

Imipenem

Antibiotic Class:

Carbapenem

Antimicrobial Spectrum:

Aerobic gram-positive microorganisms: *S. aureus* including penicillinase-producing strains, Group D streptococcus including *E.*, *Streptococcus pneumoniae*, *S. pyogenes* (Group A streptococci), *S. viridans* group

Aerobic gram-negative microorganisms: *Acinetobacter spp.*, including *A. calcoaceticus*, *Citrobacter spp.*, *Enterobacter cloacae*, *E. coli*, *H. influenzae*, *K. pneumoniae*, *Pseudomonas aeruginosa*

Anaerobic gram-positive microorganisms: *Peptostreptococcus spp.*

Anaerobic gram-negative microorganisms: *Bacteroides spp.*, *Fusobacterium spp.*

Mechanism of Action:

Cause rapid bacterial cell death by covalently binding to penicillin-binding proteins (PBPs) involved in the biosynthesis of mucopeptides in bacterial cell walls. Bactericidal effects result through inhibition of cellular growth and division and the loss of cell wall integrity, eventually causing cell wall lysis. The primary target is PBP 2.

Pharmacodynamics:

Carbapenems produce time-dependent killing

Pharmacokinetics:

C_{max}: 69.9mcg/ml

Half-life: 1.11 hours

Volume of distribution: 14.4L

Table 2

Adverse Reaction:

Hematologic: Anemia, eosinophilia, increased prothrombin time, leukopenia, myelosuppression, thrombocytopenia, and thrombocytosis

Cardiovascular System: Cardiac arrest, hypotension, tachycardia, and thrombophlebitis

Central Nervous System: Seizures, somnolence, dizziness, and vertigo

Gastrointestinal: Nausea, vomiting, oral candidiasis, pseudomembranous colitis, and taste alterations

Renal: Renal insufficiency

Hepatic: Elevated hepatic enzymes

Respiratory: Pulmonary hemorrhage, respiratory failure, hyperventilation, pulmonary infiltrates, and apnea

Dermatologic: Pruritus, urticaria, and skin rash

Dosing forms:

Intramuscular:

500mg imipenem and 500mg cilastatin power mixture for intramuscular injection

750mg imipenem and 750mg cilastatin power mixture for intramuscular injection

Intravenous:

250mg imipenem, 250mg cilastatin, and 10mg sodium bicarbonate power mixture for intravenous injection

500mg imipenem, 500mg cilastatin, and 20mg sodium bicarbonate power mixture for intravenous injection

Dosing:

Mild infections: (fully susceptible) 250 mg IV every 6 hr; (moderately susceptible including *P. aeruginosa*) 500 mg IV every 6 hr

Moderate infections: (fully susceptible) 500 mg IV every 6-8 hr; (moderately susceptible including *P. aeruginosa*) 500 mg IV every 6 hr or 1 g IV every 8 hr

Severe, life-threatening infections: (fully susceptible) 500 mg IV every 6 hr; (moderately susceptible including *P. aeruginosa*) 1 g IV every 8 hr or 1 g IV every 6 hr; maximum 50 mg/kg/day or 4 g/day, whichever is lower

Cystic fibrosis: (12 years and older) up to 90 mg/kg/day IV divided every 6 hr; maximum 4 g/day

Urinary tract infections, uncomplicated: 250 mg IV every 6 hr

Urinary tract infections, complicated: 500 mg IV every 6 hr

Gynecologic infections: 500-750 mg IM every 12 hr

Intra-abdominal infections: 750 mg IM every 12 hr

Lower respiratory tract infections: 500-750 mg IM every 12 hr

Skin/skin structure infections: 500-750 mg IM every 12 hr

Disease state based dosing:

Renal Impairment: (IV): Table 4

Renal Impairment: (IM): Not recommended with CrCl less than 20 mL/min/1.73(2) (lack of data).

Hepatic failures: Dosage adjustment is not required.

Dosing during Continuous Renal Replacement Therapy

CVVH (Continuous venovenous hemofiltration): 250mg IV q6h OR 500mg IV q8h

CVVHD (Continuous venovenous hemodialysis): 250mg IV q6h OR 500mg IV q6-8h

CVVHDF (Continuous venovenous hemodiafiltration) 250mg IV q6h OR 500mg IV q6-8h

Note: CVVH is mainly for fluid removal alone. Many institutions will employ more CVVHD or CVVHDF which combine dialysis with fluid removal.

Contraindications/Warnings/Precautions:

Contraindications: Children less than 30 kg with renal impairment, children with CNS infections (increased seizure risk), known hypersensitivity to local anesthetics of the amide type and in patients with severe shock or heart block

Precautions: History of seizures, Concomitant ganciclovir; risk for generalized seizures, Hypersensitivity to penicillins, cephalosporins, and other beta lactams

Drug Interactions:

Cyclosporine (moderate severity): Neurotoxicity (mental confusion, agitation, tremor)

Ganciclovir (major severity): CNS toxicity (seizures)

Live Typhoid Vaccine (moderate severity): A decreased immunological response to the vaccine

Theophylline (major severity): Theophylline toxicity (nausea, vomiting, palpitations, seizures)

Pregnancy Risk Factor:

Category C

Monitoring parameters:

Therapeutic:

Resolution of clinical signs of infection (fever, decreased white blood cell count), Culture and sensitivity, CBC w/differential, urinalysis, temperature

Toxicity:

Hepatic and renal function tests during therapy

Brand names/Manufacturer:

- Primaxin/Merck in the following countries: Australia, United States, Canada, United Kingdom, New Zealand, and Greece
- Tienam/Merck Sharp & Dome in the following countries: France, Italy, Spain, Netherlands, South Africa, Sweden, Switzerland, Belgium, Norway, Denmark, Portugal, Brazil, Hong Kong, Mexico, Israel, Thailand, Singapore, Finland, Malaysia, Chile, Hungary, and the Czech Republic