Gentamicin

Antibiotic Class:
Aminoglycoside

Antimicrobial Activity:

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: 2.1 hours; Volume of distribution: 0.27 L/kg; Total Clearance: 1.35 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:
Cream, topical, as sulfate: 0.1% (15 g, 30 g)
Injection, solution: 10 mg/mL, 40 mg/mL
Injection, solution (preservative free – for intrathecal administration): 10 mg/mL
Ointment, ophthalmic, as sulfate: 0.3% (3.5 g)
Ointment, topical, as sulfate: 0.1% (15 g, 30 g)
Solution, ophthalmic, as sulfate: 0.3% (5 mL, 15 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)

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.
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 ≥ 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 C: Risk unknown. Human studies inadequate.

**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 gentamicin 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 (< 1mcg/mL per American Heart Association guidelines for synergy treatment in endocarditis)

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.

**Brand names/Manufacturer:** Genoptic®/Allergan; Gentak®/Akorn; Garamycin®/Shering; Gentamicin (Various generic manufacturers worldwide)