

Meropenem

Meropenem Sodium - Group 2 Antipseudomonal Carbapenem Antibiotic

Antimicrobials / Carbapenems

Evidence status: current

ICU High-Yield Summary

Ultra-broad-spectrum antipseudomonal Group 2 carbapenem for severe ESBL Enterobacterales, MDR *Pseudomonas aeruginosa*, intra-abdominal sepsis, and post-neurosurgical meningitis.

Mechanism of Action

Penicillin-Binding Protein (PBP) Inactivation

1. Penetrates Gram-negative outer membrane via OprD porin channels. 2. Binds with high affinity to essential PBPs (PBPs 2, 3, and 4) in cell wall synthesis. 3. Inhibits peptidoglycan cross-linking transpeptidation. 4. Resistant to most beta-lactamases (TEM, SHV, CTX-M ESBLs, and AmpC enzymes). 5. Induces rapid cell wall destruction and bactericidal lysis.

ICU Clinical Reasoning

Why I Choose It

Preferred therapy for invasive ESBL-producing Enterobacterales infections such as bloodstream infection, particularly in critical illness; MERINO supports carbapenem preference over piperacillin-tazobactam for ESBL/ceftriaxone-resistant *E. coli* or *K. pneumoniae* bacteremia. | A broad antipseudomonal carbapenem option when resistance risk, prior microbiology, illness severity, or infection source justifies carbapenem coverage; it should not be the automatic empiric choice when narrower active beta-lactams are appropriate. | High CSF penetration at 2.0 g IV every 8 hours for post-neurosurgical meningitis.

Why I Avoid / Key Limitations

Inactivated by carbapenemases (KPC, NDM, VIM, OXA-48). | Drives carbapenem resistance (OprD porin loss in *Pseudomonas aeruginosa*). | Reduces serum valproic acid levels by 60-90%, triggering breakthrough seizures.

Bedside Pearl

Use prolonged/extended infusion when PK/PD optimization is important (e.g., critical illness, augmented clearance, or higher MIC pathogens) and adjust for renal/CRRT clearance. BLING III supports better clinical cure with continuous beta-lactam infusion but did not show a statistically significant primary 90-day mortality benefit.

Dosing & Administration

Routine ICU Dosing

Severe Infections / Septic Shock: 1.0 g IV every 8 hours (extended 3-hour infusion preferred).

Hemodialysis

The U.S. meropenem label states that information is inadequate to recommend a hemodialysis/peritoneal-dialysis regimen. Use an institutionally validated

intermittent-HD antimicrobial protocol, indication/MIC-specific PK/PD targets, timing relative to dialysis, and TDM where available rather than presenting a universal label dose.

CRRT

Meropenem is substantially cleared by CRRT, but the required dose varies with effluent rate, residual renal function, MIC and desired %fT>MIC. Use extended/prolonged infusion and the local CRRT dosing protocol/TDM where available rather than a universal 1 g q8-12h rule.

Renal Dose Table

CrCl > 50 mL/min: 1.0 g IV every 8 hours. | CrCl 26-50 mL/min: 1.0 g IV every 12 hours. | CrCl 10-25 mL/min: 500 mg IV every 12 hours. | CrCl < 10 mL/min: 500 mg IV every 24 hours.

Syndrome-Specific Regimens

ESBL Enterobacterales Bloodstream Infection: 1.0 g IV every 8 hours (extended 3-hour infusion). - MERINO failed to demonstrate noninferiority of piperacillin-tazobactam to meropenem for ceftriaxone-resistant E. coli/K. pneumoniae bloodstream infection and supports carbapenem preference for invasive ESBL-E infection; avoid describing the trial as proving a universal mortality benefit in every ESBL syndrome. | Post-Neurosurgical / Nosocomial Meningitis: 2.0 g IV every 8 hours (infused over 3 hours). | Ventilator-Associated Pneumonia (VAP) / MDR Pseudomonas: 1.0 g IV every 8 hours is the adult meropenem regimen listed in the 2016 ATS/IDSA HAP/VAP guideline when meropenem is selected. Higher-dose/prolonged-infusion strategies (for example 2 g q8h) may be used for selected resistant organisms, higher MICs or altered PK according to current susceptibility/PK-PD guidance, but should not be taught as the universal VAP dose.

