Material and methods Tacrolimus 0.06% adhesive gel was compounded, in a biological safety cabinet with protection equipment for the manipulator, with tacrolimus 5 mg capsules (Prograf, Astellas Pharma), glycerin (Acofarma) and a lipophilic gel (Excipiente Acofar adhesivo oral, Acofarma). The compounded drug was packed on monodoses of 4.5 g with the aim of administering 2 mg of tacrolimus in 5 mL latex free luer lock syringes (Omnifix, B Braun). Each syringe was supplied with a rectal cannula (José Mestre, SA) for patient administration (1 g of gel is retained in the cannula). Tacrolimus gel was stored at room temperature, in a dry place and protected from light.

Galenic characterisation was carried out, according to good manufacturing practices,[2] testing for homogeneity and appearance, extensibility, pH and monodose mass extraction, weekly over 28 days. Determination of pH was made with pHmeter glp21.

Results For 28 days at room temperature: tacrolimus gel kept the same appearance (granular, translucent and colourless), there were no quite different values for extensibility and pH (5.99) and monodose mass extraction (3.50 g) results differed minimally (<5–10% difference). Currently, one patient is treated in our hospital with this formulation once every 2 days, responding positively, with no adverse effects and good tolerance.

Conclusion and relevance This gel preparation is stable for 28 days at room temperature, maintaining its galenic characteristics and it can be useful in patients with difficult to treat ulcerative proctitis.

REFERENCES AND/OR ACKNOWLEDGEMENTS

1. Jaeger SU, *et al*. Tacrolimus suppositories in therapy-resistant ulcerative proctitis. *Inflamm Intest Dis* 2018;**3**:116–124. doi:10.1159/000493979
2. Ministerio De Sanidad, Servicios Sociales e Igualdad. Guía de buenas prácticas de preparación de medicamentos en servicios de farmacia hospitalaria. *Junio* 2014.

No conflict of interest.

3PC-027 LONG TERM STABILITY OF A READY TO USE TOPICAL ANAESTHETIC GEL KIT

[1]E Dijkers*, [2]H Polonini, [2]A Ferreira, [3]C Zander. *[1]Global Innovation Project Manager, Fagron Bv, Rotterdam, The Netherlands; [2]Ortofarma Analytical Services, Ortofarma Analytical Services, Matias Barbosa, Brazil; [3]Fagron Inc, Fagron Inc, Saint Paul, USA*

10.1136/ejhpharm-2020-eahpconf.74

Background and importance Undergoing small surgeries, aesthetic procedures or needle injections can be stressful, especially for paediatric patients. Various local anaesthetics have therefore been developed to numb the skin, including commercially available medications. Unfortunately, shortage of medicines, including for local anaesthesia, remains a widespread and persistent problem. LETS GEL KIT is a ready to use kit developed by Fagron to compound a topical anaesthetic gel. LETS GEL KIT contains lidocaine hydrochloride (4% w/w), epinephrine bitartrate (0.18% w/w), tetracaine hydrochloride (0.5% w/w) and sodium metabisulfite (0.075% w/w). LETS has been shown to be equivalent in providing and maintaining anaesthesia in the treatment of facial lacerations, with up to 10-fold less systemic exposure, compared with a 2.5% lidocaine/2.5% prilocaine solution.

Aim and objectives To evaluate the chemical stability of the LETS GEL KIT when stored in syringes.

Material and methods Samples were stored in plastic syringes (Comar, USA) under controlled refrigeration (2–8°C) and controlled room temperature (20–25°C). Stability was assessed by examining colour, odour and pH, and by measuring the active content at varying time points (0, 30, 60, 90, 120 and 150 days) over a 150 day period. API quantification was performed by validated high performance liquid chromatography (HPLC-UV).

Results Throughout the whole study, no phenomena, such as turbidity, macroscopically visible crystal growth or phase separation, were observed. Colour, odour and pH showed no significant change. Drug content (%) after 150 days were (for refrigerated and room temperature, respectively): lidocaine hydrochloride 94.47±0.25 and 94.86±0.70; epinephrine bitartrate 97.90±0.33 and 98.82±0.20; and tetracaine hydrochloride 102.09±0.70 and 102.18±1.15.

Conclusion and relevance In the current study, LETS GEL KIT showed excellent stability under both controlled refrigerated conditions (2–8°C) and at room temperature (15–25°C) for up to 150 days. Therefore, prefilled compounded syringes using LETS GEL KIT can be a valuable alternative when commercial medication is not suitable or available.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of interest Corporate sponsored research or other substantive relationships:

The study was sponsored by Fagron BV.

