PART III: CONSUMER INFORMATION

PrEYLEA®

Aflibercept, solution for intravitreal injection

This leaflet is Part 3 of a three-part "Product Monograph" published when EYLEA was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about EYLEA. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

EYLEA ("I-LEE-ah") is a solution which is injected into the eye (intravitreal injection) by your doctor with local anesthesia (freezing) to treat the eye conditions neovascular (wet) age-related macular degeneration – (wet) AMD, macular edema secondary to central retinal vein occlusion (CRVO), macular edema secondary to branch retinal vein occlusion (BRVO), diabetic macular edema (DME) or myopic choroidal neovascularization (mCNV). There is no clinical trial experience with EYLEA in the treatment of non-Asian patients with myopic CNV.

What it does:

Growth factors (known as VEGF-A and PIGF) can cause extra blood vessels to grow and leak in the back of the eye, which can cause loss of vision.

Vascular Endothelial Growth Factor (VEGF) and Placental Growth Factor (PlGF) are proteins that play an important role in making the abnormal blood vessels that contribute to the progression of wet AMD and the macular edema (swelling) that is seen with diabetic macular edema (DME). These blood vessels are fragile and can leak fluid and blood into the macula, leading to vision loss. DME is a swelling of the retina occurring in patients with diabetes due to leaking of fluid from blood vessels within the macula. The macula is the portion of retina responsible for fine vision. When the macula swells with fluid, central vision becomes blurry.

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).

In patients with BRVO, one or more branches of the main blood vessel that transports blood away from the retina is blocked, which cause the fluid accumulation in the back of the eye (swelling, called macular edema).

Myopic choroidal neovascularization (mCNV) is a severe form of myopia (near sightedness) which leads to elongated eyes with additional defects such as thinning, cracks and ruptures in some of the layers in the back of the eye. This triggers the abnormal formation of new blood vessels which can cause bleeding into the eye and eventually may lead to loss of vision.

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, CRVO, BRVO, DME, and myopic CNV.

These diseases may cause decreased vision.

EYLEA has been shown to slow down the progression of vision loss, improve vision, as well as the ability to perform related activities (e.g. reading, driving, etc.).

When it should not be used:

EYLEA must not be used if you:

- are allergic (hypersensitive) to aflibercept or any of the other ingredients of EYLEA listed below
- have inflammation of the eye (symptoms include eye pain, redness and trouble seeing)
- have an infection in or around the eye (ocular or periocular infection)

What the medicinal ingredient is:

The active substance in EYLEA is aflibercept.

What the nonmedicinal ingredients are:

The other inactive ingredients are: sodium phosphate, monobasic, monohydrate; sodium phosphate, dibasic, heptahydrate; sodium chloride; sucrose; polysorbate 20; and water for injection.

What dosage forms it comes in:

EYLEA is a sterile, clear, colourless to pale yellow, solution for injection which is iso-osmotic (similar properties to the inside of your eye). EYLEA is supplied as a single dose pack in a vial for the treatment of one eye.

Vials:

Each carton includes a single-dose glass vial containing a fill volume of 278 microliters solution for injection with a rubber stopper, and an 18 gauge filter needle.

WARNINGS AND PRECAUTIONS

Take special care with EYLEA:

- Injection with EYLEA may trigger an increase in eye pressure (intraocular pressure) in some patients within 60 minutes of the injection. Your doctor may monitor this after each injection. If you have glaucoma (increased eye pressure), please tell your doctor.
- 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). Please contact your doctor immediately if you develop any of these symptoms.

- Inform your doctor if you have already had a stroke or experienced transient signs of stroke (weakness or paralysis of limbs or face, difficulty speaking or understanding). This information will be taken into account to evaluate if EYLEA is the appropriate treatment for you.

Before you use EYLEA, talk to your doctor or pharmacist if:

- **You are taking other medicines:** Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.
- **You are or plan to become pregnant:** There is no experience of using EYLEA in pregnant women. In animals, high doses have been shown to have toxic effects on the fetus. Therefore, EYLEA is not recommended during pregnancy unless the potential benefit outweighs the potential risk to the fetus. If you are pregnant or planning to become pregnant, discuss this with your doctor before treatment with EYLEA. Women of childbearing potential have to use effective contraception during treatment and for at least 3 months after the last intravitreal injection of EYLEA.
- **You are breast-feeding:** EYLEA is not recommended during breast-feeding as it is not known whether aflibercept passes into human milk. A risk to the breast-fed child cannot be excluded. Ask your doctor for advice before starting EYLEA treatment. A decision must be made whether to discontinue breast-feeding or to abstain from EYLEA therapy.
- You have a history of seeing flashes of light or floaters, or if you have a sudden increase in the size or number of floaters.

The use of EYLEA in children and adolescents has not been studied and is therefore not recommended

Driving and Using Machines

After your EYLEA injection, you may experience some temporary visual disturbances. Do not drive or use machinery as long as these last.

