<Date>

Direct Healthcare Professional Communication

Leqvio (inclisiran) 284 mg solution for injection in pre-filled syringe: Important information regarding instructions for use before injection

Dear Healthcare Professional,

Novartis Europharm Limited in agreement with the European Medicines Agency and the <National Competent Authority>, would like to inform you of the following:

Summary

- Novartis has received a small number of complaints associated with difficulty moving the syringe plunger resulting in the inability to inject Leqvio. The issue occurs infrequently in the European Union (~ 0.01%).

- To ensure optimal use of Leqvio for patients and healthcare professionals while technical solutions to alleviate this issue are investigated, Novartis wants to share important information before injecting Leqvio:

- Do not remove the needle cap until you are ready to inject, as in rare cases, early removal of the needle cap prior to injection can lead to drying of the drug product within the needle, which can result in needle clogging.

    - If following insertion of the needle you cannot depress the plunger, use a new pre-filled syringe. Novartis will provide a replacement for any impacted Leqvio syringes. For product replacement, see Annex 1 below for instructions.

- The reviewed data confirm that there is no clinically relevant risk to patient safety.

Background – Labelling Guidance

Leqvio is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:

- in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin, or;
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

The recommended dose is 284 mg inclisiran administered as a single subcutaneous injection: initially, again at 3 months, followed by every 6 months. Leqvio is available in two presentations in the EU. Both are intended for administration by a healthcare professional only:

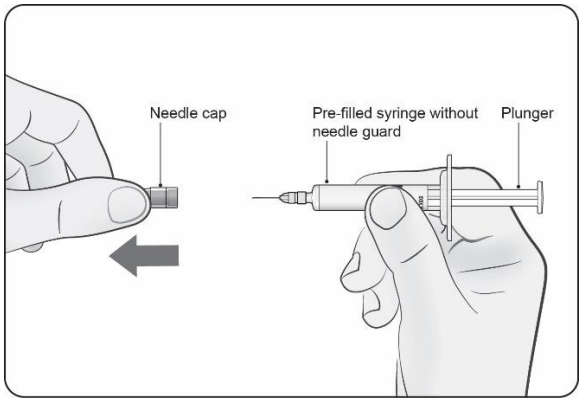
- a "pre-filled syringe" (without needle guard) which does not contain an Instruction for Use (IFU) and;
- a "pre-filled syringe with needle guard" which includes an IFU with detailed instructions on the procedure for use, including activation of the safety mechanism and an instruction not to remove the needle cap until the user is ready to inject.

Novartis wants to emphasize important information before injecting Leqvio:

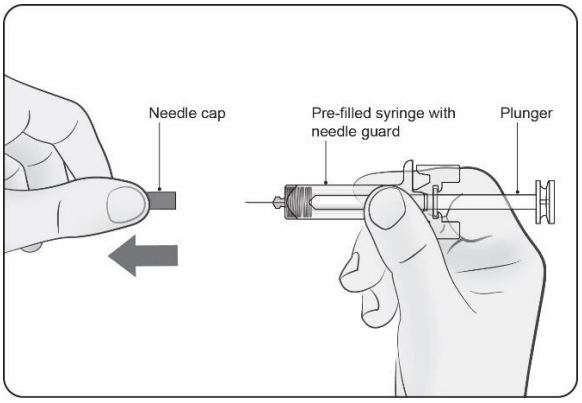
- **Do not remove the needle cap until you are ready to inject.**

This important information is already included in the IFU for the Leqvio pre-filled syringe with needle guard. Novartis will introduce an IFU for the Leqvio pre-filled syringe (without needle guard) to provide this important instruction consistently for both presentations in product labelling.

Pre-filled syringe "without" needle guard:



Pre-filled syringe "with" needle guard:



Please also note that:

- If following insertion of the needle you cannot depress the plunger, use a new pre-filled syringe. Novartis will provide a replacement for any impacted Leqvio syringes. For product replacement, please see Annex 1 below for instructions.
- The reviewed data confirm that there is no clinically relevant risk to patient safety.

Call for Reporting

Healthcare professionals should report any suspected adverse reactions associated with the use of Leqvio in accordance with the national spontaneous reporting system *<include the details (e.g. name, postal address, fax number, web address) on how to access the national spontaneous reporting system>.*

Company Contact Point

Contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address.

Yours sincerely,

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ANNEX 1: Replacement Directions

Novartis will provide a replacement for any impacted Leqvio syringes. For product replacement, please contact *<include the details of local contact point (e.g. address, phone number, email address, or other) for product replacement>.*

Communication Plan for Direct Healthcare Professional Communication

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Leqvio (inclisiran) 284 mg solution for injection in pre-filled syringe
Marketing authorisation holder(s)	Novartis Europharm Limited
Safety concern and purpose of the communication	Important information regarding instructions for use before injecting Leqvio
DHPC recipients	Healthcare providers who can administer Leqvio. The target group will be further defined at the national level, in agreement with the respective national competent authority.
Member States where the DHPC will be distributed	Unless otherwise directed by their National Competent Authority, all EU Member States where Leqvio is launched.

Timetable	Date
DHPC and communication plan (in English) agreed by CHMP/CMDh	9/11/2023
Submission of translated DHPCs to the national competent authorities for review	23/11/2023
Agreement of translations by national competent authorities	7/12/2023
Dissemination of DHPC	21/12/2023