Clinical and NHS commissioning expert statement

Cefiderocol for treating severe aerobic Gram-negative bacterial infections

Thank you for agreeing to give us your views on cefiderocol and its possible use in the NHS.

You can provide a unique perspective on cefiderocol in the context of current clinical practice that is not typically available from the published literature.

To help you give your views, please use this questionnaire. **You do not have to answer every question** – they are prompts to guide you. The text boxes will expand as you type.

**Information on completing this expert statement**

* Please do not embed documents (such as a PDF) in a submission because this may lead to the information being mislaid or make the submission unreadable.
* We are committed to meeting the requirements of copyright legislation. If you intend to include journal articles in your submission you must have copyright clearance for these articles. We can accept journal articles in NICE Docs.
* Your response should not be longer than 13 pages.

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| **About you** |  |
| 1. Your name | Aneeka Chavda |
| 2. Name of organisation | Imperial College Healthcare NHS Trust |
| 3. Job title or position | Lead Pharmacist – Infection + TB |
| 4. Please specify your role from the examples given: | X An employee or representative of a healthcare professional organisation that represents clinicians  A specialist in the treatment of people with this condition  A specialist in the clinical evidence base for this condition or cefiderocol  Commissioning services for a CCG or NHS England in general  Commissioning services for a CCG or NHS England for the condition for which NICE is considering cefiderocol  Responsible for quality of service delivery in a CCG (for example, medical director, public health director, director of nursing)  Other (please specify) |
| 5. Name of your nominating organisation | UK Clinical Pharmacy Association (UKCPA) – Pharmacy Infection Network |
| 6. Did your nominating organisation make a submission? | Yes |
| 7. Did you write your nominating organisation’s submission? | No |
| 8. If you did not write your nominating organisation’s submission, do you agree with its content? We would encourage you to complete this form even if you agree with your nominating organisation’s submission, but this is not compulsory. | Yes |
|  | **Current treatment of severe gram-negative infections, where resistance is suspected/confirmed** |
| 9. What is the main aim of treatment? | Clinical cure of severe G-ve infection and avoidance of relapse of infection or development of cefiderocol resistance |
| 10. What do you consider a clinically significant treatment response? | Resolution or substantial improvement signs and symptoms of infection towards baseline and improvement or lack of progression from an imaging perspective if applicable and microbiological eradication where this is deemed to be appropriate e.g BSI |
| 11. How are severe gram-negative infections, where resistance is suspected/confirmed, currently treated in the NHS? | With best available therapy, which includes combination antibiotics dependent on resistance profile and site of infection. This may or may not have optimal pharmacokinetics for that site of infection and associated with significant risks of toxicity in protracted courses. |
| a) Are any clinical guidelines used, and if so, which? | No – dependent on resistance profile + patient factors e.g allergies + antibiotic availability to guide decision on best treatment.  There is some consensus nationally and internationally on how these infections should be broadly treated:  <https://academic.oup.com/jacamr/article/2/3/dlaa075/5917871>  <https://www.idsociety.org/practice-guideline/amr-guidance/> |
| 1. Is the pathway of care well defined? Does it vary or are there differences of opinion between professionals across the NHS? (Please state if your experience is from outside England.) | The pathway of care varies between organisations dependent on level of expertise and availability of antimicrobials. |
| 1. What impact would cefiderocol have on the current pathway of care? | It would allow equitable access to this drug where deemed to be best treatment for the pathogen/site of infection. Therefore, it may be utilised earlier on in treatment rather than as salvage therapy. |
|  | Using cefiderocol in clinical practice |
| 12. To what extent and in which population(s) is cefiderocol currently being used in your local health economy? | It is used infrequently in severe gram-negative infections where there are limited treatment options in hospitalised patients. |
| 13. Will cefiderocol be used (or is it already used) in the same way as current care in NHS clinical practice? | Yes |
| 14. What rules will be used to start treatment? Do these include any additional testing that is not currently routinely available on the NHS? | Confirmation of cefiderocol susceptibility via lab testing – unsure if this test is widely available across the NHS.  There may have to be certain criteria for initiation/stopping of this drug to avoid overuse and minimise its impact in antimicrobial resistance. |
| 15. If information about the pathogen is very limited (i.e susceptibility data and gene testing results are not yet available) – what specific rules/criteria determine that it’s appropriate to use cefiderocol in the risk-based empiric treatment setting? | N/A |
