercept 2 mg every 8 weeks arm, aflibercept 8 mg every 12 weeks arm, and aflibercept 8 mg every 16 weeks arm, respectively).

The proportion of patients who discontinued treatment due to an ocular TEAE was 0.6% in the aflibercept 2 mg every 8 weeks arm, and 1.2% in both the aflibercept 8 mg every 12 weeks and every 16 weeks arms. In the aflibercept 2 mg every 8 weeks arm, death events were reported for 1.5% of patients. In the aflibercept 8 mg every 12 weeks arm, death events were reported for 0.9% and 0.6% in the aflibercept 8 mg every 12 weeks arm and aflibercept 8 mg every 16 weeks arm, respectively. In terms of notable harms, cataracts occurred in 3.9% of patients treated with aflibercept 2 mg every 8 weeks, 4.8% of patients treated with the aflibercept 8 mg every 12 weeks, and 4.4% of patients treated with the aflibercept 8 mg every 16 weeks. The incidence of increased intraocular pressure was 2.7% in the aflibercept 2 mg every 8 weeks arm and 3.3% in the aflibercept 8 mg every 12 weeks arm, and 3.0% in the aflibercept 8 mg every 16 weeks arm. The percentage of patients experienced retinal pigment epithelium tear was 0.9% in the aflibercept 2 mg every 8 weeks arm, 1.8% in aflibercept 8 mg every 12 weeks arm, and 0.9% in the aflibercept 8 mg every 16 weeks arm.

Results of GRADE Assessments

Table 3 presents the GRADE summary of findings for aflibercept 8 mg every 12 weeks and every 16 weeks versus aflibercept 2 mg every 8 weeks.

Table 3: Summary of Findings for Aflibercept 8 mg Every 12 Weeks and 8 mg Every 16 Weeks Versus Aflibercept 2 mg Every 8 Weeks for Patients With Treatment-Naive nAMD

Outcome and follow-up	Intervention: patients (studies), N	Relative effect (95% CI)	Absolute effects (95% CI)			Certainty	What happens
			Aflibercept 2 mg Q8W	Aflibercept 8 mg Q12W or Q16W	Difference		
Visual acuity							
Change from baseline in BCVA (letters), LS mean (SE) Follow-up: 48 weeks	Aflibercept 8 mg every 12 weeks: 671 (1 RCT)	NA	7.03	6.06 (0.77)	0.97 fewer (2.87 fewer to 0.92 more)	High	Aflibercept 8 mg every 12 weeks results in little to no clinically important difference in the change in BCVA compared with aflibercept 2 mg every 8 weeks.
	Aflibercept 8 mg every 16 weeks: 674 (1 RCT)	NA	7.03	5.89 (0.72)	1.14 fewer (2.97 fewer to 0.69 more)	High	Aflibercept 8 mg every 16 weeks results in little to no clinically important difference in the change in BCVA compared with aflibercept 2 mg every 8 weeks.
Proportion of patients gaining ≥ 15 letters in BCVA from baseline Follow-up: 48 weeks	Aflibercept 8 mg every 12 weeks: 671 (1 RCT)	NA	22.1 per 100	20.7 per 100	1.8 fewer per 100 (7.8 fewer to 4.3 more per 100)	Moderate[a,b]	Aflibercept 8 mg every 12 weeks likely results in little to no clinically important difference in the proportion of patients gaining ≥ 15 letters from baseline compared with aflibercept 2 mg every 8 weeks.
	Aflibercept 8 mg every 16 weeks: 674 (1 RCT)	NA	22.1 per 100	21.7 per 100	0.9 fewer per 100 (7.0 fewer to 5.1 more per 100)	Moderate[a,b]	Aflibercept 8 mg every 16 weeks likely results in little to no clinically important difference in the proportion of patients gaining ≥ 15 letters from baseline compared with aflibercept 2 mg every 8 weeks.
Proportion of patients with no IRF and no SRF							
Proportion of patients with no IRF and no SRF Follow-up: 48 weeks	Aflibercept 8 mg every 12 weeks: 671 (1 RCT)	NR	59.4 per 100	71.1 per 100	11.7 more per 100 (4.5 to 18.9 more per 100)	Moderate[b,c]	Aflibercept 8 mg every 12 weeks likely results in little to no clinically important difference in the proportion of patients without IRF and SRF compared with aflibercept 2 mg every 8 weeks.