PROPER USE OF THIS MEDICATION

Usual dose

EYLEA is intended for injection into the eye. It must only be administered by a doctor experienced in giving eye injections.

EYLEA will be injected under aseptic (clean and sterile) conditions. Before the injection, your doctor will use a disinfectant eyewash to clean your eye carefully to prevent infection. Your doctor will also give you a local anesthetic to reduce or prevent any pain you might have with the injection.

Treatment of AMD

The recommended dose of EYLEA is 2 mg (0.05 mL or 50 microliters). It will be administered once a month (every 4 weeks) for the first 3 months then you may receive an injection every 2 months (8 weeks) for the first 12 months of treatment. After the first 12 months of treatment, EYLEA may be administered up to every 3 months (12 weeks) based on your doctor's assessment. The interval between two doses should not be shorter than one month. Your doctor will monitor your vision regularly.

Treatment of CRVO and BRVO

The recommended dose of EYLEA is 2 mg (0.05 mL or 50 microliters). EYLEA will be administered once every month (4 weeks) and may be extended to up to every 3 months (12 weeks) based on examination by your doctor. The interval between two doses should not be shorter than one month. Your vision will be monitored by your doctor every 1 to 2 months to determine the need for continued treatment.

Treatment of DME

If you are a patient with diabetic macular edema, the recommended dose of EYLEA is 2 mg (0.05 mL or 50 microliters). You will be treated with EYLEA once a month (every 4 weeks) for the first 5 consecutive months, then you may receive one injection every 2 months (8 weeks) thereafter. Unless you experience any problems or are advised differently by your doctor, there is no need for you to see your doctor in between the injections.

Your doctor may decide to treat you with EYLEA as frequently as every month.

Treatment of myopic CNV

If you are a patient with myopic choroidal neovascularization you will be treated with one single injection of EYLEA 2 mg (0.05 mL or 50 microliters) at the beginning of your therapy. You will receive additional injections only if during examination your doctor finds that your disease persists. If your disease resolves, your treatment will stop. In case your disease recurs it will be treated like a new disease.

The interval between two doses should not be shorter than one month.

Use in children: Wet AMD does not occur in children or adolescents. Therefore, the safety and efficacy of EYLEA have not been studied in this age group.

The safety and efficacy of EYLEA have not been studied in patients who are younger than 18 years of age with CRVO, BRVO, DME, and myopic CNV.

If you missed your appointment

If a dose of EYLEA is missed, make a new appointment for an examination and injection.

Before stopping EYLEA treatment

Consult your doctor before stopping the treatment. If you have any further questions about the use of this product, ask your doctor.

Overdosage

For management of a suspected drug overdose, contact your regional Poison Control Centre.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, EYLEA can cause side effects, although not everybody gets them.

With administration of EYLEA, there may be some side effects due to the injection procedure. Some of these may be serious and include infection or inflammation inside the eye (endophthalmitis), sudden loss or change of sharpness of vision (detachment or tear of retina), increase of pressure inside the eye (intraocular pressure), clouding of the lens due to injury (cataract traumatic), and detachment of the gel-like substance inside the eye from the retina (vitreous detachment), in AMD clinical studies; endophthalmitis, cataract and vitreous detachment in CRVO clinical studies; cataract in BRVO clinical studies; retinal detachment in DME clinical studies; and macular hole in the myopic CNV clinical study. These serious side effects occurred in less than 1 in 1000 (16 of 26,780 injections in AMD studies; 3 out of 2,728 intravitreal injections in CRVO clinical studies; 1 out of 1,115 intravitreal injections in BRVO clinical studies; 1 out of 5940 intravtireal injections in DME clinical studies; and 1 out of 474 injections in the myopic CNV study.

The following is a list of the side effects reported to be possibly related to the injection procedure or to the medicine. Please do not get alarmed, you might not experience any of these. Always discuss any suspected side effects with your doctor.

Very common side effects (more than 1 in 10 patients may be affected):

- bloodshot eye caused by bleeding from small blood vessels in the outer layers of the eye (conjunctival hemorrhage)

Common side effects (between 1 and 10 in every 100 patients may be affected):

- decreased sharpness of vision (retinal pigment epithelium tear*, detachment of the retinal pigment epithelium)*
- certain forms of clouding of the lens (cataract, cataract nuclear, cataract subcapsular)
- damage to the front layer of the eyeball (corneal erosion, corneal abrasion, punctate keratitis)
- increase in eye pressure (intraocular pressure increased)
- blurred vision
- moving spots in vision (vitreous floaters)
- detachment of the vitreous (gel-like substance inside the eye) from the retina (vitreous detachment)
- a feeling of having something in the eye (foreign body sensation in eyes)
- increased tear production (lacrimation increased)
- swelling of the eyelid (eyelid edema)
- eye pain
- pain or bleeding at the injection site (injection site pain or hemorrhage)
- redness of the eye (conjunctival hyperemia, ocular hyperemia)

*) Conditions known to be associated with wet AMD; observed in wet AMD patients only.

