Dear Healthcare Professional,

Novartis Europharm Ltd. in agreement with the European Medicines Agency and the Health Products Regulatory Authority would like to inform you of the following:

- **Following issuance of an earlier DHPC on 28 August 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 patients, 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 on 28 August 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 overdosage).
• 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. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpра.ie; E-mail: medsafety@hpра.ie. Adverse events should also be reported to Novartis Ireland by calling 01-2080 612 or by email to drugsafety.dublin@novartis.com.

Company contact point

Should you have any questions or concerns, please contact Novartis medical information department. Email: medinfo.dublin@novartis.com; Telephone: 01 2601255.

Yours sincerely,

Dr. Bishember Kathuria MB BS, MBA
Chief Scientific Officer | Novartis Ireland Ltd.
Vista Building, Elm Park Business Park | Merrion Road, Dublin 4, D04 A9N6, Ireland
Mail: bishember.kathuria@novartis.com | P: +353(0)12204909 | M: +353(0)873898581
Annexes

ANNEX 1: Replacement directions
Please contact Novartis Medical Information to report any syringe that 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.dublin@novartis.com; Telephone: 01 2601255

ANNEX 2: Lucentis summary of product characteristics
Section 4.2 ‘Posology and method of administration’, Section 4.8 ‘Undesirable Effects’ and Section 4.9 ‘Overdose’ of the Irish SmPC can be found at https://www.medicines.ie/medicines/lucentis-10mg-ml-solution-for-injection-in-pre-filled-syringe-32743/smpc

ANNEX 3: Instructions for use
The Instructions For Use can be found in Section 6.6 of the Irish SmPC at https://www.medicines.ie/medicines/lucentis-10mg-ml-solution-for-injection-in-pre-filled-syringe-32743/smpc