Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

pegcetacoplan (TBC)

(Apellis Canada Inc.)

Indication: Pegcetacoplan solution for injection is indicated in adults for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

July 12, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

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CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: pegcetacoplan
Indication: Geographic atrophy secondary to age-related macular degeneration
Name of Patient Group: Fighting Blindness Canada, The Canadian Council of the Blind (CCB), CNIB, International Federation on Ageing (IFA), Vision Loss Rehabilitation Canada (VLRC), Association Québécoise de la dégénérescence maculaire (AQDM)
Author of Submission: Dr. Larissa Moniz (FBC), Dr. Keith Gordon (CCB), Thomas Simpson (CNIB), Dr. Anjali Tripathi (IFA), Jennifer Urosevic (VLRC), Sylvie Castonguay (AQDM)

1. About Your Patient Group

Fighting Blindness Canada (FBC) is the largest charitable funder of vision research in Canada.

Over our 50-year history, FBC has contributed critical funding for the development of sight-saving treatments and cures for blinding eye diseases. By raising and stewarding funds, FBC is helping drive forward research that supports our goal of understanding why vision loss occurs, how it can be slowed and how sight can be restored. We are an invaluable resource for individuals and families impacted by blindness, providing accurate eye health information through our website and educational events, as well as engaging with government and other stakeholders to advance better vision health policies.

The Canadian Council of the Blind (CCB) is a membership-based not-for-profit organization that brings together Canadians who are blind, deaf-blind or living with vision loss through chapters within their own local communities to share common interests and social activities.

CCB works to improve the quality of life for persons with vision loss through awareness, peer mentoring, socializing, sports, advocacy, health promotion and illness prevention.

The CCB was founded in 1944 by blind Canadian war veterans and schools of the blind. The national office is located in Ottawa with over 80 chapters across Canada. The CCB is the largest membership-based organization for the blind in Canada and is known as the Voice of the Blind™.

Founded in 1918, **CNIB** is a non-profit organization driven to change what it is to be blind today. We deliver innovative programs and powerful advocacy that empower people impacted by blindness to live their dreams and tear down barriers to inclusion. Our work as a blind foundation is powered by a network of volunteers, donors and partners from coast to coast to coast.

The **International Federation on Ageing** **(IFA)** is an international non-governmental organization (NGO) based in Canada whose members are government, NGOs, academia, industry, and individuals in nearly 80 countries. IFA believes that all these members working together are essential to help shape and influence policy and good practices. IFA stands to drive the agenda for the world's population ageing. We are proud to have general consultative status at the United Nations. The International Federation on Ageing is a non-State actor in official relations with the World Health Organization (WHO).

Vision Loss Rehabilitation Canada (VLRC) is a health services organization. We provide training that enables people who are blind or partially sighted to develop or restore key daily living skills, helping enhance their independence, safety and mobility. Our certified specialists work closely with ophthalmologists, optometrists and other health care professionals, providing essential care on a referral basis in homes and communities.

The Vision of VLRC is to maximize health and independence for Canadians impacted by vision loss and our mission is to provide high-quality, integrated and accessible rehabilitation and health care services that enable Canadians impacted by vision loss to live the lives they choose.

Founded in 1990, **AQDM**'s mission is to inform, guide and support people with macular degeneration and their caregivers. AMD is the most common form of the disease, but there are others, including myopic degeneration. The association also represents patients and their caregivers in dealings with government authorities. It organizes conferences, publishes a newsletter, informs the public in the province of Quebec on its phone line, and refers people to local organizations for their visual health needs.

2. Information Gathering

Information forming the basis of this submission was collected through three primary sources:

1) **Qualitative interviews** held during 2023 with two patients diagnosed with geographic atrophy (GA). Conducted by Fighting Blindness Canada, the interviews were semi-structured and designed to learn about the lived experience of GA, including visual and life challenges, economic hurdles, experiences with treatments, and more.

2) **MOSAIC: a burden of illness study** focused on patients with GA and produced by Apellis, the company that developed pegcetacoplan (SYFOVRE) for treatment of GA. Although data from MOSAIC may already be part of the company submission, it is used here as a secondary resource and analyzed from the perspective of the submitting patient groups and without any input from Apellis; the analysis takes the form of "key takeaways" that are supported by other sources of information. MOSAIC is based on survey input from patients and caregivers internationally: 251 patients, 238 caregivers, and 157 dyads (linked patients and caregivers).

   Below is an overview of the MOSAIC respondents:

Variables Patients	Australia N=21	Canada N=47	France N=12	Germany N=36	UK N=34	Europe N=81	US N=102
Mean (SD) age (years) Range	80 (6) 60-95	73 (5) 64-83	78 (9) 63-94	76 (8) 60-95	78 (8) 62-94	77 (8) 60-95	68 (4) 60-84
Sex proportion in % Male/Female/Prefer to skip	43/57	[illegible]	17/83	51/49	50/47/3	46/53/1	43/57
Employment status	76% retired	81% retired	100% retired	91% retired	82% retired	89% retired	77% retired
Living situation	52% live with someone	79% live with someone	33% live with someone	77% live with someone	59% live with someone	63% live with someone	88% live with someone
Mean (SD) age at time of diagnosis of GA (years)	69 (9)	68 (4)	64 (10)	71 (8)	69 (8)	69 (9)	62 (6)
Mean (SD) NEI VFQ-39 composite score *Range: 0-100*	57.6 (20.8)	48.3 (21.3)	48.1 (21.9)	47.9 (15.2)	46.9 (20.4)	47.5 (18.3)	44.6 (20.2)
Had to change living situation	10%	28%	0%	6%	24%	12%	38%
Need help everyday	19%	38%	33%	26%	50%	37%	68%

Variables Caregivers	Australia N=13	Canada N=46	France N=7	Germany N=35	UK N=35	Europe N=77	US N=102
Mean (SD) age (years) Range	58 (16) 38-84	44 (11) 27-78	75 (5) 69-82	64 (14) 30-87	58 (18) 23-86	62 (16) 23-87	46 (15) 19-68
Sex proportion in % Male/Female/Prefer to skip	31/69	[illegible]	57/43	34/66	9/89/2	25/74/1	47/53
Employed	69%	93%	0%	37%	51%	40%	44%
Employment status changed since becoming a caregiver	69%	22%	0%	9%	23%	14%	41%
Living with the person with GA	77%	67%	86%	69%	34%	55%	81%
Had to change living situation	31%	59%	0%	11%	14%	12%	46%
Mean (SD) ZBI score *Range 0-88*	24.7 (17.8)	42.4 (11.9)	29.9 (18.5)	18.8 (9.8)	20.0 (15.5)	20.3 (13.7)	24.8 (18.7)
Number of dyads	**N=7**	**N=3**	**N=4**	**N=35**	**N=14**	**N=53**	**N=93**
Correlation between VFQ-39 composite score and ZBI score	NA*	NA*	NA*	0.00	-0.50	-0.27	-0.63

3) **An online survey** made available to Canadians living with either wet or dry age-related macular degeneration (AMD) during the first months of 2020. Shared across networks associated with FBC and CCB, the survey is part of a larger research project titled VIEW AMD (Valuation and Interpretation of Experiences with AMD) that received ethics approval from Advarra, the largest independent provider of institutional review board (IRB) services.

   A total of 337 Canadians responded to the survey, and although the responses focus on the experience of AMD, it is possible to draw conclusions related to GA as well, particularly when connected to the qualitative interviews led by FBC and findings from the MOSAIC study. In particular—and as the interviews demonstrate—it is generally safe to assume that the experience of GA is comparable to AMD, but often more extreme in terms of vision loss and the related physical, social, psychological, etc., challenges.

   Below is an overview of the respondents to the VIEW AMD survey:

Characteristic	**n (%)**
Age (n = 320)	
Mean age (SD)	63.5 (16.5)
18 - 40 years	34 (10.6)
41 - 60 years	112 (35.0)
61 - 80 years	117 (36.6)
Over 80 years	57 (17.8)
Biological Sex (n = 322)	
Female	168 (52.2)
Male	153 (47.5)
Intersex	1 (0.3)
Province (n = 337)	
Ontario	151 (44.8)
British Columbia	68 (20.2)
Alberta	35 (10.4)
Quebec	25 (7.4)

Manitoba	13 (3.9)
Nova Scotia	12 (3.6)
Newfoundland	11 (3.3)
New Brunswick	7 (2.1)
Northwest Territories	6 (1.8)
Prince Edward Island	4 (1.2)
Saskatchewan	4 (1.2)
Nunavut	1 (0.3)
Location (n = 337)	
Urban	300 (89.0)
Rural	37(11.0)
Type of AMD (n = 337)	
Wet AMD in both eyes	111 (32.9)
Dry AMD in both eyes	60 (17.8)
Dry AMD in one eye	67 (19.9)
Wet AMD in one eye	48 (14.2)
Wet AMD in one eye and dry AMD in the other eye	43 (12.8)
Doesn't know AMD type	8 (2.4)
Other household members (n = 337)	
Partner/spouse	212 (62.9)
My child(ren)	76 (22.6)
No one	56 (16.6)
Family member(s) other than partner and child	33 (9.8)
I live in a retirement home	23 (6.8)
Roommate/friend	12 (3.6)
I live in a nursing home/long-term care facility	2 (0.6)
Employment Status (n = 322)	
Retired	178 (55.3)
Employed, working full-time	68 (21.1)
Employed, working part-time	40 (12.4)
Homemaker	18 (5.6)
Not employed, looking for work	9 (2.8)
Unemployed due to illness or disability	6 (1.9)
Taking care of a family member	2 (0.6)
Other: *In training for new career*	1 (7.7)

In the following sections, each dataset is used where it seems most relevant and connected to the original source, either through reference or with subheadings. Where possible, efforts have been made to compare the datasets.

3. Disease Experience

Both patients interviewed by FBC were diagnosed with GA within the last 5 years. For one patient, the diagnosis was a progression from dry AMD, while for the other it was from wet. In both cases, the transition from AMD to GA was thought of as a negative progression, both in terms of visual deterioration as well as emotional and psychological impact. For example, one patient explained that:

"It wasn't like he diagnosed me with that [GA], and then, suddenly, I thought I'm worse off. No, it's just been a progression, and much worse."

Although the patients described unique experiences overall, it is nonetheless possible to draw comparisons within certain categories or themes, including 1) the above point related to a progression beyond AMD, as well as 2) severity of vision loss; 3) significance of life challenges; 4) impact on emotional wellbeing; 5) impact on work; 6) hope of maintaining vision; and 7) openness to new treatments. The below table provides descriptions of the experiences within each thematic group.

