Development and stability of 40 mg/mL amiodarone suspension

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Introduction

Amiodarone: class III **antiarythmic drug**, used in the treatment of **supraventricular tachycardia**

- No commercial oral drug is suitable for the pediatric population
- Need to make capsules iteratively to adjust dose to body surface area and dosing schedule (loading or maintenance dose)

→ Develop an **oral form of amiodarone adapted to pediatrics**

→ Evaluate its **stability**

Material and methods

Choice of the concentration (1)
- 5-year **retrospective study** of prescriptions for amiodarone capsules manufactured in our hospital

Galenic formulation (2)
- Selection of **appropriate excipients** for pediatric use

Dosage method (3)
- **Developement** and **validation** of a **stability indicating method** by **UPLC-PAD**

Stability study (4)

3 batches
- ✓ 25°C ± 2°C
- ✓ 5°C ± 3°C

Packaging: brown glass vials
- *Vials « after opening »* (2 mL sample / day for 30 days): analysis at D0, D1, D3, D7, D15, D22 and D30
- *Vials « before opening »*: analysis at D0, D15, D30 and D60

Physico-chemical: concentrations, pH, osmolality, organoleptic characteristics

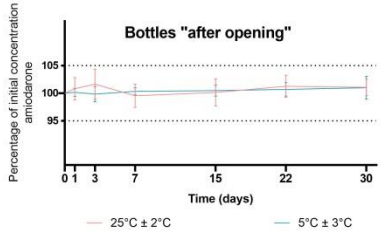
Microbiological: microbial enumeration(Eur. Ph. 2.6.12) and search for *E. coli* (Eur. Ph. 2.6.13): D0, D15, D30 and D60

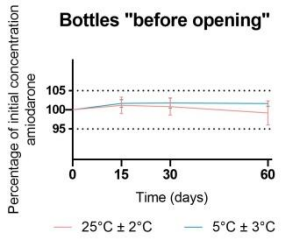
Results

47 children. Median age = 22 days. **Median dose = 90 mg** [IQR : 60 – 120 mg]
Selected concentration = **40 mg/mL**

Selected excipients: **thickener** (*HPMC*), **antimicrobial preservative** (*potassium sorbate*, evaluation of its efficacy according to Eur. Ph. 5.1.3), **citrate buffer**, **sweetener** (*sodium saccharin*) and **strawberry flavor**

- **pH** (≈ 4,3) and **osmolality** (≈ 86 mOsm/kg) remained **constant**
- **Concentrations** within the range of **95 – 105 % of the initial concentration**
- **Microbiological resultats in accordance** with specifications of the Eur. Ph.
- Appearance of crystals on the walls of the ambient vials « after opening »





Conclusion

→ **Develoment** of an **oral suspension of amiodarone at 40 mg/mL** adapted to pediatrics, with simples excipients

→ **Physicochemical and microbiological stability** at **60 days « before opening »** and **30 days « after opening »** at **5°C ± 3 °C**