3PC-028 COMPOUNDING AN ORAL LIQUID FORMULATION OF DIAZEPAM ALCOHOL FREE

[1]R Barbosa*, [1]A Capela, [1]C Sampaio, [1]S Fraga, [1]T Soares, [2]J Campos, [2]D Ferreira, [2]P Costa, [3]L Bighinati. *[1]Centro Hospitalar E Universitário São João- Epe, Pharmacy, Oporto, Portugal; [2]Faculdade De Farmácia Da Universidade Do Porto, Ucibio- Requimte-Pharmaceutical Tecnology, Oporto, Portugal; [3]Universitá Degli Studi Di Modena E Reggio Emilia, Chimica E Tecnologia Farmaceutiche, Modena, Italy*

10.1136/ejhpharm-2020-eahpconf.75

Background and importance Drug shortages is a common international problem. Pharmaceutical compounding is a viable alternative, especially relevant in paediatrics. An example of such a situation is the oral liquid formulation of diazepam, indicated for epilepsy and seizures. However, only formulations that use ethanol as a cosolvent are described in the scientific bibliographies. This excipient is not recommended in paediatrics, with children's age dependent proposed limits by EMA/FDA/WHO.

Aim and objectives To develop an oral liquid formulation of diazepam that is ethanol free.

Material and methods A compounding vehicle, B9, National Compounding Formulary, formulated with the suspending agent Avicel RC581 polymer was used to prepare an oral suspension of diazepam 0.4 mg/mL. Tablets and bulk material were used as drug sources. The stability of the drug was verified over 90 days under different temperature and storage conditions (ambient and refrigerated) with the inhouse high performance liquid chromatography (HPLC) method using the UltiMate 3000 HPLC (Thermo Fisher Scientific, USA). Particle size was measured using the Mastersizer 300 (Malvern Panalytical, UK).

Results After 7 days, more than 10% of drug loss was observed for the ambient storage preparations, both tablets and bulk, and for the refrigerated bulk preparation. The tablet refrigerated formulation maintained >90% of the drug content until the 60 day mark. No significative changes were

observed in particle size after 60 days in all samples. The organoleptic characteristics (smell, taste and texture) remained unchanged in all of the preparations until the third month.

Conclusion and relevance A stable alcohol free diazepam suspension was achieved. The tablets produced a more stable formulation than the bulk source, especially when stored at a lower temperature. This formulation can solve the problem of shortages, allowing the appropriate administration of paediatric treatments, while allowing compliance with the recommended composition limits of ethanol, by excluding this excipient from its composition.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

3PC-029 PAEDIATRIC DRUG RESISTANT EPILEPSY: NITRAZEPAM 1 MG/ML SOLUTIONS TO AVOID CLINICAL THERAPEUTIC ERROR

[1]MA Berardi*, [2]GB Ortenzi, [2]V Moretti, [2]E Adresciani, [2]AMF Garzone, [3]S Cappanera, [1]C Polidori, [2]A Pompilio. *[1]Università Degli Studi Di Camerino 'Scuola Di Scienze Del Farmaco E Dei Prodotti Della Salute', Facoltà Di Farmacia, Camerino, Italy; [2]Ospedali Riuniti Di Ancona, Sod Farmacia Pediatrica Ospedale Pediatrico G Salesi, Ancona, Italy; [3]Ospedali Riuniti Ancona, Sod Neuropsichiatria Infantile, Ancona, Italy*

10.1136/ejhpharm-2020-eahpconf.76

Background and importance The management of paediatric patient with drug resistant epilepsy (EDR) is complicated and often requires therapy and dose adjustments. The clinical pharmacist and child neuropsychiatry unit cooperate to prevent clinical therapeutic errors, common in the prescription of drugs with reduced and personalised dosages.

Nitrazepam (NTR) in children is recommended in epileptic spasms, in Dravet, West and Lennox–Gastaut syndromes. There is a probable risk of administration error due to the low prescribed dosage (125 µg/kg)[1] and crushing of commercial tablets.

Aim and objectives To make a liquid formulation with a standard concentration, easily adaptable to paediatric needs as weight changes, that is palatability, suitable and simple to use during hospitalisation and at home.

Material and methods Multiphase study:

- Phase I: data collection.