Qualitative Interview Themes: GA Patients (n = 2)

THEME	DESCRIPTION
1. PROGRESSION BEYOND AMD	▪ GA is experienced as a linear continuation or progression from AMD, with vision loss and related challenges increasing over time. ▪ Despite this, both patients made it clear that GA feels like an escalation beyond AMD, with a near-constant sense that they are now in danger of losing the remaining vision they have left. ▪ The experience of steadily worsening symptoms, and the sense that blindness is just around the corner, is a significant psychological burden, leading to fear, anxiety, and other emotional discomforts.
2. SEVERITY OF VISION LOSS	▪ The overall trajectory of vision loss over life was described by both patients as continuous, but also as becoming most acute after the GA diagnosis. ▪ On a scale of 10, with 10 being perfect vision and 0 being blindness, both patients rated their vision between 2 and 4. ▪ While GA is not experienced as an abrupt event or discontinuity, both patients described a range of increased symptoms developing post-diagnosis: - Sensitivity to sunlight - Blurriness (one patient described the appearance of "smog in the air," even when there isn't) - Difficulty seeing faces and expressions. - Lack of contrast (one patient described spraining her ankles because a set of stairs looked like "black on black") - Difficulty with small details, making activities such as reading, watching TV, etc., challenging or impossible. ▪ One patient explained that with GA, "it's difficult to see clearly" and that in grocery stores and other areas of high visual complexity, the details blur so that it looks like "one piece."

	▪ One patient described that, month after month, it feels like a discernable amount of vision is lost.
3. SIGNIFICANCE OF LIFE CHALLENGES	▪ As a result of vision loss, neither patient drives (even though one patient is still legally able to). Both describe this is a distinct loss of independence. ▪ Both patients use magnifiers for reading text and fine detail work. Though the magnifiers help, they continue to struggle with the loss of the ability to read unaided. ▪ One patient described reading as "a task" and, in relation to reading recipes, explained that the "lines aren't always where they're supposed to be." ▪ Both patients provided additional commentary on reading: - Used to read magazines but has had to cut off many subscriptions. - Hard to read measuring cups or to see dials on the stove. - When reading and performing fine detail work, "lots of lights everywhere can be helpful." - On computer forms it is easy to "place x's in the wrong places." - Friends will read placards for one of the patients at exhibits. ▪ One patient explained that grocery shopping is a significant challenge, and that differentiating products can be hard or impossible. As a result, they now only shop with their partner. ▪ Both patients described the support they receive from family members; for example, one patient's partner does all the cooking. ▪ In the context of support, both patients articulated feelings of appreciation and acknowledged the importance of support in managing daily challenges; both also expressed empathy for those who do not have similar levels of support. ▪ One patient discussed how their love of theatre has been threatened by vision loss. It has become increasingly difficult to distinguish costume and set details at ballet, for instance.
4. IMPACT ON EMOTIONAL WELLBEING	▪ One patient is a parent and grandparent and described their children as "the motor of my life." The idea of not being able to see them someday is devastating. ▪ The other patient does not have children, but explained that if they did, they would worry about them having AMD or GA when they are older. ▪ One patient sees a psychologist to help with the acceptance of their vision loss and its emotional impact. They explained that acceptance is a "step-by-step process" and that they are "making progress."

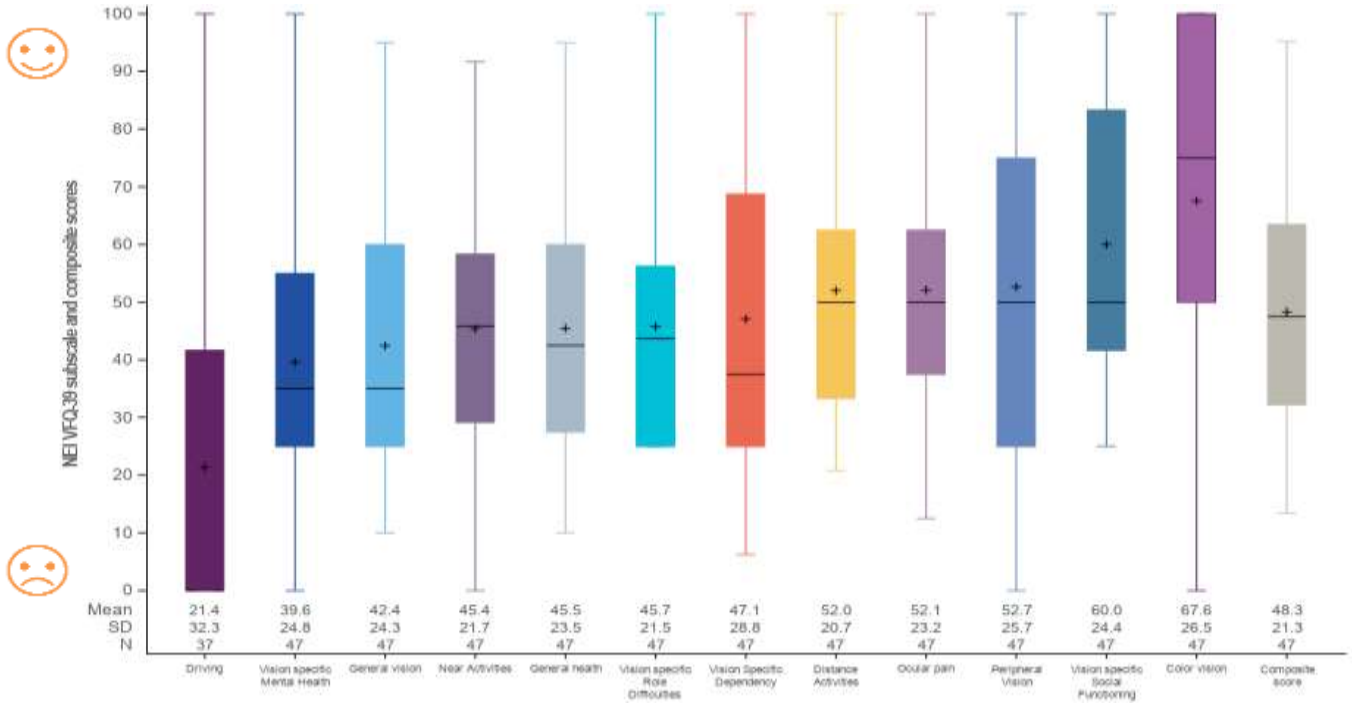
	▪ One of the interviewees emphasized their positive outlook on life, but also that they now get frustrated more easily: "frustration is one thing that happens a lot more." ▪ Both interviewees expressed concerns over the future and discussed related emotional distress. One patient explained that "I'm more anxious about the future and what the future will bring." The other explained that thinking about the future "leads to sadness." ▪ Both patients described anxiety related to asking for help, and feelings of unnaturalness when it comes to relying on others.
5. IMPACT ON WORK	▪ One of the interviewees is currently employed. They have an assistant who helps them manage daily tasks that their vision renders challenging or impossible. Recognizing that most people do not have this level of support, they expressed gratitude for the position. Despite this, they also described work as a challenge in the context of basic visual tasks; for instance, struggling to read faces and facial expressions has an impact in the workplace. ▪ The other patient does not work but is active in many other ways: travelling, concerts, condo board meetings, etc. The patient discussed challenges associated with these activities and how they would potentially impact work in a similar way—for example, not driving making it difficult to get to work, or difficulty travelling (reading signs, etc.) translating to difficulty navigating a work environment.
6. HOPE OF MAINTAINING VISION	▪ A general hope or desire to maintain as much vision as possible was expressed by both participants. They also expressed hope that a treatment will be developed for GA. ▪ Both acknowledged the impossibility—at present time, at least—of regaining lost vision, emphasizing instead the importance of keeping what they have, or even slowing the progression of their vision loss so that it does not feel so rapid. ▪ One patient explained that they want to "keep this possibility"—the possibility of reading, of living a normal life, and of maintaining some vision. ▪ If maintaining vision is not possible, both patients also underscored the value of slowing vision loss. For example, one patient explained that even if a treatment only slows vision loss for a single year, it would be worth trying.
7. OPENNESS TO NEW TREATMENTS	▪ Both participants expressed a desire to access new treatments when they become available. ▪ For the patient with wet AMD, injections are already a normal part of life and an acceptable burden if it means maintaining vision or slowing vision loss—injections are "not a big problem." For the patient with dry AMD, the idea of injections is scary but well worth confronting if they help.

	▪ The participant with wet AMD also explained that receiving another set of injections alongside the anti-VEGF regime would be acceptable—as long as there is a benefit. ▪ One patient emphasized the importance of their physician's perspective. Any new treatment would have to be recommended by this trusted source.

Other Data Sources: MOSAIC and VIEW AMD

Both the MOSAIC study and findings from VIEW AMD support the thematic groupings outlined above.

In relation to **2. SEVERITY OF VISION LOSS**, for example, the MOSAIC study shows that GA patients tend to struggle with their general vision, with driving, and with vision specific mental health, all characteristics that were emphasized by our interviewees. Among other tools, MOSAIC utilized the National Eye Institute's Visual Function Questionnaire (VFQ) to draw these conclusions (table below).



In relation to driving, MOSAIC finds that 72% of its VFQ participants no longer drive due to eyesight, and that those who do experience increased difficulty at night and in visually complicated conditions. Our interviewees articulated driving as an essential part of independence; it is safe to extrapolate that the loss of driving for a majority of the GA population is similarly experienced as a loss of independence, with all of the social, emotional, and psychological effects that such a loss entails.

From VIEW AMD, we also know that driving and travel impact a patient's ability to attend vision-related appointments, further suggesting the severity of vision loss for GA patients.

