1. General Information

Name of the therapeutic review	Anti-Vascular Endothelial Growth Factor Drugs for Retinal Conditions	
Name of patient groups	Canadian Council of the Blind (CCB) Canadian National Institute for the Blind (CNIB) The Foundation Fighting Blindness	
Patient group's contact information:	**CCB**, 20 James St., Suite 100, Ottawa ON, K2P 0T6	
	CNIB, 1929 Bayview Ave., Toronto, ON, M4G 3E8	
	The Foundation Fighting Blindness, 890 Yonge St., 12th floor, Toronto, ON, M4W 3P4	
Websites	www.ccbnational.net; www.cnib.ca; www.ffb.ca	CANADIAN COUNCIL OF THE BLIND / LE CONSEIL CANADIEN DES AVEUGLES a lack of sight is not a lack of vision cnib | inca The FOUNDATION FIGHTING BLINDNESS
Date Submitted	June 8, 2015	

1.1 Submitting Organizations

The Canadian Council of the Blind (CCB) was founded in 1944 by blind war veterans and graduates from schools of the blind. All officers and directors are blind or visually impaired which gives a unique sensitivity to the needs of the blind community. The CCB is a registered charity pursuant to the provisions of the Income Tax Act (Canada); charity number is: 11921 8899 RR0001. The CCB has over 70 chapters across Canada, and with over 1,500 members, is the largest membership-based organization for the blind. **The purpose of the CCB is to give people with vision loss a distinctive and unique perspective before governments.** The CCB deals with the ongoing effects of vision loss by encouraging active living and rehabilitation through peer support and social and recreational activities. CCB promotes measures to conserve sight, create a close relationship with the sighted community and provide employment opportunities. For the 21st century, the CCB is committed to an integrated proactive health approach for early detection to improve the quality of life for all Canadians.

CNIB – The primary objective of the CNIB is to create an inclusive, accessible, barrier-free society that provides the tools blind or partially sighted Canadians require to live safe, fulfilling and independent lives. CNIB believes in making communities accessible, caring and inclusive. We believe that people living with vision loss should have no limitations placed on their ability to succeed and we work hand-in-hand with Canadians who are blind or partially sighted to advocate for a barrier-free society. As

Canada's main provider of post-vision loss rehabilitation therapy, CNIB ensures its clients are able to receive the support they need throughout their journey through vision loss. Whether it be safety and mobility training, assistance with remaining gainfully employed, or gaining access to alternative formats of published works, CNIB operates across Canada providing these services to the best of the organization's ability and funded almost entirely by charitable donations received from the public.

The Foundation Fighting Blindness is Canada's leading charitable funder of sight-saving research. Our Charitable Registration Number is: 11912 9369 RR0001. **The mission of the Foundation Fighting Blindness is to lead the fight against blindness by advancing retinal disease research, education and public awareness.** We work with Canadian families affected by retinal diseases and with vision scientists at hospitals and universities across Canada. Over the past 40 years, the Foundation has contributed over $28 million to sight-saving research. We have a rigorous process of peer review, and the systems and processes in place to support and monitor complex research projects. We do not charge membership fees and consider our community of various stakeholders (donors, educational event participants, researchers, etc.) to be our general members.

1.2 Conflict of Interest Declarations

CCB received support from the following: VIA Rail, Cannondale, Community Foundation of Ottawa, Lions Club, Keith Communications Inc., Human Resources and Skills Development Canada (HRSDC), and the following pharmaceutical companies: Bayer, Merck, Novartis, and Pfizer. **CNIB** has received unrestricted educational grants for relatively small amounts from the following pharmaceutical companies: Alcon Canada, Bayer Canada, Novartis Canada, and Pfizer Canada. **The Foundation Fighting Blindness** receives unrestricted education grants and/or fundraising event sponsorships from Novartis Pharmaceuticals, Bayer Inc, Alcon, Allergan, Rx&D Health Foundation and Bausch & Lomb. Combined these companies contributed less than 4 per cent of the Foundation's revenues in 2014. **Together we are co-signatories on the Canadian Patient Charter for Vision Care** (included as an Appendix), which illustrates our commitment to ensuring that patients have access to the highest standard of vision care across Canada. We do not recommend specific treatments because we believe that these decisions are between the patient and her/his doctor. **We advocate for the best care.**

2. Condition and Current Therapy Information

2.1 Information Gathering

This collaborative submission relies on personal and organizational knowledge (across our three organizations) obtained from working with people living with AMD, DME, RVO and choroidal neovascularization secondary to progressive myopia. We also relied on: personal conversations with people living with these retinal diseases; an interview with a DME client; focus groups involving clients with DME; and an online survey for people living with wet-AMD.

