Background and importance Ceftolozane/tazobactam is a combination of a new third generation cephalosporin and a β-lactamase inhibitor used to treat infections caused by multidrug resistant *Pseudomonas aeruginosa*. The usual dose is 3 g/day. To the best of our knowledge, no stability data for ceftolozane/tazobactam at 62.5 mg/mL in polypropylene syringes (PS) for intensive care units or at 25.0/12.5 mg/mL in elastomeric devices (ED) for home administration have been published.
Aim and objectives The objective was to study the stability of ceftolozane/tazobactam solutions at 62.5/31.25 mg/mL, diluted in 0.9% sodium chloride (0.9% NaCl) or dextrose 5% in water (D5W), in PS after storage at 20–25°C, not protected from light, and solutions at 25.0/12.5 mg/mL diluted in 0.9% NaCl or D5W in ED after storage at 37°C, during a 48 hour period.
Material and methods Three preparations for each condition were prepared. At the time of analysis, one sample for each preparation was analysed by a validated high performance liquid chromatography method coupled to a photodiode array detector at 220 nm. Physical stability was evaluated by visual and subvisual inspection (turbidimetry by UV spectrophotometry at 350, 410 and 550 nm, as recommended by the European Consensus Conference). pH values were measured.
Results Linearity was validated with an R^2 of 0.9999. The coefficients of variation on repeatability and intermediate precision were <2%. In 0.9% NaCl and D5W, ceftolozane/tazobactam retained more than 90% of the initial concentration after 48 hours in PS. After 24 hours in ED, the concentration of ceftolozane remaining was 91% in 0.9% NaCl and 89% in D5W. A major degradation product, observed during the forced degradation, appeared progressively after 8 hours. At 24 hours in ED, it represented 3.8% of the total peak area. A second degradation product eluted with tazobactam. After 24 hours, the solutions yellowed in the ED. During the stability study, pH values were all between 5.95 and 5.26.
Conclusion and relevance In ED, ceftolozane/tazobactam was unstable at 37°C in D5W and in 0.9% NaCl. Ceftolozane/tazobactam was stable at 62.5/31.25 mg/mL in PS diluted in 0.9% NaCl or D5W for 48 hours, allowing continuous intravenous infusion.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of interest No conflict of interest

3PC-060 PHYSICOCHEMICAL STABILITY OF VANCOMYCIN SOLUTION IN ELASTOMERIC DEVICES AT 37.5 MG/ML IN 0.9% SODIUM CHLORIDE AND DEXTROSE 5% IN WATER

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Background and importance Vancomycin is a time dependent antibiotic of the glycopeptide family. The recommended dose of vancomycin is 30–40 mg/kg/day. For an adult, the maximum daily dose can reach 4 g. In clinical practice, vancomycin is mostly administered by continuous infusion. After hospitalisation, administration of concentrated solutions in elastomeric devices would allow a home care service and a better quality of life for the patient.
Aim and objectives The objective of this work was to study the stability of vancomycin solutions at 37.5 mg/mL (4.5 g in 120 mL of solvent) diluted in 0.9% sodium chloride (0.9% NaCl) or in dextrose 5% in water (D5W), in elastomeric devices, protected from light, at 37°C for 48 hours.
Material and methods Chemical stability was analysed by high performance liquid chromatography coupled to a photodiode array detector and by pH measurements after preparation, after 24 hours and 48 hours of storage. The method was validated according to the International Conference on Harmonisation Q2 (R1). Three elastomeric devices for each condition were prepared. Physical stability was evaluated by a visual and subvisual inspection at each time of analysis (turbidimetry by UV spectrophotometry at three wavelengths: 350, 410 and 550 nm).
Results For each solvent, solutions at 37.5 mg/mL retained more than 90% of the initial concentration for 48 hours: for 0.9% NaCl (minimum 96.49%±1.12%; maximum 100.94% ±0.51%) and for D5W (minimum 102.75%±1.19%; maximum 104.67%±1.15%). During the study, pH values did not decrease after 48 hours in the two solvents. During the subvisual examination, there was no significant difference between the different analysis times regardless of the solvent used. No colour change was reported during the study.
Conclusion and relevance Vancomycin solutions at 37.5 mg/mL in 0.9% NaCl and D5W were stable in elastomeric devices for 48 hours at 37°C, protected from light. Home administration for this concentration is possible.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of interest No conflict of interest

3PC-061 PHYSICOCHEMICAL STABILITY OF CLOXACILLIN SOLUTION IN POLYPROPYLENE SYRINGES AT 125 MG/ML IN 0.9% SODIUM CHLORIDE AND DEXTROSE 5% IN WATER

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Background and importance Cloxacillin is an antibiotic indicated in methicillin sensitive *Staphylococcus aureus* infections. The usual curative dosage ranges from 8 to 12 g/day, divided into 4–6 daily administrations. Continuous infusions are frequently used in the intensive care unit. The administration of concentrated solutions in an electric syringe pump would reduce the water supply and the number of daily intakes.
Aim and objectives The objective was to study the stability of cloxacillin solutions at 125 mg/mL diluted in 0.9% sodium chloride (0.9% NaCl) and in dextrose 5% in water (D5W), stored in polypropylene syringes, unprotected from light, at 20–25°C for 48 hours.
Material and methods Chemical stability was analysed by high performance liquid chromatography coupled to a photodiode array detector and by pH determination after preparation, and after storage for 6, 24 and 48 hours. The analytical method

was validated according to the International Conference on Harmonisation Q2 (R1). Four syringes for each condition were prepared. Physical stability was evaluated by visual and subvisual inspection (turbidimetry by UV spectrophotometry at 350, 410 and 550 nm).

