Amikacin

Antibiotic Class:
Aminoglycoside

Antimicrobial Activity:
Pseudomonas aeruginosa, E. coli, Proteus spp., Klebsiella spp., Enterobacter spp., Serratia spp., Providencia spp., Acinetobacter spp., and Citrobacter spp., Morganella spp., S. aureus., Staphylococcus spp., Viridans stertococci, Enterococcus spp., Mycobacterium spp.

Mechanism of Action:
Inhibition of protein biosynthesis by irreversible binding of the aminoglycoside to the bacterial ribosome 30S subunit.

Pharmacodynamics:
Aminoglycosides correlate most with peak/MIC ratio

Pharmacokinetics:
Half-life: 1.4 ± 0.41 hours; Volume of distribution: 0.21 ± 0.08 L/kg; Total Clearance: 78.6 ± 12.1 mL/min/kg; Table 1

Adverse Effects:
Otic: Ototoxicity – Auditory and/or vestibular
Kidney: Nephrotoxicity
Neuromuscular: Cause or exacerbate neuromuscular blockade, myasthenia gravis (both rarely)

Dosage:
Injection, solution, as sulfate: 50 mg/mL (2 mL, 4 mL); 62.5 mg/mL (8 mL); 250 mg/mL (2 mL, 4 mL)

Dosing in adults:
Individualization is critical because of the low therapeutic index
I.V.: Traditional dosing - 5mg/kg q8h OR 7.5mg/kg q12h
Alternatively: 15-20mg/kg q24h (once daily/extended interval dosing in this agent is poorly standardized in the literature)

Dosing in pediatrics:
Individualization is critical because of the low therapeutic index
I.V. 15mg/kg divided q8 to q12h

Disease state based dosing:
Renal failure: (note: These are general guidelines, but should not substitute for patient specific data – frequency data below based on traditional dosing only)
Clcr ≥60 mL/minute: Administer every 8 hours.
Clcr 40-60 mL/minute: Administer every 12 hours.
Clcr 20-40 mL/minute: Administer every 24 hours.

Clcr 10-20 mL/minute: Administer every 48 hours.
Clcr<10 mL/minute: Administer every 72 hours.

Dialyzable (50% to 100%)

Administer dose postdialysis or administer 2/3 normal dose as a supplemental dose postdialysis and follow levels.
Peritoneal dialysis effects: Dose as for Clcr<10 mL/minute: Follow levels.
Continuous arteriovenous or venovenous hemodiafiltration effects: Dose as for Clcr 10-40 mL/minute: Follow levels.

Contraindications/Warnings/Precautions:

Warnings: Aminoglycosides penetrate poorly into non-lean muscle mass. Use adjusted body weight for patients > 120% their ideal body weight

Precautions should be taken in patients with:

Preexisting renal, vestibular, or auditory impairment; Patients with depressed neuromuscular transmission (eg, myasthenia gravis); Risk factors for the development of aminoglycoside toxicity include the following: concomitant administration potentially neurotoxic or nephrotoxic drugs, age, and dehydration; Concomitant use with potent diuretics (eg, ethacrynic acid or furosemide); Local irrigation or application may lead to significant absorption

Drug Interactions (not inclusive):

Cidofovir: Increased risk for nephrotoxicity
Colistin: Increased risk for nephrotoxicity, respiratory depression
Cyclosporine: Nephrotoxicity (decreased renal function, decreased fractional sodium excretion, and a decline in diuresis)
Tacrolimus: Increased risk for nephrotoxicity
Vancomycin: Increased risk of nephrotoxicity

Pregnancy:

Category D: Risk established, but benefits may outweigh risk.

Monitoring Requirements:

Renal function tests including, urinalysis, serum creatinine, I & O, and BUN should be monitored every 2-3 days.
Therapeutic serum levels of amikacin typically between 15-35mg/L
Trough levels typically < 5mg/L
Pretreatment audiograms should be undertaken and repeated throughout therapy if the drug is administered for periods greater than 5 days. Particularly in patients with renal or hepatic dysfunction

Brand names/Manufacturer: Amikin®/Bristol-Myers Squibb