2.2 Impact of Condition on Patients

Each of the five retinal conditions that is being considered, including age-related macular degeneration (AMD), choroidal neovascularization (CNV), diabetic macular edema (DME), pathologic myopia (PM), and retinal vein occlusion (RVO) has a unique impact on the affected patients and their families. Although each disease has different complications, they all lead to vision loss. We therefore focus on the symptoms and problems related to central vision loss that are shared across these five diseases. **We emphasize that vision loss is a devastating diagnosis because it impacts almost every task and activity**

related to daily living. In every case, early diagnosis and an individualized approach to treatment are essential to effectively combat rapid vision loss. If administered within the window of "treatability," anti-VEGF drugs can prevent further vision loss and even restore some lost sight. If this window is missed, drugs lose their effectiveness. One patient reported: "*The Lucentis booklet was very good, but too late; I should have been forewarned*."

People living with retinal diseases reported experiencing the following challenges:

- Difficulties completing tasks that utilise central vision
- Difficulty reading
- Difficulty recognizing facial features
- Difficulty or inability to drive
- Loss of independence
- Decreased quality of life
- Depression (studies have shown that adults with vision loss experience triple the rate of depression)
- Inability to maintain adequate foot care (this particularly important for people with diabetes because they also experience a range of neuropathies in the extremities)
- Difficulty traveling to doctor's appointments
- Difficulty gaining accessible transportation
- Difficulty obtaining accessible (large print, audio, high-contrast) materials about self-care
- Difficulty finding accessible information about medications and prescriptions
- Difficulty with healthy eating because many kitchens are inaccessible
- Difficulty maintaining a job
- Difficulty paying for expensive treatments
- Fear about the future
- Difficult interacting with people "not seeing what they see"
- Loss of friends and social supports, leading to isolation
- Inability to recognize people
- Worrying about their children ("I understand that there is a genetic component")
- More frequent falls and injuries
- Difficulty watching TV (loss of leisure activities)
- Writing (e.g. taking notes at a meeting)
- Poor depth perception and balance (studies show that adults with vision loss have twice the risk of falling and four times the risk of hip fracture when compared to age-matched cohorts)
- "Having to explain my limitations when out in the community"
- Difficulty with housework (sewing on a button, ironing, setting oven temperature, etc.)
- Difficulty with household repairs (hammering nails, using a screwdriver, using power tools, etc.)

The people we heard from emphasized that reading difficulties were particularly challenging because of the broad impact that reading has on other activities (e.g., reading signs to navigate in a new area, reading recipes in the kitchen, reading small print, such as the prescription information on medicine bottles, etc.). The majority of patients reported that the need to frequently visit their eye doctor was a significant burden. People experiencing central vision loss share many of the aforementioned difficulties, but each disease also presents additional challenges, as described below.

DME – Several groups are more vulnerable to diabetes and DME. First Nations Canadians are three to five times more likely than the general population to develop diabetes. This also makes them more likely to develop DME. Other ethno-cultural groups that have a higher risk of diabetes include Canadians of South Asian, Latin American and African descent. Diabetes and DME also have a higher prevalence in

people living in poverty. Due to this economic disadvantage, access to affordable therapies is essential to the well-being and health of vulnerable Canadians. People on the lower end of the socioeconomic scale will not be able to afford new medications for DME and will suffer significant vision loss, as a result. **We have all met patients living with DME who explained the economic burden of the disease** (especially because most are below the age of 65 and therefore often not eligible for reimbursement by formularies).

PM – This is a significant cause of vision loss globally, particularly in Asian populations. Choroidal neovascularization secondary to pathologic myopia is a major complication of pathologic myopia. This condition usually affects people under the age of 50 and can lead to severe vision loss within five years if left untreated. PM's impact on the quality of life of an otherwise healthy adult can be profound, affecting their ability to gain employment and function independently.

The impact of vision loss is conveyed by the following statistics:

- Only 45% of people with vision loss have graduated from high school
- Only 35% of working age adults with vision loss are employed
- Almost half of adults with vision loss report gross annual incomes of $20,000 or less

A study conducted by CNIB (with 2012 data) estimated the total financial cost of vision loss in Canada due to AMD at $2.6 billion, and due to diabetic retinopathy at $776 million per year. This breaks down to $1.8 billion in direct health costs due to AMD and $412 million in direct health costs due to diabetic retinopathy, as well as $860 million in indirect costs due to AMD and $364 million in indirect costs due to diabetic retinopathy. The net cost of suffering (burden of disease) from AMD, over and above the financial costs, was estimated to be a further $1.9 billion annually and due to diabetic retinopathy was estimated at $801 million annually. In addition to these costs, CNIB recently estimated the cost of falls associated with vision loss at $25.8 million; the cost of depression due to vision loss at $175.2 million; cost of hip fractures due to vision loss at $101.7 million; and the cost of nursing home admission due to vision loss at $713.6 million. The costs of vision loss are so large, even a small reduction in vision loss leads to significant impacts.

