**INTRODUCTION**

- Ceftolozane (cef)/tazobactam (taz) 1/0.5 g (ZERBAXA®): combination of a new 3rd generation cephalosporin and a β-lactamase inhibitor.
- Ceftolozane/tazobactam is used to treat severe infection (multi-resistant germs as *Pseudomonas aeruginosa*).
- The usual dose is 3/1.5 g per day and 6/3 g per day for serious infection (divided in 3 injections per day).
- β-lactam antibiotics have a time-dependent activity, the continuous administration of which improves therapeutic effectiveness.
- Should be validate long term stability.

**CHEMICAL STABILITY**

Method: RP-HPLC with DAD detector at 220 nm
- C18 LiChrospher® 12.5 cm, particle size = 5 μm
- Mobile phase: isocratic: potassium phosphate buffer (50 mM) / acetonitrile 1000/26 (v/v), pH = 3.4 adjusted with HCl 1 M
- Flow rate: 1 mL/min
- Injection volume: 20 μL

**STABILITY:**
- Visual inspection: search for colour change, precipitation and gas formation
- Subvisual inspection: turbidimetry by spectrophotometry at 350, 410 and 550 nm (Safas Monaco UV m²)

**MATERIALS AND METHOD**

**METHOD VALIDATION**
- Linearity: **R² > 0.9999** (cef) and (taz)
- Repeatability and intermediate precision: **CV < 2%**
- Retention time: 8.4 min (taz) and 8.7 min (cef)
- Stability indicating capacity: detection of 13 degradation products (in all stressed conditions)

**PHYSICAL STABILITY**
- Visual aspect: yellowing at 24 hours in elastomeric devices (0.9% NaCl an DSW)
- Subvisual aspect: a significant of the absorbance values at 350 and 410 nm wavelength after 24 hours in elastomeric devices (0.9% NaCl an DSW)

**CHEMICAL STABILITY**

Storage : 20-25°C, light, concentration: 62.5/31.3 mg/mL

**RESULTS**

**PHYSICAL STABILITY**

- pH measurements: decreased slightly with maximum variation: 0.7 unit pH (5.95 → 5.26), T0h → T48h for elastomeric devices. (DSW)

**METHOD VALIDATION**

**CONCLUSION**

- Physicochemical stability of ceftolozane/tazobactam at 62.5/31.5 mg/mL in 0.9% NaCl and DSW was proved for 48h in syringes
- Administration by continuous infusion in a minimal volume of solution.
- In elastomeric devices, ceftolozane/tazobactam at 25/12.5 mg/mL was stable at 37°C in the DSW and 0.9% NaCl for 8 hours
- Possible stability of 12 hours, further study to be carried out.