Levetiracetam (Keppra and Levetiracetam UCB) oral solution (150ml bottle for children aged 6 months to 4 years): risk of medication error due to change of dosing syringe

Dear Healthcare Professional,

<Name of UCB legal entity as Marketing Authorization Holder> in agreement with the European Medicines Agency and the <National Competent Authority > would like to inform you of the following:

Summary

- **A new 5mL dosing syringe delivering up to 500mg of levetiracetam (Keppra and Levetiracetam UCB) oral solution used in children aged 6 months to 4 years (150mL bottle) will replace the 3mL dosing syringe of levetiracetam, delivering up to 300mg levetiracetam.**
- **When prescribing and dispensing levetiracetam (Keppra and Levetiracetam UCB) oral solution with the new 5mL syringe, inform caregivers about the change in the volume of the dosing syringe. Caregivers should be counselled on the correct dose and how to measure the correct dose with the 5mL syringe. Caregivers should also be warned that the new 5mL syringe has additional graduations of 0.25mL compared to the 3mL syringe.**
- **Advise caregivers to read the instructions in the Package Leaflet on how to recognize signs and symptoms of a levetiracetam overdose and what to do in this situation, as well as how to use and clean the syringe.**

Background on the safety concern

Levetiracetam (Keppra and Levetiracetam UCB) is indicated as monotherapy in the treatment of partial onset seizures with or without secondary generalisation in adults and adolescents from 16 years of age with newly diagnosed epilepsy.

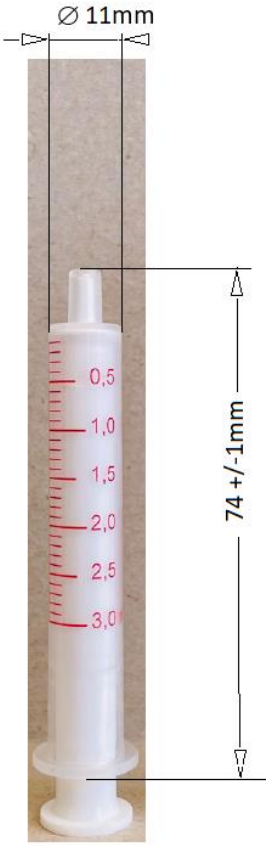
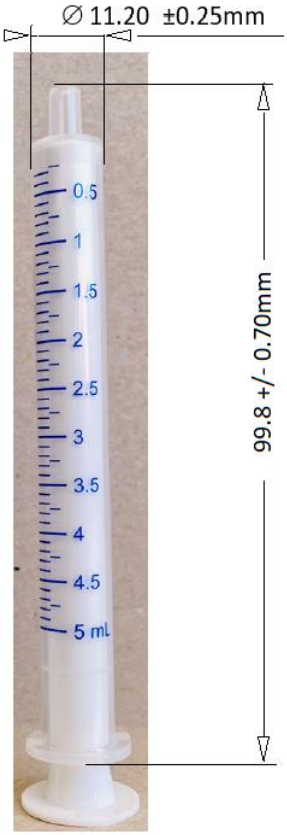
Levetiracetam (Keppra and Levetiracetam UCB) is indicated as adjunctive therapy

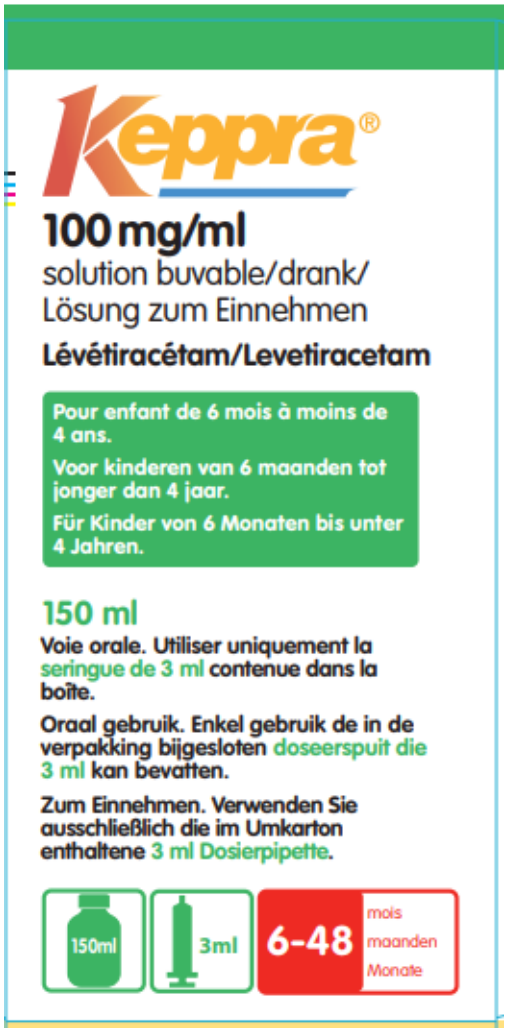
- in the treatment of partial onset seizures with or without secondary generalisation in adults, adolescents, children and infants from 1 month of age with epilepsy.
- in the treatment of myoclonic seizures in adults and adolescents from 12 years of age with juvenile myoclonic epilepsy.
- in the treatment of primary generalised tonic-clonic seizures in adults and adolescents from 12 years of age with idiopathic generalised epilepsy.