In closing, there is a clear economic benefit to sight-saving and restoring therapies, but economics should not be the only determinant. The benefit that anti-VEGFs provide to peoples' ability to function independently – to engage in the activities of everyday life that most of us take for granted – has to be the determining factor. In Canada, people should not have to suffer blindness and the related health and psychosocial impacts because they have the inability to pay for therapies. The feedback that we received from patients is bolstered by large epidemiological studies that show the impact of vision loss on quality of life as measured by objective assessment questionnaires. **Any improvement of vision loss as a result of treatment with anti-VEGF therapies leads to improvements in quality of life.**

2.2.1 Patients' Experiences With Current Therapy

Currently, patients in Canada who are living with AMD, CNV, DME, PM or RVO are treated with biweekly, monthly, or bi-monthly intra-ocular injections with one of the following three anti-VEGF drugs: bevacizumab (Avastin); ranibizumab (Lucentis); aflibercept (Eylea). Before these drugs were available, patients reported that they had been treated with cold laser, photodynamic laser therapy, and Visudyne.

Options needed for optimal patient outcomes. We gathered information from patients who are currently receiving anti-VEGF treatments, including patients who have been treated with a different anti-VEGF drug in the past. In summary, the majority of the people who we heard from were being treated with Lucentis, and the majority of those patients reported the treatment was working well for them. Some told us that a negative experience with Avastin ("severe allergic reaction, migraine, and complete vision loss") led them to switch to Lucentis. For example, in direct conversation with two patients who initially had received seven to10 injections of Avastin then changed to Lucentis, we learned that their visual acuity improved significantly after just two injections with the latter drug, enabling them to drive. In conversation, patients who were receiving Lucentis or Eylea injections reported that they experienced only very limited eye redness and fewer side effects then they had experienced on Avastin. Still, others reported that although they had been on both Avastin and Lucentis, they had never experienced a problem with either drug. This evidence illustrates that each patient has a unique experience and, as such, access to treatment options is important to achieving the best possible health outcomes.

Being coerced into treatments. Unfortunately, we heard from patients who felt they had no voice and no choice regarding their care. One caregiver described that she felt that her husband (who had received Avastin, Lucentis, and Eylea) was being **"*used as an experiment*."** She emphasized that she needed to speak for her husband because he was worried that if he spoke, the doctors would withhold treatment. Patients living in British Columbia refer to the "cartel" that determines their vision care. Patients described how they've been coerced into taking Avastin; they were told it was Avastin or nothing. One caregiver described how she always accompanied her husband to be sure he wasn't given Avastin (because he had responded poorly in one eye) – on the day when she couldn't make the treatment, her husband received Avastin in his good eye, which then became his bad eye. Since then, he has started taking Eylea, but the caregiver was reluctant to describe its effects because she does not know – in part, because it is so difficult to get visual acuity results from the doctor. We also learned that patients and caregivers have trouble accessing their treatment history, so they don't know what kind of anti-VEGF drug is being or has been used. **More than 10% of the respondents to our survey reported that they do not know which drug(s) they are taking.** This result was substantiated in conversations with people who described how difficult it was to ascertain which drug the doctor was using, especially because more than one type was used in one visit.

In general, the effectiveness and side-effects of the different anti-VEGF drugs varies from patient to patient. Patients reported experiencing the following side effects:

- Eye pain
- Dizziness
- Blurred vision
- Headaches after the injection into the eye
- Bleeding in the eye
- Floaters
- Lost vision/temporary blindness
- Feel "little bubbles" in the eye after an injection
- Elevated inner eye pressure
- Graying vision
- "Itchy eyeball"
- Severe eye pain
- Severe headaches
- "Scratches on the eyeball"

These negative side-effects often do not often prompt patients to seek alternative treatments because **they feel that other options are not available to them**. For example, a wet-AMD patient who had experienced negative side effects with both Avastin (migraines, vision loss [due to the drug not working], allergic reaction) and Lucentis (including elevated inner eye pressure, graying vision, blurred vision, severe headaches and severe eye pain) reported "*I was told there were no other treatment options in Canada, Eylea is only licensed in the USA*." **It should be noted that there is both research and anecdotal evidence that shows when one drug does not work, switching to another, often does work.** To maximize the treatment effectiveness, patients need access to different types of anti-VEGF treatments.

Equal access to most appropriate treatment needed. Patients are aware of the inequities in access to different anti-VEGF drugs across the country. For example, one wet-AMD patient who had received Avastin in the past and later switched to Lucentis (after it was covered) asked why the government wouldn't pay for Eylea. One of his friends was currently taking Eylea, and he had learned that patients often require less frequent injections, which prompted him to ask: "*Wouldn't the government save money by covering Eylea?"* The same patient described that he was having a positive experience with Lucentis, but didn't understand the rationale of limiting Eylea coverage. Another patient expressed her hope that Eylea would be covered so that she would need fewer injections.

