Recommendations for treatment with

Yesafili®

Aflibercept 40 mg/mL

solution for injection

PRESCRIBER GUIDE

This guide provides you with important information on **YESAFILI** 40 mg/mL solution for injection (2 mg aflibercept dose) in a pre-filled syringe.

It includes information on the medication itself and how to correctly administer it to your patients.

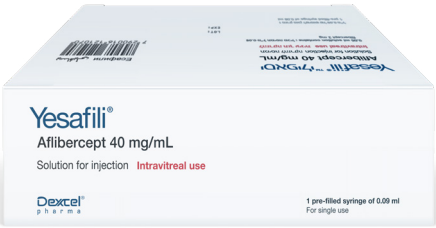
Please provide your patients with the **YESAFILI** Patient Guide, which includes a reference to an audio version (read out of the Patient Guide), and the Patient Information Leaflet.

To access the YESAFILI Prescriber Video, please scan the QR code:

The video contains information on both pre-filled syringe and vial presentations. Please note that only the pre-filled syringe is marketed.

To view the local packaging and labels of the pre-filled syringe, please refer to the Key summary information in this Prescriber Guide.

For further information on **YESAFILI**, please refer to the Summary of Product Characteristics (SmPC).

KEY SUMMARY FOR YESAFILI® 40 mg/mL	
Presentation	Pre-filled syringe
Approved indications (Adults)	• Neovascular (wet) age-related macular degeneration (AMD) • Visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO) • Visual impairment due to diabetic macular oedema (DME) • Visual impairment due to myopic choroidal neovascularisation (myopic CNV)
Dose per injection	2 mg
Injection volume	0.05 mL (50 microliters)
Pre-filled syringe packaging	
Pre-filled syringe	
Label on pre-filled syringe	

YESAFILI is a biosimilar medicinal product that has been demonstrated to be similar in quality, safety and efficacy to the reference medicinal product EYLEA®. Please be aware of any differences in the indications between the biosimilar medicinal product and the reference medicinal product. Information regarding biosimilar products can be found on the website of the Ministry of Health:

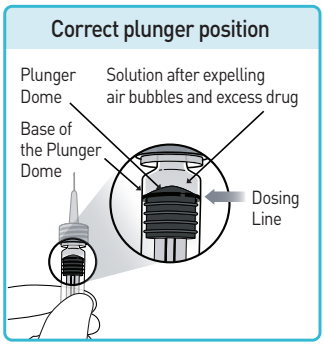
https://www.gov.il/he/Departments/General/biosimilar

Contraindications

- Hypersensitivity to the active substance aflibercept or to any of the excipients listed in section 6.1 of the Summary of Product Characteristics (SmPC).
- Active or suspected ocular or periocular infection.
- Active severe intraocular inflammation.

Key instructions for use

- The pre-filled syringe contains excess volume. Before injecting, the pre-filled syringe must be primed to the correct volume for injection according to the steps in the instructions for use.
- Ensure proper aseptic technique, including the use of a broad-spectrum microbicide, to minimize risk of intraocular infection.
- For the intravitreal injection, a **30 G x ½ inch injection needle** should be used. Use of a smaller size injection needle (higher gauge) than the 30 G x ½ inch needle may result in increased injection forces.
- Expel excess volume and air bubbles from the pre-filled syringe and adjust the base of the plunger dome (**NOT the tip**) to the dosing line before injection.
- Push the plunger slowly and with constant pressure, and do not administer any residual volume remaining in the syringe after injection.



Selected instructions for storage and handling of YESAFILI®, pre-filled syringe

	Store **YESAFILI** in the refrigerator (2°C to 8°C). Do not freeze.
	Store in the original package in order to protect from light.
	Prior to use, the unopened blister may be stored outside the refrigerator below 25°C for up to 72 hours.
	**YESAFILI** is **not licensed for multi-dose**, further compounding or splitting. Use of more than one injection from the pre-filled syringe **can lead to contamination and subsequent infection.**

Special warnings and precautions for use

In all cases, instruct patients to immediately report signs and symptoms of adverse events:

Adverse Event / Risk	Measures to Minimize Risk
Intraocular inflammation including endophthalmitis	Use proper aseptic technique when preparing the injection and during the injection itself. Use recommended antiseptic agents. Monitor patients after the injection.
Transient intraocular pressure (IOP) increase	Properly prime the syringe by removing excess volume and air bubbles from syringe before administration. Monitor patient's vision and IOP after the injection.
Medication error	Check the carton and the label on the medication to ensure you have the correct dose of **YESAFILI**.
Retinal pigment epithelial tear	Review retinal pigment epithelial detachments features for risk of retinal pigment epithelial tears. Monitor patient after the injection for symptoms such as acute decrease in (central) vision, blind spot (central scotoma) and distorted vision with deviation of either vertical or horizontal lines (metamorphopsia).
Cataract	Measure the correct site for the injection, use correct injection technique.
Off-label use/misuse	Use medication only for treatment of approved indications and use approved dose.
Embryo-fetal toxicity	Instruct patients to use effective contraception during treatment and for at least 3 months after the last intravitreal injection of **YESAFILI**. **YESAFILI** should not be used during pregnancy unless the potential benefit outweighs the potential risk to the foetus.
Exposure during breast-feeding	**YESAFILI** is not recommended in patients who are breast-feeding.

For a complete list of adverse events, please refer to the SmPC.

After the injection

- **Evaluate vision immediately after injection** (hand movement or finger counting).
- **Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure.**
- Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis (e.g., eye pain, redness of the eye, photophobia, blurring of vision) without delay.

GENERAL INFORMATION

You must explain to the patient the implications of anti-VEGF treatment. The patient guide is a tool that will help you to communicate to your patient about the disease and treatment. It contains the information on the signs and symptoms of adverse events and when the patient should seek immediate medical attention.

This guide is available upon request to Dexcel Ltd., and you should distribute it to your patients. It is available as a booklet and as an audio guide option. It is also available at the Ministry of Health website.

The Summary of Product Characteristics (SmPC) describes the properties of **YESAFILI** and the approved indications for use. It is an important source of information for healthcare professionals on how to use **YESAFILI** safely and effectively. It is available at the Ministry of Health website.

Refer to the SmPC for **YESAFILI** for complete information on posology and dosing recommendations for **YESAFILI** 40 mg/mL solution for injection (2 mg dose).

For the Ministry of Health website, please scan the following QR code:

About YESAFILI®

YESAFILI is for intravitreal injection only.
It must only be administered by a qualified physician experienced in administering intravitreal injections and familiar with the handling of the pre-filled syringe.

YESAFILI® 40 mg/mL

Presentation	Pre-filled syringe
Approved indications in adult (18 years and older) patients	• Neovascular (wet) age-related macular degeneration (AMD) • Visual impairment due to diabetic macular oedema (DME) • Visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO) • Visual impairment due to myopic choroidal neovascularisation (myopic CNV)
Recommended dose	2 mg
Volume to inject	50 microliters or 0.05 mL
Posology for approved indications	Refer to the SmPC for complete information on posology and dosing for **YESAFILI** 40 mg/mL for approved indications

IMPORTANT SAFETY INFORMATION ABOUT YESAFILI®

Contraindications

YESAFILI is contraindicated in the following:

- Hypersensitivity to the active substance aflibercept or to any of the excipients listed in section 6.1 of the Summary of Product Characteristics (SmPC).
- Active or suspected ocular or periocular infection.
- Active severe intraocular inflammation.

Special warnings and precautions for use

Please refer to section 4.4 and 4.6 of the SmPC for full information about special warnings and precautions for **YESAFILI** treatment.

Intravitreal injection-related reactions

Intravitreal injections, including those with aflibercept, have been associated with endophthalmitis, intraocular inflammation, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract.

- **Always use proper aseptic injection techniques** when administering **YESAFILI**.
- **Monitor patients during the week following injection** to permit early treatment if an infection occurs.
- **Instruct patients to immediately report any signs and symptoms** suggestive of endophthalmitis or any of the adverse reactions including those mentioned above.

The pre-filled syringe contains more than the recommended dose of 2 mg (equivalent to 0.05 mL). Expel the excess volume and air bubbles from the syringe, prior to injection.

- Administer the recommended dose and do not inject any residual volume, as increased injection volume can lead to clinically relevant intraocular pressure elevation.

Increase in intraocular pressure

Transient increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including injections with aflibercept.

- **Monitor your patient after the injection procedure** and take special precaution in patients with poorly controlled glaucoma. Do not inject **YESAFILI** while the intraocular pressure is ⩾ 30 mmHg. Both the intraocular pressure and perfusion status of the optic nerve head must be monitored and managed appropriately.
- Refer to the post-injection care section for further instruction.