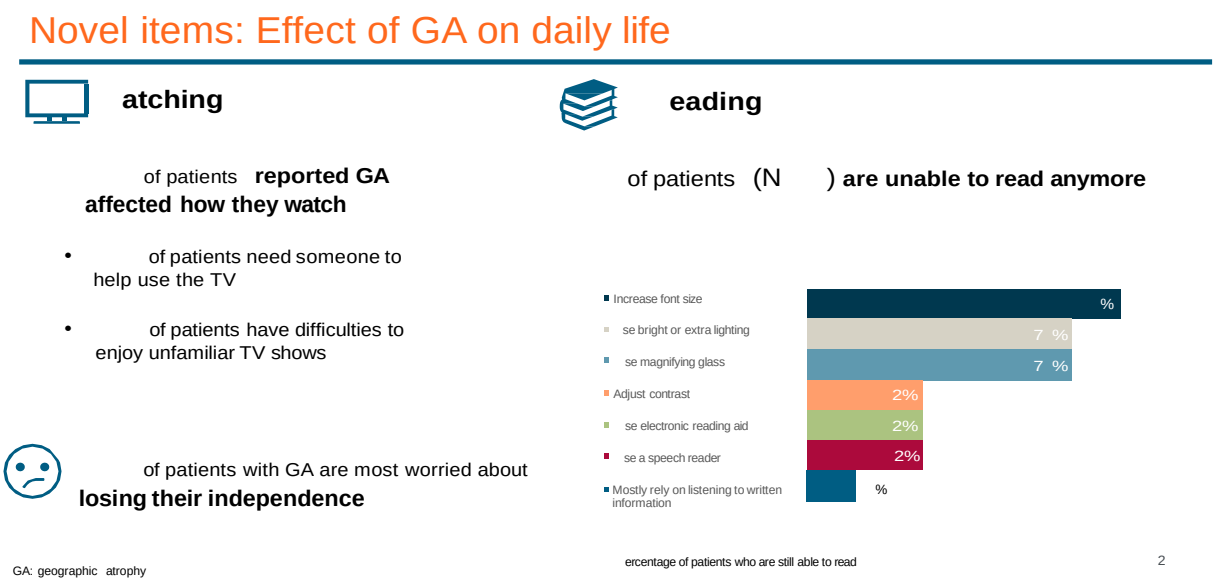
When asked what the most difficult part of attending eye injection appointments is, 27.7% of patients indicated "finding someone to drive me to/from the appointment."

Most difficult part of eye injection appointments (n = 249)

Reason	n (%)
Anxiety or fear about the injection	95 (38.2)
Long waiting time at the appointment	76 (30.5)
Cost of travel to/from the appointment	72 (28.9)
Finding someone to drive me to/from the appointment	69 (27.7)
Finding someone to help me with my daily tasks after the injection	56 (22.5)
I don't find any part difficult	52 (20.9)
Scratchiness or pain in my eye after the appointment	46 (18.5)
Taking time off work to attend	31 (12.4)
Other**	8 (3.2)

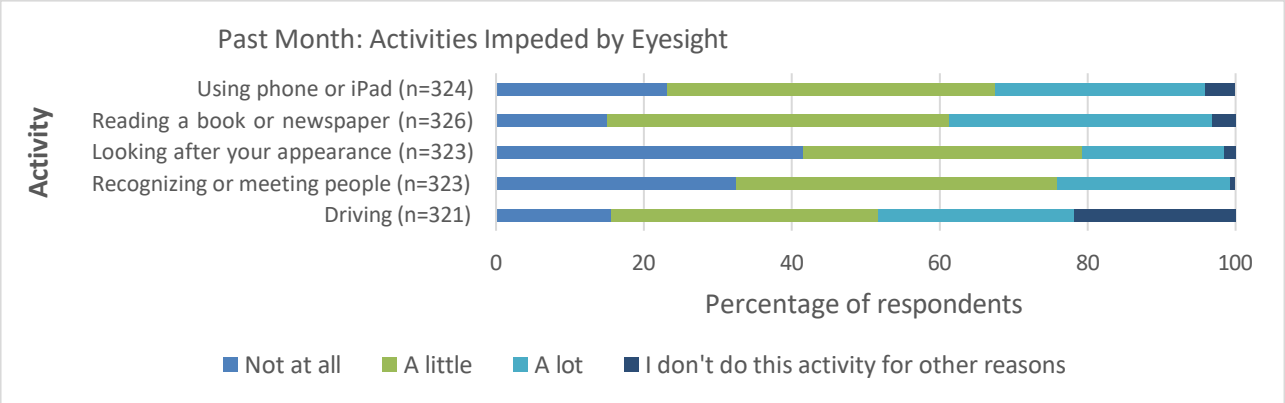
Of course, the loss of driving is more than an example of the severity of vision loss. As suggested in our interviews, it is also part of a larger theme involving the **3. SIGNIFICANCE OF LIFE CHALLENGES.**

In relation to life challenges, the MOSAIC patients were asked specifically about watching TV and reading. 57% reported that their GA affects how they watch TV, with 26% indicating they need help with the TV and 32% reporting that they have difficultly enjoying unfamiliar shows. In terms of reading, 34% of the surveyed patients reported not being able to read anymore. For those who do read, 86% use increased font size, 73% use bright or extra lighting, and 73% also use a magnifying glass.



In the VIEW AMD study, AMD patients reported on a wide range of activities that are impacted by their disease, including interacting with phones and tablets, reading books and newspapers, and more. In line with our interviews, “reading a book or newspaper” appears to be the activity that was most impacted.

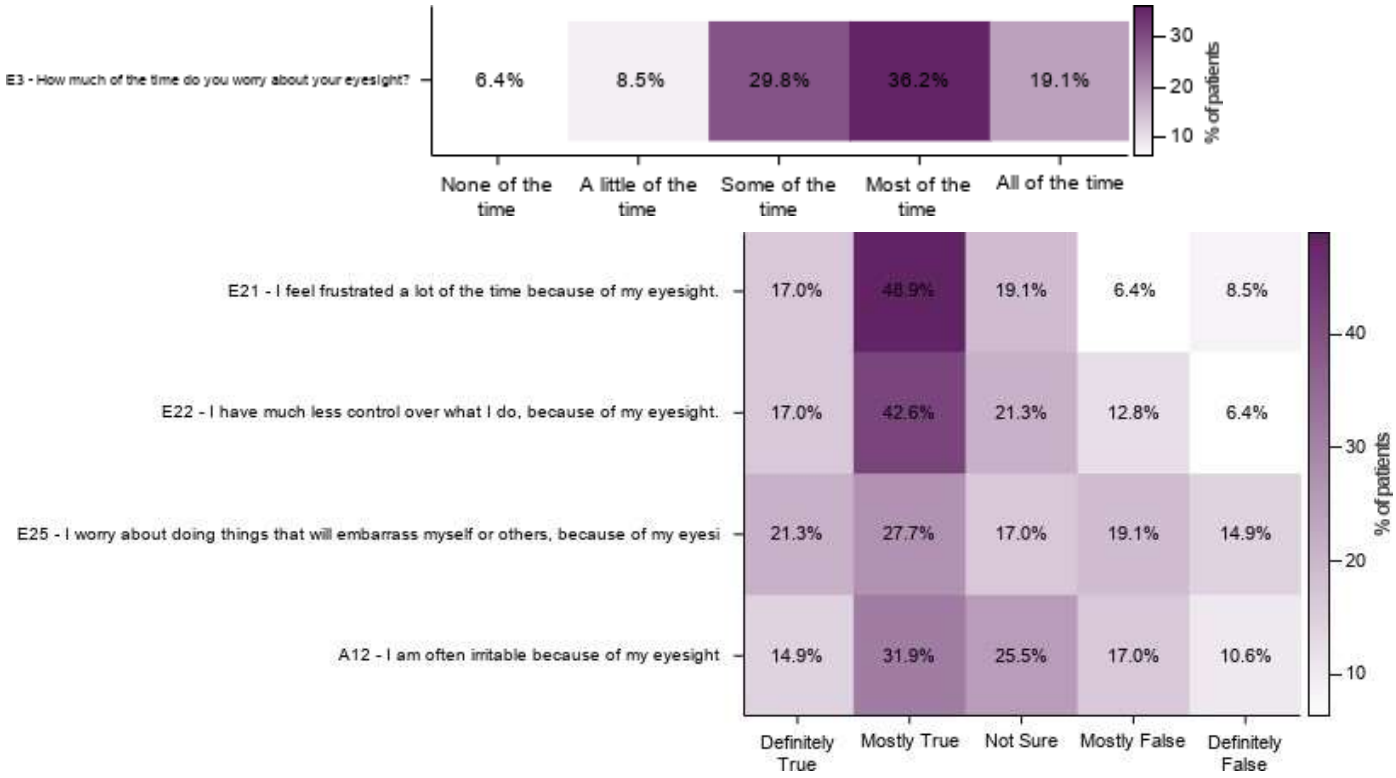
Impact on daily activities



It is clear that these impacts—on vision, activities, and more—carry an emotional burden. This was emphasized by both interviewees. Both MOSAIC and VIEW AMD show a **4. IMPACT ON EMOTIONAL WELLBEING** as well.

In MOSAIC, 55% of patients reported worrying about their vision most or all of the time, 66% reported feelings of frustration, 60% reported feeling less in control of what they do, and 49% reported worrying about doing things that would feel embarrassing.

Vision-specific mental health



Results highlighting worry and frustration align very closely with feedback from our interviewees. It is clear that GA is a difficult disease to live with in this regard, and that its emotional and psychological impacts should not be overlooked or deemphasized.

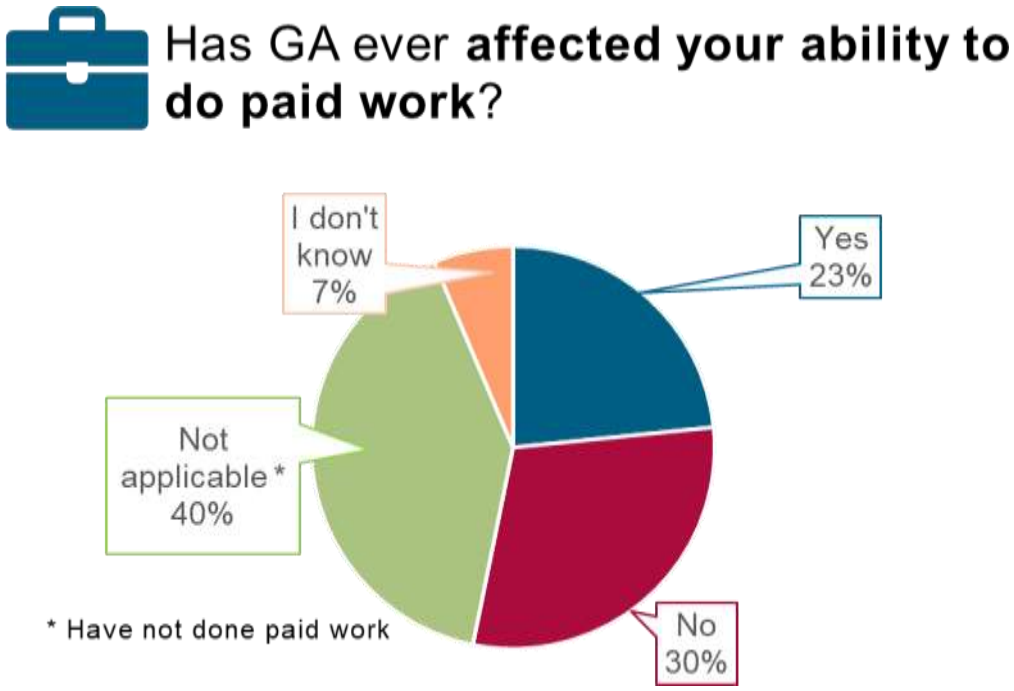
The notion of a psychological toll or burden is shown in VIEW AMD as well, particularly in relation to concerns over the future. When asked to select from a list of challenges associated with sight loss and AMD, a significant majority indicated that they “worry that my condition might worsen in the future” (77%). In a similar manner, future-oriented anxiety was discussed at length by both of the patients we interviewed.