Outcome and follow-up	Intervention: patients (studies), N	Relative effect (95% CI)	Absolute effects (95% CI)			Certainty	What happens
			Aflibercept 2 mg Q8W	Aflibercept 8 mg Q12W or Q16W	Difference		
	Aflibercept 8 mg every 16 weeks: 674 (1 RCT)	NR	59.4 per 100	66.8 per 100	7.5 more per 100 (0.1 to 14.8 more per 100)	Moderate[b,c]	Aflibercept 8 mg every 16 weeks likely results in little to no clinically important difference in the proportion of patients without IRF and SRF compared with aflibercept 2 mg every 8 weeks.
Vision-related QoL (NEI VFQ-25)							
Change from baseline in NEI VFQ-25 total score, LS mean (SE) Follow-up: 48 weeks	Aflibercept 8 mg every 12 weeks: 671 (1 RCT)	NA	4.22	3.50	0.72 less	Moderate[a,d]	Aflibercept 8 mg every 12 weeks likely results in little to no clinically important difference in the change from baseline in vision-related QoL compared with aflibercept 2 mg every 8 weeks.
	Aflibercept 8 mg every 16 weeks: 674 (1 RCT)	NA	4.22	3.35	0.87 less	Moderate[a,d]	Aflibercept 8 mg every 16 weeks likely results in little to no clinically important difference in the change from baseline in vision-related QoL compared with aflibercept 2 mg every 8 weeks.
Number of injections							
Number of injections, LS mean (95% CI) Follow-up: 48 weeks	Aflibercept 8 mg every 12 weeks: 625 (1 RCT)	NA	6.9	6.1	0.9 fewer (NR)	Low[a,e]	Aflibercept 8 mg every 12 weeks may result in little to no clinically important difference in the frequency of injections compared with aflibercept 2 mg every 8 weeks.
	Aflibercept 8 mg every 16 weeks: 621 (1 RCT)	NA	6.9	5.2	1.8 fewer (NR)	Low[a,e]	Aflibercept 8 mg every 16 weeks may result in a reduction in the frequency of injections compared with aflibercept 2 mg every 8 weeks.

Outcome and follow-up	Intervention: patients (studies), N	Relative effect (95% CI)	Absolute effects (95% CI)			Certainty	What happens
			Aflibercept 2 mg Q8W	Aflibercept 8 mg Q12W or Q16W	Difference		
Ocular SAEs							
Proportion of patients with ocular SAEs Follow-up: 60 weeks	Aflibercept 8 mg every 12 weeks: 671 (1 RCT)	NR	1.2 per 100	2.1 per 100	0.9 more per 100 (NR)	Moderate[a,f]	Aflibercept 8 mg every 12 weeks likely results in little to no difference in the proportion of patients with ocular SAEs compared with aflibercept 2 mg every 8 weeks. There may be some uncertainty about the clinical importance of the effect.
	Aflibercept 8 mg every 16 weeks: 674 (1 RCT)	NR	1.2 per 100	2.1 per 100	0.9 more per 100 (NR)	Moderate[a,f]	Aflibercept 8 mg every 16 weeks likely results in little to no difference in the proportion of patients with ocular SAEs compared with aflibercept 2 mg every 8 weeks. There may be some uncertainty about the clinical importance of the effect.

BCVA = best-corrected visual acuity; CI = confidence interval; IRF = intraretinal fluid; LS = least square; nAMB = neovascular age-related macular degeneration; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire-25; NR = not reported; Q8W = every 8 weeks; Q12W = every 12 weeks; Q16W = every 16 weeks; QoL = quality of life; RCT = randomized controlled trial; SAE = serious adverse event; SE = standard error; SRF = subretinal fluid.

