3PC-017 ASSESSING THE STABILITY OF SANDOZ RITUXIMAB BIOSIMILAR AFTER EXPOSURE TO OUT-OF-FRIDGE CONDITIONS FOR 21 DAYS

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Background and importance Studies evaluating the effect of short temperature excursions on the quality of the unopened vial of Sandoz rituximab biosimilar (SDZ-RTX) stored in the original outer box at the caregiver level are lacking.
Aim and objectives This out-of-fridge (OOF) study simulated the impact of temperature excursion on the quality of SDZ-RTX.
Material and methods The OOF study was subsequently performed after 36 months of storage in long-term conditions (5 ±3°C) by exposing three batches of SDZ-RTX to two storage conditions: (i) 25±2°C/60±5% relative humidity (RH) and (ii) 30±2°C/65±5% RH, for up to 21 days. The impact of the temperature excursion was evaluated using the following parameters: purity (cation exchange chromatography (CEX), size exclusion chromatography (SEC) and non-reducing capillary electrophoresis-sodium dodecyl sulfate (nrCE-SDS)), identity (CEX and liquid chromatography-ultraviolet (LC-UV) peptide mapping) and also potency (complement-dependent cytotoxicity (CDC)-bioactivity). Other analyses are presented in the Results section.
Results No notable change was observed after 21 days at both OOF conditions (i) and (ii) for identity (charge and primary structure), pharmaceutical tests (clarity, visible and subvisible particles, container appearance, degree of colouration, pH, osmolality, extractable volume and container closure integrity testing), protein content by UV and microbiological parameters. After 21 days, slight changes were detected with SEC (decrease in purity of up to 0.4%), CEX (decrease in the main peak up to 0.8%, decrease in the sum of basic peaks up to 2.4% and an increase in the sum of acidic peaks up to 3.9%) and nrCE-SDS (decrease in purity up to 0.9%). For CDC-bioactivity, a notable change was observed in only one out of three tested batches; however, all results complied with the shelf-life specification at both OOF conditions (i) and (ii).
Conclusion and relevance The obtained stability data support the storage of SDZ-RTX for up to 21 days up to 30±2°C/65 ±5% RH. These results may be beneficial to avoid potential wastage of product and prevent distressing the patients regarding drug quality after short-term exposure to conditions outside the intended storage of 2–8°C.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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Conflict of interest No conflict of interest

3PC-018 COMPATIBILITY AND 30-DAY STABILITY OF FOUR INTRAVENOUS MIXTURES FOR MULTIMODAL ANALGESIA

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Background and importance Multimodal analgesia is based on the combination of different drugs and analgesic techniques in order to alleviate postoperative pain. One of the limitations of this technique is the lack of evidence about the stability of these mixtures in clinical practice.
Aim and objectives To evaluate the 30-day physicochemical compatibility of four analgesic mixtures of tramadol and ketamine, combined with dexketoprofen or ketorolac, ± methadone, in saline solution bags, for patient-controlled analgesia.
Material and methods Mixtures studied:

V1: tramadol-hydrochloride 7.5 mg/mL + dexketoprofen 2.26 mg/mL + ketamine 0.19 mg/mL
V2: V1 + methadone-hydrochloride 0.075 mg/mL
V3: tramadol-hydrochloride 7.9 mg/mL + ketorolac-trometamine 0.95 mg/mL + ketamine 0.4mg/mL
V4: V3 + methadone-hydrochloride 0.08 mg/mL.

Diluent: 100 mL normal saline (polypropylene bags). Four batches of each mixture were prepared in aseptic conditions using commercially available products. Bags were protected from light, and stored at 2–8°C. The following parameters were evaluated immediately after preparation (t0), 7, 15 and 30 days after preparation (all measures by triplicate) (i) colour change and/or precipitation (visual inspection) and turbidity (nephelometry), (ii) pH (potentiometry), (iii) drug concentration (ultra-high-performance liquid chromatographic-diode array (UHPLC-DAD)) and (iv) preservation of sterility by culture in enriched soybean casein digest broth.

Two chromatographic methods were developed (M1, M2) using two different columns: Acquity-HSS-C18 (100 mm×2.1 mm×1.8 µm) (M1) and Acquity-BEH-C18 (100 mm×2.1 mm×1.7 µm) (M2). The chromatographic method consisted of a gradient with acetonitrile/water. An acidic aqueous phase was also used with a high strength silica (HSS) column ($HCOONH_4$/HCOOH) and a basic aqueous phase with an ethylene bridged hybrid (BEH) column ($HCOONH_4$/NH_3), forcing different order of drugs' elution.
Results Physical parameters and pH remained unchanged during the study; pH range for V1, V2: 7.08–7.28; V3, V4: 6.76–6.91. The chromatographic methods proved to be stable after stress tests and showed good linearity (r^2>0.999) and high selectivity, with a detection limit between 0.1 and 0.3 mg/L at 215 nm. The percentage of drug recovery remained in the range 90±110% (97%–103%) of the initial concentration (t0) for all drugs in the four mixtures during the whole study period (coefficient of variation (CV) (%) 0.1–2.4). All samples preserved their sterility during the study.
Conclusion and relevance The four analgesic mixtures of tramadol and ketamine, combined with dexketoprofen or ketorolac, ± methadone, were stable for 30 days at 2–8°C in the conditions described in the study, allowing their centralised preparation at pharmacy service.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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