Infectious Diseases Society of America 2026 Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections: Supplemental Material

The following notes relate to Table 1 "Suggested Dosing of Antibiotics for the Treatment of Antimicrobial-Resistant Infections in Adults, Assuming Normal Renal and Hepatic Function"

Agent	Notes
Amikacin	The panel suggests using adjusted body weight for patients ≥125% of ideal body weight. The panel does not suggest therapeutic drug monitoring (TDM) for single-dose amikacin. The panel suggests that multi-dose regimens of amikacin be used for complicated urinary tract infections (cUTIs) if timely, routine therapeutic drug monitoring (TDM) and subsequent dose adjustments are possible. Use of amikacin assumes isolate susceptibility has been confirmed. The panel suggests targeting an area under the curve over 24 hours (AUC_{0-24}) of 200-300 mg*h/L. An acceptable, but less preferred, approach is to target an amikacin peak concentration of ≥40 mg/L and trough concentration <5 mg/L, or use a nomogram-based approach. If TDM is too resource intensive, or the anticipated treatment duration is <72 hours, a reasonable alternative approach is to focus efforts on monitoring the amikacin trough concentration alone (i.e., targeting <5 mg/L) to minimize risk of toxicity. Data supporting the safety of amikacin AUC_{0-24}, irrespective of MIC, in excess of 300 mg*h/L are limited; such exposures are not routinely recommended. If pharmacokinetic calculations for an individual regimen suggest the use of a dose which confers an unacceptably high risk of nephrotoxicity, alternate agents may be necessary, even in the setting of organism susceptibility. The above suggested amikacin dosing strategies are informed by the following references: Rougier F, et al. Clin Pharmacokinet. 2003;42:493. Drusano GL and Louie A. Antimicrob Agents Chemother. 2011;55:2528-31. Drusano GL, et al. Clin Infect Dis. 2007; 45:753-60. Pai MP, et al. Diagn Microbiol Infect Dis. 2014;78:178-187.
Ampicillin-sulbactam	The panel suggests 9 grams total daily dose of the sulbactam component of ampicillin-sulbactam for the treatment of CRAB infections. Safety concerns with high-dose ampicillin-sulbactam were not identified in the literature. The rationale behind this dosage is described in the AMR Guidance document. Suggested dose adjustment strategies for high-dose ampicillin-sulbactam are available in Jaruratanasirikul S, et al. European Journal of Pharmaceutical Sciences. 2019;136:104940. The panel suggests reconstituting and preparing high-dose ampicillin-sulbactam to the maximum concentration reported in the FDA-approved product labeling.

Ceftazidime-avibactam PLUS aztreonam	The panel suggests administration of ceftazidime-avibactam 2.5 grams intravenously (IV) every 8 hours and aztreonam 2 grams IV every 8 hours administered simultaneously. The panel suggests 3-hour infusions of both agents to increase the time of the free drug concentrations above the MIC. Ceftazidime-avibactam and aztreonam are Y-site compatible (O'Donnell JN, et al. Clin Ther. 2020;42:1580-1586.e2). Aztreonam administered as 2 grams IV every 6 hours, infused over 3 hours, can be considered in patients with augmented renal clearance with at least weekly monitoring of liver function. The panel suggests caution with the use of aztreonam continuous infusion, particularly at doses of 8 grams daily, due to potential increased risk of liver enzyme elevation. The panel suggests developing paneled orders in the electronic medical record to facilitate simultaneous administration via Y-site administration. A hollow-fiber infection model demonstrated killing of an NDM-producing *Escherichia coli* with simultaneous administration of a two-hour infusion of ceftazidime-avibactam, 2.5 grams every 8 hours, and aztreonam 2 grams every 8 hours in some experiments; increased bacterial killing and reduced bacterial regrowth was observed when dosed as ceftazidime-avibactam 2.5 every 8 hours plus aztreonam 2 grams every 6 hours. (Lodise TP, et al. J Antimicrob Chemother. 2020;75:2622-2632). Monte Carlo simulations using a population pharmacokinetic model derived from patients receiving the combination suggested that aztreonam administered every 6 hours may only be necessary in patients with augmented renal clearance (Falcone M, et al. J Antimicrob Chemother 2021;76:1025-1031). Comparative effectiveness studies evaluating these two regimens have not been conducted. The safety of aztreonam with or without ceftazidime-avibactam was assessed in a healthy volunteer study. These data suggest a dose-dependent effect of aztreonam on elevated liver enzymes with resolution upon withdrawal of the drug. The clinical significance of these data remain unclear; caution is warranted with aztreonam at doses of 8 grams daily, especially as a continuous infusion. The above suggested dosing strategies are informed by the following references: Lodise TP, et al. J Antimicrob Chemother. 2020;75:2622-2632. Falcone M, et al. Clin Infect Dis. 2021;72:1871-1878. Falcone M, et al. J Antimicrob Chemother. 2021;76:1025-1031. Lodise TP, et al. Antimicrob Agents Chemother. 2022;66:e0093622. Lodise TP, et al. Antimicrob Agents Chemother. 2022;66:e0093522.
Ertapenem	The panel suggests administration of 1 gram of ertapenem IV every 24 hours, infused over 30 minutes. Higher doses of ertapenem (e.g., 1.5 grams) or more frequent dosing (e.g., every 12 hours) may circumvent some of the probability of target attainment issues with ertapenem in obese or critically ill patients with hypoalbuminemia, respectively. However, data supporting these alternative dosing strategies are limited: Chen M, et al. Antimicrob Agents Chemother. 2006;50:1222-1227. Lass J, et al. Case Reports in Critical Care. 2017;5310768. Goutelle S, et al. J Antimicrob Chemother. 2018;73:987-994. Ferry T, et al. Open Forum Infectious Diseases. 2016; 3(suppl_1).

