A brief guide to the management of risks associated with intravitreal injections during LUCENTIS® (ranibizumab) treatment
Introduction

This physician leaflet is part of the educational materials regarding the use of ranibizumab and provides information on the method of administration of ranibizumab and on the prevention and management of key injection-related risks associated with intravitreal injections.

Treatment with ranibizumab

Background

- Ranibizumab is a fully humanized monoclonal antibody fragment specifically designed for intravitreal use that binds and inhibits multiple isoforms of biologically active vascular endothelial growth factor A (VEGF-A).1

Indications

Ranibizumab is indicated for the treatment of adults with:1

- Neovascular age-related macular degeneration (AMD)
- Visual impairment due to diabetic macular edema (DME)
- Visual impairment due to macular edema secondary to retinal vein occlusion (branch RVO or central RVO)
- Visual impairment due to choroidal neovascularization (CNV) secondary to pathologic myopia (PM)

Please refer to SPC for further information.
Prevention and management of key injection-related risks associated with ranibizumab intravitreal injection

Intravitreal injections, including those with ranibizumab, have been associated with endophthalmitis, iatrogenic traumatic cataract, intraocular pressure (IOP) increase (see more details below), as well as intraocular inflammation, rhegmatogenous retinal detachment or retinal tear. Proper aseptic injection techniques must always be used when administering ranibizumab. In addition, patients should be monitored during the week following the injection to permit early treatment if an infection occurs. Patients should be instructed to report any symptoms suggestive of endophthalmitis or any of the above mentioned events without delay.

Although this leaflet focusses on key ocular risks, there is a potential risk of arterial thromboembolic events following intravitreal use of VEGF inhibitors. The difference in stroke rates may be greater in patients with known risk factors for stroke, including history of prior stroke or transient ischemic attack. These patients should be carefully evaluated as to whether ranibizumab treatment is appropriate.

Endophthalmitis

Characteristics

- Endophthalmitis is a serious ocular condition consisting of inflammation of the vitreous cavity, and can potentially lead to blindness
- Endophthalmitis is often caused by an intraocular infection
  - Frequently implicated pathogens include skin bacteria such as coagulase-negative staphylococci, Staphylococcus aureus and streptococci
- Streptococcus viridans (a commensal organism of the throat) has been isolated over three times more frequently in cases of endophthalmitis occurring after intravitreal injection than after intraocular surgery
- Events such as penetrating trauma, surgical procedures and intravitreal injections that disrupt the integrity of the eye globe can potentially lead to endophthalmitis
- Endophthalmitis following ranibizumab injection is uncommon; the reported incidence in ranibizumab clinical trials ranges from ≥ 1/1,000 to <1/100 patients across all indications

Prevention and management

- Ranibizumab should be prepared for intravitreal injection and administered according to the steps outlined in the prescribing information, summarized on pages 8, 9 and 10 of this leaflet
- It is essential to perform the injection procedure under aseptic conditions to prevent contamination of the eye
- The use of surgical hand disinfection, sterile gloves, a sterile drape and a sterile eyelid speculum (or equivalent), and the availability of sterile paracentesis (if required) is recommended
- Patients should be instructed to report any symptoms suggestive of endophthalmitis without delay
- Appropriate management and treatment of endophthalmitis should be followed according to local clinical practice

Iatrogenic traumatic cataract

Characteristics

Iatrogenic traumatic cataract can be caused by trauma to the intraocular lens following either penetrating or non-penetrating ocular trauma
Cataract may lead to loss of vision, and may require surgical intervention

Prevention and management

- To reduce the risk of iatrogenic traumatic cataract, ranibizumab should be prepared for intravitreal injection and administered according to the steps outlined in the prescribing information, summarized on pages 8, 9 and 10 of this leaflet
- Care should be taken to ensure the injection is inserted 3.5-4.0 mm posterior to the limbus into the vitreous cavity, avoiding the horizontal meridian and aiming towards the center of the globe
- Patients should be instructed to report any symptoms suggestive of iatrogenic traumatic cataract without delay
- Appropriate management and treatment of iatrogenic traumatic cataract should be followed according to local clinical practice

Increases in intraocular pressure

Characteristics

- Transient increases in IOP within 60 minutes of injection of ranibizumab are very common; the reported incidence is ≥1/10 patients in ranibizumab clinical trials across all indications
- Increases in IOP are caused by injection of fluid into the eye and are more likely if high volumes are administered
- Post-injection increases in IOP are often asymptomatic and usually resolve quickly (are transient)
Prevention and management

- Ranibizumab should be administered as a single intravitreal injection with an injection volume of 0.05 mL.
  > Injection volume should be accurately checked to minimize the risk of increases in IOP.
  > If an overdose occurs, IOP should be monitored and treated, if deemed necessary by the attending physician.
- IOP and perfusion of the optic nerve head must be monitored and managed appropriately.
  > The treatment of increases in IOP should follow local clinical practice.
  > Paracentesis should only be carried out in cases in which the degree of increase in IOP poses a threat to vision.

Overdose due to overfill of the pre-filled syringe

Characteristics

The pre-filled syringe contains more ranibizumab solution than is required for a single dose.

The extra volume is present to aid priming the needle and syringe in preparation for the injection.

Prevention and management

- The instructions for use in the Core Data Sheet should be closely followed to ensure accurate setting of the dose in the syringe.
- If an overdose occurs, IOP should be monitored and treated, if deemed necessary by the physician.
- IOP and perfusion of the optic nerve head must be monitored and managed appropriately.
  > Paracentesis should only be carried out in cases in which the degree of increase in IOP poses a threat to vision.

