ORPHAN EUROPE
RECORDATI GROUP

22nd July 2013

PEDEA - **DHPC** n°1

Direct Healthcare Professional Communication on PEDEA® shortage (ibuprofen solution 5mg/ml for injection) and information about an alternative product (distribution and differences in concentration)

Dear Sir / Madam,

Summary

Orphan Europe would like to draw your attention to an interruption in the supply of PEDEA®, ibuprofen solution for injection. We anticipate an out of stock situation arising by early August. This letter is sent in agreement with the Irish Medicines Board (IMB) and gives further information and advice regarding:

- Arrangement for supply of an alternative unlicensed product imported from the United States of America.
- Advice to Healthcare Professionals regarding precautions to be used when prescribing the alternative unlicensed product due to the difference in concentration.

Detailed information on the interruption in supply

Pedea® is an orphan drug centrally approved on July 29th 2004, intended to treat haemodynamically significant Patent Ductus Arteriosus in premature newborn infants of less than 34 weeks of gestational age.

Orphan Europe has recently become aware of a forthcoming shortage in product supply. This is due to visible particles forming in the vials shortly after production. The issue has been detected prior to the release of these batches on the market. So far, it is established that Pedea® batches currently on the market are not affected by this manufacturing issue. Nevertheless, Orphan Europe wishes to draw your attention to section 6.6 of the Summary of Product Characteristics for Pedea® "*As for all parenteral products, ampoules of Pedea® should be visually inspected for particulate matter and the integrity of the container prior to use.*"

To the best of our knowledge, there is no other similar medicinal product approved in the European Union for the same indication. We have therefore made it our priority to make available an alternative therapy.

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Registered in England and Wales: No. 3216698
VAT No. GB 604178359
Registered office: Chartam House, 16 College Avenue, Maidenhead, Berkshire, SL6 6AX

Alternative treatment: Neoprofen® (ibuprofen lysine) injection (10mg/mL) –
Advice for Healthcare Professionals

Neoprofen®, **approved in the US by the FDA in 2006**, but unlicensed in Ireland, is indicated for the closure of a clinically significant *Patent Ductus Arteriosus* (PDA) in premature **infants weighing between 500 and 1500 g, who are no more than 32 weeks gestational age** when usual medical management (e.g., fluid restriction, diuretics, respiratory support, etc.) is ineffective. The clinical trial was conducted among infants with an asymptomatic PDA. However, the consequences beyond 8 weeks after treatment have not been evaluated; therefore, treatment should be reserved for infants with clear evidence of a clinically significant PDA.

Neoprofen® is currently marketed in the US by Recordati Rare Diseases. Considering the seriousness and urgency of the situation, Orphan Europe and Recordati Rare Diseases are collaborating to provide Neoprofen® in the EU for the duration of the Pedea® shortage.

Neoprofen® is an intra-venous formulation of ibuprofen and is in many respects similar to Pedea®. However, some differences exist.

Neoprofen® is a clear, sterile, preservative-free solution of the L-l**ysine salt of ibuprofen**. L-lysine is used to create a water-soluble salt of the drug suitable for intravenous administration.

Caution should be exercised when dosing Neoprofen®, **as the concentration of ibuprofen lysine is 10mg/ml in contrast to 5 mg/ml ibuprofen in Pedea®**.

The recommended posology of both Neoprofen® and Pedea® are identical (an initial dose of 10mg/kg, followed by two doses of 5mg/kg each, after 24 and 48 hours).

- **Neoprofen® (ibuprofen lysine) 10mg/ml:**
  each vial of 2ml contains 20mg of ibuprofen
  3 vials per pack

- **Pedea® (ibuprofen) 5mg/ml:**
  each ampoule of 2ml contains 10mg of ibuprofen
  4 ampoules per pack

A course of therapy is three doses administered I.V. An initial dose of 10 mg/kg is followed by two doses of 5 mg/kg each, after 24 and 48 hours. All doses should be based on birth weight.
If anuria or marked oliguria (<0.6 mL/kg/hr) is evident at the scheduled time of the second or third dose, no additional dosage should be given until laboratory studies indicate that renal function has returned to normal. If the *ductus arteriosus* closes or is significantly reduced in size after completion of the first course, no further doses are necessary. If the *ductus arteriosus* fails to close, then a second course of Neoprofen®, alternative pharmacological therapy, or surgery may be needed.

For administration, Neoprofen® should be diluted to an appropriate volume with dextrose or saline. Neoprofen® should be prepared for infusion and administered within 30 minutes of preparation and infused continuously over a period of 15 minutes. The drug should be administered via the IV port that is nearest the insertion site. After the first withdrawal from the vial, any solution remaining must be discarded because Neoprofen® contains no preservative.

Neoprofen requires storage at 20 to 25°C, with excursions permitted between 15 and 30°C. Please protect from light and store vials within the carton until contents have been used.

The US Product Information of Neoprofen® is appended to this letter

Supply information on Neoprofen®

In order to simplify the distribution to hospitals, Orphan Europe has agreed to supply unlicensed Neoprofen® (ibuprofen lysine) injection (10mg/mL) directly in the EU in accordance with the regulations for supply of unlicensed medicines for the special needs of individual patients for the duration of the Pedea® shortage.

NB: It is considered Good Clinical Practice for clinicians to record in the patients` notes when an unlicensed product has been used and why, and to inform the parent/guardian of the situation.

Any enquiry regarding this information or request for Neoprofen® should be addressed to:

Kim Robinson
Office Manager, Customer Service

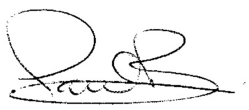
ORPHAN EUROPE UK Ltd
Isis House
43 Station Road
Henley-on-Thames
Oxfordshire RG9 1AT
United Kingdom
Tel: +44 (0) 1491 414 333
Fax: +44 (0) 1491 414 443
e-mail: krobinson@orphan-europe.com

Reporting adverse events

Suspected adverse reactions should be reported to the IMB using a Yellow Card obtained either from the IMB, or electronically via the website at www.imb.ie or by calling (01) 676 4971. Suspected adverse reactions can also be reported to:

Orphan Europe
Pharmacovigilance Department
Tel.: +33 1 47 73 64 58
Fax: +33 1 49 00 18 00
E-mail: dptpharmacovigilance@orphan-europe.com

Yours faithfully,



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