

LUCENTIS®* (ranibizumab) intravitreal injection guidelines¹

*Please refer to the approved LUCENTIS® prescribing information.

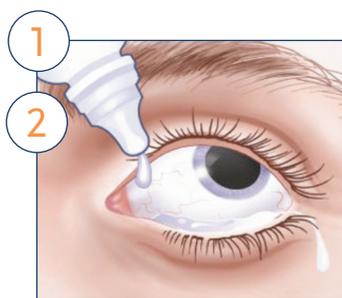
Aseptic technique should be observed during tray assembly, anesthetic preparation, drug preparation and administration. Ranibizumab must be administered by a qualified ophthalmologist experienced in administering intravitreal injections. In addition to the procedures outlined below, intravitreal injection guidelines of your specific clinic should be followed.

Injection supplies

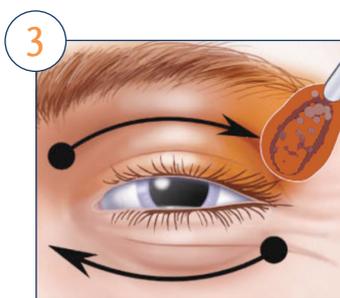
Before starting, aseptically assemble the following supplies:

- Sterile surgical gloves
- 4 x 4 sterile pads
- Pupillary dilation agent
- Povidone iodine solution 10%
- Povidone iodine eye drops 5%
- Sterile eyelid speculum
- Sterile ophthalmic drape
- Sterile caliper

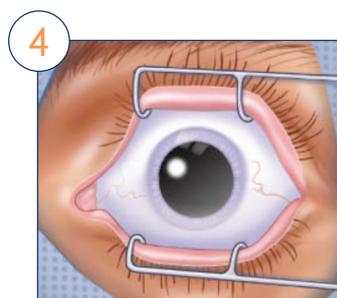
Injection procedures



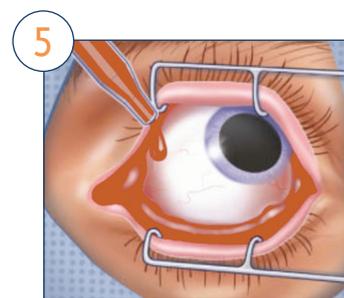
1. Dilate the pupil.
2. Apply topical anesthesia.



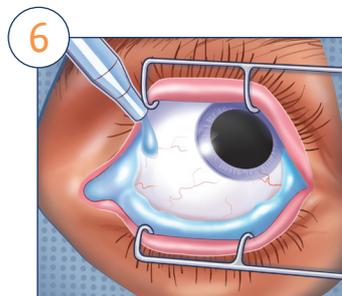
3. Apply 10% povidone iodine solution to periocular skin, lids, and eyelashes, and place sterile drape over eye.



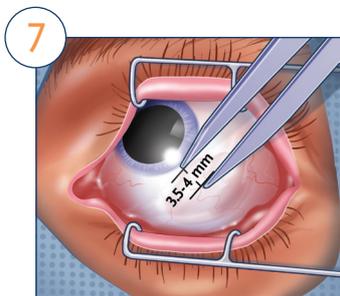
4. Apply sterile lid speculum.



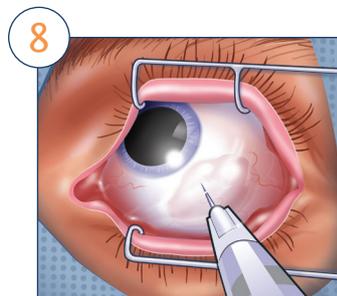
5. Instill 5% povidone iodine ophthalmic solution, and wait for 90 seconds.



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.
 - Rotate the scleral site 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

Post-injection procedures

- 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
- Evaluate light perception, indirect ophthalmoscope findings, and intraocular pressure immediately post-injection
- Instruct patient to report immediately any signs of inflammation or infection, such as eye pain or discomfort, worsening eye redness, sensitivity to light, vitreous floaters, or vision changes
- Monitor patients during the week following the injection to permit early treatment if an infection occurs

Reference: 1. Aiello LP, et al. Retina 2004;24:53-19.

Lucentis® 10mg/ml pre-filled syringe

PRESENTATION: 10mg/ml solution for injection in pre-filled syringe. Each vial contains 2.3 mg of ranibizumab in 0.23 ml solution.

INDICATIONS: The treatment of 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) and visual impairment due to choroidal neovascularisation (CNV) secondary to pathologic myopia (PM)

DOSAGE: Lucentis must be administered by a qualified ophthalmologist experienced in intravitreal injections. The recommended dose for Lucentis is 0.5 mg given as a single intravitreal injection. This corresponds to an injection volume of 0.05 ml. The interval between two doses injected into the same eye should be at least four weeks. Treatment is initiated with one injection per month until maximum visual acuity is achieved and/or there are no signs of disease activity i.e. no change in visual acuity and in other signs and symptoms of the disease under continued treatment. In patients with wet AMD, DME and RVO, initially, three or more consecutive, monthly injections may be needed. Thereafter, monitoring and treatment intervals should be determined by the physician and should be based on disease activity, as assessed by visual acuity and/or anatomical parameters. *Lucentis and laser photocoagulation in DME and in macular oedema secondary to BRVO:* When given on the same day, Lucentis should be administered at least 30 minutes after laser photocoagulation. *Hepatic impairment:* Lucentis has not been studied in patients with hepatic impairment. However, no special considerations are needed in this population. *Renal impairment:* Dose adjustment is not needed in patients with renal impairment. *Elderly:* No dose adjustment is required in the elderly. *Paediatric population:* The safety and efficacy of Lucentis in children and adolescents below 18 years of age have not been established.

CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients. Patients with active or suspected ocular or periocular infections. Patients with active severe intraocular inflammation

WARNINGS/PRECAUTIONS: *Intravitreal injection-related reactions:* Intravitreal injections, including those with Lucentis, have been associated with endophthalmitis, intraocular inflammation, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract. Proper aseptic injection techniques must always be used when administering Lucentis. *Intraocular pressure increases:* Transient increases in intraocular pressure (IOP) have been seen within 60 minutes of injection of Lucentis. Sustained IOP increases have also been identified. Both intraocular pressure and the perfusion of the optic nerve head must be monitored and managed appropriately. *Bilateral treatment:* Limited data on bilateral use of Lucentis (including same-day administration) do not suggest an increased risk of systemic adverse events compared with unilateral treatment. *Immunogenicity:* There is a potential for immunogenicity with Lucentis. Since there is a potential for an increased systemic exposure in subjects with DME, an increased risk for developing hypersensitivity in this patient population cannot be excluded. Patients should also be instructed to report if an intraocular inflammation increases in severity, which may be a clinical sign attributable to intraocular antibody formation. *Concomitant use of other anti-VEGF (vascular endothelial growth factor):* Lucentis should not be administered concurrently with other anti-VEGF medicinal products (systemic or ocular). *Withholding Lucentis:* The dose should be withheld and treatment should not be resumed earlier than the next scheduled treatment in the event of: a decrease in best-corrected visual acuity (BCVA) of ≥ 30 letters compared with the last assessment of visual acuity; an intraocular pressure of ≥ 30 mmHg; a retinal break; a subretinal haemorrhage involving the centre of the fovea, or, if the size of the haemorrhage is $\geq 50\%$, of the total lesion area; performed or planned intraocular surgery within the previous or next 28 days. *Retinal pigment epithelial tear:* Risk factors associated with the development of a retinal pigment epithelial tear after anti-VEGF therapy for wet AMD, include a large and/or high pigment epithelial retinal detachment. When initiating Lucentis therapy, caution should be used in patients with these risk factors for retinal pigment epithelial tears. *Rhegmatogenous retinal detachment or macular holes:* Treatment should be discontinued in subjects with rhegmatogenous retinal detachment or stage 3 or 4 macular holes. *Systemic effects following intravitreal use:* Systemic adverse events including non-ocular haemorrhages and arterial thromboembolic events have been reported following intravitreal injection of VEGF inhibitors. *Women of childbearing potential/contraception in females:* Women of childbearing potential should use effective contraception during treatment. *Pregnancy:* For women who wish to become pregnant and have been treated with ranibizumab, it is recommended to wait at least 3 months after the last dose of ranibizumab before conceiving a child. *Breast-feeding:* It is unknown whether Lucentis is excreted in human milk. Breast-feeding is not recommended during the use of Lucentis. *Effects on ability to drive and use machines:* The Lucentis treatment procedure may induce temporary visual disturbances, which may affect the ability to drive or use machines (see section 4.8). Patients who experience these signs must not drive or use machines until these temporary visual disturbances subside.

INTERACTIONS: No formal interaction studies have been performed.

ADVERSE REACTIONS: *Very common:* Nasopharyngitis. Headache. Vitritis, vitreous detachment, retinal haemorrhage, visual disturbance, eye pain, vitreous floaters, conjunctival haemorrhage, eye irritation, foreign body sensation in eyes, lacrimation increased, blepharitis, dry eye, ocular hyperaemia, eye pruritus. Arthralgia. Intraocular pressure increased. *Common:* Urinary tract infection. Anaemia. Hypersensitivity. Anxiety. Retinal degeneration, retinal disorder, retinal detachment, retinal tear, detachment of the retinal pigment epithelium, retinal pigment epithelium tear, visual acuity reduced, vitreous haemorrhage, vitreous disorder, uveitis, iritis, iridocyclitis, cataract, cataract subcapsular, posterior capsule opacification, punctate keratitis, corneal abrasion, anterior chamber flare, vision blurred, injection site haemorrhage, eye haemorrhage, conjunctivitis, conjunctivitis allergic, eye discharge, photopsia, photophobia, ocular discomfort, eyelid oedema, eyelid pain, conjunctival hyperaemia. Cough. Nausea. Allergic reactions (rash, urticaria, pruritus, erythema). *Please refer to the Summary of Product Characteristics for a full list of adverse events.*

LEGAL CATEGORY: POM

PACK SIZES: one pre-filled syringe, packed in a sealed tray

MARKETING AUTHORISATION HOLDER: Novartis Europharm Limited, Frimley Business Park, Camberley GU16 7SR, United Kingdom

MARKETING AUTHORISATION NUMBERS: EU/1/06/374/003

Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma Services Inc., Representative Office Malta, P.O. Box 4, MRS 1000, Marsa, Malta. Tel+35621222872.

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Suspected adverse reactions and medication errors associated with the use of Lucentis should be reported to: Malta Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000, or at: www.medicinesauthority.gov.mt/adrportal
Alternatively at: Novartis Pharma Services Inc. Representative Office Malta by phone on 21222872