

STABILITY STUDY OF 10 MG/ML CYCLOPHOSPHAMIDE SOLUTION

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BACKGROUND & OBJECTIVE

Used in oral onco-paediatric therapy for the treatment of Ewing's sarcoma or rhabdomyosarcoma, only cyclophosphamide tablets are marketed.

- Difficult to adapt for paediatric use
- Manufacture of oral liquid magistral preparations, often made with syrup containing excipients with know effects (EKE), for which few stability data are available



To perform a stability study of a 10 mg/mL oral solution of cyclophosphamide without EKE, in order to establish a shelf life

MATERIAL & METHOD

Formulation:

30 mL of cyclophosphamide solution Endoxan® 1000 mg/50 mL (reconstituted with water for injection) + 30 mL

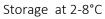
d'Inorpha[®]

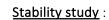
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3 batches packaged in amber glass bottles



, at 2.0°C





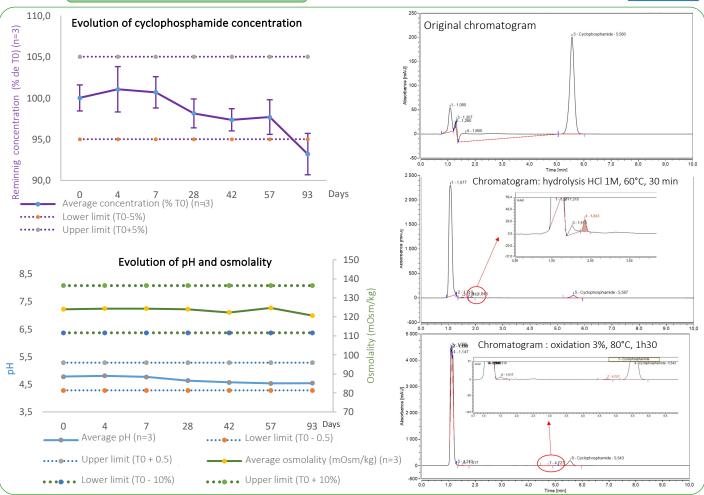
D0, D4, D7, D28, D42, D57, D93

CONCLUSION

Parameters studied:

- Organoleptic properties (color, visible particle, odor)
- pH and Osmolality
- Quantification of Cyclophosphamide content and detection of degradation products :
- Validated stability-indicating method according to ICH Q2R2
- o Analytic method parameters :
- Fig. HPLC with UV detection $\lambda = 195$ nm
- ➤ Column : Hypersil Gold®, Thermo Scientific, 100 x 2.1 ; 3 µm
- ➤ Mobile phase : water/Acetonitrile (80:20) (v/v)
- ➤ Flow rate : 0.3 mL/min
- > Injection volume : 1 μL

RESULTS



- Remaining cyclophosphamide concentration : > 95 % of the initial concentration for 57 days, no degradation product was observed
- pH and osmolality: constant throughout the study.
- Organoleptic properties: unchanged.

An EKE-free oral solution of cyclophosphamide 10 mg/mL was developed using the neutral formulation of Inorpha®. In addition to flavouring, this vehicle contains a bitterness-masking agent of particular interest for this active substance. The physicochemical properties of this preparation appear to be stable for 57 days when stored in amber glass bottles at 2-8°C.