

Tobramycin

Antibiotic Class:

Aminoglycoside

Antimicrobial Activity:

Staphylococcus spp., *Streptococci spp.*, *E Coli*, *Enterobacter*, *Serratia spp.*, *Proteus spp.*, *Pseudomonas aeruginosa*, *Citrobacter*, *Aeromonas hydrophilia*, *Klebsiella 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: 1.8 ± 0.23 hours; Volume of distribution: 0.297 ± 0.64 L/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: 10 mg/mL; 40 mg/mL

Ointment, ophthalmic: 0.3% (3.5 g)

Solution for nebulization (TOBI®): 60 mg/mL (5 mL)

Solution, ophthalmic: 0.3% (5 mL)

Dosing in adults:

Individualization is critical because of the low therapeutic index

I.V.: Traditional dosing in Gram negative infection: 1.7-2mg/kg IV q8h

Alternatively: 7mg/kg OR 5mg/kg frequency per nomogram (once daily/extended interval dosing in this agent Figure 6 for 7mg/kg nomogram) Note: nomogram for 5mg/kg dosing not shown

Traditional dosing for Gram positive synergy: 1mg/kg IV q8h (note: extended interval dosing not recommended in this situation) Note: Can NOT use tobramycin for Gram-positive synergy in *Enterococcus spp.* – in this situation use gentamicin

Topical: Eczematoid dermatitis or Impetigo: Apply small amount of cream/ointment to affected area q8h OR q6h

Ophthalmic: Ointment: Apply a small ribbon to the affected eye q12h OR q8h

Solution: One to two drops into the affected eye every 4 hours.

Pulmonary infections: Inhalation:

Standard aerosolized tobramycin: 60-80 mg 3 times/day

High-dose regimen (TOBI™): 300 mg every 12 hours (do not administer doses <6 hours apart); administer in repeated cycles of 28 days on drug followed by 28 days off drug

Disease state based dosing:

Renal failures (note: These are general guidelines, but should not substitute for patient specific data – frequency data below based on traditional dosing only):

Clcr \geq 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.

Hemodialysis effects: Dialyzable; removal by hemodialysis: 30% removal of aminoglycosides occurs during 4 hours of HD. Administer dose after dialysis and follow serum levels.

Contraindications/Warnings/Precautions:

Warnings: Aminoglycosides penetrate poorly into non-lean muscle mass. Use an 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:

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:

Urinalysis, urine output, BUN, serum creatinine; hearing should be tested before, during, and after treatment; particularly in those at risk for ototoxicity or who will be receiving prolonged therapy (>2 weeks). Peak serum levels of tobramycin in traditional dosing are:

Serious infections: 6-8 mcg/mL (SI: 12-17 mg/L)

Life-threatening infections: 8-10 mcg/mL (SI: 17-21 mg/L)

Urinary tract infections: 4-6 mcg/mL (SI: 7-12 mg/L)

Synergy against gram-positive organisms: 3-5 mcg/mL

Trough levels in traditional dosing are typically: < 2 mcg/mL

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 dysfunction.

Inhalation: Serum levels are ~1 mcg/mL one hour following a 300 mg dose in patients with normal renal function.

Brand names/Manufacturer: AKTob®/Akorn; TOBI®/Pathogenesis; Tobrex®/Alcon; Tobramycin (Various manufacturers worldwide)