| 16. Will cefiderocol be easier or more difficult to use for patients or healthcare professionals than current care? Are there any practical implications for its use (for example, any concomitant treatments, additional clinical requirements or additional monitoring needed) | Yes – in some cases will be able to use single agent as opposed to dual. This will limit nursing resources with administration of intravenous therapy, reduction in drug toxicity for patients, possible reduction in days due to effectiveness of therapy. Overall will save on nursing time and bed days. The technology is administered as a 3 hour infusion up to four times a day – this may be less preferential for the pt as this associated with increased infusion time. |
| Benefits of cefiderocol |  |
| 17. Do you expect cefiderocol to provide clinically meaningful benefits compared with current care? | Yes |
| 18. Please comment on the potential benefits of cefiderocol in relation to the 5 following elements of value, and how these elements of value could be quantified and captured in an economic analysis.  Please be aware that more detailed definitions of these elements of value are provided in chapter 7 of the [protocol for this evaluation.](https://www.nice.org.uk/Media/Default/About/what-we-do/Life-sciences/models-for-the-evaluation-and-purchase-of-antimicrobials/Cefiderocol-protocol.docx) |  |
| 1. Transmission value (avoiding onwards spread of pathogens in the population).   Please include suggestions for surrogate outcomes to measure transmission benefit, for example length of hospital stay/length of stay in an intensive care unit, and provide any available evidence that supports the link between these outcomes. | Unable to comment |
| 1. Enablement value (enabling other treatments and procedures to take place e.g. chemotherapy, organ transplant, surgical procedures).   Please comment on the potential for enablement value **beyond** the person being treated for the infection, considering the impact of the infection on other hospital patients and members of staff.  Can you suggest a specific intensive care unit which would make a good case study for modelling enablement value? | A reduction in length of stay may allow pt to be discharged, facilitate with bed flow in the hospital  May undergo a surgical procedure that is essential for the control of infection. |
| 1. Spectrum value (benefits of replacing broad spectrum antimicrobials with narrow spectrum antimicrobials). | Single agent vs multiple agents. This will impact nursing administration time if multiple agents are required.  Adverse effects associated with broad spectrum use e.g C diff, development of drug resistance |
| 1. Insurance value (having antimicrobials available for sudden increase of infections with pathogens resistant to existing antimicrobials). | Measured by antimicrobial usage reports. |
| 1. Diversity value (having a range of treatment options available) | By having more options available, will allow a more timely switch to appropriate abx if the patient is unable to tolerate current therapy due to an ADR, sub-optimal pharmacokinetics of development of antimicrobial resistance. This in turn will lead to a quicker clinical cure. |
| 19. Which of these elements of value (transmission, enablement, spectrum, insurance, diversity) does cefiderocol have the greatest potential to impact? That is, the greatest potential to improve population health outcomes? | Diversity value |
| 20. Are there any groups of people for whom cefiderocol would be more or less effective (or appropriate) than the general population? | No – Currently not licensed in paediatrics and minimal data to support appropriate dosing structure in this cohort. |
| 21. How do any side effects or adverse effects of cefiderocol affect the management of infection and the patient’s quality of life? | Minimal adverse effect profile. Lower incidence of ADRs in comparison to alternative MDR G-ve agents. |
| **Sources of evidence** |  |
| 22. Do the clinical trials on cefiderocol reflect current UK clinical practice? | Yes |
| 1. If not, how could the results be extrapolated to the UK setting? | N/A |
| 1. What, in your view, are the most important outcomes, and were they measured in the trials? | Yes in the CREDIBLE-CR study – All cause mortality and development of resistance |
| 1. If surrogate outcome measures were used, do they adequately predict long-term clinical outcomes? | N/A |
| 1. Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently? | No |
| 23. Are you aware of any relevant evidence that might not be found by a systematic review of the trial evidence? | No |
| 24. How do data on real-world experience compare with the trial data? | It is quite often used in infections outside of HAP/VAP/CAP/BSI/sepsis/cUTI such as bone infections, intra-abdominal infections which was not assessed in the clinical trials. |
| **Equality** |  |
| 25a. Are there any potential [equality issues](https://www.nice.org.uk/about/who-we-are/policies-and-procedures/nice-equality-scheme) that should be taken into account when considering cefiderocol? | No |
| 25b. Consider whether these issues are different from issues with current care and why. | N/A |
| **Key messages** |  |
| 26. In up to 5 bullet points, please summarise the key messages of your statement. |  |

Thank you for your time.

Please log in to your NICE Docs account to upload your completed statement, declaration of interest form and consent form.

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