Challenges with AMD (n = 330)

Challenges	n (%)
Worry that my condition might worsen in the future (n=331)	255 (77.0)
Not being able to do the daily activities I used to (n=331)	127 (38.4)
The long wait times for appointments	103 (31.2)
Explaining my condition to family and friends	103 (31.2)
Lack of social support	97 (29.4)
Finding answers to my questions about my condition	73 (22.1)
Socializing	68 (20.6)
Other*	34 (10.3)

A **5. IMPACT ON WORK** is explored in detail in the MOSAIC study, with a specific emphasis on financial stability: 36% of patients indicated a concern over the effect of GA on their finances in the future, and 66% indicated concern over effects on their living situations. Almost a quarter of the patient group (23%) selected that GA has affected their ability to do paid work:

Impact on ability to do paid work



4. Experiences With Currently Available Treatments

Seeing as pegcetacoplan represents the first viable treatment for GA to enter the Canadian market, we were unable to learn about experiences with “currently available treatments.” That said, the VIEW AMD study includes a robust review of attitudes and feelings

about existing anti-VEGF treatments which similar to pegcetacoplan are delivered by intravitreal injection. Below is a summary of what can be considered relevant insights:

Satisfaction and Adherence

The largest group of respondents showed that they are “satisfied” with their injections (%) and that “they helped me avoid losing more eyesight” (72.7%).

Level of satisfaction with injections (n = 252)

	n (%)
Very dissatisfied	1 (0.4)
Dissatisfied	8 (3.2)
Neither satisfied nor dissatisfied	46 (18.3)
Satisfied	116 (46.0)
Very satisfied	81 (32.1)

How the injections have helped (n = 253)

	n (%)
They helped me avoid losing more eyesight	184 (72.7)
They improved my eyesight	112 (44.3)
Dried up fluid/blood in my eye(s) (n=252)	104 (41.3)
They have had no effect but I receive injections because my doctor recommends them	43 (17.0)
I don't know	7 (2.8)
Other*	8 (3.2)

Difficulty of Eye Injection Appointments

Most difficult part of eye injection appointments (n = 249)

Reason	n (%)
Anxiety or fear about the injection	95 (38.2)
Long waiting time at the appointment	76 (30.5)
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Taking time off work to attend	31 (12.4)
Other**	8 (3.2)

Emotional and Physical Effects

The largest group of patients underscored “anxiety or fear about the injection” (.2%) as the most difficult part of the appointment. This is interesting, considering that many patients also indicated being “satisfied” with their injections, as well as appreciative of the impact on their sight. It may show that those with AMD tend to manage their fear and anxiety in relation to injections as a matter of course. Injections still carry an emotional or psychological impact, but this has become internally managed in such a way as to be common or matter of fact—an insight supported by the patient we interviewed whose GA is secondary to wet AMD.

5. Improved Outcomes

As discussed, the two patients interviewed as part of this submission stressed their desire for a treatment for GA. For them, improved outcomes would involve either a) the preservation of their existing vision; or b) a slowing of the vision loss they are currently experiencing.

Both patients acknowledged that preserving vision is unlikely. At the same time, both emphasized that slowing vision loss—even for a small amount of time—would be desirable, and that the treatment burden of intravitreal injections, would be acceptable to achieve these outcomes.

The patient whose GA is secondary to wet AMD made it clear that injections have been normalized and are part of their life. The prospect of more injections is not a barrier. The patient with dry AMD expressed a generalized nervousness and uncertainty related to injections, but also stated that they would be willing to try an injection-based treatment. So again, injections are not a barrier to trying a treatment.

6. Experience With Drug Under Review

None of the patients involved in this submission have received pegcetacoplan as a treatment for their GA. This is unsurprising, given that assessments of the drug by Canadian HTA agencies have not yet completed.

7. Companion Diagnostic Test

Not applicable

8. Anything Else?

To summarize, the insights from our interviewees allowed us to develop a set of core themes or ideas that were shared by both participants: 1) progression beyond AMD; 2) severity of vision loss; 3) significance of life challenges; 4) impact on emotional wellbeing; 5) impact on work; 6) hope of maintaining vision; and 7) openness to new treatments. Many of these ideas are echoed within the MOSAIC and VIEW AMD studies, which we have attempted to highlight in section 3 of this submission.

The below table reiterates these themes in relation to the data sources that support them.

	DATA SOURCE		
THEME	INTERVIEWS	MOSAIC	VIEW AMD
1. Progression beyond AMD	X		
2. Severity of vision loss	X	X	X
3. Significance of life challenges	X	X	X
4. Impact on emotional wellbeing	X	X	X
5. Impact on work	X	X	

6. Hope of maintaining vision	X		
7. Openness to new treatments	X		

As organizations that represent patients with GA, AMD, and other eye diseases, our overarching goal is to contribute meaningfully to the discussion and potential implementation of new treatments in this space—in particular, to guide that discussion along lines that are patient-centered, that focus on optimal and equitable outcomes, and that recognize the expertise of patients with lived experience of GA and their value in the review process of new treatments.

We look forward to continuing to work with CADTH to support Canadians living with GA, and to advance our collective understanding of how the disease and its treatments impact their lives.

Appendix: Patient Group Conflict of Interest Declaration

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

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.
    - FBC contracted Dr. Chad Andrews as an independent consultant with expertise in patient centered research to draft this submission.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.
    - FBC contracted Dr. Chad Andrews as an independent consultant with expertise in patient centered research to interview patients and analyze data.

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Apellis				X
Roche				X

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

Name: Dr. Larissa Moniz
Position: Director, Research and Mission Programs

Patient Group: Fighting Blindness Canada
Date: February 9, 2024

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Apellis			X	

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

Name: Dr. Keith Gordon
Position: Senior Research Officer
Patient Group: The Canadian Council of the Blind
Date: February 9, 2024

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Bayer				X
Novartis				X

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

Name: Thomas Simpson
Position: Vice President, CNIB Voice
Patient Group: CNIB
Date: February 8, 2024

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Bayer				X
Roche				X

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

Name: Dr. Anjali Tripathi
Position: Secretary General
Patient Group: International Federation on Ageing
Date: February 5, 2024

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
None to Declare				

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

Name: Jennifer Urosevic
Position: President and CEO
Patient Group: Vision Loss Rehabilitation Canada
Date: January 2, 2024

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Apellis			X	

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

Name: Sylvie Castonguay
Position: Executive Director
Patient Group: AQDM
Date: January 30, 2024

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0810-000
Generic Drug Name (Brand Name): Pegcetacoplan
Indication: Geographic Atrophy secondary to age-related macular degeneration
Name of Clinician Group: Canadian Ophthalmological Society
Author of Submission: Dr. Phil Hooper

1. About Your Clinician Group

The Canadian Ophthalmological Society (COS) is the national, recognized authority on eye and vision care in Canada. As eye physicians and surgeons, we are committed to assuring the provision of optimal medical and surgical eye care for all Canadians by promoting excellence in ophthalmology and by providing services to support our members in practice. Our membership includes over 900 ophthalmologists and 200 ophthalmology residents. We work collaboratively with government, other national and international specialty societies, our academic communities (ACUPO), our provincial partners and affiliates, and other eye care professionals and patient groups to advocate for health policy in Canada in the area of eye and vision health. COS is an accredited, award-winning provider of Continuing Professional Development (CPD) through the Royal College of Physicians and Surgeons of Canada (RCPSC) and is an affiliate of the Canadian Medical Association (CMA).

www.cos-sco.ca

2. Information Gathering

We convened a working group composed of ophthalmologists who responded to a notification sent to our membership. This yielded a pool of ophthalmologists at varying stages in their careers and degree of specialization. The group has representation across Canada, including many academic based retina specialists and we included a representative who is the liaison to the Canadian Retinal Society.

3. Current Treatments and Treatment Goals

At the present time, there are no treatments for patients with Dry Age-related Macular Degeneration (dAMD) who develop geographic atrophy (GA). Our current treatment paradigm consists of counselling on modifiable risk factors such as smoking and diet, use of anti-oxidant vitamins and minerals as was done in the AREDS trials to lower the risk of progression to wAMD, advice about optical low vision aids where appropriate, and information about the symptoms of, and monitoring for, the development of Wet Age-related Macular Degeneration (wAMD).

An ideal treatment for dAMD would reverse the loss of photoreceptors and restore visual function to the affected retina. This would be expected to improve functioning on critical visual tasks such as those involved in medication recognition and administration, self-care, and ability to function independently. Quality of life would improve as the individual could resume activities like reading, and the many hobbies which depend on good vision, as well as be able to recognize friends at a distance. (Loss of these functions has been shown to increase self-isolation and depression in those with this disease[1]). In the scenario involving the drug under review, slowing the loss of retinal function would be expected to provide a longer time window for an individual to retain the functions outlined above thereby improving long-term quality of life and reducing dependence.

1)Crews JE, Campbell VA. Vision impairment and hearing loss among community-dwelling older Americans: Implications for health and functioning. American Journal of Public Health. 2004;94:823–829

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

As there are no treatments for this disease currently available, the disease progresses over time. The AREDS study[2] demonstrated that over a 5-year period approximately 20% of individuals with intermediate dAMD (those with extensive drusen and RPE changes) will develop areas of GA and suffer associated vision loss. Use of anti-oxidant vitamins and minerals has been shown in the AREDS1 and 2 trials to reduce the risk of the development of wAMD in patients with dAMD above threshold but this does not affect the progression of dAMD.

2)Keenan TD, Agrón E, Domalpally A, et al. Progression of geographic atrophy in age-related macular degeneration: AREDS2 Report Number 16. Ophthalmology. 2018;125:1913–1928.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

The drug under review is the first drug that has been demonstrated to slow the progression of GA in dAMD. As such, it is expected to produce a major shift in our treatment paradigm as individuals with GA within the macula can be offered an intervention that will slow the growth of the atrophy and reduce scotoma growth. It would be our first line therapy for these individuals.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

In order to benefit from treatment, the eye must have dAMD and show area(s) of GA within the macula which is defined as the retina from the foveal centre to the major vascular arcades above and below, the edge of the optic disc nasally, and a similar distance temporally. The closer the atrophy comes to centre and the larger retinal area involved, the more it will affect visual function; once the atrophy involves the fovea, visual acuity as measured on an eye chart will be reduced. The ideal candidate for treatment will be an individual who has GA in the macula, retains good visual function, and has a life expectancy long enough that the atrophy would be expected to progress enough to cause functional impairment. Eyes which already demonstrate disabling scotomas or with significant vision loss to the level of legal blindness are unlikely to benefit from therapy.

