Stability study of an injectable hospital preparation of naloxone hydrochloride as part of a clinical trial

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INTRODUCTION

Injectable hospital preparation of naloxone hydrochloride (0.4 mg/ml) is administered by parenteral route as part of a multicentric double-blind clinical trial. This clinical research focuses on the evaluation of efficacity of the administration of naloxone 0.4 mg or placebo (0.9% Sodium chloride solution) in the reduction of severe dysfunction of post-critical tonic-clonic seizures. To meet regulatory requirements and have ready to use preparation with an expiration date, a stability study was realised.

MATERIALS AND METHOD

Hospital preparation was realised in an isolator under aseptic conditions associated with sterilizing filtration, then conditioning type II glass vials (5 ml filled to 1 ml) and finally stored in a climatic chamber at 25°C +/- 2°C. To assess the stability for preparation, physicochemical (naloxone assay by high performance liquid chromatography, sodium concentration, pH, osmolality, particles counting) and microbiologicals (bacterial endotoxin and sterility) were realised for preparation one year from a pilot batch.

RESULTS AND DISCUSSION

	Naloxone concentration (mg/mL)	Sodium concentration (mM)	pH	Osmolality (mOsm/kg)	Particles counting		bacterial endotoxin (UI/mL)	sterility
					≥10µm	≥25 µm		
Spécifications	0.4 +/- 10%	154 +/- 10%	3-5	290 +/- 10%	≤ 6000/mL	≤ 600/mL	≤ 0.5	Sterile
J0	0.42	146.7	4.32	305	43	12,4	< 0.05	Sterile
M3	0.40	153.3	4.42	294	12	< 1	NR	NR
M6	0.40	151.9	4.49	289	3	< 1		
M9	0.39	152.3	4.10	294	25	< 1		
M12	0.40	153.9	4.37	291	35	1.2	< 0.05	Sterile

J0 = First day of stability study M = Period of stability defined in month NR = Not realised

Throughout the stability study, neither significant naloxone concentration and sodium concentration nor pH and osmolality variations were observed. The variation of the concentration of naloxone remaining relative to the initial concentration was between 98.9% and 103.6%. Particles counting, the bacterial endotoxin and sterility were in accordance with the European Pharmacopoeia attesting limpidity, apyrogenicity and sterility of this injectable preparation.

CONCLUSION

The hospital preparation was stable over one year at 25°C +/- 2°C ensuring to safe a parenteral administration for human as part of the clinical trial.

BIBLIOGRAPHICAL REFERENCE

- *ICH Topic Q1A (R2) : Stability testing of new Drug Substance and Products. European Medicines Agency, 2003.*