**Organisation name: APRHAI (Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infections)**

**Disclosure:** Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry:

None

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| **Comment no.** | **Page** **no.** | **Section no.** | **Comment** Insert each comment in a new row.Do not paste other tables into this table, because your comments could get lost – type directly into this table. |
| 1 | 13 | summary | Network meta analysis is appropriate but only MBL organisms are included. EUCAST criteria have recently been revised and interpretation of sensitivities may have been affected (see section 4). Sensitivity appears to be the sole evaluator used. Review 4 examined other resistant organisms. |
| 2 | 14 | summary | QALYS and number of patients are small nationally but should include non MBL patients where this antibiotic was used.  |
| 3 | 17 | 1.4.2 | Do not suggest differences in sensitivity when OR shows not significant |
| 4 | 21 | 1.5.2 | EUCAST breakpoints have recently been changed relative to CLSI. |
| 5 | 32 | 4.2.1 | Although many trials of efficacy include sensitive organisms many more patients are included and demonstrate efficacy against species not just those strains with resistance to other antibiotics. Hence these studies need to be taken into account in clinical evidence.  |
| 6 | 33 | 4.2.2 | CRE screening was suspended during Covid. Different labs and studies will use different methods of sensitivity testing so comparison without stating the test method may be difficult. |
| 7 | 39 | 5 | Outcome relates to penetration of the antibiotic to the site of infection as well as the susceptibility |
| 7 | 39 | 5.1.1 | Carbapenem-susceptible infections may nevertheless provide useful indicator of efficacy of this antibiotic when susceptible and many more results available than for MBL  |
| 8 | 41 | 5.1.1.1 | Submission of isolates to reference labs is variable and biased towards suspected resistance or transmission so not a representative sample. Not only do labs observe different methods but interpretation has changed with the new EUCAST criteria. |
| 9 | 54 | 5.4.2 | Efficacy assessment of cefciderocol should not be limited to MBL – if the organism is susceptible is there evidence would efficacy any different? |
| 10 | 67 | 5.5.1 | Unclear whether the mistake with excluding two studies has been corrected fully – please explain  |
| 11 | 94 | 5.8 | Differences are stated repeatedly where the odds ratio includes 1. The impression should not be given that there are differences, just not statistically significant. In fact, there is no significant difference.  |
| 12 | 93 | 6.2.1 | 9 experts may not be sufficient number to be independent |
| 13 | 109 | 8.2.2 | Ototoxicity is common if audiograms are used – not all symptomatic |
| 14 | 121 | 8.2.3.2 | Association of outcome and susceptibility are not necessarily accurate as pharmacokinetics and post antibiotic effects re important. This review relies on sensitivity alone. |
| 15 | 145 | 8.2.5.1 | Is there evidence that BSI correlate with other infections – depends on definitions and colonization rates. May not be a valid assumption |
| 16 | 149 | 8.2.5.2 | In practice national trends in resistance have not necessarily followed reduction in usage – for example cephalosporins.  |
| 17 | 161 | 8.2.6.3 | How are 9 respondents representative even of 25 asked? Assumptions seem unjustified. |

**Insert extra rows as needed**

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