Assessment to determine candidacy will involve ascertainment that the retinal changes are because of dAMD and determination of visual function through assessment by a skilled Ophthalmologist, supplemented by Optical Coherence Tomography (OCT) and Fundus Autofluorescence (FAF) testing. Although it does not preclude treatment and long-term benefit, it is also important to ascertain the presence or absence of wAMD as the two diseases can coexist and treatment of wAMD, if present, should occur to prevent accelerated vision loss. Other retinal diseases may have features that overlap, in part, with dAMD and can be excluded by history and clinical examination supplemented, on occasion, by additional testing. It is more likely that candidacy for treatment will be over diagnosed prior to definitive assessment rather than underdiagnosed.

At the present time, only patients with dAMD have been evaluated for treatment with this drug. No systemic or ocular factors have yet been associated with better or worse response to this drug, and as such, criteria to determine eligibility would need to be determined based upon the registry trials: size of the GA, proximity to the foveal centre, and visual acuity at baseline. As well, an understanding of the need for ongoing treatment and commitment to the therapy course would be a requirement.

We anticipate that patients who would most benefit from intervention are those who are monocular due to prior GA or wAMD in the fellow eye with early GA now affecting the only remaining eye, or patients with bilateral GA that is threatening the centre of the fovea.

Visual acuity and clinical examination including a dilated fundus examination by an Ophthalmologist with additional training and interest in AMD would be required. In addition, an OCT would be necessary to exclude wAMD and FAF to determine lesion location and extent would be helpful.

Potential candidates for treatment would be identified by referring optometrists and/or comprehensive ophthalmologists using clinical exam findings, OCT and fundus autofluorescence (FAF) imaging when available.

Some referring optometrists and general ophthalmologists may not have FAF testing readily available in their offices. This is more likely to lead to over referral rather than under referral, however. OCT imaging is currently not covered by provincial health insurance in some provinces in optometry offices and may limit access to care for some patients. FAF is not currently reimbursed in most settings.

The diagnosis of dAMD is quite clear when the above tests are included in the baseline examination. If all testing outlined is required and clear guidelines for eligibility implemented, underdiagnosis and over diagnosis at the point of initial treatment should be limited.

Data from registry trials is still being collected and no clear sub-characteristics are known. It seems likely, however, that the impact of treatment is likely to be greatest in eyes with lesions which are close to the fovea but do not extend beneath it.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Given the fact that the disease is expected to progress despite treatment, determination of response to therapy in clinical practice will be more difficult than during a clinical trial as at this time there is no good normative data on the growth of GA in a population. At a population level, preservation of visual function (not exclusively visual acuity) is the most important outcome but measures on an individual patient do not determine if treatment has successfully slowed progression. However, evaluation of FAF for progression once or twice yearly will assist in developing population level data.

Despite the lack of patient specific indicators of success, it is important that patients be regularly monitored for the development of wAMD via OCT testing as treatment appears to increase the risk of this developing.

Patients self-report visual function data during visits but visual function testing is not routinely performed beyond recording a standardized visual acuity. This measure is not sensitive to the rate of growth of GA unless it is subfoveal. There is no clear agreement on a reproducible, rapid, sensitive test of visual function that can be performed in an office setting.

As the response is preservation of visual function and daily life activities, a clinically meaningful response would be a reduction of the loss of these functions over time. Similar to determining the reduction of growth in size of GA lesions, this reduction in the rate of loss of function cannot be measured at an individual level, only within a population with control subjects. At a population level, this preservation of visual function should lead to a reduction in the need for care supports in the community and a prolongation of the ability to live independently. Unfortunately, there is no one measure that will be directly sensitive to this improvement in visual function at a population level.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Treatment discontinuation should be considered if severe inflammation develops in response to the injection, or if central vision is lost from dAMD or for another reason making treatment irrelevant in preserving visual function. Similarly, if an individual's health deteriorates so that life expectancy is shorter than the likely time to functional vision loss, consideration should be given to discontinuing therapy. Persons who no longer can attend for injections at least every 2 months fall outside known parameters for benefit and probably should be discontinued

5.5 What settings are appropriate for treatment with the drug under review? Is a specialist required to diagnose, treat, and monitor patients who might receive the drug under review?

The drug will be given through a series of intraocular injections every one to two months on an ongoing basis. Experience in treating wAMD has demonstrated that intraocular injection can be performed safely in a community office setting. As the treatment protocol will continue for life following initiation, it is important that determination of the need to begin therapy be done by an Ophthalmologist who is well versed in the disease and who has the tools (OCT and FAF) to determine the extent of the disease at the outset. Monitoring through skilled clinical examination and OCT is needed if new visual symptoms develop that are possibly indicative of the development of wAMD or findings suggestive of this are observed during the course of therapy.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   No

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

   The Canadian Ophthalmological Society requested and received from Apellis USA post marketing usage data and 3 year post trial data. Apellis had no further involvement in the group's deliberations.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr Phil Hooper
Position: President COS
Date: 03/02/2024

☒ **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.

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name	No conflicts to declare			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr Thomas Sheidow
Position: Associate Professor, Ophthalmology Western University
Date: 04/02/2024

☒ **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.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: David A. L. Maberley, MD, MSc (Epid), FRCSC
Position: Chairman and Head, Department of Ophthalmology, University of Ottawa, The Ottawa Hospital
Date: 05/02/2024

☒ 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.

Table 3: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Bayer	X			
RegenXBio	X			
Apellis	X			
Novartis	X			
Roche	X			
Ionis	X			
Ophthea	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Gareth Mercer
Position: Clinical Fellow
Date: 07-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.

Table 4: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Bayer			X (research funding)	

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: Parnian Arjmand
Position: Vitreoretinal surgeon
Date: 07-02-2024

☒ **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.

Table 5: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Bayer	X			
YoungMD Connect	X			
Roche			X	

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 6

Name: Alan Cruess
Position: Professor of Ophthalmology and Visual Sciences at Dalhousie University, Halifax, NS
Date: 07-02-2024

☒ **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.

Table 6: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Bayer	X			
Apellis	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Canadian Ophthalmological Society

Name: Elisabeth Fowler
Position: Canadian Ophthalmological Society, CEO
Date: 05/02/2024

☒ 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.

Table 7: Conflict of Interest Declaration for Canadian Ophthalmological Society

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Apellis			X	

The Canadian Ophthalmological Society received sponsorship in the amount of $30,000 to support the COS Annual Meeting and Exhibition. The COS Annual Meeting is the largest gathering of ophthalmologists in Canada and in 2023, the meeting had 27 sponsors, including Apellis. The COS uses the sponsorship funds to off-set the costs of hosting the meeting (rental of conference space, food and beverage, speaker costs, etc.) All sponsorship dollars received go into one fund, without attribution to any sponsoring organization.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0810-000
Generic Drug Name (Brand Name): pegcetacoplan (TBC)
Indication: For treatment of GA secondary to age-related macular degeneration
Name of Clinician Group: Island Health Group
Author of Submission: Dr. Rajan Nirwan

1. About Your Clinician Group

Island Health is a group of practicing physicians on Vancouver Island, focusing on comprehensive ophthalmology and medical/surgical retina care.

2. Information Gathering

Our group held a conference call on February 6th to discuss the information we thought was most relevant to include as part of the submission. A medical writer captured our discussion. The submission was then circulated via email for final approval.

3. Current Treatments and Treatment Goals

There is currently no available treatment for patients with geographic atrophy. Vitamins are occasionally used for patients with intermediate AMD, but they primarily just slow sown conversion to wet/exudative AMD. Therefore, we can only monitor patients with geographic atrophy (approximately every 6 months following diagnosis) to confirm the extent of progression and ensure the disease has not developed into exudative age-related macular degeneration.

The most important goal of treatment would be to slow the progression of the geographic atrophy lesion growth to prevent further vision loss, whereas in our experience, retinal vitamin supplementation does not effectively address these needs. Instead, our understanding of retinal vitamins is they are more so effective to prevent progression from dry to wet age-related macular degeneration.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

A treatment for geographic atrophy should effectively slow the progression of lesion growth to maintain remaining vision for as long as possible. Additionally, the safety profile for the treatment should be considered, as a treatment for geographic atrophy should be well-tolerated overall and not further complicate or impair visual function.

When considering disease course and natural history, it is important to understand geographic atrophy is a slow, progressive disease, in which the maintenance of current lesion state should be seen as an improvement. Parallels can be drawn to congestive heart failure, in which long-term changes in the cardiac tissue can result in prevention of further cardiac damage and assocaited events, resulting in an overall lasting impact on heart function .

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Pegcetacoplan would be the first drug which effectively treats the underlying pathogenesis of geographic atrophy and managing symptoms (i.e. loss of visual function). While the 1-year clinical trial data may not show a drastic reduction in lesion growth, the goal of pegcetacoplan treatment would not be curative in nature, but rather important to maintain the current lesion state as best as possible.

Pegcetacoplan will be used first-line being the only treatment option available for geographic atrophy, though it will be important to generate appropriate selection criteria to treat patients expected to benefit most from therapy.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

First and foremost, many patients with geographic atrophy are highly motivated to receive treatment, given the progressive and irreversible nature of the disease. While there may not be drastic changes in visual function visit to visit, patients are willing to go to great lengths to prevent this irreversible vision loss and maintain what function they do have for as long as possible. It is also important to highlight geographic atrophy is almost always bilateral, so pegcetacoplan use should not be limited to one eye.

The patients with only an island of vision/photoreceptors left, or the patients in which we see a rapid growth of the geographic atrophy lesion over time, would be the most important to prioritize for pegcetacoplan treatment to spare further loss of visual function.

There are some cases in which pegcetacoplan treatment should be limited, based on both patient- and disease-related factors. If the patient has significant vision loss (i.e. 20/400), they would likely be past the point of benefiting from treatment. If the patient has had previous inflammation in the eye, there may be hesitation to treat given the reported ischemic optic neuropathy from the trial. Finally, monocular patients represent an interesting decision point, as on the one hand, we want to do everything possible to preserve remaining vision, but potential adverse events would be more impactful given theses only have vision in the remaining eye.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

While there are currently no set criteria to determine which patients would respond to treatment, there are potential factors such as initial rate of geographic lesion growth, which could be used as a prognostic indicator. While it may be difficult to measure response in the short-term, long-term reductions s in geographic atrophy lesion reduction will be easier to monitor.

