HEALTHCARE
CELLTRION

Recommendations for treatment with

Eydenzelt® ▼ 40 mg/mL

solution for injection

aflibercept

Prescriber Guide

This Guide provides important information on EYDENZELT® 40mg/mL solution for injection (2 mg aflibercept dose), the medication itself, and how to correctly administer it to your patients.
Please provide the adult patient with the EYDENZELT Patient Information Leaflet. In addition, please also provide the adult patient with the EYDENZELT Patient Guide, including its audio version (read out of the patient guide). The above information is available on www.medicines.ie

This Guide is additional risk minimisation material and is provided by Celltrion Healthcare as a condition of the product's marketing authorisation. For further information and additional details on EYDENZELT, please see the Summary of Product Characteristics (SmPC) on www.medicines.ie

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events to HPRA Pharmacovigilance via www.hpra.ie. You should also report side effects to Celltrion by emailing medinfoie@celltrionhc.com or calling (01) 564 5074.

INTRAVITREAL INJECTION PROCEDURE VIDEO

PLEASE SCAN:

OR VISIT:
www.medicines.ie
(under the Educational Materials – HCP tab)

Contents

KEY SUMMARY FOR EYDENZELT USE IN ADULTS

Contraindications

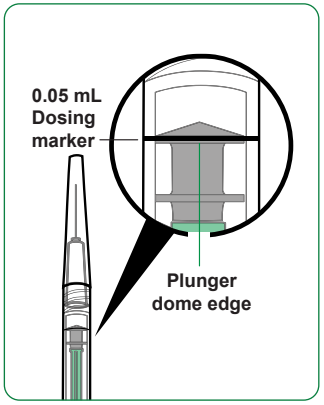
- Hypersensitivity to aflibercept or to any of the excipients listed in section 6.1 of the Summary of Product Characteristics (SmPC)
- Active or suspected ocular or periocular infection
- Active severe intraocular inflammation

Key instructions for use in adults

- Each vial/pre-filled syringe is for single use only.
- The vials and the pre-filled syringes come with excess volume. Before injecting, syringes with solution withdrawn from the vial and the pre-filled syringes must be primed to the correct volume for injection according to the steps in the instructions for use.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 broad-spectrum microbicide to minimise the 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 30G x ½ inch needle may result in increased injection forces.

EYDENZELT 40 mg/mL pre-filled syringe (2 mg dose):

- Expel excess volume and air bubbles from the pre-filled syringe and adjust the base of the plunger dome (NOT the tip) to the dose 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

- **Store EYDENZELT in the refrigerator** (2°C to 8°C)
- **Prior to use, the unopened 40 mg/ml vial may be stored outside the refrigerator, below 25°C, for up to 31 days in the original package.**
- **Prior to use, the unopened 40 mg/ml pre-filled syringe blister may be stored outside the refrigerator, below 25°C, for up to 7 days. If necessary, the unopened blister may be returned to the refrigerator for later use until the end of shelf-life. If the product is exposed to temperatures above 25 °C, do not use.**
- EYDENZELT is **not licensed for multi-dose**, further compounding or vial splitting. Use of more than one injection from the vial or the pre-filled syringe **can lead to contamination and subsequent infection.**

GENERAL INFORMATION FOR ADULT PATIENTS

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 adult patient about the disease and treatment. This guide is available upon request to Celltrion, and you should distribute it to your adult patients. It is available as a booklet and as an audio guide option for your adult patients. It contains information on the signs and symptoms of adverse reactions and when they should seek medical attention.

To order additional copies of the EYDENZELT patient guide and/or the prescriber guide, please contact Celltrion Healthcare Ireland Ltd at Enquiry_IE@celltrionhc.com or (01) 223 4026.

The patient guide and its audio version are also available on www.medicines.ie. Please bring this to the patient's attention, for ease of access.