Organ Failure Considerations

Renal Failure & AKI

Cleared primarily by glomerular filtration. Mandatory dose reduction in renal impairment to avoid neurotoxicity/seizures.

Hepatic Impairment

Minimal hepatic metabolism; no dose reduction required in isolated liver failure.

Toxicity & Safety

Major Warnings

Seizures & Neurotoxicity: Seizure risk (0.5% in general, higher in renal failure or pre-existing CNS disease). | Valproic Acid Interaction: Severe drop in valproate levels within 24 hours. | Clostridioides difficile Colitis risk.

Organ Toxicities

Central Nervous System: Seizures, encephalopathy, confusion, myoclonus. | Gastrointestinal: Diarrhea, nausea, vomiting, C. difficile colitis. | Hepatic: Transient elevation of ALT, AST, alkaline phosphatase.

Drug Interactions

Bedside Interactions

Valproic Acid / Divalproex Sodium: Inhibition of acyl-glucuronide valproate hydrolysis and clearance acceleration; consequence: Rapid 60-90% reduction in valproate levels leading to status epilepticus; ICU action: Avoid co-administration; use alternative antiepileptic. | Probenecid: Inhibition of tubular secretion; consequence: Increases meropenem half-life and exposure; ICU action: Co-administration not recommended.

Monitoring & TDM

Monitoring

Calculated CrCl and serum creatinine daily for dose adjustment | Neurologic assessment for seizure activity or encephalopathy | Valproic acid level if co-administered | Clinical response and body temperature

Antimicrobial Spectrum

Gram Positive

Covered: Methicillin-susceptible *Staphylococcus aureus* (MSSA) | *Streptococcus pneumoniae* | *Streptococcus pyogenes* | *Enterococcus faecalis* (variable/intermediate) | Not covered: Methicillin-resistant *Staphylococcus aureus* (MRSA) | *Enterococcus faecium* | *Listeria monocytogenes*

Gram Negative

Covered: *Pseudomonas aeruginosa* | ESBL-producing *Escherichia coli* | ESBL-producing *Klebsiella pneumoniae* | AmpC *Enterobacter cloacae* | *Citrobacter freundii* | *Acinetobacter baumannii* (susceptible) | *Haemophilus influenzae* | Not covered: *Stenotrophomonas maltophilia* | *Burkholderia cepacia* | Carbapenemase producers (KPC, NDM, OXA-48)

Anaerobes

Covered: *Bacteroides fragilis* | *Bacteroides thetaiotaomicron* | *Peptostreptococcus* spp. | *Fusobacterium* spp. | Not covered: *Clostridioides difficile*

Notable Gaps

MRSA | *Enterococcus faecium* | *Stenotrophomonas maltophilia* | KPC / NDM Carbapenemase producers

Evidence & Source Traceability

Claim-Level Citations

The MERINO trial did not demonstrate noninferiority of piperacillin-tazobactam to meropenem for ceftriaxone-resistant *E. coli*/*K. pneumoniae* bloodstream infection; the mortality direction favored meropenem and supports carbapenem preference for invasive ESBL-E infection. - Harris PN et al. Effect of Piperacillin-Tazobactam vs Meropenem on 30-Day Mortality in ESBL Bacteremia: MERINO RCT. JAMA 2018;320(10):984-994. (<https://pubmed.ncbi.nlm.nih.gov/30208454/>) | IDSA 2026 AMR Guidance recommends Meropenem as first-line therapy for ESBL-producing Enterobacterales bloodstream infections. - Tamma PD, et al. IDSA 2026 Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections. Infectious Diseases Society of America; published July 2026 (online guidance). (<https://www.idsociety.org/practice-guideline/amr-guidance/>)

Guideline IDs

mdr-organisms-guideline-idsa-amr-2026 | vap-guideline-idsa-ats-2016

Trial IDs

merino-trial-jama-2018