Currently, optical coherence tomography is used to determine presence of geographic atrophy, but following pegcetacoplan approval, fundus autofluorescence will be instructive to determine how the lesion develops over time. Response to treatment would likely be most appropriately assessed every 3-4 months, with the potential for slightly more frequent monitoring early in treatment to determine patients' tolerance to therapy. Month-to-month follow-up is not necessary, as it is unlikely there will be significant change in geographic atrophy lesion growth over that time frame.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Several factors should be used to determine appropriate stoppage criteria for pegcetacoplan, including significant loss of vision or progression of the geographic atrophy lesion such that it covers the fovea. If a patent's geographic atrophy converts to exudative age-related macular degeneration, treatment would likely need to be prioritized. It is difficult to determine appropriate stoppage criteria, as the disease itself is slowly progressive and patients could benefit from treatment indefinitely if their lesion does not show significant growth.

5.5 What settings are appropriate for treatment with pegcetacoplan? Is a specialist required to diagnose, treat, and monitor patients who might receive pegcetacoplan?

Currently, many patients with geographic atrophy are likely being followed by optometrists, given the lack of available treatment. Following approval of pegcetacoplan, however, it is likely most patients will be followed by retinal specialists. Retina specialists should ultimately be the ones responsible for managing patients with pegcetacoplan, as these specialists can best recognize geographic atrophy in patients and manage potential adverse events/conversion to exudative age-related macular degeneration.

6. Additional Information

We feel CADTH will be doing a disservice if pegcetacoplan is not reimbursed for use in Canada, as we have already seen our US neighbors readily and freely using pegcetacoplan. We have many patients who would rather pay for pegcetacoplan in the US, in hope they can do something rather than nothing to prevent the progression of geographic atrophy and irreversible blindness. Pegcetacoplan represents an important drug in our armament which currently lacks any suitable alternative, and its non-coverage would be a disaster for this patient population who knows their lesions are progressing and getting worse.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   Yes, we received support from a medical writer to schedule our meeting and document discussion.

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

   N/A

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Rajan Nirwan
Position: Ophthalmologist and Vitreoretinal Surgeon
Date: February 7th 2024

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

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*

	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Apellis		X		
Bayer	X			
Roche		x		

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Brett Williams
Position: Comprehensive Ophthalmologist
Date: February 7th, 2024

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

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
I do not have any conflicts of interest to declare				

* Place an X in the appropriate dollar range cells for each company.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0810-000
Generic Drug Name (Brand Name): pegcetacoplan (TBC)
Indication: For treatment of GA secondary to age-related macular degeneration
Name of Clinician Group: New Brunswick Ophthalmology Group
Author of Submission: Dr. Nir Shoham-Hazon

1. About Your Clinician Group

Our group represents a major treatment centre in New Brunswick, which includes Dr. Nir Shoham-Hazon and Dr. Vijay Sharma. We are all comprehensive ophthalmologists, heavily involved with administering intravitreal injections in our practice.

2. Information Gathering

Our group met virtually over Microsoft Teams on February 6, 2024 for 1 hour to discuss the submission. A medical writer captured our discussion. The final submission was then approved by all signing group members.

3. Current Treatments and Treatment Goals

For current management, our group employs a monitoring strategy in which we follow-up with patients with geographic atrophy (GA) every few months, using optical coherence tomography (OCT) and fundus autofluorescence (FAF) to measure potential growth of the GA scar. We also monitor to ensure there is no transition of the disease to wet AMD.

Our group is ultimately forced to use a “watch-and-wait” approach for these patients, as the only considerable management option for GA is AREDS vitamin supplementation every few months. However, we do not believe vitamin supplementation addresses the underlying disease. Instead, vitamin supplementation is largely a psychological benefit to patients, just to feel they are doing something instead of nothing for their disease.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Our group feels, in the absence of a pharmacologic treatment, the current role of treatment is simply to provide reassurance to the patient, and doing our best to prevent total vision loss. “Blindness” will be individually defined based on a different threshold for each patient, and so ensuring we have appropriate therapy which can address varying levels of vision loss will be key. While the ideal treatment outcome would be to restore vision, we feel that at least the preservation of remaining visual function is imperative.

The best way to curb loss of visual function would be to halt the progression of the growth of the GA scar over time, which would be viewed by our group as a positive and clinically meaningful treatment outcome. Meanwhile, in our experience, AREDS vitamin supplementation does not effectively achieve this outcome.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Our group believes, based on the data available, pegcetacoplan will be the first (and only) treatment available for treating the underlying causes of GA. Our group already has a list of patients interested in the medication, and have been preparing both ourselves and our patients for treatment.

We see potential to continue AREDS vitamins in combination with pegcetacoplan, as many patients do not have symmetrical disease so any potential benefit of vitamin supplementation may still be derived. At this time, our group feels any patient diagnosed with GA would likely benefit from pegcetacoplan.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

In our group, we plan to treat a variety of patients ranging from relatively good vision to poor vision, the worst of which being in the 20/100 – 20/200 range. Patients with more severe vision loss may be most appropraite to start on pegcetacoplan in order to maintain any remaining visual function, and represent those patients most motivated for treatment were one available. The location of the GA scar will also determine the need for treatment, as patients with the scar closer to the macular fovea will be better candidates for treatment based on preventing spread of the atrophy into the macula itself. Finally, fellow eye status will be a large determinant, as our group and our patients will feel more motivated to receive treatment if already blind in the fellow eye, to maintain remaining visual acuity.

Our group has internally discussed patients we feel would be less suitable for pegcetacoplan, and have outlined the following criteria:

- Patients who still have very good visual function (~20/50 or better)
- Patients in which the GA scar is not threatening central vision
- Patients with GA scars which do not show appreciable growth over successive follow-ups.

Ultimately, our group feels our GA management approach will be most appropriately decided using shared decision-making with the patient. We feel their comfort and desire for pharmacological treatment will play a large role in determining the suitability of treatment, as the threat of progressive blindness is a large weight many of our patients with GA carry.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

In our practice, our group currently uses OCT to identify GA and monitor patients for any signs of progression. We also use fundus photography (not autofluorescence) to measure the relative size of GA scar, and will measure on successive visits to determine any potential scar growth. Our group has been using this imaging approach for at least a year in anticipation of pegcetacoplan approval, in order to have a good idea of which of our patients are progressing most rapidly and may be a priority for treatment when it becomes available.

We feel any treatment which has the potential to slow the progression of the GA scar, and therefore spare remaining visual function, would be valuable in the clinical setting.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Our group would consider pausing treatment if any adverse event arose which requires direct management, or discontinuing if we observe a decrease in visual acuity beyond a certain point where treatment would no longer be of functional benefit to patients (although this will be different for each patient). However, our group recognizes progression of GA is a slower process, and so evaluation should be occurring at each and every visit to monitor progression and determine response to treatment over time.

5.5 What settings are appropriate for treatment with pegcetacoplan? Is a specialist required to diagnose, treat, and monitor patients who might receive pegcetacoplan?

In Canada, the landscape is different across provinces regarding who can and cannot administer intravitreal injections. In New Brunswick, ophthalmologists can perform IVT injections, and our group believes anyone currently performing injections for wet AMD should be able to prescribe and administer pegcetacoplan for GA, as well as conduct the necessary follow-up and monitoring. While IVT injections were traditionally performed in hospital, we currently perform the bulk of our injections in clinic, with other provincial practices adopting this strategy due to changes in practice during COVID-19. That said, administration can be performed in any setting the physician feels comfortable.

6. Additional Information

Our group believes this a much needed and anticipated GA treatment in the Canadian setting, especially given there is no other current GA treatment option. We feel it is important to provide Canadian physicians and patients the opportunity to choose to treat GA instead of just monitor it, and are confident our patients with GA will benefit from pegcetacoplan treatment when it becomes available.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   Yes, we received support from a medical writer to schedule our meeting and document discussion.

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

   N/A

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for <u>each clinician</u> who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Nir Shoham-Hazon
Position: Ophthalmologist - Owner - Dr. Shoham-Hazon EyeCare PC Inc
Date: 06-02-2024

☒ **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.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
No conflicts to declare	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Vijay Sharma
Position: Ophthalmologist ; Dr. Vijay Sharma Prof. Corp.
Date: 06-02-2024

☒ 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.

Table 3: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
No conflicts to declare	x			

* Place an X in the appropriate dollar range cells for each company.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0810-000
Generic Drug Name (Brand Name): pegcetacoplan (TBC)
Indication: For treatment of GA secondary to age-related macular degeneration
Name of Clinician Group: Ocular Health Centre
Author of Submission: Dr. Jaspreet Rayat

1. About Your Clinician Group

Ocular Health Centre is the largest ophthalmology practice in Kitchener & Waterloo and one of the largest centres in Ontario. Each year our institution administers ~8000 injections for wet age-related macular degeneration (AMD).

2. Information Gathering

Our group met virtually via conference call on February 8, 2024, for 1 hour to discuss the submission. A medical writer captured our discussion. The submission was then circulated via email for final approval.

3. Current Treatments and Treatment Goals

In addressing the chronic, slowly progressive, and irreversible nature of GA, the current paradigm consists of no viable treatments to counter its progression. While light-based interventions like photo biomodulation exist, they are in their infancy, lacking robust evidence of clinical significance. Beyond fringe technologies, the predominant recourse for managing GA is vitamins; however, these relevant studies were conducted over two decades ago using the formulations available at the time, which questions their current usefulness.

In managing patients with GA, the primary therapeutic objective is ideally the prevention of further atrophy, although the pragmatic focus remains on slowing GA progression to preserve vision and optimize patient quality of life as long as possible.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Vitamins, which serve as the predominant management strategy for GA currently, prove insufficient in altering the underlying disease course or providing clinically meaningful impacts on preserving remaining vision. Additionally, the high cost of vitamins can impede accessibility to patients and some patients find vitamin ingestion challenging or experience gastric discomfort upon consumption. These reasons in addition to the fact patients with GA present a socioeconomic burden and strain on the healthcare system as they lose their independence, underscore the urgency for innovative, effective and affordable treatments to combat GA.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Based on the available data, pegcetacoplan would be the first and only option available to treat the underlying causes of GA.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

We would consider most patients with GA as ideal candidates for pegcetacoplan. The patients we would consider ideal candidates for pegcetacoplan include those with early symptoms of GA, such as a scotoma, and patients who have already lost vision in one eye due to GA. Individuals showing a linear growth of GA lesions, particularly in the perifoveal regions, are potential candidates, with studies indicating the longer the duration on the drug, the more effectively the disease progression is slowed down.

While we would prefer to initiate pegcetacoplan in most patients, their motivation and preference for treatment varies by disease severity. As such, a “watch-and-wait” approach may be considered for patients who have yet to experience vision loss, as they may be hesitant to initiate pegcetacoplan due to the frequency of injections every two months. These patients would be monitored, reserving treatment for cases where the GA lesions grow. Additionally, prioritizing patients with large GA lesions could strategically manage the demand on healthcare resources.

