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.

|  |  |
| --- | --- |
| **About you** |  |
| 1. Your name | Alicia Demirjian |
| 2. Name of organisation | Public Health England (soon to become UK Health Security Agency); Evelina London Children’s Hospital (Guy’s and St. Thomas’ NHS Foundation Trust) |
| 3. Job title or position | Consultant epidemiologist; consultant in paediatric infectious diseases and immunology |
| 4. Please specify your role from the examples given: | **An employee or representative of a healthcare professional organisation that represents clinicians**A specialist in the treatment of people with this conditionA specialist in the clinical evidence base for this condition or cefiderocolCommissioning services for a CCG or NHS England in generalCommissioning services for a CCG or NHS England for the condition for which NICE is considering cefiderocolResponsible 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 | Public Health England |
| 6. Did your nominating organisation make a submission? |  |
| 7. Did you write your nominating organisation’s submission? |  |
| 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. |  |
|  | **Current treatment of severe gram-negative infections, where resistance is suspected/confirmed** |
| 9. What is the main aim of treatment? | Treatment of severe, invasive infections caused by Gram-negative bacteria not susceptible to other agents |
| 10. What do you consider a clinically significant treatment response? | Clinical improvement (e.g. less requirement for cardiorespiratory support), resolution of fever, decreased inflammatory markers, recovery of organ function |
| 11. How are severe gram-negative infections, where resistance is suspected/confirmed, currently treated in the NHS?  | Broad-spectrum antibiotics, at our Trust commonly with aminoglycosides +/- beta-lactam |
| a) Are any clinical guidelines used, and if so, which?  | NICE guidance available for several conditions |
| 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.)
 | Difference of opinion between professionals; this variability is a common issue in the treatment of infectious diseases in general and highlights the need for better antimicrobial stewardship + research into the optimal treatment for most patients. This is consistent with my international experience. |
| 1. What impact would cefiderocol have on the current pathway of care?
 | One of the last-resort options for patients with suspected resistant Gram-negative; could be used upfront as suggested by antimicrobial susceptibility testing profile |
| Using cefiderocol in clinical practice |  |
| 12. To what extent and in which population(s) is cefiderocol currently being used in your local health economy? | Cefiderocol is not commonly used in clinical practice in England; paucity of data in children |
| 13. Will cefiderocol be used (or is it already used) in the same way as current care in NHS clinical practice?  | There will need to be protocols to justify the use of cefiderocol over other antibiotics targeting Gram-negative bacteria |
| 14. What rules will be used to start treatment? Do these include any additional testing that is not currently routinely available on the NHS?  | Severe/invasive infection, lack of response to first-line/second-line therapy, or microbiological data strongly supporting the use of cefiderocol |
| 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? | Severe/invasive infection, lack of response to first-line/second-line therapy, results of a risk assessment: untreated/partially treated infection vs. adverse events of cefiderocol |
| 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) | More difficult, especially in infections/populations where less data/no licensing are available |
| Benefits of cefiderocol |  |
| 17. Do you expect cefiderocol to provide clinically meaningful benefits compared with current care?  | Yes, major benefit in select situations |
| 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.  | Good value. Local (ward/hospital-level) surveillanceDecreased length of stay/exposure to healthcare |
| 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?  | This would be similar for other treatment of an infection, except in this case there may not be other options |
| 1. Spectrum value (benefits of replacing broad spectrum antimicrobials with narrow spectrum antimicrobials).
 | Good value. Benefits of not using unnecessary Gram-positive or anaerobic spectrumTo consider measuring antimicrobial spectrum use in a more granular manner than “broad-spectrum vs. narrow-spectrum” |
| 1. Insurance value (having antimicrobials available for sudden increase of infections with pathogens resistant to existing antimicrobials).
 | Excellent value. This would be difficult to model prospectively, would suggest modelling studies |
| 1. Diversity value (having a range of treatment options available)
 | Excellent value |
| 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? | All impacted, would highlight transmission value in infections not treated by other agents. This value is also the more likely to contribute to improved population health outcomes. |
| 20. Are there any groups of people for whom cefiderocol would be more or less effective (or appropriate) than the general population?  | Would kindly request more studies in children, especially PK/PD |
| 21. How do any side effects or adverse effects of cefiderocol affect the management of infection and the patient’s quality of life? | Similar profile to other beta-lactams |
| **Sources of evidence** |  |
| 22. Do the clinical trials on cefiderocol reflect current UK clinical practice? |  |
| 1. If not, how could the results be extrapolated to the UK setting?
 | Would be good to collect more data in UK setting; Data on children and young people; different populations such as minoritised communities and people with chronic conditions, including obesity |
| 1. What, in your view, are the most important outcomes, and were they measured in the trials?
 | Resolution of infection/test of cure, adverse events, long-term risk for antimicrobial resistance. Some were measured in the trials. |
| 1. If surrogate outcome measures were used, do they adequately predict long-term clinical outcomes?
 |  |
| 1. Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently?
 |  |
| 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? |  |
| **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? | Addressing inequity in access to care when enrolling into trials – this will affect the level of care received by patients receiving cefiderocol in the future, for example due to lack of data in some populations, including minoritised communities and children/young people |
| 25b. Consider whether these issues are different from issues with current care and why. | Similar issues but need improvement in addressing these |
| **Key messages** |  |
| 26. In up to 5 bullet points, please summarise the key messages of your statement. | -cefiderocol has added value in the current NHS, in the treatment of severe/invasive infections not susceptible to currently available agents-more data are needed in specific populations: children/young people (including PK/PD), minoritised communities, individuals with chronic conditions including obesity -clear protocols describing appropriate use (vs. other agents) and monitoring (including measurement of long-term effects, such as potential for antimicrobial resistance) should be in place before cefiderocol is used widely |

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.

Your privacy

The information that you provide on this form will be used to contact you about the topic above.

 [ ]  Please tick this box if you would like to receive information about other NICE topics.

 For more information about how we process your personal data please see our [privacy notice](https://www.nice.org.uk/privacy-notice).