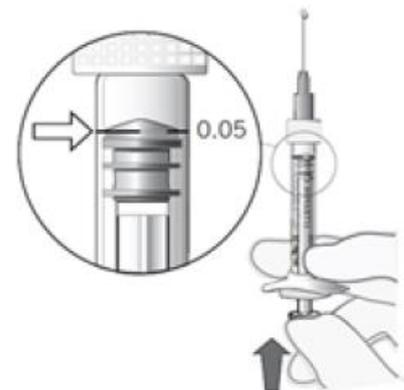
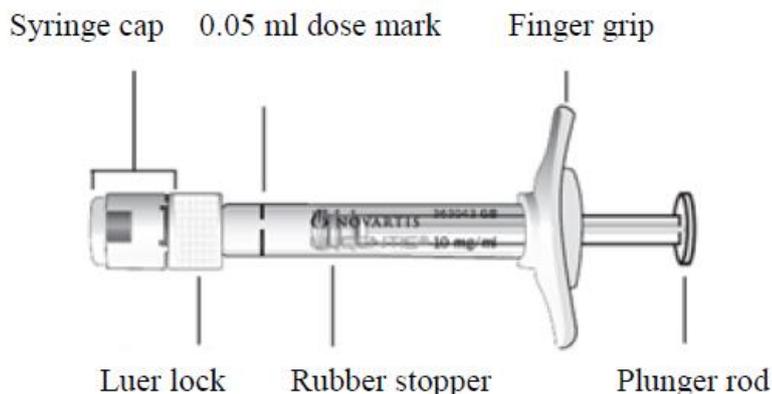


Updated Direct Healthcare Professional Communication (DHPC) Update on Lucentis® (ranibizumab) 10 mg/ml pre-filled syringe – plunger on syringe too stiff

Dear Healthcare Professional,

Novartis Pharmaceuticals in agreement with the European Medicines Agency and the Medicines and Healthcare products Regulatory Agency (MHRA), would like to inform you of the following update:

- **Following issuance of an earlier DHPC (06 September 2019), difficulties are still being reported with the movement of the plunger of some Lucentis pre-filled syringes, which may result in reduced doses of Lucentis being injected into the patient's eye.**
- **Proceeding to inject a patient with a syringe that does not appear to operate properly may harm the patient, if the needle shifts inside the eye.**
- **Always check that the pre-filled syringe plunger can be pushed easily when setting the dose (see figure below).**
- **Do not start to inject if the plunger cannot be pushed easily. Use a new pre-filled syringe instead.**
- **Stop the injection immediately if it has already started and the plunger cannot be pushed easily.**
- **Return any syringe which does not appear to operate properly to Novartis for evaluation and for notification of potential defect (see Annex 1 below for instructions).**



CHECK BEFORE INJECTION: Ensure that the pre-filled syringe plunger can be freely and easily pushed when setting the dose during step 11 of the instructions for use (see package leaflet provided with each pre-filled syringe; see also Annex 3, below).

Background information

Lucentis pre-filled syringe indicated in adults for:

- The treatment of neovascular (wet) age-related macular degeneration (AMD)
- The treatment of visual impairment due to diabetic macular oedema (DME)
- The treatment of proliferative diabetic retinopathy (PDR)
- The treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO)
- The treatment of visual impairment due to choroidal neovascularisation (CNV)

Novartis has received complaints from physicians of difficulties with a stiff plunger in Lucentis pre-filled syringes. Release-testing data from the batches of syringes for which complaints were received ('signal batches') have been reviewed and we have confirmed that the signal batches conformed to the specifications for manufacture. The root cause investigation has been concluded and additional measures have been introduced. Most recent complaint trend analysis shows a consistent decline in complaints for this type of defect.

Following issuance of an earlier [DHPC](#) (06 September 2019), additional complaints with the movement of the plunger of some Lucentis pre-filled syringes were received for syringes from the same signal batches as above, including reports on incomplete injections due to difficult to move plungers. This update is provided to remind you of the following instructions should you identify a syringe which does not appear to operate as expected: If the Lucentis pre-filled syringe plunger does not move freely, the syringe must not be used. If the injection has already started, it should be stopped immediately. When an injection has been stopped and if re-injection at the same session (using a new pre-filled syringe) is imperative, it is important to consider the possibility of excessive dosage (see SmPC in Annex 2 of this letter, section 4.8 on adverse effects and 4.9 on overdose).

