Common Drug Review
Patient Group Input Submissions

Aflibercept (Eylea) for Macular edema, diabetic & secondary to retinal vein occlusion (RVO)

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.
Canadian Council of the Blind — permission granted to post.

CADTH received patient group input for this review on or before October 8, 2014

CADTH posts all patient input submissions to the Common Drug Review received on or after February 1, 2014 for which permission has been given by the submitter. This includes patient input received from individual patients and caregivers as part of that pilot project.

The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations. While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

Canadian Council of the Blind

Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	EYLEA® Aflibercept Macular edema, diabetic & secondary to retinal vein occlusion (RVO)
Name of patient group	Canadian Council of the Blind
Name of primary contact for this submission:	[redacted]
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1.1 Submitting Organization

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 65 chapters across Canada, and with over 1,500 members, is the largest membership-based organization for the blind.

1.2 Conflict of Interest Declarations

a) We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:

In 2011, 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 Frosst, Novartis, and Pfizer.

b) We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:

Nothing to declare. This submission was prepared by CCB staff.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

Information was obtained from online literature searches, conversations with some patients, and product monogram.

2.2 Impact of Condition on Patients

- Available coverage and lack of choice of Health Canada approved drugs for the treatment of eye diseases such as DME and RVO are the most important aspects of this condition.
- Quality of life and daily living is severely impacted with impaired vision. Because the patients can no longer drive, they need to find ways to attend medical appointments, shopping and social activities. Assistance is required for what were formerly simple tasks such as preparing meals, daily household chores, reading, etc. Patients with DME & RVO are unable to read regular print (books, newspapers, food labels, menus, greeting cards, etc.) as they have in the past.
- There is a social impact: often when someone develops a condition such as vision loss, friends seem to disappear basically because they don't know how to deal with the situation. People become isolated because they cannot move independently in their former environment.
- The patient has to learn how to deal with new challenges as they arise. Depression can also set in due to the pending loss of independence, potential loss of employment, loss of driving privileges, and the sheer uncertainty of diminished quality of life and of a life with no vision.
- Vision loss can cause patients to fall and injure themselves more frequently.
- There is often an economic impact and higher costs to vision loss due to loss of employment and the cost of treatment.
- Family dynamics change.
- Patients can no longer drive, thread a needle, ID medications, cook/prepare food, and much more.

2.3 Patients' Experiences With Current Therapy

Current therapies include laser therapy, Vitalux, ASA, Lutein, Lucentis and Avastin. Many patients are using currently Health Canada approved injections with good results. Some are being treated with "off-label" drugs. These drugs may need to be repeated many more times than Eylea would need to be used – i.e. every four weeks after initial regime, where Eylea can be effective for up to 8 weeks after initial 3-month set of treatments.

Some patients are receiving injections of a drug that has not been tested or approved by Health Canada. The long term effects of untested drugs are not known and could lead to adverse results due to the unknown.
Some patients are restricted in choice of treatment due to cost incurred from travel to regional clinics and therefore do not receive the optimal treatment they should be getting. Some provinces only provide a certain amount of money for use of current approved drug therapy.

Patients need to have a choice in approved treatment; currently there is only one medication available. Physicians need to have an alternate treatment should one not be available or may not meet the current needs of their patients. Physicians need to be able to provide approved medications for DME and RVO. Sometimes some patients may have an adverse reaction to an additive in the solution that may not be in Eylea so that they can receive the best care for their condition. Sometimes there may be some irritation which could be avoided with a second choice of medication.

Eylea provides an alternate choice should there be a shortage of current therapy or an adverse reaction to current therapy.
Other treatments may not be readily available due to short supply and Eylea is available therefore less chance of patient having to miss treatment or receive a drug that is currently not approved for RVO or DME by Health Canada

Patients need to receive the best-approved care for DME & RVO wherever they live so that the cost factor of travel and medication out-of-pocket expenses does not prevent them from getting this care.

2.4 Impact on Caregivers

With diagnosis of DME or RVO of a loved one, caregivers have to deal with all the emotional effects of vision loss in someone who had been previously independent, and deal also with their own emotions. Caregivers need to provide a safe environment for the patient. They may need to possibly take time off work to transport patient to medical appointments, shopping, etc. They may need to do more household chores especially if the patient live alone. They may need to provide comfort and reassurance to the patient.

Caregivers are dealing with an added financial burden due to both patient and caregiver having to take additional time from employment or arranging childcare for other family members as they care for a parent, etc. Due to lack of knowledge or understanding they may not know how to deal with the personal feelings/depression of the patient.

Should a patient not receive proper treatment the caregiver needs to arrange daily living care for the patient – most especially if there is a resulting injury due to decrease in vision.

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

Information was obtained from internet searches, one-to-one conversations with patients, and printed sources.

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

It is expected that the lives of patients will be improved with Eylea. According to research the macular edema should decrease and therefore improve vision.

The lack of choice as to approved therapy is currently not available. Eylea now would give the patient/physician two drugs to improve eye health.

EYLEA® (aflibercept) Injection is indicated for the treatment of patients with Diabetic Macular Edema and Retina Vein Occlusion The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg once every 8 weeks (2 months). Although EYLEA may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated when EYLEA was dosed every 4 weeks compared to every 8 weeks, therefore fewer trips to physician and less time for caregivers to miss from work.

