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 | xxxxxxxxxxxx |
| 2. Name of organisation | British Society for Antimicrobial Chemotherapy (BSAC) **Royal College of Pathologists** |
| 3. Job title or position | xxxxxxxxxxxxxxxxxxxxxxxxxxxxx, Cambridge University Hospitals NHS Foundation Trust, Cambridge |
| 4. Are you (please tick all that apply): | 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 British Society for Antimicrobial Chemotherapy (BSAC) is a professional society and registered charity that works to influence antimicrobial use globally. It does this through the development, funding and delivery of relevant initiatives that inform and enhance knowledge about practices that drive responsible antimicrobial use. The Society owns and publishes the Journal of Antimicrobial Chemotherapy and this is its main source of income. Membership is free. The Royal College of Pathologists is a professional membership organisation with charitable status, concerned with all matters relating to the science and practice of pathology. The College is a charity with over 11,000 members worldwide. The majority of members are doctors and scientists working in hospitals and universities in the UK. The College oversees the training of pathologists and scientists working in 17 different specialties, which include cellular pathology, haematology, clinical biochemistry and medical microbiology. The College is funded from subscriptions, examinations and related fees, investment income, grants from outside bodies and charitable donations. |
| 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. | Neither BSAC or the RCPath have received any funding from the manufacturer(s) of the technology and/or comparator products in the last 12 months, published any position on the technology or a comparator in the last 12 months, or have any other interests in the last 12 months relevant to the technology or comparator. |
| 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? | Clinical cure as determined by resolution of symptoms. These principles would be the same for any infection irrespective of the presence of any resistant causative organisms, these being the principle focus of the use of ceftazidime-avibactam. |
| 7. What do you consider a clinically significant treatment response? | Resolution of symptoms, settling of any fever and reduction in the inflammatory response (wbc, CRP etc). (Microbiological eradication would be another outcome, but would not usually be a major priority in the types of infection where this treatment would be given**,** apart from in bloodstream infection) |
| 8. In your view, is there an unmet need for patients and healthcare professionals? | The unmet need is in the treatment of infection due to carbapenem-resistant organisms, especially those due to organisms producing carbapenemase enzymes. |
| 9. How is the condition currently treated in the NHS? | Current treatments are usually empirical and based on regimens proposed in the literature. These most often include agents such as colistin, amikacin and tigecycline. The first two of these agents are nephrotoxic and tigecycline has poor efficacy in the most severe infections. |
| * Are any clinical guidelines used in the treatment of the condition, and if so, which? | Wilson APR et al. Prevention and control of multi-drug-resistant Gram-negative bacteria: recommendations from a Joint Working Party. *Journal of Hospital Infection* 2016; 92: S1-S44 |
| * 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.) | Knowledge in the field is advancing rapidly and the above guideline is probably out of date now. Most clinicians would refer to publications on the treatment of resistant Gram negative infection in the literature, much of which is based on experience in the US and is based on small case series rather than more robust evidence.  The geographical setting for any study in this field is very important. The local epidemiology of different resistance mechanisms varies around the world and experience in one area is not necessarily applicable to another. An example relevant to this technology is the epidemiology of KPC carbapenemase enzymes. These are seen most frequently in the US, but are less common in Europe, where other carbapenemase enzymes predominate. |
| * What impact would the technology have on the current pathway of care? | A key impact would be a reduction in the use of more toxic alternative agents. |
| **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? | It is likely that most clinical use of cetazidime-avibactam would be overseen by infection specialists and the drug would probably be reserved for restricted use following approval. Most NHS Trusts have systems in place to restrict the use of various drugs and thus this would not be unusual. |
| * To what extent and in which population(s) is the technology being used in your local health economy? | Currently, ceftazidime-avibactam is only used following recommendation and approval of infection specialists. It is only used in secondary care. It is mainly used in immunocompromised patients (mostly haematology or solid organ transplant) and most often on ICU.  It is infrequently used. Perhaps one patient treated each month |
| * How does healthcare resource use differ between the technology and current care? | It is the same |
| * What investment is needed to introduce the technology? (For example, for facilities, equipment, or training.) | None |
| 11. Do you expect the technology to provide clinically meaningful benefits compared with current care? | There would be an expected reduction in drug-related toxicity as a result of a reduction in the use of alternative agents, particularly colistin and aminoglycosides. As yet, there are no data from RCTs that I am aware of that demonstrate improved patient outcomes. |
| * Do you expect the technology to increase length of life more than current care? | Probably not. |
| * Do you expect the technology to increase health-related quality of life more than current care? | Possibly, if drug-related toxicities are avoided. This would mainly relate to nephrotoxicity. |
| 12. Are there any groups of people for whom the technology would be more or less effective (or appropriate) than the general population? | No |
| 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.) | Similar |
| 14. Will any rules (informal or formal) be used to start or stop treatment with the technology? Do these include any additional testing? | Antimicrobial susceptibility testing will be required (but this is performed as routine already).  Future guidance could usefully provide recommendations for starting and stopping. For example, which resistant microorganisms might respond to treatment and when. Also recommended course lengths. |
| 15. What is the outcome of any evaluations or audits of the use of the technology? | Most data are non-inferiority studies in comparison with carbapenems or other standard of care that have been company sponsored and performed for licencing purposes. |
| **Sources of evidence** |  |
| 16. Do the clinical trials on the technology reflect current UK clinical practice? | No. Studies have often been performed in areas of the world where the epidemiology of bacterial resistance to antibiotics is different to the UK. In particular, in the US the prevalence of KPC carbapenemases is much higher than in the UK. This means that ceftazidime-avibactam would be expected to be a more frontline treatment in the US than in the UK, where it would be a reserved agent used on approval by infection specialists only. |
| * If not, how could the results be extrapolated to the UK setting? | It is useful to understand which infections due to resistant microorganisms respond to treatment with ceftazidime-avibactam. This information can only be obtained in areas of the world where it is more frequently used. |
| * What, in your view, are the most important outcomes, and were they measured in the trials? | Generally, trials have been non-inferiority design and performed for licencing purposes. Real world use experience would be more informative. |
| * 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? | No |
| 17. Are you aware of any relevant evidence that might not be found by a systematic review of the trial evidence? | The emergence of resistance to cetazidime-avibactam is well described and might not feature in the type of study included in a systematic review. |
| 18. How do data on real-world experience compare with the trial data? | There are limited data so far. |
| **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? | Not in UK practice. |
| 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. | * Ceftazidime-avibactam provides a less toxic alternative treatment option for the treatment of resistant Gram-negative infections * It’s use would need to be restricted to require approval from an infection specialistThe epidemiology of resistance in Gram-negative bacteria varies significantly around the world and it is possible that use of ceftazidime-avibactam in the UK would be lower than in the US or elsewhere, at least initially. * Studies demonstrating improved efficacy compared to current options are lacking and would be useful. |

Thank you for your time.

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