Results For each solvent, solutions at 125 mg/mL retained more than 90% of the initial concentration for 24 hours: for 0.9% NaCl (minimum 96.57%±1.69%; maximum 95.96% ±1.38%) and for D5W (94.96%±1.38%; 98.08%±0.48%). After 48 hours of storage, the solutions contained <90% of cloxacillin: a minimum of 89.58%±0.43% for 0.9% NaCl and 89.47%±0.79% for D5W. During the study, pH values decreased progressively during the 48 hours of storage and pH differences were >1 pH unit after 48 hours for both solvents. During the subvisual examination, absorbance values at 410 and 550 nm increased after 48 hours. A colour change was observed at 48 hours (from colourless to very slight yellow) in 0.9% NaCl. In D5W, the solutions stained more quickly; a very slight yellow colouration was visible after 6 hours of storage which intensified after 24 and 48 hours.

Conclusion and relevance Cloxacillin solutions at 125 mg/mL in 0.9% NaCl and D5W were stable in polypropylene syringes for 24 hours at room temperature. The solutions were unstable after 48 hours of storage.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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3PC-062 IMPACT OF THE PREPARATION OF 1.0 MG/ML NIVOLUMAB CLINICAL SOLUTION ON THE PARTICULATES (AGGREGATION) MEASURED BY DYNAMIC LIGHT SCATTERING: NACL AND GLUCOSE CONCENTRATION AND AGITATION EFFECT

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Background and importance Nivolumab (Opdivo) is a human immunoglobulin G4 monoclonal antibody that binds to programmed death receptor 1 (PD-1) and blocks its interaction with PD-L1 and PD-L2. As a complex protein, routine handling or unintentional mishandling of its solutions may cause degradation that could remain unnoticed but could potentially compromise the clinical safety and efficacy of the drug product.[1]

Aim and objectives To assess the impact on the nivolumab (Opdivo) aggregation process promoted by slight modification in the concentration of the compound (NaCl 0.9% or glucose 5%) used to prepare the clinical diluted solution of nivolumab at 1.0 mg/mL. Also, to assess the impact on the aggregation on nivolumab clinical diluted solutions (1.0 mg/mL, in NaCl 0.9% and glucose 5%) promoted by agitation stress.

Material and methods Nivolumab (Opdivo, 10 mg/mL) was diluted at 1 mg/mL using different NaCl (from 0.5% to 1.5%) and glucose (from 1% to 10%) solution concentrations. Also, clinical diluted solutions were subjected to manual gentle agitation (for 30 s and 1 min) and vortex agitation (Vortex VibraMix, 3000 rpm for 10 s, 30 s and 1 min). Particulate was tracked by dynamic light scattering (DLS) using a Malvern Zetasizer Nano ZS90.

Results Reference samples of diluted nivolumab at 1.0 mg/mL in NaCl 0.9% and 5% glucose showed a single particulate population with a hydrodynamic diameter (HD) of 9.66±2.96 nm and 10.67±2.68 nm, respectively, attributed to nivolumab monomers. No significant changes were obtained for HD when the concentration of the diluents was changed. Also, no significant changes were observed after performing the agitation stresses, showing that the HR values were always in the interval of the size of the monomers.

Conclusion and relevance Variation in NaCl and glucose concentrations around the clinical concentrations of 0.9% and 5% did not promote aggregation in a 1 mg/mL nivolumab solution detected by DLS. Also, agitation did not have any impact on aggregation on this clinical nivolumab solution.

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3PC-063 PERFORMANCE QUALIFICATION OF ROBOTIC SYSTEM FOR CYTOTOXIC DRUG PREPARATION IN A FULLY GMP COMPLIANT HOSPITAL PHARMACY

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Background and importance A robotic system for automated preparation of cytotoxic drugs, such as APOTECAchemo, ensures reduced occupational exposure to toxic substances and aseptic conditions. The most critical operations are performed by a robotic arm; the operator's intervention is limited to loading/unloading materials in a rotating warehouse through an unloading/loading area enclosed within a laminar airflow barrier. In European hospital pharmacies which comply with good manufacturing practice (GMP), the performances of the robot are assessed by GMP qualification to confirm that the technology meets the set quality standards.

Aim and objectives The aim of this study was to evaluate microbiological performances and environmental conditions during fully automated preparation with APOTECAchemo in a grade B cleanroom.

Material and methods Effectiveness of laminar airflow retention was checked by potassium iodide (KI) discus test in the unloading/loading area of the APOTECAchemo robot. Aseptic preparation of cytotoxic drugs was evaluated with media fill simulation tests on three consecutive days. In total, 240 products (180 infusion bags, 30 syringes, 30 elastomeric pumps) were automatically filled with single/double strength tryptic soy broth in lieu of drug products. Microbiological environmental controls were performed by passive air sampling (settle plates, four locations), surface sampling (contact plates/swabs, 14 locations), and active air sampling (three locations). Samples were taken for each shift. Media fill products were