IMPORTANT SAFETY INFORMATION

Special warnings and precautions for use

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 intravitreal injections
- **Monitor patients following injections as per local practice** to permit early treatment if an infection occurs
- **Instruct adult patients to immediately report any signs and symptoms** suggestive of endophthalmitis or any of the adverse reactions mentioned below
- Refer to the post injection care section for further instructions

Increase in intraocular pressure

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

- **Monitor the adult patient after the injection procedure** and take special precaution in patients with poorly controlled glaucoma. Do not inject aflibercept 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 instructions

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

Adverse event/ risk	Measures to minimise risk
Intraocular inflammation including endophthalmitis	Use proper aseptic technique when preparing the injection and during the injection itself. Use recommended antiseptic agents. Monitor patient after the injection
Transient intraocular pressure (IOP) increase	Properly prime the syringe by removing excess volume and air bubbles from the 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 aflibercept
Retinal pigment epithelial (RPE) tear	Review PED* features for risk of RPE 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-foetotoxicity	Instruct women of childbearing potential to use effective contraception during treatment and for at least **3 months** after last intravitreal injection of aflibercept (2 mg dose). Aflibercept should not be used during pregnancy unless the potential benefit outweighs the potential risk to the foetus
Exposure during breast-feeding	Aflibercept is not recommended in patients who are breast-feeding

* pigment epithelial detachment

Adverse drug reactions

See section 4.8 of the EYDENZELT SmPC for the full list of potential adverse reactions and their frequency categories.
Key signs and symptoms of intravitreal injection-related adverse reactions in adult patients include:

Adverse Drug Reaction	Key signs and symptoms
Transient increased intraocular pressure	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 in 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

Post-Injection Care

Immediately after intravitreal injection :

- Evaluate the patient's vision (hand movement or finger counting).
- 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.

Management of adverse reactions

In case of any adverse reactions that concern your patient, they 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 standardised guidelines.

Healthcare Professionals are asked to report any suspected adverse reactions to HPRA Pharmacovigilance via www.hpra.ie.
You should also report adverse reactions to Celltrion via medinfoie@celltrionhc.com.

Risk of medication error

EYDENZELT 40 mg/mL solution for injection (2 mg dose) is available in a pre-filled syringe or vial. The pre-filled syringe and vial contain more than the adult recommended dose of 2 mg aflibercept (equivalent to 0.05 mL).

Expel the excess volume, to avoid overdosing, and air bubbles from the syringe prior to injection.

Pregnancy and breast-feeding

The following recommendations are made:

• Women of childbearing potential

Use effective contraception during treatment and for at least 3 months after the last intravitreal injection of aflibercept 40 mg/ml (2 mg dose).

• Pregnancy

There are no data on the use of aflibercept in pregnant women. Studies in animals have shown embryo-foetal toxicity. **Aflibercept 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 aflibercept.

STORAGE AND HANDLING OF EYDENZELT

The EYDENZELT 40 mg/mL (2 mg dose) solution is clear to slightly opalescent, and colourless to very pale brownish-yellow, iso-osmotic solution.

Inspect the solution visually before use for any foreign particulate matter and/or unusual colour (the solution can be pale yellow, which is normal) **or any variation in physical appearance. If any of these are observed, do not use the product.**

Inspect the pre-filled syringe. If any part is damaged or loose, or if the syringe cap is detached from the Luer Lock, do not use.

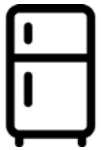
Do not split a vial/pre-filled syringe into more than one dose. Each vial/pre-filled syringe is for single use in one eye only. Extraction of multiple doses from a single vial/pre-filled syringe may increase the risk of contamination and subsequent infection in the patient.

EYDENZELT 40 mg/mL pre-filled syringe and vial for use in adults:

Each 40 mg/mL solution for injection in a pre-filled syringe (2 mg dose) **contains more than the recommended 0.05 mL dose of aflibercept.**
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 from the syringe, prior to injection.

Each 40 mg/mL solution for injection in a vial (2 mg dose) **contains more than the recommended 0.05 mL dose of aflibercept.**
Correct handling of the 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 from the disposable syringe, prior to injection.