EYLEA is indicated for the treatment of patients with Macular Edema following Central Retinal Vein Occlusion (CRVO). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly). Branch retinal vein occlusion (BRVO) and Central retinal vein occlusion (CRVO) are retinal vascular diseases which are associated with a decrease in vision-related quality of life.

The hemorrhaging that occurs with RVO, along with the macular edema resulting loss of vision causes the patient to become very apprehensive. The need to stop bleeding is most important to prevent further vision loss which would compound the above problems. Also, the increased intraocular pressure – glaucoma - needs to be controlled to decrease the incidence of peripheral vision loss.

An unmet need is that sometimes patients may have an adverse reaction to current therapy and therefore have no second choice of approved medication and therefore continue to lose vision.

It is expected that there will be improvement with this new drug by arresting the progress and possibly regaining sight. There may be a reduction in the number of drops needed in the future, therefore, alleviating adverse reactions or irritations. There will be less macular edema and less bleeding.

If the patient felt they were going to regain sight or prevent further loss, they would often be willing to experience some temporary adverse effects. Patients indicate that they have nothing to lose if the treatment doesn't work or cause adverse side effects so will be willing to give it a try with the anticipation that they will regain their sight. Regaining sight, controlling bleeding, fewer hospital visits, returning to work, and regaining independence to a greater degree than prior to treatment would be considered adequate improvement and worth the risk of side effects.

Mild irritation for short time is acceptable. Infection is not acceptable but if properly administered and proper patient compliance to post-injection this should not be a problem. With individual dosing as Eylea is prepared, infection would be minimized greatly.

b) EYLEA is the only anti-angiogenic therapy approved for wet age-related macular degeneration (AMD) with a proactive, treat-and-extend dosing approach without the need for interim monitoring. **EYLEA has demonstrated efficacy in a proactive, treat-and-extend dosing approach to treatment-naive patients with wet AMD:**

- Monthly treatment with ranibizumab or bevacizumab produced better efficacy outcomes compared with PRN or scheduled quarterly dosing regimens
- Relative to ranibizumab 0.5 q4 regimens, aflibercept 2q8 requires 5 fewer injections per year and the mode of treatment remains proactive
- Aflibercept 2q8 is also less intensive and less subject to equipment, operator, and interpretive variability

EYLEA®–Demonstrated Efficacy in a Proactive Approach for the Treatment of Wet AMD in Treatment-naive patients
Proven once every 2 months dosing in the first year. Fewer clinic visits.

- Treating proactively instead of reactively means patients spend less time at the clinic and less time travelling
- More independence

With fewer monthly clinic visits, patients have more time for what matters

- Predictability

A predictable injection schedule offers patients reduced impact of disease management on their personal lives

- Less burden on clinic staff

Staff no longer needs to spend time coordinating monthly monitoring and unscheduled injections

- Proactive approach

Ability to proactively extend time between combined monitoring/injection visits based on visual and anatomic response

- Serious adverse reactions related to the injection procedure have occurred in less than 1 in 1,000 intravitreal injections with Eylea and included endophthalmitis, traumatic cataract, and transient increased intraocular pressure.
- The vials are for single use only.
- Long term health is expected to improve greatly as mentioned previously

3.3 Growth factors (known as VEGF-A and PlGF) can cause extra blood

vessels to grow and leak in the back of the eye, which can cause loss of vision.
In Central Retinal Vein Occlusion (CRVO), a blockage occurs in the main blood vessel that transports blood away from the retina (the light sensitive back part of the eye), where fluid accumulates in the back of the eye, causing swelling (called macular edema). Aflibercept, the active substance in EYLEA, blocks these growth factors, and has been shown to help improve vision or slow vision loss from wet AMD and CRVO

EYLEA is supplied as a single dose pack in a vial. Injection with EYLEA may trigger an increase in eye pressure (intraocular pressure) in some patients within 60 minutes of the injection
Although uncommon, all intravitreal injections, including those with EYLEA, carry a risk of serious infection or inflammation inside the eye (endophthalmitis), detachment
or tear of the retina at the back of the eye (symptoms include eye pain, worsening eye redness, blurred or decreased vision, sensitivity to light, sudden loss of vision, flashing
lights and black spots), and cataracts (clouding of the lens in the front of the eye).

Usual dose EYLEA is intended for injection into the eye. It must only be administered by a doctor experienced in giving eye injections. Treatment of CRVO and DME
The recommended dose of EYLEA is 2 mg (0.05 mL or 50 microliters). EYLEA will be administered once every month and may be extended to up to every 3 months based on examination by your doctor. Following the initial doses the time frame for subsequent doses will be extended so that there will be fewer injections required compared to current therapy.

If the patient felt they were going to regain sight or prevent further loss, they would often be willing to experience some temporary adverse effects. Patients indicate that they have nothing to lose if the treatment doesn't work or cause adverse side effects so will be willing to give it a try with the anticipation that they will regain their sight. Regaining sight, controlling bleeding, fewer hospital visits, returning to work, and regaining independence to a greater degree than prior to treatment would be considered adequate improvement and worth the risk of side effects.
Mild irritation for a short time is acceptable. Infection is not acceptable but if properly administered and proper patient compliance to post-injection this should not be a problem. With individual dosing as Eylea is prepared, infection would be minimized greatly.

Section 4 — Additional Information

Having new drugs available can allow patients more choice and would allow for better quality of care.

The questions are clear.

It is clear to the Canadian Council of the Blind (CCB), that the Common Drug Review (CDR) should recommend this treatment for listing by all participating drug plans and make it accessible to patients who need this treatment.