



Development of ready-to-use cefuroxime syringes for use in ophthalmology

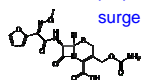
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Background

Cefuroxime: prophylaxis of postoperative endophthalmitis after cataract surgery (intravitreal injection)



Usually reconstituted just before injection due to the **low stability** in aqueous solution



RTU syringes of cefuroxime at 10 mg.mL⁻¹ in NaCl 0.9% (0.5 mL)



Batch production of RTU syringes of cefuroxime

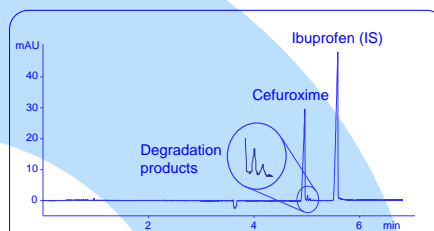
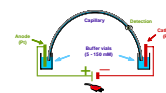
Preparation's **safety**
Medicine's **availability**



Stability-indicating method

Experimental conditions

CE: HP3DCE (Agilent Technologies, Germany)
Cap: Fused-silica cap., length 64.5 cm, i.d. 50 µm
BGE: Phosphate buffer 20 mM pH 7.2
Injection: 10 s 40 mbar
Voltage: 30 kV
UV: 200 nm



Electropherograms obtained for the CE-UV analysis of RTU cefuroxime syringes produced the HUG pharmacy

+ Separation from degradation products
+ Satisfactory quantitative performances
+ Stability-indicating method

-18°C Analysis immediately after thaw up

Time (d)	cefuroxime (%)	Degradation products (%)*
90	107	3
135	100	4

* Percent of peaks areas of degradation products with regard to cefuroxime peak area

Sterility & endotoxine determination were found negative in all cases. pH & osmolarity were constant. Particle counts were well within the limits specified by European Pharmacopeia during all the stability test.

Syringes of cefuroxime at 10 mg.mL⁻¹ can be stored **4 months at -18°C** without loss of potency. After defrosting, they must be used without delay given the rapid increase of degradation products.

Stability testing

4°C After 90 days at -18°C, syringes were stocked at 4°C 24 h, 7, 14, 21 and 33 days

Time	cefuroxime (%)	Degradation products (%)*
24 h	106	3
7 d	100	3
14 d	101	5
21 d	93	7
33 d	91	10

* Percent of peaks areas of degradation products with regard to cefuroxime peak area

The validation was based on ICH recommendations following the guidelines of SFSTP [1] and carried out over three series. Each series involved:

3 calibration standards at 80, 100 and 120% of cefuroxime in water
4 validation standards at 80, 100 and 120 % of cefuroxime in NaCl 0.9%.

100% corresponded to 0.2 mg.mL⁻¹ of cefuroxime

Theoretical conc. (%)	Trueness	Repeatability (CV)	Intermediate precision (CV)
80	100.7%	1.3%	1.4%
100	100.9%	1.3%	1.6%
120	99.0%	1.5%	1.6%

[1] P. Hubert et al., *Stp Pharma Pratiques* 13 (2003) 101-138

Validation Stability-indicating method