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# Population Pharmacokinetics of Doripenem in Critically III Patients with Sepsis in a Malaysian Intensive Care Unit

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## Abstract

Dorlpenem has been recently introduced in Malaysia and is used for severe infections in the intensive care unit. However, limited data currently exist to guide optimal dosing in this scenario. We almed to describe the population pharmacokinetics of doripenem in Malaysian critically III patients with sepsis and use Monte Carlo dosing simulations to develop clinically relevant dosing guidelines for these patients. In this pharmacokinetic study, 12 critically III adult patients with sepsis receiving 500 mg of doripenem every 8 h as a 1-hour infusion were enrolled. Serial blood samples were collected on 2 different days, and population pharmacokinetic analysis was performed using a nonlinear mixed-effects modeling approach. A two-compartment linear model with between-subject and between-occasion variability on clearance was adequate in describing the data. The typical volume of distribution and clearance of doripenem in this cohort were 0.47 liters/kg and 0.14 liters/kg/h, respectively. Doripenem clearance was significantly influenced by patients' creatinine clearance (CLCR), such that a 30-milmin increase in the estimated CLCR id increase doripenem CL by 52%. Monte Cario dosing simulations suggested that, for pathogens with a MIC of 8 mg/liter, a dose of 1,000 mg every 8 h as a 4-h Infusion is optimal for patients with a CLCR of 30 to 100 milmin, while a dose of 2,000 mg every 8 h as a 4-h infusion is best for patients manifesting a CLCR of > 100 milmin. Findings from this study suggest that, for doripenem usage in Malaysian critically III patients, an alternative dosing approach may be mentorious, particularly when multidrug resistance pathogens are involved.

## Keywords

KeyVVords Plus: AUGMENTED RENAL CLEARANCE; BETA-LACTAM ANTIBIOTICS; ASIA-PACIFIC REGION; IN-VITRO ACTIVITY; NOSOCOMIAL PNEUMONIA; TARGET ATTAINMENT, MEROPENEM; CARBAPENEMS; PATHOGENS; PHARMACODYNAMICS

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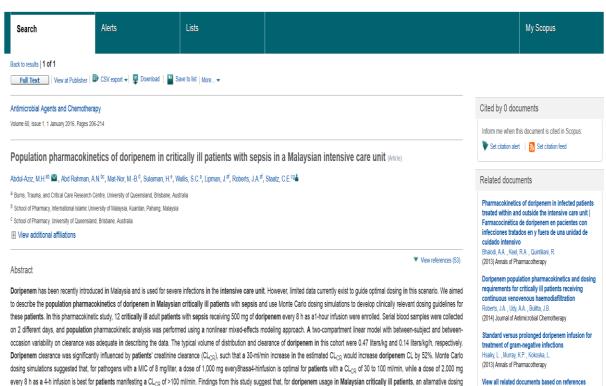
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