Special precautions for storage of the EYDENZELT vial and pre-filled syringe

	• Store the pre-filled syringe in the sealed blister in the outer carton in a refrigerator (2–8°C). • Store the vial in the outer carton in a refrigerator (2–8°C).
	• Prior to use, the unopened pre-filled syringe blisters may be stored outside the refrigerator, below 25°C, for up to 7 days. If necessary, the unopened blister may be returned to the refrigerator for later use until the end of shelf-life. • Prior to use, the unopened vials may be stored outside the refrigerator, below 25°C, for up to 31 days.
	• Do not freeze.
	• Keep the pre-filled syringe in its blister and in the outer carton in order to protect it from light. • Keep the vial in the outer carton in order to protect from light.

The inside of the sealed pre-filled syringe blister packaging, and the pre-filled syringe itself are sterile. Do not open the pre-filled syringe blister outside the clean administration room.

After opening the blister or vial, proceed under aseptic conditions.

INSTRUCTIONS FOR USE IN ADULTS

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 vial/pre-filled syringe.
- Surgical hand disinfection, aseptic gloves, a sterile drape and a sterilised 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 30G x ½ inch needle may result in increased injection forces.

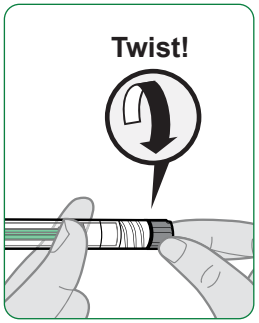
Pre-filled syringe 40 mg/mL (2 mg dose), solution for injection (for use in adults)

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 or if the expiration date has passed. 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 an aseptic 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 aseptic gloves 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.

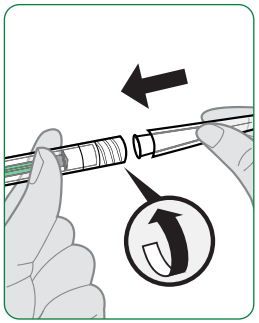
2 **Twist off the syringe cap**

Twist off the syringe cap by holding the pre-filled syringe in one hand and the syringe cap with the thumb and forefinger of the other hand. **Twist off – do not snap off – the syringe cap. Do not pull back on the plunger rod**, to avoid compromising the sterility of the drug product.



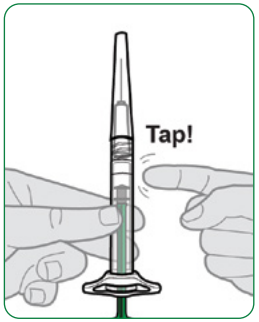
3 **Attach the needle to the pre-filled syringe**

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



4 **Check for air bubbles**

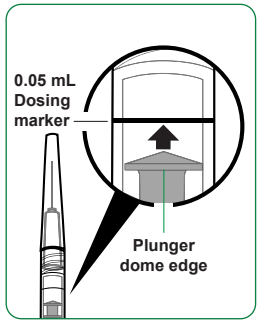
Hold the pre-filled syringe with the needle pointing up and **check the pre-filled syringe for bubbles. If there are bubbles, gently tap the pre-filled syringe with your finger until the bubbles rise to the top.**

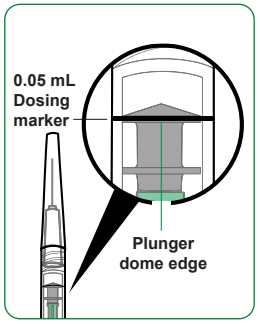


5 **Remove air bubbles and set the dose**

To remove **all bubbles and expel excess drug, SLOWLY depress the plunger rod to align the plunger dome edge (not the tip of the dome) with the dosing marker shown on the barrel of the pre-filled syringe (equivalent to 0.05 mL, i.e. 2 mg aflibercept).**

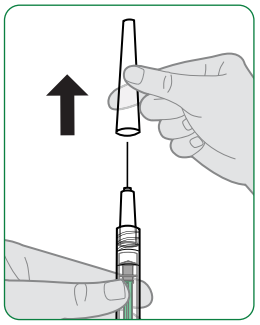
Note: This accurate positioning of the plunger is very important because incorrect plunger positioning can lead to delivering more or less than the labelled dose.





6 **Remove the needle shield**

When ready to administer the medicine, remove the plastic needle shield from the needle.