Note: Study limitations (which refer to internal validity or risk of bias), inconsistency across studies, indirectness, imprecision of effects, and publication bias were considered when assessing the certainty of the evidence. All serious concerns in these domains that led to the rating down of the level of certainty are documented in the table footnotes.

[a]There was not a hypothesis test for this outcome in the trial; the result can be considered as supportive evidence.

[b]Rated down 1 level for serious concerns about risk of bias due to missing outcome data. Did not rate down for imprecision; a between-group difference of greater than 20% was clinically significant according to the clinical expert; the entire CI is compatible with little to no difference.

[c]There is no multiplicity adjustment; the result can be considered as supportive evidence.

[d]Rated down 1 level for serious concerns about risk of bias due to missing outcome data. Did not rate down for imprecision. Based on the literature, a 6-point change from baseline in NEI VFQ-25 total score was clinically important; the point estimate and entire CI suggest little to no difference.

[e]Rated down 1 level for serious concerns about risk of bias due to missing outcome data. Did not rate down for imprecision; the clinical expert considered a difference of 2 injections in this time frame to be clinically important; the sample size was adequately large. Rated down 1 level for serious indirectness because the number of injections was driven by the protocol and not reflective of how injections would be provided in practice.

[f]The clinical expert consulted by CADTH was unable to estimate a threshold for clinically important effects, so the null was used. Rated down 1 level for serious imprecision due to the small number of events.

Economic Evidence

Table 4: Cost and Cost-Effectiveness

Component	Description
Type of economic evaluation	Cost-utility analysis Markov model
Target population	Adults with nAMD
Treatment	Aflibercept 8 mg, administered every 16 weeks[a]
Dose regimen	8 mg administered by intravitreal injection every 4 weeks for first 3 doses, followed by 8 mg at a dosing interval of every 8 to 16 weeks
Submitted price	Aflibercept 8 mg, 30 mg per 0.263 mL, single-use vial: $1,250.00
Treatment cost	$6,250 to $10,000 in the first year, based on 5 to 8 injections. $5,000 to $8,750 in subsequent years, based on 4 to 7 injections.
Comparators	• Aflibercept 2 mg • Bevacizumab • Brolucizumab • Faricimab • Ranibizumab
Perspective	Canadian publicly funded health care payer
Outcomes	QALYs, life-years
Time horizon	Lifetime (25 years)
Key data sources	• PULSAR trial to inform clinical efficacy of aflibercept 8 mg • Comparative clinical efficacy (change in BCVA) and administration frequency were informed by a sponsor-submitted ITC
Key limitations	• The comparative efficacy and safety of aflibercept 8 mg every 16 weeks relative to other anti-VEGFs is uncertain owing to a lack of head-to-head trials and limitations with the sponsor's ITCs. Indirect evidence submitted by the sponsor suggests that there may be no meaningful difference in the efficacy or safety for aflibercept 8 mg compared to other currently available treatments for nAMD due to uncertainty in the ITC results. • The relative frequency of administration for aflibercept 8 mg and comparators is uncertain owing to limitations with the sponsor's submitted evidence for administration frequency and the individualized approach to administration frequency in clinical practice
CADTH reanalysis results	• There is insufficient clinical evidence to justify a price premium for aflibercept 8 mg relative to currently available treatments for nAMD.

BCVA = best-corrected visual acuity; ICER = incremental cost-effectiveness ratio; ITC = indirect treatment comparison; nAMD = neovascular age-related macular degeneration; QALY = quality-adjusted life-year.

[a]In the sponsor's base case, aflibercept 8 mg was assumed to be administered every 16 weeks. Administration of aflibercept 8 mg every 12 weeks was considered in scenario analysis.

