Professional and NHS organisation submission template

Ceftazidime with avibactam for treating severe aerobic Gram-negative bacterial infections

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| Thank you for agreeing to give us your organisation’s views on this technology and its possible use in the NHS.  You can provide a unique perspective on the technology 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 submission**   * 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 | xxxxxxxxxxxxx |
| 2. Name of organisation | UK Cystic Fibrosis Medical Association (UKCFMA) |
| 3. Job title or position | xxxxxxxxxxxxxx **xxxxxxxxxxxxxxxxxxxxxxxxxxxxx** |
| 4. Are you (please tick all that apply): | 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 technology (for example, an investigator in clinical trials for the technology)?  commissioning services for a CCG or NHS England in general?  commissioning services for the condition for which NICE is considering this technology?  responsible for quality of service delivery in the CCG (e.g. medical director, public health director, director of nursing)?  other (please specify): |
| 5a. Brief description of the organisation (including who funds it). | **The UKCFMA supports the work of specialist medical clinicians in the UK in improving clinical outcomes for people with CF through**   * **Consultation and communication with members to develop and promote representative positions/statements** * **Providing evidence and value-based care in line with best international standards** * **Working collaboratively with partner and stakeholder organisations** * **Developing and supporting processes of quality improvement** * **Supporting Training and Career Development**   **The UKCFMA does not receive any funding. Some administrative time has been provided to the CFMA by the CF Trust.** |
| 5b. Has the organisation received any funding from the manufacturer(s) of the technology and/or comparator products in the last 12 months? [Relevant manufacturers are listed in the stakeholder list.]  If so, please state the name of manufacturer, amount, and purpose of funding. | no |
| 5c. Do you have any direct or indirect links with, or funding from, the tobacco industry? | no |
| **Current treatment of severe gram-negative infections, where resistance is suspected/confirmed** |  |
| 6. What is the main aim of treatment? | Cystic fibrosis is an inherited clinical condition affecting over 10000 people in the UK. The majority of people with CF die prematurely as a result of respiratory failure caused by progressive loss of lung function due to chronic endobronchial infection and inflammation. People with CF experience infective exacerbations that frequently require 2 weeks or more of intravenous antibiotic therapy delivered as an outpatient or as an inpatient. During exacerbations there is an acute decline in lung function which can be permanent without therapy. Treatment of infective exacerbations aims to prevent permanent loss of lung function and restore the patient to their previous clinical baseline.  In addition, lung transplantation is a potential treatment for people with CF with end stage lung disease. At the peri-lung transplant period intensive IV antibiotic therapy is usually required. |
| 7. What do you consider a clinically significant treatment response? | Stabilisation of an exacerbation with a return to previous baseline health status and lung function. |
| 8. In your view, is there an unmet need for patients and healthcare professionals? | Antibiotic resistance is commonly encountered in clinical isolates of gram negative organisms from patients with CF. *Pseudomonas aeruginosa* is the most common pathogen, and MDR *P. aeruginosa* isolates are frequently encountered in CF. Other gram-ve organisms are also encountered including *Burkholderia cepacia* complex, *Burkholderia gladioli, Achromobacter* species, *Stentrophomonas maltophilia, Pandoraea* species, and *Ralstonia* species. |
| 9. How is the condition currently treated in the NHS? | Treatment is supervised and delivered through specialist CF centres. These adhere to NHSE service specification. |
| * Are any clinical guidelines used in the treatment of the condition, and if so, which? | * **Antibiotic Treatment for cystic fibrosis. CF Trust, 2002** * **Cystic fibrosis: diagnosis and management - NICE guideline [NG78]** * **ECFS best practice guidelines, 2018** |
| * 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.) | Treatment is supervised and delivered through specialist CF centres. These adhere to NHSE service specification |
| * What impact would the technology have on the current pathway of care? | At present the draft technology assessment effectively excludes cystic fibrosis. |
| **The use of the technology** |  |
| 10. Will the technology be used (or is it already used) in the same way as current care in NHS clinical practice? | Ceftazidime/avibactam is used in at least some CF centres as a rescue IV antibiotic for patients with multi-resistant gram-ve organisms not responding to other IV antibiotic combinations. One large UK CF centre has published its experience of use of ceftazidime/avibactam (Use of ceftazidime/avibactam for the treatment of MDR *Pseudomonas aeruginosa* and *Burkholderia cepacia* complex infections in cystic fibrosis: a case series. J Antimicrob Chemother 2019;74(5):1425-1429) |
| * To what extent and in which population(s) is the technology being used in your local health economy? | **see comments in section above** |
