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Fosphenytoin sodium, Pro-Epanutin® 75mg/ml (50 mg/ml Phenytoin sodium Equivalents (PE)) Concentrate for solution for infusion/Solution for injection: Medication Errors and Off-label Use in Children under 5 Years of Age

Dear Healthcare Professional,

Pfizer Healthcare Ireland would like to inform you of the following important safety information for Pro-Epanutin (fosphenytoin sodium, an antiepileptic drug):

Summary

- Pro-Epanutin is not indicated for use in children under 5 years of age and should not be administered to this patient group. Spontaneous reports received by Pfizer indicate that while medication errors leading to fatal overdoses have occurred in all age groups, a disproportionate percentage of fatal overdose cases have been reported when Pro-Epanutin is used off-label in patients under the age of 5 years.
- The Summary of Product Characteristics (SmPC) has been updated to emphasize the approved age range for the use of Pro-Epanutin in children, which is 5 years of age and older.
- Medication errors with Pro-Epanutin continue to be received, including reports involving doses which are too high or intravenous (IV) infusion rates which are too rapid. In some cases, these medication errors have been associated with cardiac arrest and/or death.
- It is essential that Pro-Epanutin is administered at the correct dose and correct rate of administration (for IV infusions), in accordance with the SmPC.
- The SmPC has been updated to clarify the dosing information and to provide a new warning about medication errors and the need to closely monitor patients during IV administration of Pro-Epanutin. Paediatric and adult Dosing Aids have also been developed to provide a simplified summary for administering Pro-Epanutin to patients with status epilepticus and are attached to this letter. The Dosing Aids will be enclosed with the packs of Pro-Epanutin vials.

This information is being sent to you in agreement with the Health Products Regulatory Authority (HPRA).

Further information on the safety concern and the recommendations:

Medication Errors

Medication errors with Pro-Epanutin are an important issue due to the use of this product in emergency situations (where mistakes can often be made), the vulnerable patient group being

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treated (who are seriously ill), and the potential serious medical sequelae of overdose (including fatal cardiac arrest).

Due to the complex posology of Pro-Epanutin, there are several mechanisms by which confusion can arise and can result in medication errors including: confusion regarding Phenytoin sodium Equivalents (PE), product name confusion, product preparation errors, drug infusion/administration errors, and incorrect dose calculations.

Pro-Epanutin should always be prescribed and dispensed in Phenytoin sodium Equivalents (PE).

Medication errors have occurred when the CONCENTRATION of drug in the vial was mistaken for the TOTAL AMOUNT of drug in the vial. Pro-Epanutin is marketed in 10 ml vials containing a total of 500 mg PE. Errors have occurred when the concentration of drug in the vial (50 mg PE/ml) was misinterpreted to mean the total content of the vial, which is actually 500 mg PE, resulting in a 10-fold overdose. Fatal overdoses have been reported, including in children under 5 years of age.

Medication errors have also occurred when a maintenance dose of Pro-Epanutin was administered shortly after the initial loading dose, and/or when the total daily maintenance dose was repeated within the same day. The maintenance dose of Pro-Epanutin should be adjusted according to the patient`s therapeutic response and plasma phenytoin concentrations. Section 4.2 of the SmPC has been updated to clarify that “After administration of a loading dose, maintenance doses should typically be started at the next identified dosing interval. For example, if the intended dose frequency is every 12 hours then the first maintenance dose of fosphenytoin should be administered 12 hours after the loading dose.”

When administering Pro-Epanutin by IV infusion, it is mandatory to strictly adhere to the recommended rate of infusion described in the SmPC. Section 4.4 Special Warnings and Precautions for Use of the SmPC has been updated to clarify that for adults “Pro-Epanutin should be administered intravenously at a rate no greater than 150 mg PE/min, due to the risk of cardiovascular toxicity (see Section 4.2)” and for children (5 years and older) “Pro-Epanutin should be administered at a rate no greater than 3 mg PE/kg/min or 150 mg PE/min, whichever is slower, due to the risk of cardiovascular toxicity (see Section 4.2)”.

When ordering and storing Pro-Epanutin, including in computer systems, prescriptions and automated dispensing cabinet databases, consider displaying the total drug content (500 mg PE/10 ml) instead of the concentration per ml to help ensure that the total drug content can be clearly identified.

Please refer to the attached Pro-Epanutin Dosing Aids (a simplified summary for administering Pro-Epanutin to patients with status epilepticus) and the SmPC, which can be found on the following website: http://www.medicines.ie/.

Off-label Use in Children under 5 Years of Age
Pro-Epanutin is not indicated for use in children under 5 years of age because the safety and efficacy of Pro-Epanutin has not been established in this patient group.

Further information

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Pro-Epanutin (fosphenytoin sodium) is indicated in adults and children aged 5 years and older:

- for the control of status epilepticus of the tonic-clonic (grand mal) type.
- for prevention and treatment of seizures occurring in connection with neurosurgery and/or head trauma.
- as substitute for oral phenytoin if oral administration is not possible and/or contra-indicated.

Call for reporting

You can assist us with monitoring the safety of Pro-Epanutin by reporting suspected adverse reactions. Suspected adverse drug reactions (ADRs) should be reported to the Health Products Regulatory Authority (HPRA):

- Online reporting via the HPRA Website www.hpra.ie
- Using downloadable form from the HPRA website. An adverse reaction report form can be downloaded from the HPRA Website. This can be sent by Freepost to the HPRA or by email to medsafety@hpra.ie.
- By telephoning the Pharmacovigilance Section of the HPRA, (01) 676 4971

Suspected adverse drug reactions may also be reported to Pfizer Medical Information on 1800 633 363.

Company contact point

For more information about Pro-Epanutin, please contact Pfizer Medical Information at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS or Tel: 1800 633 363 and ask for Medical Information.

Annexes
Pro-Epanutin Dosing Aid For Adults Only
Pro-Epanutin Dosing Aid For Children 5 Years and Older

Yours sincerely,

Dr Declan O'Callaghan
Medical Director
Pfizer Healthcare Ireland