carbohydrates (polynuclear iron (III)-oxyhydroxy cores stabilised by carbohydrates), glatiramoids (polypeptides) and liposomal drugs [1]. Like biological MPs, NBCDs are complex MPs consisting of non-HOMO molecular, partially nanoparticle, structures. Composition, in vitro and in vivo characteristics are defined by manufacturing. Subtle changes of the manufacturing modify quality, efficacy and safety of the MP. NBCDs are not fully characterised physicochemically. In contrast to biosimilars, a regulatory framework is not established.

Purpose Intended copies of NBCDs such as the iron sucrose similars have been approved in several countries by the classical generic pathway. Growing scientific evidence in the non-clinical and clinical setting has raised doubts about interchangeability and/or substitutability.

Material and Methods

Science-based statements for comparability of intended copies and reference MPs were discussed among experts from regulatory science, clinicians, hospital pharmacists and industry in a Workshop at FIP 2012. The conclusions were used to propose regulatory requirements for NBCDs.

Results The FIP 2012 consensus meeting confirmed the lack of an appropriate regulatory market authorization of intended copies of NBCDs. For liposomes, physicochemical equivalence testing seems to be more likely to be achievable, but clinical efficacy trials are needed on a case-by case base (EMA). Nanoparticle iron sucrose similars show almost no comparability and therapeutic equivalence has to go through quality, efficacy and safety assessments [2]. Glatiramoids, with a not-understood mode of action, also need a broad, as yet to be defined, regulatory approach. Nanoparticle assessment includes sizing and morphology (FDA) and also evaluation of in vivo biodisposition (EMA). The upcoming Terminology and a White Paper will integrate these conclusions.

Conclusions For NBCDs and their specific characteristics a regulatory pathway is needed to assess comparability and eventually therapeutic equivalence of originator and intended copy MPs. In multiprofessional medicines management specific attention to the limits of interchangeability and substitutability is mandatory.

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No conflict of interest.

GRP-125 OBSERVATIONAL PROSPECTIVE STUDY ON PULMONARY ARTERIAL HYPERTENSION AND DRUG EXPOSURE

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Background Pulmonary arterial hypertension (PAH) is a rare disease characterised by an elevation of the pulmonary vascular resistances leading to right cardiac failure and death. Among different aetiologies of PAH, association with drug exposure was proved forty years ago with aminorex and more recently with benfluorex. Other drugs such as dasatinib or interferons seem to be associated with PAH development and/or severity. Pharmacovigilance is critical to improve our knowledge of PAH associated with drug exposure.

Purpose To confirm the feasibility of collecting the drug exposure history in PAH patients during hospitalisation by a systematic interview.

Materials and Methods This pilot study was performed in the French national PAH reference centre. Patients with idiopathic, heritable PAH, PAH known to be associated with drug exposure and pulmonary veno-occlusive disease were included. A standard questionnaire to collect the past and current medicines history was designed and approved by pharmacists and pneumologists. For each patient, this questionnaire was systematically assessed by a pharmacist after patient consent had been obtained.

Results Interviews were performed in 57 PAH patients. The median time of interview was 30 minutes. 16% of patients had a history of anorexigen exposure which led to 5 pharmacovigilance reports. The remaining four other patients were already known to the pharmacovigilance centre. Twenty seven patients (47%) had been exposed to psychoactive drugs, two patients to cytotoxic agents and one patient to interferon. Interestingly, a quarter of all patients had a history of nasal vasoconstrictor exposure.

Conclusions This pilot study demonstrates the feasibility of collecting the history of drug exposure in PAH patients during hospitalisation. Our observations match those reported in the literature except for the nasal vasoconstrictors, for which no epidemiological data have been published yet. Further studies are warranted to investigate the potential harmfulness of nasal vasoconstrictors.

No conflict of interest.

GRP-126 OFF-LABEL PRESCRIPTIONS IN THE NEONATAL INTENSIVE CARE UNIT AT MARSEILLES NORTH HOSPITAL

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Background The availability of drugs specifically assessed for use in neonates is limited as evaluation is more difficult in neonates than in adults. The result is a widespread off-label use of drugs, especially in neonatal intensive care units. Such practise is an essential part of their care and should be based on the best available evidence.

Purpose To describe and analyse the off-label use of medicines in a neonatal intensive care unit.

Materials and Methods Prospective observational study conducted over three months, from 27 February 2012 to 27 May 2012. All the drugs prescribed were analysed with regard to their licence status for the: indication, dose, route of administration, mode of administration, age category, formulation (compounding of capsules, oral suspensions, eye drops), contraindications and warnings specified in the summary of product characteristics of the marketing authorization.

Results In total, 638 prescriptions, comprising 59 different medicines were written, 107 newborn babies were admitted (60 male, 47 female). Their age varied from 0 to 27 days (average: 2 days), their mean gestational age was of 34 weeks of amenorrhea (65% premature), their weight ranged from 630 g to 4700 g (average: 2230 g). A total of 487 prescriptions were written off-label (76%), with 101 patients (94%) receiving at least one drug used off-label. Drugs were prescribed off-label mostly concerning the indication (48%), then came off-label use for the dose and the age category. The medicine most often prescribed off-label was caffeine citrate.

Conclusions Critically ill neonates are exposed to numerous medicines, a significant proportion of which are not yet approved for use in this vulnerable group of patients. Despite European initiatives aiming to promote greater awareness and research in the paediatric population, there is still a high percentage of unlicensed or off-label drug use in neonatal intensive care. This study underlines the need for clinical research and approval of the clinical data acquired within the neonatal population.

No conflict of interest.