Altogether, the burden of GA, especially for the elderly population already facing a loss of independence and associated reduction in quality of life, underscores the critical need for accessible treatments. The anxiety induced by GA, where patients live in constant fear of losing their remaining sight, emphasizes the urgent requirement for an effective and affordable intervention to halt the progression of this debilitating condition.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

In evaluating treatment response to GA in clinical practice, there is a lack of quantifiable and objective measures as seen with other retinal disorders, such as wet AMD. This can be attributed to the lack of data evaluating the long-term impact of GA treatments over extended periods of time (i.e. 5+ years). Unlike studies for other retinal disorders which aim for visual gain, GA treatment should prioritize visual stability, as the irreversible nature of the damage precludes the possibility of improvement, necessitating a focus on halting further deterioration. With this focus, imaging techniques like fundus autofluorescence (FAF) or optical coherence tomography (OCT) should be used to assess the impact of treatment on GA lesion growth. Additionally, evaluating treatment response should extend to visual function questionnaires to gauge improvements in patients' quality of life.

The timing and frequency of assessing treatment response should be tailored to the individual patient's needs and the evolving nature of GA progression. For example, patients who have already experienced significant vision loss should be assessed at each visit (every 1-2 months), whereas patients earlier in their disease state could be evaluated every 4-6 months.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Discontinuation of pegcetacoplan would only be considered if the treatment no longer meaningfully maintains vision, or if an unmanageable adverse event is experienced. Analogous to glaucoma management, where stopping drops may lead to a gradual loss of vision over time, the decision to stop GA treatment hinges on the balance between maintaining healthful vision and the potential for vision loss.

In cases where treatment burden becomes overwhelming over an extended period, adjustments in injection frequency can be explored. With this, monitoring GA lesions through imaging will be crucial in assessing disease progression. Individual patient preferences and response to treatment also contribute to the nuanced decision-making process, with a constant need for reassessment based on the evolving nature of the disease and the patient's vision trajectory.

5.5 What settings are appropriate for treatment with pegcetacoplan? Is a specialist required to diagnose, treat, and monitor patients who might receive pegcetacoplan?

Administration of pegcetacoplan should be performed in a physician's office or clinic, with a potential for hospital administration as well. It should be administered by any trained ophthalmologist who treats retinal disorders.

6. Additional Information

Pegcetacoplan is a vital solution for the urgent unmet need in treating GA. We strongly emphasize its potential to address the profound impact of vision loss on patients' quality of life. Beyond its clinical benefits, pegcetacoplan can play a pivotal role in alleviating the financial and resource burden to the healthcare system associated with patients' loss of vision and independence.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   Yes, we received support from a medical writer to schedule our meeting and document discussion.

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

   N/A

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Jaspreet Singh Rayat
Position: Ophthalmologist, Assistant clinical professor (adjunct) McMaster University
Date: 08-02-2024

☒ **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.

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*

	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Bayer	X			
Novartis	X			
Roche	X			
AbbVie/Allergan	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Richard Weinstein
Position: Ophthalmologist
Date: 08-02-2024

☒ 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.

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Bayer	X			
Novartis	X			
Roche	X			
AbbVie/Allergan	X			

* Place an X in the appropriate dollar range cells for each company.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0810-000
Generic Drug Name (Brand Name): pegcetacoplan (TBC)
Indication: Geographic atrophy secondary to age-related macular degeneration
Name of Clinician Group: Retina Centre of Ottawa
Author of Submission: Dr. Thomas Lee

1. About Your Clinician Group

The Retina Centre of Ottawa serves a large cohort of patients living with geographic atrophy (GA) in the Ottawa region. The centre provides retinal care to over 60,000 patients in Ottawa and the surrounding National Capital Region. It is the largest retinal centre outside of Toronto.

2. Information Gathering

Our group discussed our opinions on each of the categories below, with a Medical Writer capturing and synthesizing our input. The submission was then circulated via email for final input and approval by each member of our group.

3. Current Treatments and Treatment Goals

Our group currently monitors patients with GA on a semi-frequent basis, typically every few months. Our group monitors disease progression using imaging such as optical coherence tomography (OCT), which is sufficient for diagnosis and monitoring. We also monitor for the development of other retinal diseases, such as exudative or wet age-related macular degeneration (AMD).

Our group is currently resigned to using a “watch-and-wait” management approach for patients with GA, given the lack of treatment options available in Canada. Desperate seniors have been leaving Canada to go to the United States for treatment with pegcetacoplan, which has been available for over a year. In some instances, vitamin supplementation can be used to support ocular health, but our group does not believe this is effective in addressing the underlying causes of GA.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

The loss of vision and independence to perform activities of daily living creates an incredible physical, emotional and financial burden on patients with GA. Our group believes it is important to consider treatment goals for GA in a larger context, with a change in attitude toward focusing on strategies that slow or prevent further loss of healthy tissue in the retina. While gains in visual function may be minimal, we feel any delay of disease progression may be significant based on the characteristics of the GA itself (i.e. disease close to the fovea).

Current strategies sorely lack an impact on the progression of disease itself, and instead we are simply left to monitor patients as their vision slowly deteriorates to eventual blindness. Our group believes a treatment for GA should prioritize slowing disease progression through hindering lesion growth, thereby preserving remaining retinal tissue. The preservation of tissue is believed to impact long-term vision conservation in patients with GA.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Our group views pegcetacoplan as the first and only option available to manage GA, representing a significant need in the community.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

Our group believes treatment is most appropriate for patients who have clearly defined GA secondary to AMD. It is important to ensure the disease is differentiated from other retinal disorders that also result in atrophy of retinal tissue (i.e. Stargardt disease). This should be done through imaging and identification of drusen using OCT. FAF can also provide an additional tool for differential diagnosis and be used to visualize the area of atrophy, which may help with treatment and management compliance.

Our group feels it is important to treat patients with GA who are both symptomatic and asymptomatic, as the ultimate goal of pegcetacoplan is to control/reduce their lesion growth. We do believe patients with significant vision loss should not be treated, as they would likely derive no long-term benefit.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

When assessing a meaningful response to treatment, our group believes pegcetacoplan has demonstrated a meaningful biological effect, being the reduction of lesion growth, which is a key predictor of visual function. Specific treatment goals will differ for each patient based on their disease presentation. These differentiating factors could include, but are not limited to, laterality, monocular vs. both eyes have remaining visual function, or level of symptoms (i.e. number of scotomas or other visual distortions). Any delay of progression can be significant to these various patient profiles, to buy time to delay vision loss.

While the change in lesion growth can be assessed at each clinic visit, the actual assessment of treatment response in relation to delay in vision loss does not need to be measured in the initial treatment stages. This is because the overall impact will be gradual and well outside the expected response to previous treatments in the retina space, such as anti-VEGFs.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Reasons for discontinuing pegcetacoplan would fall primarily under two categories: if the patient has complete vision loss (i.e. levels of 20/400 vision) or if there were adverse events that would suggest stopping therapy.

While exudative AMD is a known safety concern related to pegcetacoplan injections, our group is not concerned about managing its occurrence. Firstly, as patients will be monitored closely based on the frequency of injections, we

anticipate adverse events will be caught in their early stages of development. Secondly, a large portion of the patient population currently being managed by our group already has both exudative AMD and GA, and therefore would need both anti-VEGF and pegcetacoplan injections.

5.5 What settings are appropriate for treatment with pegcetacoplan? Is a specialist required to diagnose, treat, and monitor patients who might receive pegcetacoplan?

Administration of pegcetacoplan should be performed by a trained ophthalmologist who treats retinal disorders, in a setting in which intravitreal injections are normally administered (i.e. clinic, hospital).

6. Additional Information

Pegcetacoplan is an immediate need in ophthalmology to finally provide patients with a treatment to address GA progression. While the primary endpoint at 12 months observed in the DERBY Phase III study did not reach statistical significance, our group feels this is not important because the disease does not progress fast enough on average to detect a difference at 12 months. The key point is that the effects of treatment are seen long-term (i.e. +24 months), which is reinforced by the increasing effect over time found in both the OAKS and DERBY studies.

7. Conflict of Interest Declarations

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

   A Medical Writer supported with statement development and editing.

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

   N/A

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for <u>each clinician</u> who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Thomas Lee
Position: Ophthalmologist, Clinical Assistant Professor, Department of Ophthalmology, University of Ottawa
Date: 05-07-2024

☒ **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.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Bayer	X			
Roche	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. William A. Britton Jr.
Position: Ophthalmologist, Clinical Assistant Professor, Department of Ophthalmology, University of Ottawa
Date: 05-07-2024

☒ **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.

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Bayer	X			
Roche	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Dr. Adam McLaughlin
Position: Ophthalmologist, Clinical Assistant Professor, Department of Ophthalmology, University of Ottawa
Date: 05-07-2024

☒ **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.

Table 3: Conflict of Interest Declaration for Clinician 3

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Bayer	X			
Roche	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Dr. Raman Tuli
Position: Ophthalmologist
Date: 05-07-2024

☒ **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.

Table 4: Conflict of Interest Declaration for Clinician 4

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Bayer	X			
Roche	X			

* Place an X in the appropriate dollar range cells for each company.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0810-000
Generic Drug Name (Brand Name): pegcetacoplan (TBC)
Indication: Geographic atrophy secondary to age-related macular degeneration
Name of Clinician Group: Sunnybrook Retina Specialists
Author of Submission: Dr. Peter Kertes

1. About Your Clinician Group

The Sunnybrook Retina Specialists serve a patient population with a range of retina diseases. A subset of which are patients affected with age-related macular degeneration, where geographic atrophy (GA) is a secondary consequence. The team is composed of medical and surgical units that manage the diagnosis, treatment, and follow up of their patient population.

2. Information Gathering

Our group met virtually over Teams on July 10th for 1 hour to discuss the submission. A medical writer captured our discussion. The submission was then circulated via email for final approval.

3. Current Treatments and Treatment Goals

Our group focuses on a range of retina diseases. A large portion of which are patients with wet age-related macular degeneration (AMD), where some may develop secondary GA. Unfortunately, we are not referred patients with GA and we do not actively monitor for it as there is no treatment available. For patients who do develop GA secondary to their AMD, we monitor the progression of their macular degeneration.

With respect to treatment, our patients are recommended to initiate vitamin supplementation to support ocular health. Since we do not monitor patients' GA long-term, we cannot comment on the potential clinical benefits of vitamin supplementation in this population as GA progression is not monitored. However, we do not believe vitamin supplementation addresses the underlying causes of GA. We do not believe that this intervention addresses the underlying causes of GA.

