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INTRODUCTION

Bortezomib is widely used mainly for the treatment of multiple myeloma. The stability of reconstituted bortezomib solution is 8 hours in syringes according to the manufacturer, and only 5 days at 2-8°C and 3 days at room temperature according to Andre and al¹. This short stability makes difficult to prepare in advance standardized doses in syringes without any risk of losing the syringes if the administration is cancelled or postponed.

OBJECTIVE

The aim of our study is to investigate the long-term stability of 1mg/mL bortezomib solution in syringes over 35 days to prepare the syringes in advance.

METHOD

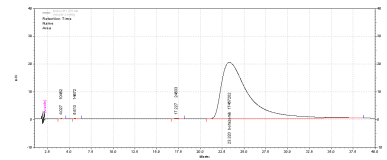
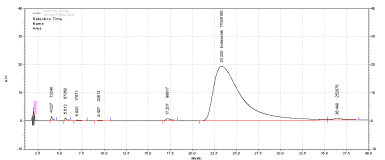
Four syringes were prepared after reconstitution of 3.5mg of bortezomib with 3.5mL 0.9% sodium chloride to obtain a 1mg/mL solution. Two were stored under refrigeration (2-8°C) and two at room temperature. Criteria of stability were defined as retention of at least 95% of the initial drug concentration and as percentage of degradation products below 1%. After a visual inspection, samples of each syringe were analysed after preparation (day 0) and on days 2, 4, 7, 14, 21, 28, 35 with a stability-indicating high-performance liquid chromatography assay².

STORAGE AT ROOM TEMPERATURE

RESULTS

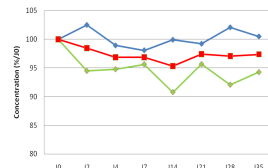
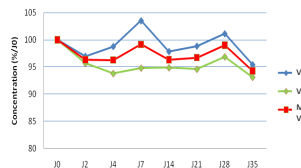
STORAGE UNDER REFRIGERATION

Chromatograms after 35 days



Percentage of bortezomib compared to the initial value at day 0

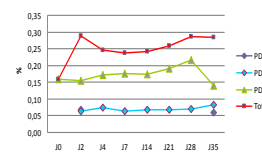
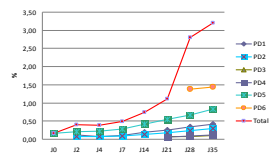
Solution retained over 95% of the initial bortezomib concentration until day 28



Solution retained over 95% of the initial bortezomib concentration until day 35

Percentage of the areas of the degradation products compared to the sum of the areas of all products

Six products of degradation appeared corresponding to 3% of the total peaks areas at day 35



Three degradation products appeared corresponding to 0.4% of total peaks areas at day 35

DISCUSSION - CONCLUSION

Bortezomib 1 mg/mL solution in syringe was stable for 35 days between 2-8°C
Bortezomib 1 mg/mL solution in syringe was stable for 14 days at 25°C

APPLICATIONS

Preparation in advance of a large number of syringes at standardized doses with an expiry date at 35 days

Immediate availability after addition of a label with the name of the patient on the day of the administration

No waiting time for the patient

Preparation in advance of standardized doses labelled for one patient

Immediate availability

No waiting time for the patient

Reallocation of syringe if injection is cancelled or postponed

Relabel with a secure procedure

No additional cost due to the advance preparation

At the University hospital of Nancy, France, during a six months period (July to december 2011) we have prepared standardized doses labelled for each patient the day before the administration.

247 syringes of Velcade® prepared in advance : considerable reduction of the waiting time for the patient in the wards
10 syringes reallocated (4%) : more than 8 000 euro of loss avoided

¹ Ref : ANDRE and al
Ann Pharmacotherapy 2005;39:1462-66.

² Ref : WALKER and al
Can J Hosp Pharm 2008; 61,1:14-20.