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Physicochemical stability of rocuronium bromide injection solution 10 mg/mL as bulk solution and in 10 mL ready-to-administer syringes

Objectives

Ready-to-administer (RTA) of Rocuronium bromide (Ro-Br) injection solutions prepared in the pharmacy department increase patient safety and efficiency during administration.

The objective of this study was to evaluate the physicochemical stability of 10 mL RTA syringes containing Ro-Br 10 mg/mL and prepared batch wise as pharmacy preparation.

Methods

Manufacture of Ro-Br bulk solution 10 mg/mL

- Dosage form: solution for injection, 500 mL glass bottles (type I), autoclaved (120°C, 15 min)
- Active substance: Ro-Br Ph. Eur.
- Excipients: NaCl, sodium acetate trihydrate, acetic acid 30%, distilled water

Aseptic preparation of Ro-Br 10 mg/mL RTA syringes 10 mL

- Source solution: released bulk solution Ro-Br 10 mg/mL
- Primary containers:10 mL BD plastipaK syringes
- Filling: semiautomatic filling and stoppering with Plümatex pump (Plümat, Espelkamp, Germany).
- Labelling: according to the German Pharmacy Ordinance
- Storage: refrigerated at 2-8°C

Stability test

- 6 months for RTA-syringes ,1 year for bulk solution
- Quality control: measurement of pH, osmolality, subvisible particles, sterility and endotoxin tests according to Ph. Eur. 9.0
- Content and purity: determination of Ro-Br concentrations by a stability-indicating reversed-phase high-performance liquid chromatography (RP-HPLC) method with photodiode array-detection (PDA) adapted from Ph. Eur. 9.0

Column	Orbit Sil 5 µm 250 x 4.6 mm
Flow rate	2,0 mL/min
Temperature column oven	30 °C
Injection volume	10 µl
Run time	10 min
PDA at	220 nm
Mobile phase	30% Tetramethyl ammonium hydroxide buffer (4,38 g/L) pH 7,4 70% ACN
Linearity	0,9901
Intraday Precision [RSD]	0,93%
Interday Precision [RSD]	3,41%
Timepoints of stability measurement	0,(7, 14), 28 days, 3, 6, (9 and 12) months

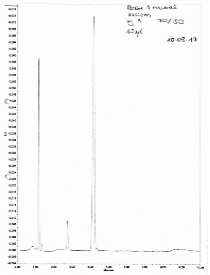

Fig. 1: HPLC chromatogram of Ro-Br

Results

The concentration of the Ro-Br injection solution in 500 mL glass bottles and in 10 mL PP syringes remained unchanged so far over a period of 6 months. After 6 months of refrigerated storage, the Ro-Br concentration amounted to 99% of the initial concentration in the RTA-syringes and 98% in the bottles, respectively (s. Fig. 2).

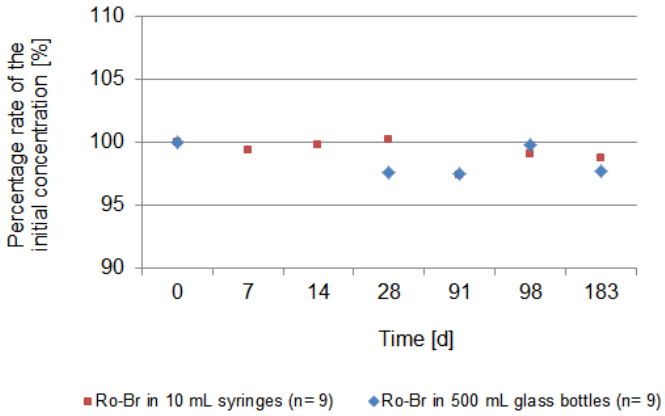

Fig.2: Stability of Ro-Br in 500 mL bottles and in 10 mL syringes over 6 months under refrigeration

No changes for pH and osmolality became obvious (Table 1).

Table 1 : pH and osmolality of Ro-Br in 500 mL bottles and in 10 mL syringes over 6 months under refrigeration

	Ro-Br in 10 mL syringes			Ro-Br in 500 mL glass bottles		
Days	0	28	183	0	28	183
pH (n=3)	4,07	4,15	4,10	4,08	4,15	4,09
Osmolality [mosmol/kg] (n=3)	282	286	288	276	284	281

Degradation products were not detected during the study period.

Conclusion

Pharmacy based aseptic preparation of 10 mL RTA syringes containing Ro-Br injection solution 10 mg/mL is feasible and efficient by starting with the powder and batchwise manufacturing of bulk solution. The bulk solution is stable for at least 6 months. Further stability data will be compiled.

The physicochemical stability of the batch wise aseptic preparation of 10 mL RTA syringes containing Ro-Br 10 mg/mL is given over a period of at least 6 months.

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