STABILITY STUDY OF 100 MG/ML PAEDIATRIC PYRAZINAMIDE ORAL SUSPENSION IN SYRSPEND

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BACKGROUND
Pyrazinamide (PZA) is an antituberculosis agent used in adjunctive treatment of tuberculosis infection in combination with other antituberculosis agents as isoniazid, rifampicin and ethambutol. Tablet form is unsuitable for pediatric patients and leads the pharmacist to produce oral suspension. Data about PZA stability in oral suspension are scarce and were got several decades ago. Thus, new stability informations are needed.

POURPOSE
Determine the stability of 100 mg/mL PZA oral suspension in commercial compounding excipic : Syrspend® SF PH4.

MATERIAL AND METHODS
Stability study according to the ICH guidelines
3 batches of oral suspension of PZA at 100 mg/mL → storage at room temperature in amber vials
Day : D0 → D3 → D5 → D8 → D15 → D30 → D60 → D90

Physical Stability
- Mesure of pH
  - phenomenal® VWR pHmeter
- Mesure of osmolality
  - Advanced Instruments Model 3250®
- Visual inspection

Chemical Stability
- Using a validated analytical method
  - Quantification of PZA
    - High Performance Liquid Chromatography with Ultraviolet detection
    - Mobile phase : acetonitrile/phosphate buffer pH 3 (40:60 v/v)
    - Column : WATERS C18 ATLANTIS T3 column (150 x 4.6 mm, 5 μm)
    - Flow rate : 1 ml/min; λ=270 nm
- Detection of degradation product

Microbiological Stability
- Test using colony counts on media platings
  - Trypticase Soja (35°C)
  - 1/10e dilution of suspension in water
- D0
- D15
- D30
- D60
- D90

RESULTS
- Physical stability
  - No change of physical properties was observed during the studied period
- Chemical stability
  - No degradation product
  - Variation of pH and osmolality of PZA oral suspension 100 mg/mL
  - Variation of pH and osmolality of PZA oral suspension 100 mg/mL
- Quantification of PZA
  - Measured concentrations within ± 5% of the nominal concentration

CONCLUSION
Finally, 100 mg/mL pyrazinamide oral suspension in Syrspend® SF PH4 is stable for at least 90 days at room temperature, so we determine a shelf life of 90 days for this preparation. Eventually this oral suspension could be used in children with tuberculosis infection throughout all the treatment duration usually recommended (3 months).