- If the injection into the patient's eye is incomplete (i.e. less than the recommended 0.05 ml dose has been injected), the medicine's efficacy may be reduced. Monitor treatment efficacy according to current practice.
- Follow the recommendation on treatment interval for Lucentis injection, taking into account a minimal interval of 4 weeks between consecutive injections in the same eye as described in Section 4.2 'Posology and method of administration' in the summary of product characteristics (SmPC, see Annex 2).
- Only consider re-injection during the same session if it is imperative for an individual patient, and after you have considered the possibility of excessive dosage (see Section 4.9 'Overdose' in the SmPC in Annex 2 of this letter). Always use a new pre-filled syringe for re-injection.

Call for reporting

You are reminded to report adverse reactions to Lucentis or product quality complaints with the pre-filled syringe in accordance with the national spontaneous reporting system, as applicable.

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme. Please report:

- all suspected ADRs that are serious or result in harm. (Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.)
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼

It is easiest and quickest to report ADRs online via the Yellow Cards website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gov.uk
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- or by downloading and printing a form from the Yellow Card section of the MHRA website

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.

Adverse events should also be reported to Novartis online through the patient safety information (PSI) tool at www.report.novartis.com or via uk.patientsafety@novartis.com.

Company contact point

Should you have any questions or concerns, please contact Novartis Medical Information department on 01276 698370 or email medinfo.uk@novartis.com.

Yours faithfully,



Dr Mark Toms, MBChB
Chief Scientific Officer, Novartis Pharmaceuticals UK Ltd.

Annexes

ANNEX 1: Replacement directions

Please contact Novartis Medical Information to report any syringe which does not appear to operate properly, in order to arrange collection and evaluation. Novartis Medical Information can be contacted using the following contact details:

Email: medinfo.uk@novartis.com

Telephone: 01276 698370

ANNEX 2: Lucentis summary of product characteristics (SmPC)

Full UK SmPC can be found at <https://www.medicines.org.uk/emc/product/5418/smpc>

4.2 Posology and method of administration (excerpt only, see SmPC for full information)

Lucentis must be administered by a qualified ophthalmologist experienced in intravitreal injections.

Posology

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.

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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.

Monitoring for disease activity may include clinical examination, functional testing or imaging techniques (e.g. optical coherence tomography or fluorescein angiography).

Lucentis and verteporfin photodynamic therapy in CNV secondary to PM

There is no experience of concomitant administration of Lucentis and verteporfin.

Method of administration

Single-use pre-filled syringe for intravitreal use only. The pre-filled syringe contains more than the recommended dose of 0.5 mg. The extractable volume of the pre-filled syringe (0.1 ml) is not to be used in total. The excess volume should be expelled prior to injection. Injecting the entire volume of the pre-filled syringe could result in overdose. To expel the air bubble along with the excess medicinal product, slowly push the plunger until the edge below the dome of the rubber stopper is aligned with the black dosing line on the syringe (equivalent to 0.05 ml, i.e., 0.5 mg ranibizumab).

Lucentis should be inspected visually for particulate matter and discoloration prior to administration.

The injection procedure should be carried out under aseptic conditions, which includes 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). The patient's medical history for hypersensitivity reactions should be carefully evaluated prior to performing the intravitreal procedure (see section 4.4). Adequate anaesthesia and a broad-spectrum topical microbicide to disinfect the periocular skin, eyelid and ocular surface should be administered prior to the injection, in accordance with local practice.

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 centre of the globe. The injection volume of 0.05 ml is then delivered; a different scleral site should be used for subsequent injections. Each pre-filled syringe should only be used for the treatment of a single eye.

4.9 Overdose

Cases of accidental overdose have been reported from the clinical studies in wet AMD and post-marketing data. Adverse reactions associated with these reported cases were intraocular pressure increased, transient blindness, reduced visual acuity, corneal oedema, corneal pain, and eye pain. If an overdose occurs, intraocular pressure should be monitored and treated, if deemed necessary by the attending physician.

ANNEX 3: Instructions for use

See above for an excerpt from SmPC.