Immunogenicity

YESAFILI is a therapeutic protein and has potential for immunogenicity.

- **Instruct patients to report any signs or symptoms of intraocular inflammation** (e.g. pain, photophobia or redness), which may be attributable to hypersensitivity.
- Refer to the post-injection care section for further instructions.

Systemic effects

Systemic adverse events including non-ocular haemorrhages and arterial thromboembolic events have been reported following intravitreal injection of VEGF inhibitors, and there is a theoretical risk that these may relate to VEGF inhibition.

- Exercise caution when treating patients with a history of stroke, transient ischaemic attacks or myocardial infarction within the last 6 months as there are limited data on safety of aflibercept in these groups.

Special populations

The following recommendations are made:

- **Women of childbearing potential**

  Women of childbearing potential have to **use effective contraception during treatment** and **for at least 3 months** after the last intravitreal injection of **YESAFILI** 40 mg/mL (2 mg dose).
- **Pregnancy**

  YESAFILI should not be used during pregnancy unless the potential benefit outweighs the potential risk to the foetus.
- **Breast-feeding**

  Based on very limited human data, aflibercept may be excreted in human milk at low levels. Aflibercept is a large protein molecule and the amount of medication absorbed by the infant is expected to be minimal. The effects of aflibercept on a breast-fed newborn/infant is unknown. As a precautionary measure, breast-feeding is not recommended during the use of **YESAFILI**.

Post-injection care

Immediately after intravitreal injection:

- Monitor the patient for elevation in intraocular pressure. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or conducting a tonometry test. Sterile equipment for paracentesis should be readily available if anterior chamber paracentesis needs to be done.
- Instruct the patient to report any signs and symptoms suggestive of endophthalmitis (e.g. eye pain, redness of the eye, photophobia, blurring of vision) without delay.
- Instruct the patient to report any signs or symptoms after the injection that get worse over time.

Adverse drug reactions

Key signs and symptoms of adverse reactions include:

Adverse Drug Reaction	Key Signs and Symptoms
Transient increased intraocular pressure (IOP)	Patients may experience vision changes such as temporary vision loss, eye pain, halos around lights, red eye, nausea and vomiting.
Tear of the retinal pigment epithelium	Patients may experience acute decrease in (central) vision, blind spot (central scotoma), and distorted vision with deviation of either vertical or horizontal lines (metamorphopsia).
Tear or detachment of the retina	Patients may experience sudden flashes of light, a sudden appearance or an increase of the number of vitreous floaters, a curtain over a portion of their visual field and vision changes.
Intraocular inflammation including endophthalmitis	Patients may experience eye pain or increased discomfort, worsening eye redness, photophobia or sensitivity to light, swelling, and vision changes, such as a sudden decrease in vision or blurring of vision.
Cataract (traumatic, nuclear, subcapsular, cortical) or lenticular opacities	Patients may experience less vivid lines and shapes, shadows and colour vision than before, and vision changes.

See section 4.8 of the SmPC for full list of potential adverse reactions, and their frequency categories.

Management of adverse reactions

In case of any adverse reactions that concern your patient, he or she must have immediate access to an ophthalmologist.

Appropriate management of ALL adverse reactions, including those associated with the intravitreal injection, should be carried out according to clinical practice and/or following standardized guidelines.

It is important to advise your patients to inform their doctor, pharmacist or nurse if they experience any side effects. This includes any possible side effects not listed in the Package Leaflet.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: *https://sideeffects.health.gov.il*

Additionally, adverse events can be reported to Dexcel Ltd. via email at the following address: *customerservice@dexcel.com*

STORAGE AND HANDLING OF YESAFILI®

- The **YESAFILI** solution is clear, colourless to pale yellow. It is an iso-osmotic solution.
- **Inspect the solution visually before use, for any foreign particulate matter and/or discolouration or any variation in physical appearance. If any of these are observed, do not use the product.**
- **Do not split a pre-filled syringe into more than one dose.**

  Each pre-filled syringe is for single use in one eye only.

  Extraction of multiple doses from a single pre-filled syringe may increase the risk of contamination and subsequent infection in the patient.
- Each **YESAFILI** solution for injection in pre-filled syringe contains more than the recommended 0.05 mL dose of aflibercept.

  The excess volume and any air bubbles in the syringe must be expelled before injecting the patient with the recommended dose.