One of the current presentations of levetiracetam (Keppra and Levetiracetam UCB) 100mg/mL oral solution in 150mL bottle includes a 3mL dosing syringe and is intended for

use in children aged 6 months to 4 years. The 3mL dosing syringe (delivering up to 300mg of levetiracetam) is being replaced with a 5mL dosing syringe (delivering up to 500mg levetiracetam). While the new 5mL syringe is graduated every 0.1mL, it also has additional graduations of 0.25mL compared to the 3mL syringe. Please see Table 1 below for more information.

Table 1: Differences between the 3- and 5mL dosing syringe for patients aged 6 months to 4 years for levetiracetam (Keppra and Levetiracetam UCB) oral solution(150mL bottle)

	Old 3mL dosing syringe	**New 5mL dosing syringe**
Presentation		
Graduation markings	From 0.3mL to 3mL in 0.1mL intervals	From 0.3mL to 5mL in 0.1mL intervals and from 0.25mL to 5mL in 0.25mL intervals.

	Old 3mL dosing syringe	New 5mL dosing syringe
Outer packaging		

The product information, including immediate and outer packaging, are being updated to reflect this change.

There is a potential risk of medication error due to the changes related to the dosing syringe for this presentation of levetiracetam (Keppra and Levetiracetam UCB) oral solution. Overdose of levetiracetam (Keppra and Levetiracetam UCB) due to medication error could result in somnolence, agitation, aggression, depressed level of consciousness, respiratory depression, and coma. Further information related to the management of overdose can be found in the section 4.9 of the Summary of Product Characteristics.

When prescribing and dispensing levetiracetam (Keppra and Levetiracetam UCB) oral solution with the new 5mL dosing syringe to children aged 6 months to 4 years, caregivers should be informed about the change in the volume of the syringe and about the additional graduations of 0.25mL on the new syringe. They should also be advised to read the updated instructions for using the new 5mL syringe to measure the appropriate dose for the patient in the Package Leaflet.

Caregivers should also be informed about the updated instructions in the Package Leaflet for cleaning the syringe. The syringe should be cleaned by rinsing it with cold water and moving the plunger several times up and down to take up and expel the water, without separating the 2 components.

There are no changes to the dosing syringes in the following presentations of levetiracetam (Keppra and Levetiracetam UCB) oral solution:

- 150mL bottle with 1mL dosing syringe (for children aged 1 month to 6 months);
- 300mL bottle with 10mL dosing syringe (for children aged 4 years and older).

<FOR NATIONAL DECISION: Additional information to warn healthcare professionals and caregivers that the new dosing device provided with levetiracetam (Keppra and Levetiracetam UCB) oral solution intended for the population of children aged 6 months to 4 years may differ from the dosing device provided with generic presentations of levetiracetam oral solution intended for the similar age group.>

Call for reporting

Healthcare professionals should report any suspected adverse reactions, including medication errors to < Insert details of the national spontaneous reporting system e.g. name, postal address, fax number, website>.

Company Contact Point

Should you have any questions, please contact <add details>

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

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Levetiracetam oral solution (Keppra and Levetiracetam UCB)
Marketing authorisation holder(s)	UCB Pharma SA
Safety concern and purpose of the communication	To inform healthcare professionals of potential risk of medication errors due to change of the dosing syringe
DHPC recipients	Neurologists, pediatricians, community pharmacists, hospital pharmacists and their relevant learned societies. The target group should be further defined at national level, in agreement with the respective national competent authority.
Member States where the DHPC will be distributed	All EU Member States where the oral solution in 150mL bottles for 6-48-months old patients is marketed.

Timetable	Date
DHPC and communication plan (in English) agreed by PRAC	3 Oct 2024
DHPC and communication plan (in English) agreed by CHMP	17 Oct 2024
Submission of translated DHPCs to the national competent authorities for review	2 Dec 2024[a]
Agreement of translations by national competent authorities	9 Dec 2024[a]
Dissemination of DHPC	16 Dec 2024[a]