Our ideal treatment for GA would cure the underlying mechanism of disease and restore central vision to our patients. At the present time, and in the absence of a cure, a treatment that slows GA progression would be highly important to maintain remaining vision. We anticipate pegcetacoplan being satisfactory to our patients, especially in the context of having no alternative, as it will maintain their vision and function for a longer term.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Without intervention, the progression of GA will lead to central blindness. This loss of vision has wide-reaching implications for patient well-being including a loss of independence, financial burden and emotional hardship. As patients' function deteriorates, the responsibility of care is placed on family/caregivers. Numerous patients mention the burden of vision loss on their personal lives. Unfortunately, in the current landscape, we are resigned to disappointing discussions around possible future therapies as nothing can currently be done.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Our group expects pegcetacoplan to be used first-line in patients with GA, given there is no alternative treatment.

For this group, the approval of pegcetacoplan would allow for referrals of GA to be received and for therapy to be initiated. Currently, there is a tendency for GA referrals to be withheld as there is no treatment. While there are other retinal diseases that have atrophy as a component of their disease, the markers of macular degeneration assessed by OCT and FAF provide confidence in an accurate diagnosis of GA. This group does not believe there to be an issue with GA diagnosis or misdiagnosis. As there is no current GA treatment, however, this group believes there are undoubtedly many patients who are being monitored by their optometrists who do not make it to the retina specialists.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

Our group believes there will be patients that are better and worse suited for this treatment, given their nuanced situations. However, it will be a primary option for all patients with GA. The overarching goal is to preserve central vision; therefore, patients in whom central vision is not imminently threatened would serve to gain the most, as they would have more function to preserve. Additionally, patients in whom GA is progressing at an accelerated rate would be most in need of intervention.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

When assessing GA treatment outcome measures, this group believes there is an alignment between clinical practice and clinical trials. In practice, however, these patients have not historically been followed to the same extent that they were in the trials. That does not mean the outcomes are not important for the patients, as this population has not received the attention that they deserve.

In an ideal situation, this group looks forward to the day when a treatment can reverse GA. However, as there is no current treatment for GA, this group believes that slowing the progression of GA is a clinically meaningful response, quantified by a reduction of lesion growth and a maintenance of central vision. Any patients with GA who receive treatment would be followed regularly for treatment administration, with imaging done every 3-6 months to monitor GA progression.

This group notes that, as pegcetacoplan will not improve visual function according to the clinical trial data, it will require trust from patients that it will preserve central vision. The choice to proceed with treatment is the choice of the individual

patient and requires the assessment of a multitude of factors (age, comorbidities, travel to site, burden of care, etc.). A portion of this population has both neovascular or wet AMD and GA and would require both an anti-VEGF and pegcetacoplan injection. Some patients may choose to not receive the treatment, and others would be excited to finally have an option.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

The main reason for discontinuing pegcetacoplan would be a development of an adverse event, such as inflammation following the administration. While some patients may not be suited for treatment due to the frequency and mode of administration, the group feels most patients will be encouraged a treatment is finally available.

5.5 What settings are appropriate for treatment with pegcetacoplan? Is a specialist required to diagnose, treat, and monitor patients who might receive pegcetacoplan?

Ideally, the administration of pegcetacoplan would be performed by a retina specialist. Additionally, it would be appropriate for general ophthalmologists to administer pegcetacoplan as they currently administer anti-VEGF therapy. This would be especially helpful in areas where there are no retina specialists and therefore would increase patient's access to treatment.

6. Additional Information

There are no other treatments that are currently available to address GA – pegcetacoplan would address a need for a large number of patients who are suffering with progressive vision loss. Furthermore, this group believes that pegcetacoplan reimbursement would relieve some of the financial burden associated with treatments.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   Yes, we received support from a medical writer to schedule our meeting and document discussion.

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

   N/A

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each**

clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.

Declaration for Clinician 1

Name: Dr. Peter Kertes
Position: Ophthalmologist, Retina Specialist at Sunnybrook Health Sciences Centre
Date: 12-07-2024

☒ **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.

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AdMare Bioinnovations				
Amgen				
Apellis				
Bayer				
Boehringer Ingelheim				
Biogen				
Janssen				
Kriya Therapeutics				
Novartis				
Novelty Nobility				
RegenxBio				
Roche				
Viatris				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Radha Kohly
Position: medical retina specialist , Sunnybrook hospital, department of ophthalmology and vision sciences
Date : <11/07/2024 >

☒ 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.

Table 2: Conflict of Interest Declaration for Clinician 2
No conflicts of interests to declare at this time

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
None				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Gary Yau
Position: Staff Ophthalmologist, Medical Retina Specialist at Sunnybrook Health Sciences Centre
Date: <12-07-2024>

☒ 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.

Table 3: Conflict of Interest Declaration for Clinician 3
No conflicts of interests to declare at this time

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
None				

* Place an X in the appropriate dollar range cells for each company.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: SR0810-000
Generic Drug Name (Brand Name): pegcetacoplan (TBC)
Indication: For treatment of GA secondary to age-related macular degeneration
Name of Clinician Group: University Health Network
Author of Submission: Dr. Brian Ballios

1. About Your Clinician Group

Our group at University Health Network represents a major treatment facility in Ontario. Our group consists of ophthalmologists and retina specialists who diagnose, treat and manage patients with retinal disorders, including geographic atrophy (GA).

2. Information Gathering

Our group met virtually over Microsoft Teams on February 7, 2024, for 1 hour to discuss the submission. A medical writer captured our discussion. The submission was then circulated via email for final approval.

3. Current Treatments and Treatment Goals

GA is a chronic and slowly progressive disorder that deprives individuals of their vision yet, has no established standard treatment to counter its progression. While there is evidence suggesting that certain vitamins may reduce the risk of progression from intermediate to severe AMD in age-related disease studies, in our experience, this does not seem applicable to GA.

Our current strategy for managing GA employs a “watch-and-wait” approach, where we monitor patients for potential sequalae (e.g. wet macular degeneration) and/or observe progression to a different disease with an established treatment. In the absence of a definitive treatment paradigm for GA, we advise patients on corrective measures for modifiable risk factors contributing to the development or progression of GA. This includes urging smoking cessation and collaborating with family physicians to co-manage uncontrolled high blood pressure or cholesterol. The prevailing emphasis on observation instead of treatment refrains from actively modifying the disease trajectory, and underscores the importance of the urgent need for effective treatments for GA.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

We believe treatment goals for GA should prioritize slowing disease progression, hindering anatomical degeneration, preserving light-sensitive cells and maintaining retinal health. We emphasize a shared decision-making approach to ensure physician goals align with patient preferences. We often find patients express a preference for interventions that maintain their remaining visual rather than focusing on vision regeneration.

Although historical clinical trials and studies have traditionally centered on achieving gains or improvements in vision, we believe it is crucial to reconsider treatment goals for GA; shifting the focus towards strategies that slow or prevent further loss of light-sensitive cells or healthy tissue in the retina. This shift in perspective is essential, particularly in contrast to other areas of ophthalmology where vision improvements are possible with treatment. Ultimately, we believe the focus of treatment goals in GA should strive for an extended duration of better visual health to optimize patient quality of life.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Based on the available data, pegcetacoplan would be the first and only treatment available to treat the underlying causes of GA.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

Pegcetacoplan shows potential in slowing macular degeneration for all patients. In particular, we believe patients without ocular comorbidities/contraindication to intravitreal (IVT) injections would be most suitable for treatment with pegcetacoplan.

Still, we believe there may be patients more likely to experience more significant benefits in disease and vision preservation based on the post-hoc analyses of the OAKS and DERBY studies. There is also evidence suggesting patients with GA lesions not involving the foveal center are most likely to benefit from the drug, preserving vision and function for a more extended period. However, even with foveal involvement, we believe the retina will respond positively to pegcetacoplan vs. no treatment.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

We acknowledge determining treatment response for GA in clinical practice is challenging due to the absence of an established standard of care. Given this and considering the mechanism of GA disease, we believe any reduction in lesion growth rate would be clinically meaningful.

We believe relying solely on visual acuity as an outcome measure may not fully encapsulate all aspects of visual function. While important, visual acuity does not capture the entire health of the macula. Considering patient-centric outcomes, we believe there should be a shift in focus from achieving a specific visual acuity number to maintaining overall retinal health and optimizing patient quality of life.

We believe regular assessments of patients with GA are essential, with monitoring scheduled monthly or every two months. At each visit, both anatomy and treatment response are assessed, recognizing that a response may take 6-18 months based on the available pegcetacoplan data and clinical observations.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

When contemplating the discontinuation of pegcetacoplan, we believe patient-driven factors should take precedence, with a focus on addressing the treatment burden and aligning with visual maintenance. Anatomically, a waiting period of 6-18 months is crucial to determine whether or not there is a meaningful response to pegcetacoplan before classifying the patient as a non-responder. We

acknowledge continuous vigilance for complications is essential, recognizing that response profiles can vary, and monitoring over time is crucial, particularly as pegcetacoplan will be the first-in-class medication for GA.

5.5 What settings are appropriate for treatment with pegcetacoplan? Is a specialist required to diagnose, treat, and monitor patients who might receive pegcetacoplan?

We believe the appropriate setting for pegcetacoplan administration is a physician office, and it can be administered by both academic ophthalmologists in a hospital or community ophthalmologists in a community practice. Monitoring GA progression with imaging (i.e. optical coherence tomograph [OCT] and fundus autofluorescence [FAF]) can be effectively done in either setting, whether by retina specialists or comprehensive ophthalmologists. From a regulatory perspective, we do recommend any restrictions to one specific specialist or healthcare provider; anyone capable of monitoring disease progression in an office setting is suitable for administering pegcetacoplan.

6. Additional Information

Our group believes that despite over half a century of research into GA and the associated advancements in imaging and tracking disease progression, which have led to accurate diagnosis and patient identification, there remains a significant treatment gap. With the available data, we believe pegcetacoplan would be a critical first-and-only treatment for GA. We also believe, without its adoption in clinical practice, research and development in the GA field may stagnate, impeding or discouraging future research into alleviating the significant burden of GA.

7. Conflict of Interest Declarations

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Declaration for Clinician 1

Name: Dr. Brian Ballios
Position: Clinician-Scientist, Ophthalmologist
Date: 07-02-2024

☒ **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.

Table 1: Conflict of Interest Declaration for Clinician 1

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Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis Pharmaceuticals Canada Inc.	X			
GelMEDIX Inc.	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Alexander Kaplan
Position: Ophthalmologist
Date: 10-02-2024

☒ 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.

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Bayer	X			
AbbVie	X			

* Place an X in the appropriate dollar range cells for each company.