Special precautions for storage

	Store **YESAFILI** in the refrigerator (2°C to 8°C). Do not freeze.
	Store in the original package in order to protect from light.
	Prior to use, the unopened blister may be stored outside the refrigerator below 25°C for up to 72 hours.
	The inside of the sealed pre-filled syringe blister packaging of **YESAFILI** is sterile. Do not open the pre-filled syringe blister outside the clean administration room. **After opening the blister, proceed under aseptic conditions.**

INSTRUCTIONS FOR USE OF YESAFILI® PRE-FILLED SYRINGE

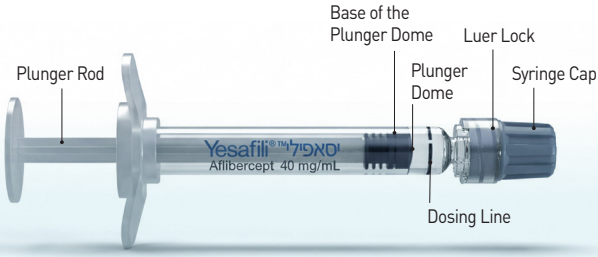
General preparation for injection

- Intravitreal injections must be carried out according to medical standards and applicable guidelines by **a qualified physician, experienced in administering intravitreal injections and familiar with the handling** of the pre-filled syringe.
- Surgical hand disinfection, sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent) are recommended.
- For the intravitreal injection, a **30 G x ½ inch injection needle** should be used. Use of a smaller size injection needle (higher gauge) than the 30 G x ½ inch needle may result in increased injection forces.

NOTE: Become familiarized with how to use this syringe before using it on patients.

The **YESAFILI** 40 mg/mL pre-filled syringe is a glass syringe with a rubber plunger that requires slightly more force to depress compared with plastic syringes.

The pre-filled syringe and contents must be inspected before use. Do not use the pre-filled syringe if any part is damaged or loose. Do not use it if the syringe cap is detached from the Luer-lock. Look for any particulate matter and/or unusual colour or any variation in physical appearance. If any of these are observed, do not use the product.



1

Prepare the pre-filled syringe for administration

It is important to prepare the pre-filled syringe using aseptic technique.

An assistant should carry out the following steps:

Remove the carton containing the pre-filled syringe from the refrigerator. Open the carton and remove the blister containing the syringe. The blister must not be placed on a sterile surface because the outside surface of the blister is not sterile. The inside of the sealed blister and the pre-filled syringe are sterile. Carefully peel open the blister.
Aseptic technique must be used once the blister is opened.

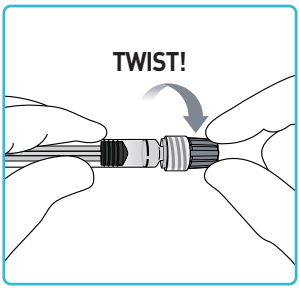
The qualified physician carries out the remainder of the steps with sterile technique including the use of sterile gloves (white gloves in pictures) when handling:

With two fingers, remove the pre-filled syringe from the blister. Visually inspect the syringe. Place the syringe in a sterile tray until ready for assembly.

2

Remove the syringe cap

Hold the syringe in one hand while using the other hand to grasp the syringe cap with the thumb and fore finger.
Twist off – do not snap off – the syringe cap.



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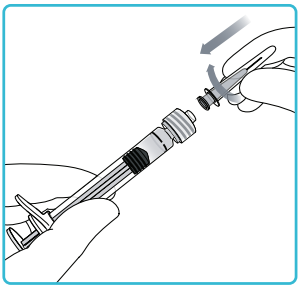
Do not pull back the plunger. This may compromise the sterility of the product.

4

Attach the needle

Using aseptic technique, **firmly twist the 30 G x ½ inch injection needle onto the Luer-lock syringe tip.**



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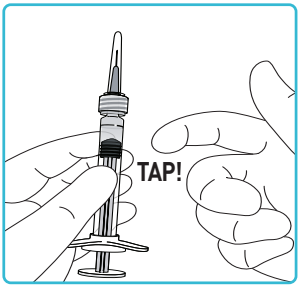
Check for bubbles

Holding the syringe with the needle pointing up, **check the syringe for bubbles. If there are bubbles, gently tap the syringe with your finger until the bubbles rise to the top.**



6

Eliminate air bubbles and excess drug

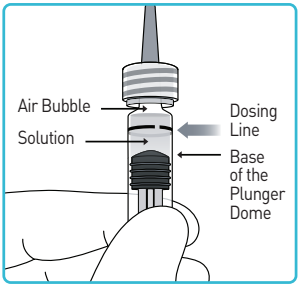
Correct handling of the pre-filled syringe is important in order to avoid the risk of medication errors. This includes removal of the excess volume (to avoid overdosing) and air bubbles.

