Ertapenem's long half-life makes it a potential option for outpatient parenteral antimicrobial therapy. Ertapenem has been used for treatment of infections where once daily parenteral administration is an advantage or where a single 1 g dose has improved patient outcomes, such as for prophylaxis following transrectal biopsy of the prostate. Frequently these 1 g single doses are administered as 100 mg/mL solutions.

Previous studies of ertapenem stability have evaluated concentrations of 10 and 20 mg/mL in normal saline (NS) and have recommended storage at 4C for 5 days or 24 hours at room temperature. However, the degradation rate of ertapenem has been reported to be concentration dependent. Therefore, it is apparent that the stability of 10 and 20 mg/mL solutions of ertapenem should not be extrapolated to 100 mg/mL solutions.

The current Canadian product monograph for ertapenem (Invanzem®) states that a reconstituted 100 mg/mL solution should be used within 6 hours following reconstitution. However, a 2014 AJHP paper (Jain et al) reported more than 12% loss of the initial concentration within 1 hour at room temperature. This observation suggests a very different degradation rate and suggests that each dose be freshly reconstituted.

Therefore, the inconsistencies between the recommendations in the product monograph and those of Jain et al (AJHP 2014) need to be reconciled.

**OBJECTIVES**

The objective of this study was to evaluate the stability of the a 100 mg/mL solution of ertapenem stored in both polypropylene syringes and the manufacturer’s original glass vial at both room temperature (23°C) and 4C over 18 days. During the 18-day study period, the drug concentration was determined on 6 study days (days 0, 1, 2, 4, 7, 11, 14 and 18).

**METHODS**

**LIQUID CHROMATOGRAPHIC METHOD**

A liquid chromatographic stability–indicating method with UV detection at 226 nm was developed and validated.

**STABILITY STUDY**

On study-day zero, 12 x 1000 mg vials of ertapenem (Invanz®, Merck Canada) were reconstituted according to the manufacturer’s instructions with 10 mL of 0.9% sodium chloride to prepare 100 mg/mL solutions. The contents of 6 vials were each drawn into 10-mL polypropylene syringes. Three of the original manufacturer’s glass vials and 3 syringes were stored at room temperature (23°C), unprotected from fluorescent room light, and 3 vials and 3 syringes were stored in the refrigerator (4°C). The objective of this study was to evaluate the stability of the a 100 mg/mL solution of ertapenem stored in both polypropylene syringes and the manufacturer’s original glass vial at both room temperature (23°C) and 4C over 18 days. During the 18-day study period, the drug concentration was determined on 6 study days (days 0, 1, 2, 4, 7, 11, 14 and 18).

**DATA REDUCTION AND STATISTICAL ANALYSIS**

Analysis of variance was used to test differences in observed concentration between the storage temperatures and container combinations. A 95% Confidence Interval was constructed around the degradation rate and the Time to Achieve 90% of the initial concentration (T-90) was calculated.

**RESULTS**

The current Canadian product monograph for ertapenem (Invanz®) states that 100 mg/mL solutions should be used within 6 hours following preparation. A recently published evaluation of the stability of 100 mg/mL solutions reported 12.2% loss during the first hour. However, the rate of loss reported by Jain et al is inconsistent between test solutions and with time. The rate of loss declines dramatically to 1.7% per hour between 4 and 24 hours. A rate of loss of 1.7% per hour is very consistent with the 6 hour recommendation found in the product monograph and observed in this study.

We have analyzed our results assuming a first order rate of loss based on the rate of loss observed in our accelerated degradation study and the slightly better correlation coefficients observed with our study data (r-values = 0.997 for first order compared to 0.987 for zero order rate analysis). This improved the prediction of the degradation rate and reduced the error between 3 and 4.5 fold. The data of Jain et al can also be fit to a first order decline in concentration (r-value of 0.972 for first order compared to 0.930 for the zero order rate analysis at 28°C) and reduces the error by more than half; however, the rate of loss continued to change during the study period.

We conclude that reconstituted solutions of 100 mg/mL of ertapenem stored in the manufacturer’s original glass vial or polypropylene syringes are chemically stable for up 48 hours at 4C. This may allow for preparation in advance to optimize workload when multiple patients are scheduled for outpatient procedures requiring ertapenem for pre-procedure prophylaxis.

**DISCUSSION & CONCLUSION**

The current Canadian product monograph for ertapenem (Invanz®) states that 100 mg/mL solutions should be used within 6 hours following preparation. A recently published evaluation of the stability of 100 mg/mL solutions reported 12.2% loss during the first hour. However, the rate of loss reported by Jain et al is inconsistent between test solutions and with time. The rate of loss declines dramatically to 1.7% per hour between 4 and 24 hours. A rate of loss of 1.7% per hour is very consistent with the 6 hour recommendation found in the product monograph and observed in this study.

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