Gentamicin	The panel suggests using adjusted body weight for patients ≥125% of ideal body weight. The panel does not suggest TDM for single-dose gentamicin. The panel suggests that multi-dose regimens of gentamicin be used for cUTI if timely, routine TDM and subsequent dose adjustments are possible. Use of gentamicin assumes that isolate susceptibility has been confirmed. The panel suggests targeting an AUC_{0-24} of 80–120 mg*h/L. An acceptable, but less preferrable, alternative approach is to target a gentamicin peak concentration of ≥10 mg/L and trough concentration <1 mg/L, or use a nomogram-based approach. If TDM as outlined above is too resource intensive or anticipated treatment duration is <72 hours, an alternative approach is to focus efforts on monitoring the gentamicin trough concentration alone (i.e., targeting <1 mg/L) to minimize toxicity. Data supporting the safety of gentamicin AUC_{0-24}, regardless of MIC, in excess of 120 mg*hr/L are limited; such exposures are not routinely suggested. If pharmacokinetic calculations for an individual dosage regimen suggest a dose which confers an unacceptably high risk of nephrotoxicity, alternate agents may be necessary, even in the setting of reported organism susceptibility. The above suggested gentamicin dosing strategies are in part informed by the following references: Rougier F, et al. Clin Pharmacokinet. 2003;42:493. Drusano GL and Louie A. Antimicrob Agents Chemother. 2011;55:2528-31. Drusano GL, et al. Clin Infect Dis. 2007;45:753-60. Pai MP, et al. Diagn Microbiol Infect Dis. 2014;78:178-187.
Imipenem-cilastatin	The imipenem-cilastatin dose only includes imipenem. As an example, 500 mg imipenem-cilastatin is equivalent to 500 mg imipenem. A prolonged infusion (i.e., 3 hours) is suggested for infections other than uncomplicated UTI (uUTI) when using the 500 mg dose. This may be challenging given the short stability of imipenem-cilastatin once reconstituted; it is not suggested for 1,000 mg dosing. If 3-hour infusions are logistically challenging, 30-minute infusions can be considered. Doses of 1,000 mg every 6 hours are suggested for isolates with intermediate susceptibility; however, alternate antibiotic therapies are preferred in those situations.
Meropenem	Meropenem has limited availability as 2-gram vials for IV infusion. If 2-gram vials are unavailable, when the agent is stored in automated drug cabinets and prepared using reconstitution drug delivery systems, the panel suggests administering two 1-gram vials successively over 90 minutes each, if administering meropenem over 3 hours. Doses of 2000 mg given over 3 hours every 8 hours are recommended for select clinical scenarios (e.g., obesity, central nervous system infections, extracorporeal membrane oxygenation, creatinine clearance ≥130 mL/min). Doses of 2,000 mg given over 3 hours every 8 hours are suggested for isolates with intermediate susceptibility; however, alternate antibiotic therapies are preferred in those situations.
Plazomicin	The panel suggests using adjusted body weight for patients ≥125% of ideal body weight. The panel does not suggest TDM for single-dose plazomicin. The panel suggests that multi-dose regimens of plazomicin be used for cUTIs if timely,

