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Worldwide Biopharmaceutical Businesses

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Fosphenytoin sodium, Pro-Epanutin® 75 mg/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 Limited would like to inform you of the following important safety information for Pro-Epanutin (fosphenytoin sodium, an antiepileptic drug for use in patients aged 5 years or older):

Summary

- Pro-Epanutin is not indicated for use in children under 5 years of age and should not be administered to this patient group. Its safety and efficacy have not been established in this age group.
- We have received reports of medication errors, some of which led to fatal overdose. A disproportionate number of fatal overdose cases have been reported when used off-label in patients under the age of 5 years.
- The medication errors report administration of doses that are too high or intravenous (IV) infusion rates that are too rapid, some cases of which led to cardiac arrest or death.
- The Summary of Product Characteristics (SPC) has been updated to clarify the dosing information and the need to closely monitor patients during IV administration, and to warn about medication errors.
- Paediatric and adult dosing aids have been developed to provide a summary for administration of Pro-Epanutin to patients with status epilepticus. The dosing aids are attached to this letter and will be enclosed with packs of Pro-Epanutin vials.

This information is being sent to you in agreement with the Medicines and Healthcare Products Regulatory Agency (MHRA).

Further information on the safety concern of medication error

Medication errors with Pro-Epanutin are an important issue because of: the use of this product in emergency situations; the vulnerable patient group being treated; and the potential serious medical sequelae of overdose (including fatal cardiac arrest).

The complex posology of Pro-Epanutin means there are several mechanisms by which errors can arise, including: confusion regarding Phenytoin sodium Equivalents (PE); incorrect dose calculations; product name confusion; product preparation errors; and drug infusion or administration errors.

Registered in England: No 526209
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Phenytoin sodium Equivalents (PE)

Pro-Epanutin should always be prescribed and dispensed in PE.

Medication errors have occurred when the concentration of drug in the vial was mistaken for the total amount. 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 (ie, 500 mg PE, a 10-fold overdose). Fatal overdoses have been reported, including in children under 5 years of age.

Administration of maintenance dose

Medication errors have also occurred when a maintenance dose of Pro-Epanutin was administered shortly after the initial loading dose, or when the total daily maintenance dose was repeated in the same day.

The maintenance dose should be adjusted according to the patient's therapeutic response and plasma phenytoin concentrations. 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 should be administered 12 hours after the loading dose.

IV infusion

For adults, Pro-Epanutin should be administered intravenously at a rate no greater than 150 mg PE/minute because of a risk of cardiovascular toxicity.

For children (aged 5 years or older), Pro-Epanutin should be administered at a rate no greater than 3 mg PE/kg/minute or 150 mg PE/minute, whichever is slower, due to a risk of cardiovascular toxicity.

Medicines management

When ordering and storing Pro-Epanutin, including details in computer systems, prescriptions, and automated dispensing cabinet databases, consideration should be given to displaying the total drug content (ie, 500 mg PE/10 mL) for clear identification of contents.

Further information

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 contraindicated.

Please refer to the attached Pro-Epanutin dosing aids and the SPC, which can be found on the following website: https://www.medicines.org.uk.

Call for reporting

Suspected adverse drug reactions (ADRs) should be reported to the Medicines and Healthcare product Regulatory Agency (MHRA) through the Yellow Card Scheme online at www.mhra.gov.uk/yellowcard.

Alternatively, prepaid Yellow Cards for reporting are available:

- upon request by mail: "FREEPOST YELLOW CARD"
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- Or by electronic download through the Yellow Card section of the MHRA website

Suspected adverse drug reactions may also be reported to Pfizer Medical Information on 01304 616161.
When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset and treatment dates.

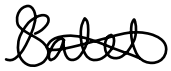
Company contact point

If you have any questions about this letter or for more information about Pro-Epanutin, please contact Pfizer Medical Information at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS or Telephone: 01304 616 161

Annexes

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

Yours sincerely,



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