Are Zavicefta® and Zerbaxa® sufficiently stable for Outpatient Parenteral Antimicrobial Therapy?

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Introduction

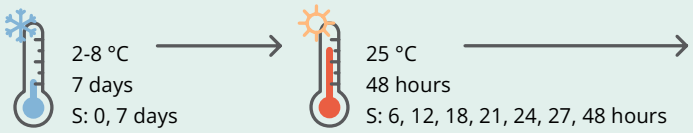
Parenteral antibiotic therapy is essential for the treatment of severe infections but often results in elongated hospitalization. Therefore the interest in outpatient parenteral antimicrobial therapy (OPAT) is growing. OPAT is usually performed with a continuous antibiotic infusion administered over 24 hours through an elastomeric device that allows outpatient administration. Especially for fragile beta-lactam antibiotics, stability needs to be investigated thoroughly. Aim of this work was to determine whether the reserve antibiotics Zavicefta® (Ceftazidime/Avibactam) and Zerbaxa® (Ceftolozane/Tazobactam) are suitable for OPAT.

Materials and Methods

Hospital Pharmacy

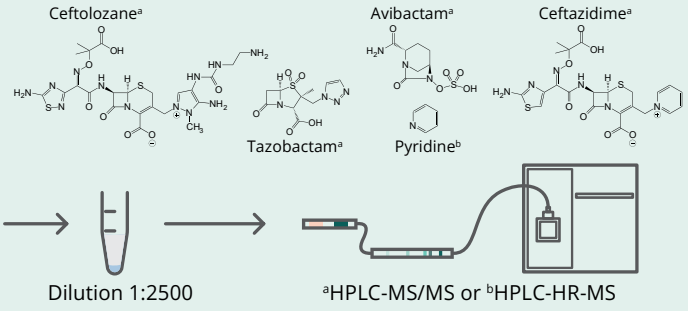
1. Preparation of 15 OPAT pumps (240 mL)

2. Incubation and sampling (S)



Laboratory Medicine

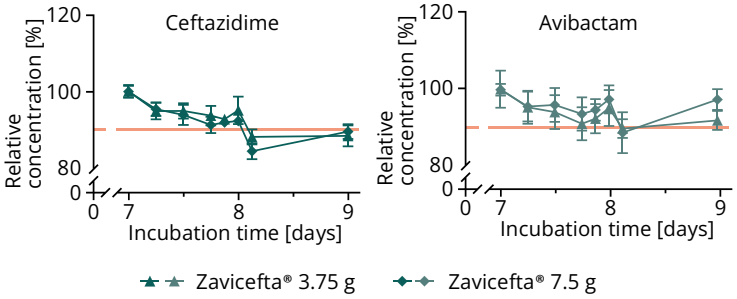
3. Quantification analytes of interest



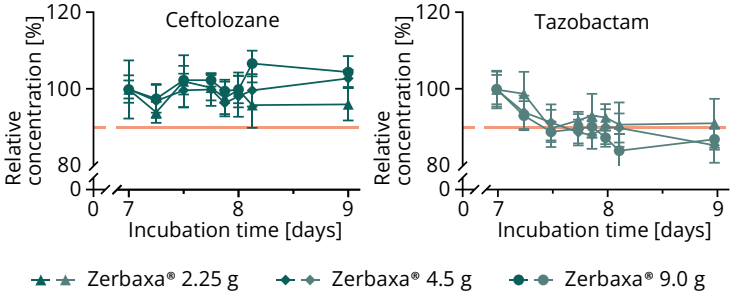
Results

Mean values for each time point were calculated out of the concentrations of 3 samples of all 3 pumps for ceftazidime, avibactam, ceftolozane and tazobactam and out of 1 sample of all 3 pumps for pyridine. The pumps were incubated for 7 days at 2-8 °C and thereafter for 2 days at 25 °C.

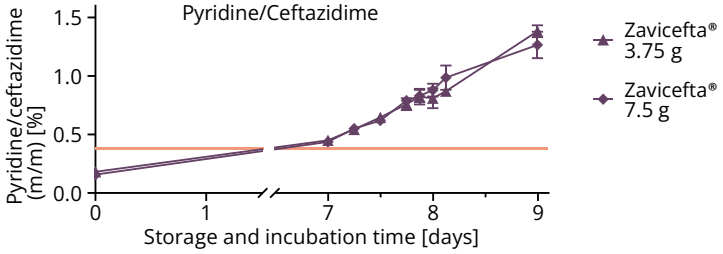
Zavicefta®



Zerbaxa®



Zavicefta® degradation product Pyridine



The European Pharmacopoeia allows 0.38 % pyridine/ceftazidime (m/m) in ceftazidime solutions for infusion [1]. This limit was already exceeded after 7 days storage at 2-8 °C. The ratios pyridine/ceftazidime (m/m) were calculated per mean ceftazidime concentrations for each sampling time point.

Conclusion

In the investigated compositions of Zavicefta® and Zerbaxa® pumps, stability could not be guaranteed over the usual application time of OPAT despite the relatively mild incubation conditions. Both seem therefore not to be recommendable for OPAT.

The toxic degradation product pyridine was already formed in Zavicefta® during storage at 2-8 °C and the formation rate was even increased during incubation at 25 °C. The exposure to a toxic analyte should always be prevented and since an essetial part of OPAT is the application at home, which requires time between preparation and application, the pyridine formation appears to be a serious limitation for Zavicefta® use in OPAT.

References

[1] European Pharmacopoeia 10.0, Monograph 2344

GSASA
Schweizerischer Verein der Amts- und Spitalapotheker
Association suisse des pharmaciens de l'administration et des hôpitaux
Associazione svizzera dei farmacisti dell'amministrazione e degli ospedali
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