	routine TDM and subsequent dose adjustments are possible. The panel suggests targeting an AUC_{0-24} 80–120. An acceptable, but less preferred, alternative approach is to use a nomogram-based approach. If TDM as outlined above is too resource intensive, or the anticipated treatment duration is <72 hours, a reasonable alternative approach is to focus efforts on monitoring the plazomicin trough concentration alone to minimize toxicity. Data supporting the safety of plazomicin AUC_{0-24}, irrespective of MIC, in excess of 315 mg*hr/L are limited; such exposures are not routinely recommended. The panel suggests maintaining plazomicin trough concentrations <3 mg/L as they are associated with a reduced risk of toxicity. If pharmacokinetic calculations for an individual regimen suggest the use of a dose which confers an unacceptably high risk of nephrotoxicity, alternate agents may be necessary, even in the setting of reported organism susceptibility. The above suggested plazomicin dosing strategies are in part informed by the following reference: Plazomicin Prescribing Information: https://zemdri.com/assets/pdf/Zemdri-plazomicin-pescribing-information-Feb-2023.pdf.
Sulbactam-durlobactam	Sulbactam-durlobactam is available as a co-packaged kit containing 1 single-dose vial of sulbactam 1 gram and 2-single-dose vials of durlobactam 0.5 grams that must be reconstituted and further diluted prior to IV infusion. Dosing is listed for each respective component (i.e., sulbactam 1 gram and durlobactam 1 gram versus the combined dose of 2 grams). Special attention should be given to the ordering, preparation, and administration of this product to avoid medication-related errors.
Tobramycin	The panel suggests using adjusted body weight for patients ≥125% of ideal body weight. The panel does not suggest TDM for single-dose tobramycin. The panel suggests that multi-dose regimens of tobramycin be used for cUTIs if timely, routine TDM and subsequent dose adjustments are possible. The panel suggests targeting an AUC_{0-24} of 80–120. An acceptable, but less preferred, alternative approach is to target a peak of ≥10 mg/L and trough concentration <1 mg/L, or use a nomogram-based approach. If TDM as outlined above is too resource intensive, or the anticipated treatment duration is <72 hours, a reasonable alternative approach is to focus efforts on monitoring the tobramycin trough to evaluate for nephrotoxicity. Data supporting the safety of tobramycin AUC_{0-24}, irrespective of MIC, in excess of 120 mg*hr/L are limited; such exposures are not routinely recommended. If pharmacokinetic calculations for an individual dosage regimen suggest the use of a dose which confers an unacceptably high risk of toxicity, alternate agents may be necessary, even in the setting of reported organism susceptibility. The above suggested tobramycin dosing strategies are in part informed by the following references: Rougier F, et al. Clin Pharmacokinet. 2003;42:493. Drusano GL and Louie A. Antimicrob Agents Chemother.

	2011;55:2528-31. Drusano GL, et al. Clin Infect Dis. 2007;45:753-60. Pai MP, et al. Diagn Microbiol Infect Dis. 2014;78:178-187.
Trimethoprim-sulfamethoxazole (TMP-SMX)	The panel suggests a dose range of 8-15 mg/kg (trimethoprim component) of TMP-SMX for patients with *S. maltophilia* infections based on multiple factors: (1) the varied and potentially dose-limiting toxicities associated with TMP-SMX (e.g., nausea/vomiting, hyperkalemia, fluid overload, cytopenias, nephrotoxicity, hypersensitivity), (2) the suggested dose-response relationship for many of those toxicities (Chen WP, et al. J Antimicrob Chemother. 2025 Jun 3;80(6):1716-1725), (3) the lack of an established dose-response relationship for antibacterial effectiveness (Lasko MJ, et al. Antimicrob Agents Chemother. 2022;66(3):e0216721), (4) the limited clinical evidence supporting any particular dose, and (5) the evidence that TMP dosing of >15 mg/kg/day may lead to serum sulfamethoxazole levels higher than necessary (Dao BD, et al. Curr Ther Res Clin Exp. 2014;76:104-109). TDM of sulfamethoxazole and/or TMP should be considered, if feasible, for patients at high risk for supratherapeutic exposures that may increase toxicity risks (e.g., patients with acute or chronic renal dysfunction, patients receiving renal replacement therapy, or patients with obesity or critical illness).