Administration of ranibizumab

- Ranibizumab is available as a vial kit, vial with filter needle, vial or pre-filled syringe.
- Ranibizumab should be inspected visually for particulate matter and discoloration prior to administration.
- Both the vial and the pre-filled syringe are for single use only. Ranibizumab is not licensed for multi-dose, further compounding or vial splitting. Use of more than one injection from the vial may lead to contamination and subsequent infection.
- The injection procedure should be carried out under aseptic conditions:
  > The use of surgical hand disinfection, sterile gloves, a sterile drape and sterile eyelid speculum (or equivalent) is recommended.
  > The periocular skin, eyelid and ocular surface should be disinfected.
- Adequate anesthesia and a broad-spectrum topical microbicide should be administered prior to the injection.
- Prophylactic topical antibiotics should be used according to local clinical practice.
- The patient’s medical history should be carefully evaluated for hypersensitivity reactions prior to performing the intravitreal procedure.

References

Preparation of ranibizumab for intravitreal injection using the pre-filled syringe

To prepare the ranibizumab pre-filled syringe for intravitreal administration, please adhere to the following instructions for use:

1. Make sure that your pack contains a sterile pre-filled syringe in a sealed tray.
2. Peel the lid off the syringe tray and, using aseptic technique, carefully remove the syringe.
3. Check that:
   - The syringe cap is not detached from the Luer Lock
   - The syringe is not damaged
   - The solution looks clear, colorless to pale yellow and does not contain any particulates.
4. If any of the above is not true, discard the pre-filled syringe (Figure 1) and use a new one.
5. Snap off (do not turn or twist) the syringe cap (Figure 2).
6. Dispose of the syringe cap (Figure 3).
7. Attach a 30-gauge x ½-inch sterile injection needle firmly onto the syringe by screwing it tightly onto the Luer lock (Figure 4).
8. Carefully remove the needle cap by pulling it straight off (Figure 5).
   - Note: do not wipe the needle at any time.
9. Hold the syringe upright.
10. If there are any air bubbles, gently tap the syringe with your finger until the bubbles rise to the top (Figure 6).
11. Hold the syringe at eye level and carefully push the plunger until the mark on the syringe (Figure 7). This will expel the air and the excess solution and set the dose to 0.05 mL.
   - Note: the plunger rod is not attached to the rubber stopper this is to prevent air being drawn into the syringe.

The injection procedure should be carried out under aseptic conditions.

12. The injection needle should be inserted 3.5-4.0 mm posterior to the limbus into the vitreous cavity, avoiding the horizontal meridian and aiming towards the center of the globe.
13. Inject slowly until the rubber stopper reaches the bottom of the syringe to deliver the volume of 0.05 mL.
14. A different scleral site should be used for subsequent injections.
15. After injection, do not recap the needle or detach it from the syringe.

Dispose of the used syringe together with the needle in a sharps disposal container or in accordance with local requirements.

Preparation of ranibizumab for intravitreal injection using the vial

To prepare the vial for intravitreal administration, please adhere to the following instructions:

1. Before withdrawal, the outer part of the rubber stopper of the vial should be disinfected.
2. Assemble the 5 μm filter needle (18-gauge) onto the 1 mL syringe using aseptic technique. Push the blunt filter needle into the center of the vial stopper until the needle touches the bottom edge of the vial.
3. Withdraw all the liquid from the vial, keeping the vial in an upright position, slightly inclined to ease complete withdrawal (Figure 1).
4. Ensure that the plunger rod is drawn sufficiently back when emptying the vial in order to completely empty the filter needle.
5. Leave the blunt filter needle in the vial and disconnect the syringe from the blunt filter needle. The filter needle should be discarded after withdrawal of the vial contents and should not be used for the intravitreal injection (Figure 2).
6. Aseptically and firmly assemble the injection needle (30-gauge x ½-inch) onto the syringe.
7. Carefully remove the cap from the injection needle without disconnecting the blunt filter needle. The filter needle should be discarded after withdrawal of the vial contents and should not be used for the intravitreal injection (Figure 3).
8. Carefully expel the air from the syringe and adjust the dose to the 0.05 mL mark on the syringe (Figure 4). The syringe is ready for injection.
   - Note: grip at the yellow hub of the injection needle while removing the cap.

The injection needle should be inserted 3.5-4.0 mm posterior to the limbus into the vitreous cavity, avoiding the horizontal meridian and aiming towards the center of the globe. The injection volume of 0.05 mL is then delivered; a different scleral site should be used for subsequent injections.

After injection, do not recap the needle or detach it from the syringe. Dispose of the used syringe together with the needle in a sharps disposal container or in accordance with local requirements.
Preparation of the eye and administration of ranibizumab

**Preparation**

1. Dilate the pupil.
2. Apply topical anesthesia.
3. Apply 10% povidone iodine solution to periciliar skin, lids and eyelashes, and place sterile drape over eye.
4. Apply sterile eyelid speculum.
5. Instill 5% povidone iodine ophthalmic solution and wait for 90 seconds.
6. Rinse the eye with ophthalmic saline solution.
7. Direct the patient to look away from the injection site. Mark an injection site at an area 3.5 mm to 4.0 mm posterior to the limbus, avoiding the horizontal meridian.
8. The injection needle should be inserted aiming toward the center of the globe. Slowly deliver the injection volume, then remove the needle slowly. - A different scleral site should be used for subsequent intravitreal injections so that the same site is not injected repeatedly.

**Note:** prophylactic topical antibiotics should be used according to local clinical practice.
You can report any problem or adverse events through:

**Novartis Consulting AG.**

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you can report any problem through
Toll free phone: 8002490000
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Or by online: https://ade.sfda.gov.sa