

<Date>

## Direct Healthcare Professional Communication

### EYLEA 40 mg/mL (aflibercept solution for intravitreal injection): Higher risk of intraocular pressure increase with the pre-filled syringe

Dear Healthcare professional,

<Name of the MAH/local representative in the member state>, in agreement with the European Medicines Agency and <name of national competent authority>, would like to inform you of the following.

#### Summary

- **Cases of increased intraocular pressure have been reported more frequently (estimated up approximately seven-fold) when using the Eylea pre-filled syringe, compared with administration with Luer-lock syringe of Eylea solution for injection in a vial.**
- **Incorrect handling in the preparation and injection is suspected as the most probable root cause of the observed cases of increased intraocular pressure with the Eylea pre-filled syringe. Injections should be performed by health care professionals familiar with the handling of this presentation.**
- **Correct handling of the pre-filled syringe and training are key to mitigate this risk:**
  - **use a 30G x 13mm injection needle;**
  - **always check that the excess volume/air bubbles in the pre-filled syringe is eliminated before use: the base of the plunger dome (not the tip of the dome) must be aligned with the black dosing line on the syringe (see below);**
  - **carefully depress the plunger rod;**
  - **administer the exact recommended dose and do not inject any residual volume, as increased injection volume can lead to clinically relevant intraocular pressure elevation.**
- **Evaluate the patient's vision and monitor intraocular pressure immediately after the intravitreal injection.**

#### Background information

Eylea pre-filled syringe is indicated in adults for the treatment of:

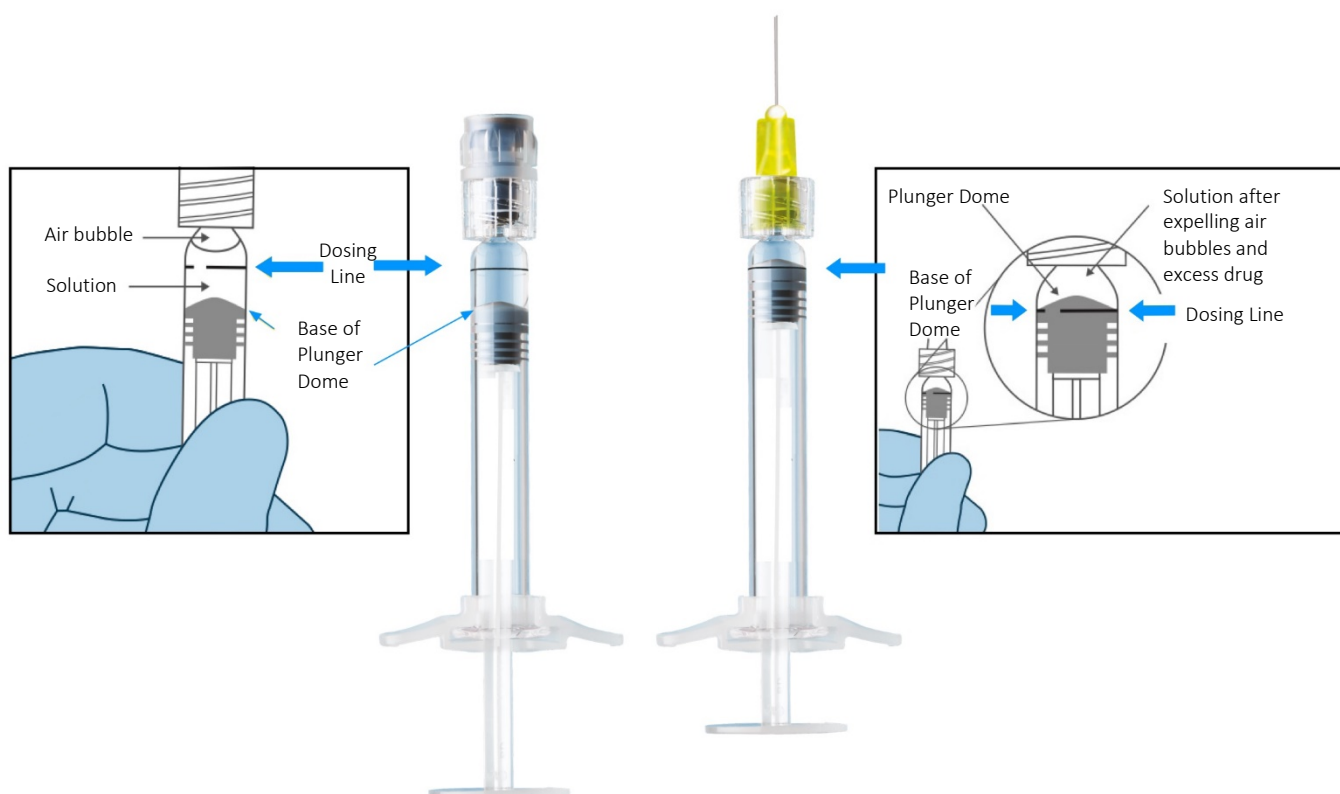
- neovascular (wet) age-related macular degeneration (AMD)
- visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO)
- visual impairment due to diabetic macular oedema (DME)
- visual impairment due to myopic choroidal neovascularisation (myopic CNV).

