

## General and risk management, patient safety

**GRP-001 1ST ESNEE EXCIPIENT MONOGRAPH: INFORMATION NEEDED TO FORMULATE, PREPARE AND PRESCRIBE MEDICINES FOR NEONATES CONTAINING PROPYLENE GLYCOL AS AN EXCIPIENT**

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**Background** Neonates are particularly vulnerable to the adverse effects of medicines and excipients because their organs are immature. ESNEE (European Study of Neonatal Exposure to Excipients) is a European research consortium created in 2011 after the PRIOMED-CHILD call for proposals.

**Purpose** The aim of ESNEE workpackage 2 was to conduct a literature review of excipients used in medicines for neonates and to establish a monograph of information for each excipient.

**Materials and Methods** A systematic review of the literature was conducted with 6 key databases (i.e. Medline, Web of Science, Pascal, International Pharmaceutical Abstracts, Biosis previews, Embase). Hits were selected for their relevance according to criteria set by toxicology experts. Summaries of relevant papers were prepared with underlying critical information in a table. A face to face meeting was organised with experts to validate the data. Experts from European Medicines Agency Paediatric Committee (EMA PDCO) were involved.

**Results** The search strategy identified around 1500 papers of which 87 were relevant to our purpose. Among those papers, 17, 20, and 15 corresponded to non-clinical, case report, and epidemiological data respectively. The remaining 35 reported miscellaneous data observed in adults. The monograph includes some general information (chemical structure, pharmaceutical use), the list of all (propylene glycol) PG-containing medicines used in Europe for neonates collected by ESNEE workpackage 1 during a point prevalence study, the kinetic characteristics of PG, the first signs of toxicity (biological perturbation, clinical signs, etc.), the organ to target for monitoring and follow up for short or long term effects, some estimations of Acceptable Daily Intake (ADI), and Permitted Daily Exposure (PDE) and finally some recommendations to manage PG toxicity.

**Conclusions** This is the first monograph on PG that includes the most available and relevant information validated by a panel of European experts. This documented, accurate and practical information should help the pharmaceutical industry and hospital pharmacists when formulating/preparing medicines and neonatologists when prescribing such PG-containing medicines. It also provides a clear image of which information is lacking and warrants further experimental investigation.

No conflict of interest.

**GRP-002 A CASE REPORT: MANAGEMENT OF PAIN AFTER SUBCUTANEOUS INJECTION OF TREPROSTINIL**

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**Background** Treprostinil is a prostacyclin analogue indicated for the treatment of Pulmonary Arterial Hypertension (PAH) for

patients with functional NYHA class III. The administration is a continuous subcutaneous infusion. It is recommended that the treatment is initiated incrementally to reach a target dose, in intensive care. Injection site pain and local reactions (respectively 85% and 83% of patients) cause treatment cessation in 8% of cases [1].

**Purpose** To describe the role of multidisciplinary care in the management of pain due to treprostinil treatment.

**Materials and Methods** A descriptive study of a patient with pain due to subcutaneous injection of treprostinil. We collected information from the clinical and pharmacotherapeutic histories. A systematic literature search was performed about practical considerations for subcutaneous treprostinil in PAH. At Grenoble Hospital, the pain of treprostinil is managed by patient education [2] conducted by pharmacists, doctors and nurses belonging to different units.

**Results** Treprostinil treatment was initiated on 19 May 2011, on a 43 year-old patient with idiopathic pre-capillary NYHA III PAH (bosentan and tadalafil not effective; right-heart catheterization 80/30/50 mmHg PAP). The 6-minute-walk test was 544 metres. The initial dose is 1 ng/kg/min for a target dose of 40 ng/kg/min. The initial tolerance was good (Visual Analogue scale (VAS): 3; controlled by paracetamol). Doses were increased with an increment of 1 ng/kg/day. On May 30, 2011, with 10 ng/kg/min dose, the pain was intense (VAS: 8) despite analgesic treatment (paracetamol + tramadol), application of hot/cold packs and diclofenac gel. Mathier's work suggested changing the injection site (abdomen) and limiting the rotation. On July 08, 2011, the pain was controlled (VAS: 2) decreasing 4 days after changing the injection site [1]. The dose was 38 ng/kg/min, the NYHA stage was going down to II, while echocardiography showed persistent right dysfunction. By September 13 the desired dose had been reached (40 ng/kg/min), the pain had disappeared (VAS: 0), the patient was not taking analgesics and the injection site was being changed every 3 weeks. The effectiveness of the treprostinil treatment was demonstrable clinically and echographically.

**Conclusions** Intense pain due to treprostinil may require discontinuation of effective treatment. This case shows that multidisciplinary care with the use of simple measures allows this common side effect to be managed and cessation of treatment prevented.

**References**

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**GRP-003 A MEDICINES RECONCILIATION PROCESS IN FRAIL ELDERLY PEOPLE**

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**Background** Medicines reconciliation may be effective in reducing clinically important medicines errors among high-risk patients such as elderly polymedicated people.

**Purpose** To standardise a home medicines reconciliation process in frail elderly people admitted to hospital.

**Materials and Methods** In this two-month pilot study in a 280-bed hospital, a reconciliation process was designed by a multi-disciplinary team. Geriatricians obtained medical information to verify home medicines by interviewing patients with the help of nurses and also from other medical reports. Pharmacists were