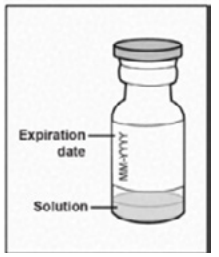
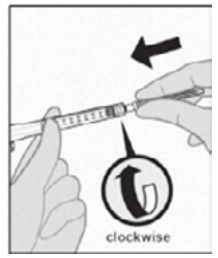
7 **When ready, complete the intravitreal injection**

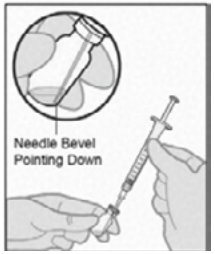
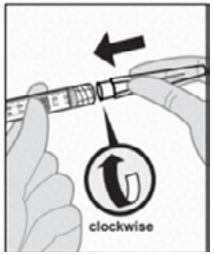
The intravitreal injection procedure should be carried out under controlled aseptic conditions, which include surgical hand disinfection and the use of sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent). Adequate anaesthesia and a topical broad–spectrum microbicide should be given prior to the injection.

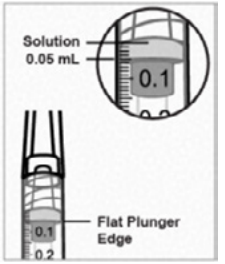
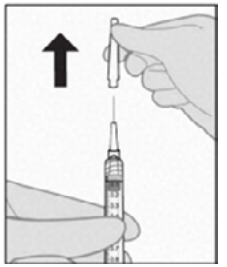
Each sterile, pre-filled syringe should only be used for the treatment of a single eye. If the contralateral eye requires treatment, a new sterile, pre-filled syringe should be used and the sterile field, syringe, gloves, drapes, eyelid speculum, filter, and injection needles should be changed before aflibercept is administered to the other eye.

	Inject by pressing the plunger rod carefully and with constant pressure. • **Do not** apply additional pressure once the plunger rod has reached the bottom of the syringe. A small residual volume may remain in the syringe after a full dose has been injected. This is normal. • **Do not** administer any residual solution observed in the syringe.
8	**The pre-filled syringe is for single use 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.
9	**After the injection, monitor the patient.** Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry. If required, a sterile paracentesis needle should be available. Following intravitreal injection, patients and/ or caregivers should be instructed to report any signs and/or symptoms suggestive of endophthalmitis or retinal detachment (e.g., eye pain, redness of the eye, photophobia, blurring of vision) without delay.

Vial 40mg/mL (2 mg dose) solution for injection (for use in adults)

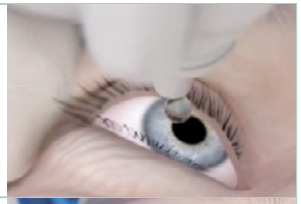
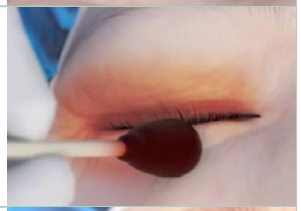
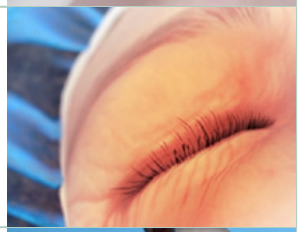
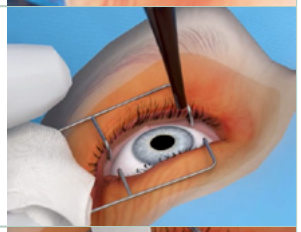
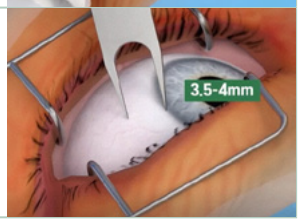
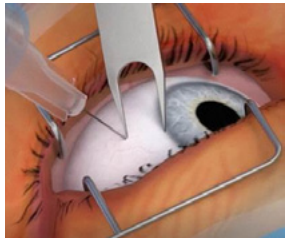
1	**Inspect vial** Look at the vial and make sure you have the correct medicine and dosage. Check the expiration date on the label to make sure it has not passed. • Do not use if particulates, cloudiness, or discoloration are visible in the solution. • Do not use if the expiration date has passed.	
2	**Remove the protective plastic cap from the vial**	
3	**Disinfect the outer part of the rubber stopper of the vial with an alcohol wipe**	
4	**Attach the filter needle to the syringe.** Remove the 18 G × 1 ½-inch, 5-micron filter needle, supplied in the carton, and a 1 mL Luer lock syringe, not included in the carton, from their packaging. Attach the filter needle to the syringe by twisting it onto the Luer lock syringe tip.	