The high cost of drugs is a problem. One patient described that before Lucentis was covered it had taken him several months to apply for and receive special authorization from the Alberta Blue Cross Plan. One patient reported her wish that "*our provincial government will cover eye injections and other treatments for patients under the age of 60. Because right now they do not!!!"* Another patient described how her costly treatments were not covered by OHIP, but said that it was worth it because her vision stabilized. Patients in BC described how challenging it was to try and get private coverage for Lucentis and Eylea without needing to go through the "cartel."

The most important issues to patients are restoring vision and preventing further loss of vision. To achieve these goals, patients are willing to risk almost any side effect or procedure. Patients say that their lives "*will not be worth living without vision*." Existing treatment is monthly intra-ocular injections – patients report fearing injections into their eyes. "*I would be very apprehensive, worried days before. I was so nervous and upset while I waited. Still what was the trade-off?*" Some patients experience pain for hours after treatment, while others do not. The unpredictable nature of these side effects adds to their unease.

Travel to and from appointments can be a major burden for patients and families. Patients, mostly seniors who are already concerned about losing their independence, must depend on family and friends to travel to a specialist to receive monthly eye injections. This is especially true in rural and remote areas. Although many doctors now elect to lengthen the treatment interval over time, the burden of the schedule may lead to sub-optimal treatment decisions. *"[After five monthly injections,] I told my doctor I'd have to keep it to [every] two months. It is too hard getting there, you know winter is coming on, and it is a three-hour drive. Then we come right back. The roads are not so good either."*

2.3 Impact on Caregivers

Caregivers experience many challenges. They may be needed to act as a sighted guide for people who are blind or partially sighted, and assist them with activities of daily living such as reading, managing medications, testing blood and administering insulin. Caregivers may be asked to take people to multiple doctor's appointments. If complications arise from therapy, the requirements placed on a caregiver can increase.

Impact extends beyond the patient. It is often said that vision loss affects at least one additional family member directly. In order to provide the kind of care needed to help a person with vision loss as described above, a caregiver usually has to take time off work or stop working entirely. The social impact on the caregiver in doing this is significant and the financial cost in terms of lost productivity and earning ability has an additional impact on the economy. Caregivers reported that one of the main challenges was the need to assist with travel to and from clinic appointments. For example, caregivers reported needing to schedule time off from work for this reason. Caregivers also reported that they felt discouragement and even depression around their loved one's loss of independence and inability to do their favourite hobbies. Caregivers also reported that the frequent scheduling of appointments posed challenges for their entire family because it affected their ability to visit relatives who live far away ("*appointments cut visits short*").

3. Information about New Drugs

3.1 Information Gathering

Together, we drew on personal knowledge and experiences working closely with people living with vision loss. We also relied on printed sources and information gathered from presentations and professional conferences, and responses from an online survey.

3.2 What Are the Expectations for New Drugs or What Experiences Have Patients Had With New Drugs?

a) **Based on no experience using new drug(s):** The vast majority of people whom we gathered information from reported that they were very hopeful that new drugs would be developed to treat their condition. Many hope for a treatment that could be administered at home without the need for an injection. **Yet many respondents felt that they would not have access to new treatments.**

People are hoping for a treatment that is "*more successful and less painful than the present one*." Many people are hoping for a cure – recognizing that the current approaches treat the symptoms, but do not cure the disease.

b) **Based on patients' experiences with new drug(s) as part of a clinical trial or through a manufacturer's compassionate supply:** Eylea is particularly appealing to patients, who are often "panicked" about their rapid vision loss and are burdened by the need for frequent injections. The promise from the outset of reduced injection frequency is powerful. Patients are reassured that this is "*the way the drug [Eylea] is supposed to work*" rather than having their doctor watch, wait and experiment with a longer treatment interval, which is what happens with Lucentis, although patients are aware that it is supposed to be administered monthly. None of the patients we spoke with reported side effects, although ophthalmologists with patients on Eylea

say the side effects are similar to existing drugs. However, the bi-monthly injection schedule means less exposure to side effects or injection-related complications. Patients generally see Eylea as a sensible advance that will reduce drug costs for the province, as well as the burden on themselves and their families. In the words of one trial patient who was forced to switch back to monthly treatments of Lucentis at the conclusion of the Eylea trial, "*They give me one shot [of Eylea] every two months and OHIP is way ahead [financially, because they pay for fewer injections]! Why would they throw money away like that?*" Patients receiving Eylea frequently express gratitude, crediting it with saving their vision and facilitating their daily activities. Patients are hopeful for a better future, but question if they are currently receiving the best care because they do not understand how doctors are deciding to use Avastin, Lucentis or Eylea.