Intraocular pressure increase is a known adverse drug reaction associated with intravitreal injections in general, including the use of Eylea. A seven-fold higher reporting rate of increased intraocular pressure has been reported with the prefilled syringe (approximately 1.1 cases per 10,000 sold prefilled syringes versus 0.15 cases per 10,000 sold vials) following the recent European launch of this product in April 2020. There have been reports of transient increases of the intraocular pressure

and reversible visual impairment after intravitreal injections. Of the cases with known outcome, the majority resolved without permanent sequelae.

No quality defects have been detected with Eylea prefilled syringes or the solution being injected. After further review of the reported cases, an administration of excessive product due to incorrect handling in the preparation and injection is suspected as the cause of the increased intraocular pressure. Further, Eylea pre-filled syringe is a glass syringe with a rubber plunger that requires slightly more force to be used compared to plastic syringes (such as the ones used with the vial presentation). In order to further minimise this risk, the following recommendations on appropriate handling of the Eylea pre-filled syringe should be strictly followed:

- A 30 gauge x 13mm injection needle should be used.
- To eliminate all bubbles and to expel excess medicinal product, the plunger must be correctly positioned. **The base of the plunger dome** (not the tip of the dome) must be aligned with the black dosing line on the syringe, as described in section "Instructions for use of pre-filled syringe" of the product information and in the figure below.
- When administering the dose into the eye, the plunger rod must be carefully depressed with constant pressure until the plunger reaches the bottom of the syringe. A small residual volume of solution may be observed in the syringe after the plunger has reached the bottom of the syringe. Do not attempt to administer it by exerting additional pressure on the plunger.



Intraocular pressure should be monitored, and appropriate treatment should be instituted, if necessary. Immediately after the intravitreal injection:

- Evaluate vision (hand movement or finger counting).
- Appropriate monitoring of intraocular pressure may consist of a check for perfusion of the optic nerve head or tonometry. Sterile equipment for paracentesis should be available.

It is recommended to consult the training materials provided and the distributed information on the correct use of the pre-filled syringe presented in the prescriber guide and injection video of the educational materials for Eylea. The educational materials including the patient guide are also available on [<link to platform/website>](#) or can additionally be made available on request, along with training sessions.

The product information and the educational material for healthcare professionals are being updated to contain additional instructions/recommendations about the handling of the pre-filled syringe to mitigate the risk of intraocular pressure increase.

### **Call for reporting**

Reporting suspected adverse reactions after authorisation of Eylea 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 via the national reporting system: [<details of national reporting system>](#).

### **Company contact information**

For further questions or additional information on the correct use of the Eylea pre-filled syringe, please contact the medical information department at [<name of the MAH/local representative in the member state>](#) at the following e-mail address: [< e-mail address>](#) or phone number: [< phone number>](#).

## Communication Plan for Direct Healthcare Professional Communication

DHPC COMMUNICATION PLAN	
<b>Medicinal product(s)/active substance(s)</b>	Eylea® (aflibercept) 40 mg/ml solution for injection in pre-filled syringe
<b>Marketing authorisation holder(s)</b>	Bayer AG, Germany
<b>Safety concern and purpose of the communication</b>	DHPC for Eyla regarding the reported cluster of IOP increase, including key messages regarding IOP surveillance and management of IOP increase, how to use the product in an appropriate way to avoid the occurrence of this serious ADR, the size of the recommended needle (30G) as well as the recommendations to administer exactly the recommended dose and reduce the risk of overdose/medication errors.
<b>DHPC recipients</b>	Ophthalmologists, hospital pharmacists; final list of recipients to be agreed at national level incl. professional societies and national associations, depending on the national healthcare system
<b>Member States where the DHPC will be distributed</b>	All member states where the Eylea® pre-filled syringe is marketed
Timetable	Date
<b>DHPC and communication plan (in English) agreed by PRAC</b>	11 March 2021
<b>DHPC and communication plan (in English) agreed by CHMP</b>	25 March 2021
<b>Submission of translated DHPCs to the national competent authorities for review</b>	1 April 2021
<b>Agreement of translations by national competent authorities</b>	8 April 2021
<b>Dissemination of DHPC</b>	15 April 2021