NM ASP Protocol for Restricted Multidrug-Resistant Gram-Negative Antibiotics

I. Carbapenem-resistant Enterobacterales (CRE)

- ID consult is required for use in all patients receiving ceftazidime-avibactam, meropenem-vaborbactam, imipenem-relebactam, and cefiderocol.
- **Empiric therapy:** Use of these agents in patients with infections associated with new or pending carbapenemase molecular (e.g., BioFire with positive NDM/VIM/IMP/KPC/OXA-48-like) or culture results, or in critically ill patients with recent (past 6 months) CRE in cultures is permitted by using guidance outlined in **Table 1** below; however, the primary team must consult ID within 24 hours after starting the order for recommendations on continuation therapy.
- **Directed therapy:** Non-beta-lactam agents such as nitrofurantoin (cystitis only), TMP-SMX, ciprofloxacin, and levofloxacin should be considered first line when susceptible and no patient-specific contraindications exist. These oral agents should also be considered for oral step-down therapy, if susceptible, for patients with source control achieved, no absorption/intake issues, and clinical stability. Otherwise, the restricted agents are available for the duration of an appropriate course for the infectious disease syndrome.

Table 1. Empiric Recommendations for Suspected CRE Infections Based on Molecular Tests or Prior Culture Results

Infection	1st Line	2nd Line	3rd Line
Cystitis	Nitrofurantoin, TMP-SMX, Ciprofloxacin, levofloxacin, single-dose aminoglycoside	Ceftazidime-avibactam, Meropenem-vaborbactam, Imipenem-relebactam	Cefiderocol
Pyelonephritis Complicated UTI	Ceftazidime-avibactam	Meropenem-vaborbactam, Imipenem-relebactam	Cefiderocol
All Other Non-Urine Infections	Ceftazidime-avibactam	Meropenem-vaborbactam, Imipenem-relebactam	Cefiderocol
NDM/VIM/IMP	Ceftazidime-avibactam + Aztreonam	Cefiderocol	
OXA-48-like	Ceftazidime-avibactam		
KPC	Ceftazidime-avibactam	Meropenem-vaborbactam, Imipenem-relebactam	Cefiderocol

NM ASP Protocol for Restricted Multidrug-Resistant Gram-Negative Antibiotics

II. Multidrug-Resistant (MDR) and Difficult-to-Treat Resistance (DTR) *Pseudomonas aeruginosa*

- ID consult is required for use in all patients receiving ceftazidime-avibactam, ceftolozane-tazobactam, imipenem-relebactam, and cefiderocol.
- Multidrug resistant (MDR) *P. aeruginosa* is defined as non-susceptibility to at least 3 of the following: penicillins, cephalosporins, fluoroquinolones, aminoglycosides, and carbapenems.
- Difficult-to-Treat Resistance (DTR) in *P. aeruginosa* is defined as non-susceptibility to all of the following: piperacillin-tazobactam, ceftazidime, cefepime, aztreonam, meropenem, imipenem-cilastatin, ciprofloxacin, and levofloxacin.
- **Empiric therapy:** Critically ill patients with history of MDR- or DTR-*P. aeruginosa* isolates within the past 6 months may benefit from empiric treatment with these restricted drugs (**Table 2**).
- **Directed therapy**: Susceptibilities should be reviewed when available.

Table 2: Empiric Recommendations for MDR *P. aeruginosa* Infections Based on Molecular Tests or Prior Culture Results

Infection	1st Line	2nd Line	3rd Line
Cystitis	Ceftolozane-tazobactam[1], single-dose aminoglycoside	Ceftazidime-avibactam[2]	Imipenem-relebactam, Cefiderocol
Pyelonephritis Complicated UTI	Ceftolozane-tazobactam[1]	Ceftazidime-avibactam[2]	Imipenem-relebactam, Cefiderocol
All Other Non-Urine Infections	Ceftolozane-tazobactam[1]	Ceftazidime-avibactam[2]	Imipenem-relebactam, Cefiderocol

1. The NMH antibiogram suggests 97.7% ceftolozane-tazobactam susceptibility for *P. aeruginosa* MICs ≤ 4 (CLSI breakpoint) and 94.8% for MICs ≤ 2 (one dilution below breakpoint) [n=794 isolates]
2. The NMH antibiogram suggests 99% ceftazidime-avibactam susceptibility for *P. aeruginosa* MICs ≤ 8 (CLSI breakpoint) and 93.9% for MICs ≤ 4 (one dilution below breakpoint) [n=820 isolates]

References:

1. Tamma PD, Aitken SL, Bonomo RA, et al. *Clin Infect Dis*. 2021;72(7):1109-16.