PP-044

STABILITY OF 50 AND 100µG/0.1ML INTRAOCULAR SOLUTIONS OF VORICONAZOLE AT 2-8°C

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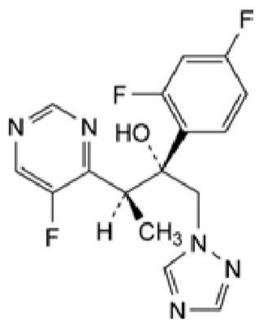
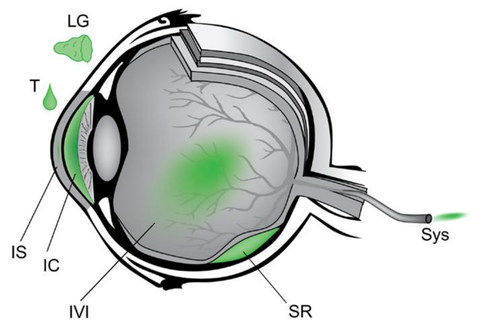


Background

Voriconazole is a triazole antifungal agent effective on most keratitis causative fungi.
Off-label use of extemporaneously compounded intraocular (intrastromal (IS), intracameral (IC)) Voriconazole has shown promising results in deep fungal ophthalmic infections and abscessed, recurrent or drug-resistant eye infections[1].
Stability studies on Voriconazole intraocular solutions (VIS) are lacking.



LG : lacrymal gland, T : Topical, IVI: Intra vitreal, SR: Sub retinal and Sys: Systemic

Purpose

To assess the stability of 50 and 100µg/0.1mL VIS stored in 3 part syringes at 2-8°C

Material and Methods

Voriconazole concentration was assessed using a stability-indicating HPLC-UV Diode-Array-Detector method (Ultimate 3000® Thermo Scientific, France).

Non visible particle count was performed using light obscuration particle count test (APSS-2000, Particle measuring systems, Boulder, USA) in regards to the European Pharmacopoeia 2.9.19 monography.

Statistical analysis were led using a Mann and Whitney's non parametric tests (α<5%). Degradation rates were compared with a Student's T test.

Compounding of Voriconazole intraocular solutions

Ringer's Lactate solution (BAXTER®)

Vfend® (PFIZER®)

Batch 1: 50µg/0.1mL
Batch 2: 100µg/0.1mL
X 66

Two batches of VIS (2mL) were aseptically compounded and **stored at 2-8°C** in 3mL 3 part syringes (ref 002022420, Pentaferte, Villeparisis, France).

Stability study led according to the GERPAC-SFPC stability studies guidelines

D0 D1 D3 D6 D10 D13 D30 D44

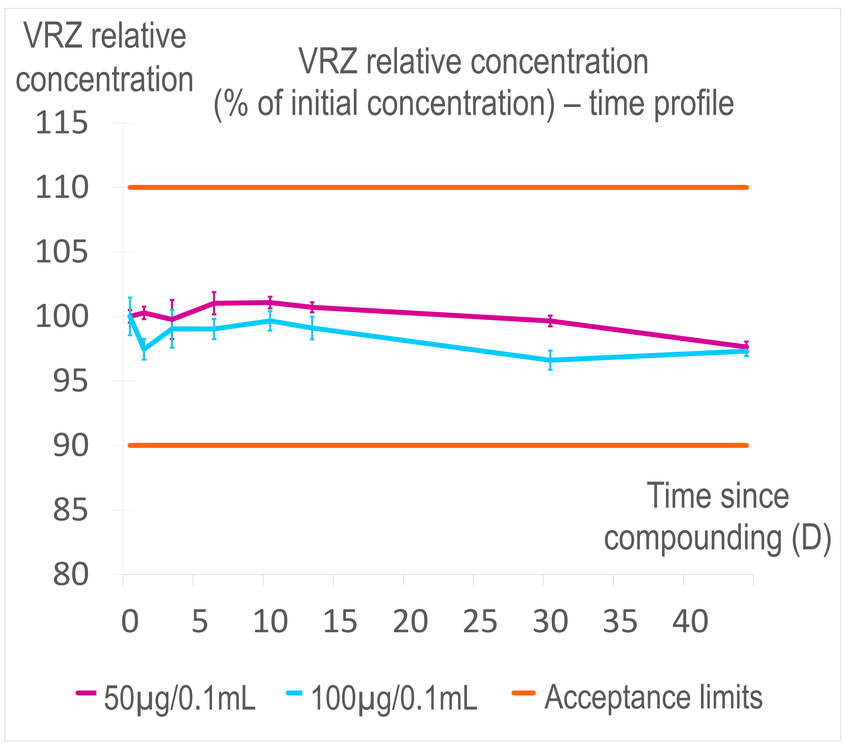
At each time point:

- Visual aspect
- And Voriconazole relative concentration (% of initial concentration)
- pH
- Osmolality

At D0 and D13:

- Non-visible particles count for particle size ≥10µm and ≥25µm (Eur Pharm 2.9.19 threshold: 6000 and 600 particles/recipient respectively)
- Sterility assay

Results



	D0 50µg/0.1mL	D13 50µg/0.1mL	D44 50µg/0.1mL	D0 100µg/0.1mL	D13 100µg/0.1mL	D44 100µg/0.1mL
Osmolality (mOsm/kg)	281.2	281.7	282.2	298.2	299.8	299.8
pH	6.78	6.86	7.11	6.64	6.88	7.09
Particles >10µm (particle/syringe)	240.3	339.07	Not measured	363.2	487.6	Not measured
Particles>25µm (particle/syringe)	3.3	4.4	Not measured	5.2	6.9	Not measured

Discussion

Considering every time point, confidence intervals for relative concentration are:

-For 50µg/0.1mL :]0.993;+∞[

-For 100µg/0.1mL :]0.951;+∞[

Relative concentration remained superior to 95% (p<0.0001)

NO CONCENTRATION EFFECT

No difference was shown in degradation rates between the two concentrations (p=0.497)

-50µg/0.1mL : 0.008 ± 0.120

-100µg/0.1mL : -0.231 ± 0.961

About Voriconazole degradation products (toxicity unknown), areas increased by maximum 1.3 (D13) and 2 (D44), remaining unquantifiable.

Sterility was preserved for at least D13 with no change in visual aspect

Osmolality remained stable for both concentrations for 44 days (p=0.490) and pH slightly increased (p=0.150)v

VIS remained stable for at least 13 days, based on sterility assays and non visible particles count.

Conclusion

Voriconazole intraocular solutions remained stable for thirteen days at 2-8°C.

We advise a shelf life of maximum thirteen days for both Voriconazole intraocular solutions kept at 2-8°C

[1] *Sharma N. et al. Evaluation of intrastromal voriconazole injection in recalcitrant deep fungal keratitis: case series. Br J Ophthalmol (2011); 95(12):1735-7.*