

Impact of temperature on the physico-chemical stability of Azacitidine Zentiva 25 mg/ml suspensions packaged in polypropylene syringes



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INTRODUCTION

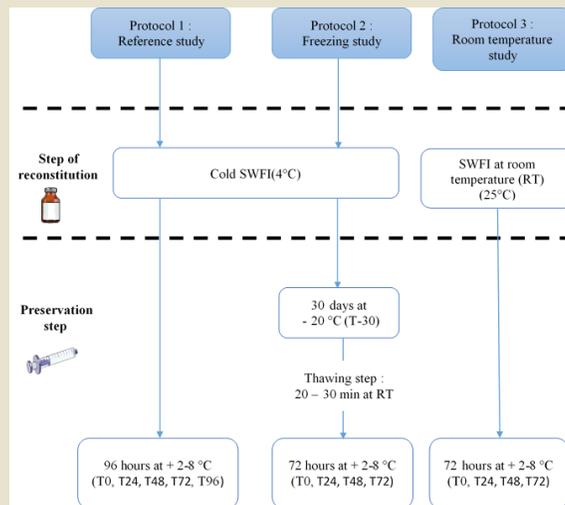
The arrival of generics makes it necessary to confirm the applicability of stability data. Previous studies on the originator have established a maximum stability time of 5 days at 4°C and up to 30 days for conservation at -20°C.

OBJECTIVE

The objective of this study was therefore to evaluate the impact of temperature on the physicochemical stability time of Azacitidine Zentiva suspensions contained in polypropylene syringes.

MATERIAL & METHOD

3 study protocols have been completed (see diagram)



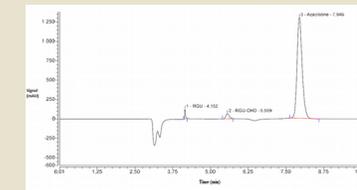
The physico-chemical stability of Azacitidine was estimated using the following validated methods:

- visual inspection
- High Performance Liquid Chromatography (HPLC)
- optical microscopy analysis
- turbidity measurement by UV-visible spectroscopy (500 nm)

RESULTS

Suspension is a cloudy, uniform, whitish suspension.

No changes in visual appearance were observed regardless of the conservation protocol.



The HPLC method was validated in a previous study. Azacitidine has a retention time of 7.9 min. The 2 degradation products (RGU-CHO and RGU) have retention time at 4.15 and 5.56 min respectively.



The suspension has been shown to be inhomogeneous with the presence of crystals of variable size, length and width. The appearance and shape of the crystals were unchanged after 96h of preservation at +4°C and after 30 days of freezing followed by 3 days at 4°C. The use of SWFI at room temperature did not affect the appearance of the suspension.

DISCUSSION- CONCLUSION

The stability of the Zentiva Azacitidine suspension at 25mg/ml is therefore 96 hours if reconstitution is carried out with refrigerated water and 48 hours if reconstitution is carried out with water at room temperature. If the suspension is kept at -20°C, it can be kept for 30 days followed by a period of 72 hours of storage between +2 and +8°C after thawing. These new stability data allow to maintain the current organization of the Pharmaceutical Technology Unit Hospital for the preparation of Azacitidine syringes with the Zentiva generic, i.e. the advance preparation. The study carried out with water at room temperature for reconstitution provides an answer to the pharmacy having difficulties to respect this parameter.

