UCB (Pharma) Ireland Limited
United Drug House, Magna Drive, Magna Business Park, Citywest Rd, Dublin 24

Direct Healthcare Professional Communication

14th November 2016

Levetiracetam containing products 100 mg/ml oral solution presentations: Risk of medication errors associated with overdose

Dear Healthcare Professional,

UCB Pharma Limited in agreement with the European Medicines Agency and the HPRA would like to inform you of the following:

Summary

- Cases of an up to 10-fold accidental overdose with Keppra (levetiracetam) oral solution have been reported. The majority of cases occurred in children aged between 6 months and 11 years. The use of an inadequate dosing device (e.g. confusion between a 1ml and a 10ml syringe, resulting in a 10-fold overdose) was identified as an important cause.
- Physicians should always prescribe the dose in mg with ml equivalence based on the correct age.
- Pharmacists should ensure that the appropriate presentation of levetiracetam oral solution is dispensed. In the event that provision of the age appropriate presentation of levetiracetam oral solution to paediatric patients is not feasible due to supply issues, then pharmacists should use their discretion so as to ensure that the patient's medication is not interrupted.
- With every prescription, physicians and pharmacists should advise the patient and/or caregiver on how to measure the prescribed dose.
- With every prescription, physicians and pharmacists should remind patients or caregivers to use only the syringe delivered with the medicine. Once the bottle is empty the syringe should be discarded and not kept.

Background on the safety concern

Levetiracetam overdose can lead to serious adverse events, like depressed level of consciousness,

respiratory depression and coma.

In the cases where the cause of the reported accidental overdosing could be retrieved, it was either due to the use of an inappropriate syringe or the misunderstanding of the caregiver about how to properly measure the dose.

- Physicians should prescribe the recommended presentation of Keppra oral solution with the appropriate syringe according to the age/bodyweight of the patient. The pharmacist should ensure the right syringe is dispensed with the corresponding presentation: :
  - 150 ml bottle with 1 ml syringe for infants from 1 month to less than 6 months;
  - 150 ml bottle with 3 ml syringe for children 6 months to less than 4 years and below 50 kg bodyweight;
  - 300 ml bottle with 10 ml syringe for children 4 years and older and below 50 kg bodyweight;
  - 300 ml bottle with 10 ml syringe for children, adolescents and adults with 50 kg and more bodyweight.

UCB will revise the patient information leaflet as well as the outer packaging of its Keppra 100 mg/ml oral solution (and Levetiracetam UCB 100mg/ml oral solution where marketed) presentations to improve the clarity of the dose recommendations and to avoid confusion about the appropriate bottle size and syringe (due to be completed around May 2017). To further minimise the risk of dosing error, MAHs marketing more than one presentation of levetiracetam oral solution have been encouraged to use colour codes and pictograms to: (i) differentiate one presentation from another, (ii) clearly state the age range for whom the presentation is intended (front warning on packaging and labelling), and (iii) clearly state on the packaging/labelling which dosing device should be used with a specific presentation.

Keppra (levetiracetam) 100 mg/ml oral solution is indicated

- as adjunctive treatment of partial onset seizures with or without secondary generalization from 1 month of age
- as adjunctive treatment of myoclonic and/or generalized tonic-clonic seizures from 12 years of age
- as monotherapy in the treatment of partial onset seizures with or without secondary generalization from 16 years of age.

Call for reporting

Reporting suspected adverse reactions after authorisation of the medicinal product 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL-Dublin 2; Tel: +3531 6764971; Fax: +3531 6762517. Website: www.hpra.ie; Email: medsafety@hpra.ie.

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