**Organisation name: British Infection Association**

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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 | Overall | Overall | A thorough review though at nearly 400 pages it is difficult to be thorough as a reviewer. It is an amazing document which clearly represents a huge amount of thorough work and most of my comments on the introductory sections were then clearly addressed later in the text but might be simply worth highlighting as having been addressed in the first section with the detail in the later sections. |
| 2 | 13 | 1.3 | “Empiric setting”. The use in empiric situations will encourage over-prescribing and resistance. We do not believe this should have been included in the economic model nor should the treatment be widely available in this way at this time given the low current UK rates of resistance. We realise calculations were then done for % of these actually infected with resistant organisms but encouragement of empiric prescribing is a high-risk approach. We cannot see the % who require this treatment in the text but it is referred to as having been used in the calculation. This is important information which should be clear throughout. |
| 3 | 13 | 1.3 | “Microbiology directed setting”- it seems this has included the situation in which there are clear alternative antibiotics. Cefiderocol should be reserved for when there is no alternative due to resistance, intolerance, toxicity or allergy. Even the presumed toxicity of aminoglycosides may have been excess in the calculation as is limited when doses are correct and hydration correct. It seems 8.2.2.1 suggests this so perhaps it’s accounted for but unclear in the introduction. |
| 4 | 14 | 1.4 | In review 3 those with in vitro susceptibility were included but it seems even if other alternative agents may have been available and more suitable. |
| 5 | 16 | 1.4.2 | Whilst CREDIBLE-CR and APEKS-UTI and APEKS-NP may have high risk of bias and unsuitable numbers it is good there is later discussion of these trials. |
| 6 | 19 | Figure 1 | There appears no section in this figure of this agent being only used where alternatives are not available. |
| 7 | 21 | 1.5.2 | I am struggling to find in the document the information on which the risk of empiric treatment being given when not required. There is clear mention of this information being obtained from PHE but I cannot see the numbers clearly in the text. |
| 8 | 22 | 1.5.2 | HAP/VAP- there seems a presumption that treatment is required but there will be cases of HAP/VAP which would respond to aminoglycosides alone without toxicity expected with a short course such as 3 days. It is possible there would be recovery without antibiotic treatment as the organism may be a coloniser and the CXR change for other reasons such as inflammation, fluid overload or aspiration. HAP/VAP is difficult to diagnose with certainty. |
| 9 | 28 | 2.2 | It would be helpful context to understand how much cefiderocol has already been prescribed in the UK and at what cost if this could be added here. |
| 10 | 30 | Box 1 | Is the context of attributable and non-attributable morbidity accounted for? If not these QALYs may be overestimated as these patients may be unwell for other reasons. I see attributable and non-attributable AKI is discussed later and this too. Please include clearly this aspect in the introduction. |
| 11 | 32 | 4.2.1 | Consultation stated reserved for those with carbapenem-resistance but should this statement also state ‘and without other non-toxic available options based on susceptibility’? |
| 12 | 100 | 6.1.2 | Were no infectious diseases consultants recruited to this? If they were this should be listed. |
| 13 | 101 | 6.2.1 | Were the two with inplausible answers removed from the entire analysis (all questions) or just this question? |
| 14 | 111 | 8.2.2.1 | It seems aminoglycoside toxicity is being considered as the same as colistin toxicity but in clinical practice the risk from colistin in terms of nephrotoxicity is higher than from aminoglycoside (approximately double the risk with colisin at brief review). Therefore the colistin is a realistic treatment to avoid but aminoglycosides could continue to be safely administered with appropriate mechanisms in place- of course these mechanisms have cost too (such as serum levels and the care required to ensure safety) so this may enter calculations. In table 16 however it would be preferable to compare colistin only to those in whom aminoglycosides could be use given the lower risk profile associated with aminoglycosides than colistin and the overall implications of stewadship |
| 15 | 117 | 8.2.2.1 | The thorough discussion of AKI and CKD in this section is excellent and shows clear consideration of the potential long-term impacts of this condition and treatments. |
| 16 | 119 | 8.2.3.2 | Could the sentence at bottom link to the next page as it seems to end in mid-air (though I realise relates to table 18 which is stated on the next page) |
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**Insert extra rows as needed**

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