5	**Insert the filter needle into the vial** Using aseptic technique, push the filter needle into the centre of the vial stopper until the needle is completely inserted into the vial, and the tip touches the bottom or bottom edge of the vial. Tilt the vial during withdrawal, keeping the bevel of the filter needle submerged in the liquid to deter the introduction of air. Withdraw all of the vial contents into the syringe. Note: Ensure that the plunger rod is drawn sufficiently back when emptying the vial in order to completely empty the filter needle. 
6	**Remove the filter needle** Remove the filter needle from the syringe. Properly dispose the filter needle. • **Do not** use the filter needle for intravitreal injection. • **Do not** recap the filter needle to prevent pre-injection needle sticks.
7	**Attach the injection needle to the syringe (to be done immediately after withdrawal of the vial content)** Remove the 30 G × ½-inch injection needle, not included in the carton, from its packaging. Using aseptic technique, attach the injection needle to the syringe by firmly twisting the injection needle onto the Luer lock syringe tip. 
8	**Check for air bubbles** Holding the syringe with the injection 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. 

9	**Remove air bubbles and confirm correct dose** To remove all of the bubbles and to **expel excess drug, SLOWLY depress the plunger** so that the plunger edge aligns with the line that marks 0.05 mL on the syringe. 
10	**When ready to administer the medicine, remove the plastic needle cap from the needle** 
11	**When ready, complete the intravitreal injection** The intravitreal injection procedure should be carried out under controlled aseptic conditions, which include surgical hand disinfection and the use of sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent). Adequate anaesthesia and a topical broad–spectrum microbicide should be given prior to the injection. Each vial should only be used for the treatment of a single eye. If the contralateral eye requires treatment, a new vial should be used and the sterile field, syringe, gloves, drapes, eyelid speculum, filter, and injection needles should be changed before aflibercept is administered to the other eye.
12	**The vial is for single-use only** Any unused medicinal product or waste material should be disposed of in accordance with local requirements. Extraction of multiple doses from a single vial may increase the risk of contamination and subsequent infection.
13	**After the injection, monitor the patient** Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry. If required, a sterile paracentesis needle should be available. Following intravitreal injection, patients and/or caregivers should be instructed to report any signs and/or symptoms suggestive of endophthalmitis or retinal detachment (e.g., eye pain, redness of the eye, photophobia, blurring of vision) without delay.

Injection Procedure for Adults

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. Eye dilation prior to the injection procedure is **not** necessary.	
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 at least 30 seconds.[1]	
3	A disinfectant (e.g. 10% povidone iodine solution or equivalent) should also be applied to the periocular skin, eyelids and eyelashes, avoiding extensive pressure to the periocular glands. The disinfectant should be on the surface for at least 30 seconds.[1]	
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 at least 30 seconds.[1]	
5	Tell patient to look away from the injection site. Position the eye adequately. At an area of 3.5–4.0 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. Inject the recommended dose, 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.	

[1] Grzybowski, A *et al.* 2018 Update on intravitreal injections: EURETINA expert consensus recommendations. Ophthalmologica. 2018;239 (4): 181-193.

LOCAL SAFETY INFORMATION

Reporting of suspected adverse reactions

Reporting suspected adverse events or reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Healthcare professionals are asked to report any suspected adverse reactions to HPRA Pharmacovigilance via www.hpra.ie.
Adverse reactions or quality complaints should also be reported to Celltrion Healthcare Ireland on (01) 564 5074 or by email: medinfoie@celltrionhc.com.

Where possible, healthcare professionals should report adverse events or reactions by brand name and batch number.

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IE-EYD-PV-1225-01 December 2025, ver 1.0
HPRA Approved: December 2025