# Protocol addendum for the technology evaluation of cefiderocol for treating severe aerobic Gram-negative bacterial infections

**Table 1: Population, intervention, comparators, outcomes and study design (PICOS) for the high value clinical scenarios (HVCSs)**

| **Element** | **Microbiology-directed treatment** | **Risk-based empiric treatment** |
| --- | --- | --- |
| **Population - Patients** | Where microbiological susceptibility testing has been performed with or without gene testing | With clinically urgent disease with high risk of an infection caused by a resistant pathogen. Suspicion of infection may be based on knowledge of the local epidemiology where a patient was previously hospitalised, outbreak in the ward where the patient is currently admitted, or previous cultures (taken during previous hospitalisations stays) showing the patient was colonised by a metallo-beta-lactamase (MBL)-producing enterobacterales or *Pseudomonas spp*. |
| **Population - Pathogen/mechanism** | Infections (enterobacterales and *Pseudomonas spp)* suspected or confirmed to be caused by metallo-beta-lactamases of the following subtypes:   * NDM, VIM, IMP | Infections (Enterobacterales or *Pseudomonas spp)* suspected to be caused by MBLs of the following subtypes:   * NDM, VIM, IMP |
| **Population - Site of infection** | * Complicated urinary tract infection (cUTI) * Hospital associated pneumonia (HAP)/ ventilator associated pneumonia (VAP) | HAP/ VAP |
| **Intervention** | Cefiderocol alone or in combination | Cefiderocol alone or in combination |
| **Comparators**  Please note: These comparators reflect NHS practice based on clinical advice. The available evidence will determine which of those listed (and possible additional products including combinations) will be formally incorporated into the modelling | Comparators used in clinical practice in England, as defined by susceptibility testing and/or gene testing and considering infection site and infiltration data. Potential comparators include:  **Enterobacterales:**   * Tigecycline + colistin * Fosfomycin + colistin * Aztreonam + colistin * aminoglycosides (gentamicin, amikacin, tobramycin)   **Pseudomonas aeruginosa:**   * Fosfomycin + colistin * Fosfomycin + meropenem | Comparators used in clinical practice in England, as defined by suspected infection, considering knowledge of the local epidemiology where a patient was previously hospitalised, outbreak in the ward where the patient is currently admitted, or previous cultures (taken during previous hospitalisations stays) showing the patient was colonised by an MBL-producing gram-negative bacteria.  Potential comparators in the risk-based empiric high value clinical scenarios include:   * tigecycline + colistin * fosfomycin + colistin * aztreonam + colistin * aminoglycosides (gentamicin, amikacin, tobramycin) (+ meropenem?) * Fosfomycin + meropenem |
| **Outcomes** | The outcome measures to be considered include:   * All-cause mortality * Clinical cure (complete resolution of signs/symptoms of the index infection such that no further antimicrobial therapy is needed) * Microbiologic eradication * Emergence of resistance * Hospital days * Intensive care unit (ICU) days * Readmission rate within 90 days of treatment * Number of treatment days * Health-related quality of life * Adverse events (including those associated with Clostridium Difficile infection and renal toxicity) | Same as for microbiology-directed treatment |
| **Study designs** | The types of studies and data to be considered include:   * Randomised controlled trial (RCTs) * Observational studies * In-vitro susceptibility data * National, regional or international datasets * Pharmacokinetic and pharmacodynamic (PK/PD) | As for microbiology-directed treatment |