Retrospective study examined the medical records of children born 2008–2019 with a certain diagnosis of EDR: patient number, sex, age, epilepsy classification according to the International League Against Epilepsy criteria,[2] antiepileptic therapy and dose of drug were collected.

- Phase II: subject study of nitrazepam, its dosage and the galenic compounding formulation it was possible to use.
- Phase III: chemical–physical–microbiological stability analysis of nitrazepam 1 mg/mL.

Samples were stored for 30 days at 2–8°C and/or ambient at 25°C. Chemical–physical stability was measured by quantitative determination of the molecular ions of nitrazepam C282.1/C236, using high pressure liquid chromatography (HPLC), equipped with a UV detector, interfaced with a triple quadrupole mass detector (mass spectrometer, MS/MS), column Luna C1850 mm, standard nitrazepam D5 100 µg/mL.[3] Microbiological stability was assessed according to the Italian Ufficial Farmacopea (FUI).[4]

Results A total of 101 children with EDR (54 males, 47 females) were studied, aged mainly 3–4 years (20%) and 9–10 years (33%). Classifications: focal onset in 34.86%, focal to bilateral tonic–clonic in 17.10%, generalised onset in 47.36% and unclassified in 0.65%. Thirty-one drugs are prescribed, the most used were: levetiracetam (27%), clobazam (25%), topiramate (21%) and NTR (12%). Required dosages of NTR difficult to administer: 0.625 mg, 0.83 mg, 1.25 mg, 1.66 mg and 2.5 mg. Three liquid galenic formulations were set up (NTR from Mogadon 5 mg tablets): NTR 1 mg/mL simple syrup methylcellulose 1%, NTR 1 mg/mL suspension tragacanth gum and NTR 1 mg/mL Syrspend SFAlkaDry.[5]

HPLC MS/MS analysis confirmed uniform and steady dosage, and 30 day stability for NTR 1 mg/mL suspension and NTR 1 mg/mL Syrspend SFAlkaDry.

Conclusion and relevance Good clinical practice and collaboration between departments allowed better management of epileptic seizures in children affected by severe EDR. Reproducible and safe therapy means improving patient's life and therapeutic compliance.

REFERENCES AND/OR ACKNOWLEDGEMENTS

1. British National Formulary for Children 2014
2. https://www.ilae.org/files/ilaeGuideline
3. https://www.sigmaaldrich.com
4. Farmacopea Ufficiale Italiana XII ed.
5. https://fagron.com/en/product/syrspendr-sf-alka-dry

No conflict of interest.

3PC-030 ANALYTICAL METHOD VALIDATION TO CARRY OUT PHYSICOCHEMICAL STABILITY STUDIES OF METHADONE ORAL SOLUTIONS

[1]EA Álvaro Alonso*, [2]MP Lorenzo García, [2]FJ Rupérez Pascualena, [2]A Aguilar Ros, [1]P Tejedor Prado, [1]A Lázaro Cebas, [1]I Cañamares Orbis, [1]S Esteban Casado, [1]A Such Díaz, [1]I Escobar Rodríguez. *[1]Hospital Universitario Infanta Leonor, Pharmacy, Madrid, Spain; [2]Universidad Ceu San Pablo, Pharmacy, Madrid, Spain*

10.1136/ejhpharm-2020-eahpconf.77

Background and importance On the basis of resolution 189/2018 published by our city health council, the hospital pharmacy service was entrusted with the centralisation of the procedure for the acquisition, compounding, distribution and dispensing of methadone to drug addicts in integral attention centres. In order to improve and increase the beyond use date (BUD) of methadone oral solutions, we carried out a physicochemical stability study.

Aim and objectives To develop an analytical method and validation to carry out a physicochemical stability study of two oral solutions of methadone to increase their BUD. Method development should be made in an effective and reproducible manner.

Material and methods The study was carried out on two formulations of methadone 10 mg/mL, which were prepared with and without parabens as preservatives. A high performance liquid chromatography (HPLC) Agilent 1100 was used, provided with a quaternary pump and an ultraviolet diode array detector to determine methadone. First we carried out the analytical method development to achieve the analytical performance characteristics. Then we performed validation of the analytical method obtaining linearity, instrumental intra-assay and inter-assay precision, and accuracy and recovery percentage.

Results Chromatographic conditions were: flow rate 1.6 mL/min, 55% acetonitrile and 45% phosphate buffer (adjusted to pH=10) as the mobile phase. Injection volume was 50 µL,