Budget Impact

CADTH identified the following key limitations with the sponsor's analysis: the administration frequency for aflibercept 8 mg and other anti-VEGF inhibitors is uncertain, the number of administrations per vial for some

comparators may be underestimated, the displacement of comparators by aflibercept 8 mg is uncertain, and the price of drugs paid by the public drug plans is uncertain. In the absence of more reliable input values to estimate the key parameters of the budget impact analysis, the sponsor's base case was maintained. The sponsor's analysis estimates that reimbursing aflibercept 8 mg for the treatment of nAMD will be cost-saving for the public drug plans (3-year incremental budgetary savings of $158,158,913). CADTH explored uncertainty in this estimate via scenario analyses that included adopting alternative assumptions about the administration frequency of anti-VEGF drugs, vial sharing, displacement of anti-VEGFs by aflibercept 8 mg, and the introduction of an aflibercept 2 mg biosimilar. Results of CADTH's scenario analyses suggest that the budget impact of reimbursing aflibercept 8 mg for nAMD is highly sensitive to administration frequency of anti-VEGFs, vial sharing, and the availability of an aflibercept 2 mg biosimilar. Results of these analyses ranged from a cost savings of $171 million to an incremental cost of $21.5 million over the first 3 years of reimbursement. As such, whether there is cost savings, and the extent of any savings realized by the drug plans, is highly uncertain.

Request for Reconsideration

The sponsor filed a Request for Reconsideration for the draft recommendation for aflibercept 8 mg for the treatment of nAMD. The sponsor requested that CDEC reconsider their review of aflibercept 8 mg and the conditions for reimbursement based on the following:

- The sponsor is of the view that that reimbursement of aflibercept 8 mg should not be restricted to patients with nAMD who are naive to anti-VEGF therapy.
- The sponsor believes that achieving a gain of 15 or more letters in BCVA by month 6 is not based on current evidence to determine adequate response for continuation (i.e., renewal) of anti-VEGF treatment. The sponsor is of the view that a 5 to 10 letter gain can provide additional benefit for patients.
- The sponsor believes that a prescribing condition stating that injections should not be given more frequently than 12-week intervals does not align with the dosage recommendation in the Health Canada product monograph or with how patients are treated in clinical practice using a treat-and-extent approach.

In the meeting to discuss the sponsor's Request for Reconsideration, CDEC considered the following information:

- information from the initial submission related to the issues identified by the sponsor
- feedback from 1 clinical expert with expertise in diagnosing and treating patients with nAMD
- feedback on the drug recommendation from the public drug plans
- feedback on the draft recommendation from 25 clinician groups: Atlantic Coast Retina Consultants, North GTA Ophthalmology, Dr. Kathy Cao, Central Alberta Eye Surgery and Clearfield Eye Physicians and Surgeons, Dr. R. Geoff Williams, Canadian Ophthalmological Society, Retina surgeon, Dalhousie University, Canadian Retina Society, Eye Physicians and Surgeons of Manitoba (EPSOM),

Saskatchewan Health Authority, Retina Specialists of Vancouver Island Health Authority, Mississauga Retina Institute, Southwestern Ontario Community Ophthalmologists, Niagara Ophthalmologists, EPSNB, Northeastern Ontario Ophthalmology Group, Retina Division of The Ottawa Hospital, Toronto Ophthalmologists, Toronto Retina Institute, Waterloo Eye, GTA Ophthalmology, West Coast Retina Consultants Inc., and Scarborough Ophthalmologists.

- 1 joint feedback on the draft recommendation from 5 patient groups: Fighting Blindness Canada, the CCB, CNIB, Vision Loss Rehabilitation Canada, and the IFA
- feedback on the draft recommendation from the sponsor.

All stakeholder feedback received in response to the draft recommendation is available on the CADTH website.

CDEC Information

Members of the Committee

Dr. James Silvius (Chair), Dr. Sally Bean, Mr. Dan Dunsky, Dr. Edward Xie, Mr. Bob Gagne, Dr. Ran Goldman, Dr. Peter Jamieson, Mr. Morris Joseph, Dr. Christine Leong, Dr. Kerry Mansell, Dr. Alicia McCallum, Dr. Srinivas Murthy, Dr. Trudy Huyghebaert, Dr. Danyaal Raza, and Dr. Peter Zed.

Initial meeting date: January 24, 2024

Regrets: One expert committee member did not attend.

Conflicts of interest: None

Reconsideration meeting date: May 22, 2024

Regrets: One expert committee member did not attend.

Conflicts of interest: None

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