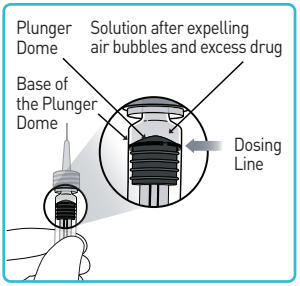
Remove the air bubbles and excess drug from the syringe by slowly depressing the plunger rod to align the base of the plunger dome (not the tip of the dome) with the dosing line on the syringe (equivalent to 0.05 mL i.e. 2 mg aflibercept). Remember that the feel with this syringe is different from disposable syringes.

The remaining volume after aligning to the dosing line ensures appropriate dosing.

Accurate positioning of the plunger is critical.

Incorrect plunger positioning can lead to overdosing or underdosing.





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*Inject **YESAFILI***

- Inject the solution into the eye carefully with constant pressure on the plunger.
- Do not apply additional pressure once the plunger has reached the bottom of the syringe.
- Do not administer any residual solution observed in the syringe.

8

*The pre-filled syringe is for **SINGLE USE IN ONE EYE ONLY***

- Extraction of multiple doses from a pre-filled syringe may increase the risk of contamination and subsequent infection.
- Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Injection procedure

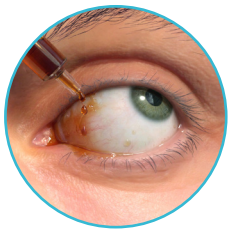
For further information on intravitreal injection procedure, sterile techniques (including periocular and ocular disinfection) and anaesthesia, please refer to local and/or national clinical guidelines.

1

Administer topical anaesthesia.

2

Apply disinfectant (e.g. 5% povidone iodine solution or equivalent) to the eyelids, eyelid margins and into the conjunctival sac. The disinfectant should be on the surface for the length of time recommended in local practice guidelines.



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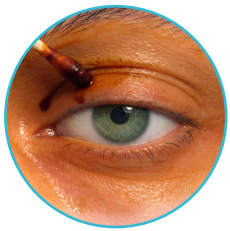
A disinfectant (e.g. 10% povidone iodine solution or equivalent) should also be applied to periocular skin, eyelids and eyelashes, avoiding excessive pressure to the periocular glands. The disinfectant should be on the surface for the length of time recommended in local practice guidelines.

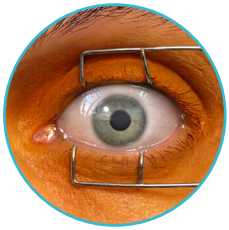


4

Cover with sterile drape and insert sterile lid speculum.

A second application of disinfectant, e.g., 5% povidone iodine solution, may be made to the conjunctival sac.

Disinfectant should be on the surface for the length of time recommended in local practice guidelines.



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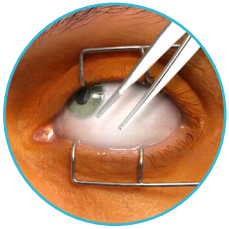
Tell the patient to look away from the injection site.

Position the eye adequately. At an area of 3.5 to 4.0 mm posterior to the limbus, mark an injection site.



6

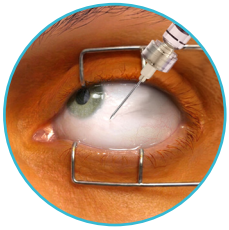
Insert the injection needle into the vitreous cavity, avoiding the horizontal meridian and aiming towards the centre of the globe.

The injection volume of 0.05 mL of **YESAFILI** 40 mg/mL is then delivered, with careful and constant pressure on the plunger.

Do not apply additional pressure once the plunger has reached the bottom of the syringe.

Do not inject any residual volume remaining in the syringe after the injection.

Use a different scleral site for subsequent injections.



ADDITIONAL INFORMATION

For more information, please refer to the SmPC.

Additional information about **YESAFILI**, including the **YESAFILI** Prescriber Video, is also available in the following QR code:

This Prescriber Guide was approved according to MOH guidelines in July 2026.