Uncommon side effects (between 1 and 10 in every 1,000 patients may be affected):

- abnormal sensation in the eye
- infection or inflammation inside the eye (endophthalmitis)
- irritation at the injection site
- irritation of the eyelid
- decreased sharpness of vision (retinal detachment, retinal tear)
- generalized allergic reactions (hypersensitivity)**
- inflammation of certain parts of the eye (iridocyclitis, anterior chamber flare)
- certain forms of clouding of the lens (cataract cortical, lenticular opacities)
- damage of the front layer of the eyeball (corneal epithelium defect)
- swelling of the front layer of the eyeball (corneal edema)
- inflammation in the iris of the eye (iritis)

** Allergic reactions like rash, itching (pruritus), hives (urticaria), and a few cases of severe allergy (anaphylactic/anaphylactoid) reactions were reported

Rare side effects *(between 1 and 10 in every 10,000 patients may be affected)*:

- inflammation of certain parts of the eye (uveitis, vitritis)
- pus in front of the iris (coloured part of the eye) (hypopyon)
- clouding of the lens due to injury (cataract traumatic)

The use of VEGF inhibitors similar to those contained in EYLEA, but which have an effect throughout the body (systemic effect) is potentially related to risk of arterial thromboembolic events (of blood clots blocking blood vessels) which may lead to heart attack or stroke. There is a theoretical risk of such events following injection of EYLEA into the eye.

As with all therapeutic proteins, EYLEA may cause an immune reaction (formation of antibodies).

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom/ Effect		Talk with your doctor or pharmacist	
		Only if severe	In all cases
Common (between 1 and 10 in every 100 patients may be affected)	Detachment of the outer layer of the retina (symptoms can include sudden appearance of floaters, flashes of light or a shadow over a portion of the visual field)		✓
	Clouding of vision		✓
	Damage to the cornea (the front layer of the eyeball) (symptoms can include eye pain, blurred vision, tearing, redness and extreme sensitivity to light)		✓
	Visual disturbances caused by detachment of the inner layer of the eye (sudden loss of vision, flashing lights, black spots)		✓
	Signs of stroke, such as weakness or paralysis of limbs or face, trouble speaking or understanding, sudden blurring or loss of vision: seek emergency medical care immediately*		✓
Uncommon (between 1 and 10 in every 1,000 patients may be affected)	Infection or inflammation inside the eye (symptoms can include eye pain, swelling around the eye, light sensitivity, and worsening of vision) (endophthalmitis)		✓
	Increased pressure in the eye		✓
	Shock (Hypersensitivity) – fast pulse, low blood pressure, sweating)		✓
	Disturbed or blurred vision (retinal tear)		✓
	A sudden increase in new moving spots in vision and flashes of light in your side vision (vitreous detachment)		✓
	A feeling that you have something in your eye, a teary red eye, blurred vision in one eye, headache or unusual sensitivity to light (corneal abrasion)		✓

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom/ Effect		Talk with your doctor or pharmacist	
		Only if severe	In all cases
Rare (between 1 and 10 in every 10,000 patients may be affected	Hypopyon (pus in the eye)		✓
	Macular hole (symptoms can include distortion or blurriness in straight-ahead vision, straight lines or objects begin to look bent or wavy)		✓

** There is a theoretical risk of ATEs, including stroke, following injection of EYLEA into the eye.*

This is not a complete list of side effects. For any unexpected effects while taking EYLEA, contact your doctor or pharmacist.

HOW TO STORE IT

- Keep EYLEA out of the reach and sight of children.
- Store in a refrigerator (2ºC to 8ºC). Do not freeze.
- Prior to usage, the unopened vial may be stored at room temperature (25ºC) for up to 24 hours
- Keep the vial in its outer carton in order to protect from light.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada through the Canada Vigilance Program collects information on serious and unexpected side effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug you may notify Canada Vigilance:

REPORTING SUSPECTED SIDE EFFECTS

Canada Vigilance Program:

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to:
    Canada Vigilance Program
    Health Canada
    Postal Locator 1908C
    Ottawa, Ontario
    K1A 0K9

  Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Website at www.healthcanada.gc.ca/medeffect.

Note: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

For more information, please contact your health professional or pharmacist first, or Bayer Medical Information at 1-800-265-7382 or canada.medinfo@bayer.com.

This document plus the full product monograph, prepared for health professionals can be found at: http://www.bayer.ca or by contacting the manufacturer, at the above-mentioned phone number and e-mail address.

This leaflet was prepared by:

Bayer Inc.
2920 Matheson Boulevard East
Mississauga, Ontario
L4W 5R6
Canada

Last revised: May 19, 2017