Proposed disc zone breakpoints for doripenem for use with the BSAC disc susceptibility testing method

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Sir,

Doripenem is a new carbapenem, recently licensed in the European Union for treatment of nosocomial pneumonia (including ventilator-associated pneumonia), complicated intra-abdominal infections and complicated urinary tract infections. A 10 µg doripenem disc has been proposed for routine susceptibility testing. We determined provisional zone breakpoints corresponding to European Committee on Antimicrobial Susceptibility Testing (EUCAST) MIC breakpoints for these 10 µg doripenem discs in the BSAC disc method.

Isolates (n=810) were selected from the BSAC Bacteraemia Resistance Surveillance Project (2005–06), supplemented with additional, more-resistant, isolates from other survey collections and reference submissions held by the UK HPA’s Antibiotic Resistance Monitoring and Reference Laboratory. Care was taken, whenever possible, to select isolates for which the MICs corresponded with or were within one or two dilutions of the breakpoints. Zones and agar dilution MICs were determined by the BSAC methods. Results were reviewed against EUCAST/European Medicines Agency (EMEA) MIC breakpoints, as also adopted by the BSAC, of: susceptible, \( \leq 1 \text{ mg/L} \) and resistant, \( > 1 \text{ mg/L} \) for streptococci; and susceptible, \( \leq 1 \text{ mg/L} \) and resistant, \( > 4 \text{ mg/L} \) for staphylococci, enterococci, Enterobacteriaceae, Acinetobacter spp. and Pseudomonas spp. Error minimization was used to optimize the values.

Zone breakpoints corresponding to these MIC breakpoints were as follows:

(i) Enterobacteriaceae (n=237): susceptible, \( \geq 24 \text{ mm} \); and resistant, \( \leq 18 \text{ mm} \) (Figure 1).

(ii) Acinetobacter (n=61): susceptible, \( \geq 24 \text{ mm} \); and resistant, \( \leq 17 \text{ mm} \) (Figure 1).

(iii) Pseudomonas (n=63): susceptible, \( \geq 32 \text{ mm} \); and resistant, \( \leq 24 \text{ mm} \) (Figure 1).

Figure 1. Scatter diagram showing the correlation between zones of inhibition caused by the 10 µg doripenem disc and doripenem MICs for Gram-negative organisms.
(iv) α- and β-Haemolytic streptococci and *Streptococcus pneumoniae* (n = 167): susceptible, ≥ 23 mm; and resistant, ≤ 22 mm. A caveat is that these breakpoints were determined by extrapolation from highly susceptible populations, and their robustness cannot be fully evaluated until streptococci with doripenem MICs of ≥1 mg/L emerge (Figure 2).

(v) *Staphylococcus aureus* and coagulase-negative staphylococci (n = 200): susceptible, ≥ 32 mm; and resistant, ≤ 27 mm. However, non-susceptibility to doripenem was best inferred from methicillin resistance (Figure 2).

(vi) *Enterococcus* spp. (n = 82): susceptible, ≥ 22 mm; and resistant, ≤ 18 mm (Figure 2).

Using the above breakpoints there was only one major error (a susceptible isolate reported as resistant) and one very major error (a resistant isolate reported as susceptible) among all 810 organisms tested. These comprised a mecA-positive coagulase-negative *Staphylococcus* and an *Enterococcus durans* for which doripenem MICs were 1 and 16 mg/L, respectively. There were 38 minor errors, half of which (n = 19) concerned staphylococci, which would not be routinely tested with doripenem.

The 10 μg doripenem discs effectively differentiated between susceptible, intermediate and resistant for most bacterial groups. As with all antibiotics, MIC determinations (for example by Etest) should be performed on isolates with zones close to the susceptible breakpoint if the drug is intended for clinical use.

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**References**