| * How does healthcare resource use differ between the technology and current care? | **Ceftazidime/avibactam is used in at least some CF centres as a rescue IV antibiotic for patients with multi-resistant gram-ve organisms not responding to other IV antibiotic combinations. One large UK CF centre has published its experience of use of ceftazidime/avibactam (Use of ceftazidime/avibactam for the treatment of MDR Pseudomonas aeruginosa and Burkholderia cepacia complex infections in cystic fibrosis: a case series. J Antimicrob Chemother 2019;74(5):1425-1429). The current draft technology submission does not include CF as a clinical condition.** |
| * What investment is needed to introduce the technology? (For example, for facilities, equipment, or training.) | CF centres are staffed by clinical teams with considerable experience of delivering IV antibiotics and would not need additional training, equipment or facilities for this technology. |
| 11. Do you expect the technology to provide clinically meaningful benefits compared with current care? | The prevalence of MDR Gram negative pathogens in CF is rising and there is a clinical need for new antimicrobial therapies. Ceftazidime/avibactam presents an option for treating patients with CF with MDR *P. aeruginosa* or *Burkholderia cepacia* complex where other antibiotics have not resolved the infection. |
| * Do you expect the technology to increase length of life more than current care? | The premature mortality in CF is due to progressive lung damage, accelerated during infective exacerbations. Optimising treatment of severe infective exacerbations requiring IV antibiotics will reduce chances of permanent decline as a result of the exacerbations, and in turn improve life expectancy.  **In addition, at the time of lung transplantation IV antibiotics are essential to improve survival. Patients with severe chronic CF lung disease (those who will require a lung transplant) are likely to be infected with MDR *P. aeruginosa* and/or other gram-negative organisms.** |
| * Do you expect the technology to increase health-related quality of life more than current care? | IV antibiotic treatment options for CF are limited; measures to enhance recovery from an exacerbation will improve quality of life for people with CF |
| 12. Are there any groups of people for whom the technology would be more or less effective (or appropriate) than the general population? | Renal dysfunction and allergies are more common in patients with CF than in the general population therefore antibiotic options for severe infections are more limited |
| 13. Will the technology 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 needed, additional clinical requirements, factors affecting patient acceptability or ease of use or additional tests or monitoring needed.) | **The technology will be no more easy or difficult to use than current similar treatments (IV antibiotics) delivered in CF**. |
| 14. Will any rules (informal or formal) be used to start or stop treatment with the technology? Do these include any additional testing? | **ceftazidime/avibactam is usually reserved as a rescue IV therapy when other IV antibiotic options have failed or are contraindicated (e.g. due to allergy) and initiated only with liaison with local senior microbiologists** |
| 15. What is the outcome of any evaluations or audits of the use of the technology? | **See publications:**  **Use of ceftazidime/avibactam for the treatment of MDR *Pseudomonas aeruginosa* and *Burkholderia cepacia* complex infections in cystic fibrosis: a case series. J Antimicrob Chemother 2019;74(5):1425-1429**  **Avibactam confers susceptibility to a large proportion of ceftazidime-resistant Pseudomonas aeruginosa isolates recovered from cystic fibrosis patients*. Journal of Antimicrobial Chemotherapy*, Volume 70, Issue 5, May 2015, Pages 1596–1598,**  **Lung transplantation in two cystic fibrosis patients infected with previously pandrug-resistant *Burkholderia cepacia* complex treated with ceftazidime–avibactam Infection 47, pages289–292 (2019)** |
| **Sources of evidence** |  |
| 16. Do the clinical trials on the technology reflect current UK clinical practice? | See above papers, especially **Use of ceftazidime/avibactam for the treatment of MDR Pseudomonas aeruginosa and Burkholderia cepacia complex infections in cystic fibrosis: a case series. J Antimicrob Chemother 2019;74(5):1425-1429** |
| * If not, how could the results be extrapolated to the UK setting? |  |
| * What, in your view, are the most important outcomes, and were they measured in the trials? |  |
| * If surrogate outcome measures were used, do they adequately predict long-term clinical outcomes? |  |
| * Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently? |  |
| 17. Are you aware of any relevant evidence that might not be found by a systematic review of the trial evidence? |  |
| 18. How do data on real-world experience compare with the trial data? |  |
| **Equality** |  |
| 19. 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 this treatment? | Cystic fibrosis is an inherited condition. |
| 20. Consider whether these issues are different from issues with current care and why. |  |
| **Key messages** |  |
| 21. In up to 5 bullet points, please summarise the key messages of your submission. | * **CF is an inherited disease; patients suffer from damaging respiratory exacerbations and ultimately die prematurely from respiratory failure** * **MDR gram negative organisms are frequently encountered in CF and treatment options are limited** * **Ceftazidime/avibactam is currently being used in at least some CF centres as a rescue IV antibiotic for patients with multi-resistant gram-ve organisms not responding to other IV antibiotic combinations** * **the current draft submission does not include CF; consideration should be given to including CF** * **Ceftazidime/avibactam may also provide a treatment option at times of lung transplantation for patients with cf** |

Thank you for your time.

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