PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrYESAFILI™ (Yes-A-Fill-Ee)
(Aflibercept)
Aflibercept injection, solution for intravitreal injection

This patient medication information is written for the person who will be taking **YESAFILI**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again. This patient medication information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **YESAFILI**, talk to a healthcare professional.

YESAFILI *is a biosimilar biologic drug (biosimilar) to the reference biologic drug EYLEA®. A biosimilar is authorized based on its similarity to a reference biologic drug that was already authorized for sale.*

What is YESAFILI used for?

Pr YESAFILI™ (Yes-A-Fill-Ee) is a solution which is injected into the eye (intravitreal injection) by your doctor with local anesthesia (freezing).

In adults, YESAFILI is used 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)
- Myopic choroidal neovascularization (mCNV). There is no clinical trial experience with Aflibercept in the treatment of non-Asian patients with myopic CNV.

How does YESAFILI work?

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 YESAFILI, 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.

What are the ingredients in YESAFILI?

Medicinal ingredients: aflibercept

Non-medicinal ingredients: histidine, histidine hydrochloride monohydrate, polysorbate 20, trehalose dihydrate, and water for injection.

YESAFILI comes in the following dosage forms:

YESAFILI is a sterile, clear, colourless to pale yellow, solution for injection which is iso-osmotic (similar properties to the inside of your eye). Solution for intravitreal injection 2 mg / 0.05 mL in vial or pre-filled syringe.

Pre-filled Syringes:
Each carton includes a single-dose pre-filled syringe containing a fill volume of 170 microliters solution for injection. One package insert in each carton.

Vials:
There are 2 Cartons of YESAFILI available containing the following:

1. YESAFILI Carton contains (FULL Kit):
    - one YESAFILI 2 mg/0.05 mL single-dose glass vial containing a fill volume of 278 microliters solution for injection with a rubber stopper
    - one 18-gauge x 1½-inch, 5-micron, filter needle for withdrawal of the vial contents
    - one 30-gauge x ½-inch injection needle for intravitreal injection
    - one 1-mL syringe for administration
    - one package insert

2. YESAFILI Carton contains (HALF Kit):
    - one YESAFILI 2 mg/0.05 mL single-dose glass vial containing a fill volume of 278 microliters solution for injection with a rubber stopper
    - one 18-gauge x 1½-inch, 5-micron, filter needle for withdrawal of the vial contents
      one package insert

Do not use YESAFILI if:

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

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take YESAFILI. Talk about any health conditions or problems you may have, including if you:

Take special care with YESAFILI:

- Injection with YESAFILI 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 YESAFILI, carry a risk of serious infection or inflammation inside the eye (endophthalmitis), inflammation of the vessels of the retina (retinal vasculitis with or without occlusion), 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 YESAFILI is the appropriate treatment for you.
- **Tell your doctor immediately if you develop signs of a possible allergic reaction** (for example, fast pulse, low blood pressure, sweating, allergic skin reactions such as rash, itching or stinging).

Before you use YESAFILI, 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 YESAFILI in pregnant women. In animals, high doses have been shown to have toxic effects on the fetus. Therefore, YESAFILI 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 YESAFILI. Women of childbearing potential have to use effective contraception during treatment and for at least 3 months after the last intravitreal injection of YESAFILI.
- **You are breast-feeding:** YESAFILI 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 YESAFILI treatment. A decision must be made whether to discontinue breast-feeding or to abstain from YESAFILI 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 YESAFILI in children and adolescents has not been studied and is therefore not recommended.

Driving and Using Machines

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

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take YESAFILI:

Usual dose:

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

YESAFILI will be injected under aseptic (clean and sterile) conditions. Before the injection, the 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 YESAFILI is **2 mg** (0.05 mL or 50 microliters). It will be administered once a month (every 4 weeks) for the first 3 months (12 weeks) then you may receive an injection every 2 months (8 weeks) thereafter. Your doctor will decide whether the treatment interval between injections may be maintained at every 2 months (8 weeks) or it may be extended by 2 weeks. The maximum of interval between two doses is 16 weeks.

Based on examination by your doctor, you may be prescribed an YESAFILI injection every month (4 weeks) after the first 3 months. 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 YESAFILI is **2 mg** (0.05 mL or 50 microliters). YESAFILI 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 YESAFILI is **2 mg** (0.05 mL or 50 microliters). You will be treated with YESAFILI once a month (every 4 weeks) for the first 5 consecutive months, then you may receive one injection every 2 months (8 weeks) thereafter. The treatment interval may be kept at every two months (8 weeks) or extended, by up to 2 weeks at a time, based on your doctor's examination. Your doctor will decide on the schedule for follow up examinations.

Based on examination by your doctor, you may be prescribed an YESAFILI injection every month (4 weeks) after the first 5 months.

Treatment of myopic CNV

If you are a patient with myopic choroidal neovascularization you will be treated with one single injection of YESAFILI **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: The safety and efficacy of YESAFILI have not been studied in patients who are younger than 18 years of age. Health Canada has not authorized YESAFILI for pediatric use.

Before stopping YESAFILI treatment:

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

Overdose:

If you think you or a person you are caring for, have taken too much YESAFILI, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no symptoms.

Missed Dose:

If a dose of YESAFILI is missed, make a new appointment for an examination and injection as soon as possible.

What are possible side effects from using YESAFILI?

These are not all the possible side effects you may have when taking YESAFILI. If you experience any side effects not listed here, tell your healthcare professional.

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

With administration of YESAFILI, 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 intravitreal 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)
- eye pain

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

Frequency not known (frequency cannot be estimated from the available data):
- inflammation of the white part of the eye associated with redness and pain (scleritis)

The use of VEGF inhibitors similar to those contained in YESAFILI, 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 YESAFILI into the eye.

As with all therapeutic proteins, YESAFILI 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 Section, please tell your doctor.

Serious side effects and what to do about them			
Frequency/ Side Effect/ Symptom	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	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		√	

Serious side effects and what to do about them			
Frequency/ Side Effect/ Symptom	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
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)		√	
Bleeding in the eye (vitreous hemorrhage, hyphema)		√	
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)		√	
FREQUENCY NOT KNOWN			
Damage to the white part of the eye (symptoms can include eye pain, blurred vision, tearing, redness, extreme sensitivity to light) (scleritis)		√	
** There is a theoretical risk of ATEs, including stroke, following injection of YESAFILI into the eye.*			

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store in a refrigerator (2°C to 8°C). Do not freeze.
- Keep out of reach and sight of children.

Pre-filled Syringe:

- Prior to usage, the unopened blister pack may be stored at room temperature (25°C) for up to 24 hours.
- Keep the pre-filled syringe in its blister pack and in the outer carton in order to protect from light.

Vials:

- Prior to usage, the unopened vial may be stored at room temperature (25°C) for up to 4 hours.
- Keep the vial in its outer carton in order to protect from light.

If you want more information about YESAFILI:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; by calling 1 833 986 1468 or medical.informationCanada@biocon.com

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