<table>
<tr><td>Alert</td><td>The Antimicrobial Stewardship Team has listed this drug under the following categories :
Unrestricted – treatment up to 48 hours
Obtain approval from the Infectious Diseases Team − treatment > 48 hours</td></tr>
<tr><td>Indication</td><td>Treatment of suspected or proven gram negative infection.
Often used in combination with a beta-lactam antibiotic as empiric therapy for sepsis in the newborn.</td></tr>
<tr><td>Action</td><td>Bactericidal agent that acts by inhibiting protein synthesis in susceptible bacteria.</td></tr>
<tr><td>Drug Type</td><td>Aminoglycoside</td></tr>
<tr><td>Trade Name</td><td>DBL gentamicin, Gentamicin BP (Pfizer)</td></tr>
<tr><td>Presentation</td><td>10 mg/mL ampoule – paediatric strength
80 mg/2 mL ampoule – adult strength</td></tr>
<tr><td>Dosage / Interval</td><td>5mg/kg/dose. Dosing interval as per Tables below
<table>
<tr><th colspan="2">Method (First 2 doses)</th><th rowspan="2">Interval (hours)</th></tr>
<tr><th>Corrected Gestational Age/Postmenstrual Age</th><th>Route</th></tr>
<tr><td>< 30^{+0} weeks</td><td>IV/IM</td><td>48 hourly</td></tr>
<tr><td>30^{+0}–34^{+6} weeks</td><td>IV/IM</td><td>36 hourly</td></tr>
<tr><td>≥ 35^{+0} weeks</td><td>IV/IM</td><td>24 hourly</td></tr>
</table>
Subsequent dose interval is based on a gentamicin concentration at 22 hours after the administration of the 2nd dose as indicated in the table below.
<table>
<tr><th>Gentamicin level</th><th>Interval</th></tr>
<tr><td>≤ 1.2 mg/L</td><td>Every 24 hours after previous dose</td></tr>
<tr><td>1.3 mg/L – 2.6 mg/L</td><td>Every 36 hours after previous dose</td></tr>
<tr><td>2.7 mg/L – 3.5 mg/L</td><td>Every 48 hours after previous dose</td></tr>
<tr><td>≥ 3.6 mg/L</td><td>Hold dose, repeat concentration at 24 hours</td></tr>
</table>
Gentamicin monitoring is required ONCE only, except when renal function is compromised. Refer to monitoring section below.</td></tr>
<tr><td>Route</td><td>IV
IM</td></tr>
<tr><td>Preparation/Dilution</td><td>10 mg/mL – paediatric strength: Add 1 mL (10 mg) of gentamicin to 4 mL sodium chloride 0.9% to make a final volume of 5 mL with a concentration of 2 mg/mL.
80 mg/2 mL – adult strength: Add 1 mL (40 mg) of gentamicin to 19 mL sodium chloride 0.9% to make a final volume of 20 mL with a concentration of 2 mg/mL.</td></tr>
<tr><td>Administration</td><td>IV: Slow infusion over 5 minutes.
IM: Variable absorption by the IM route, use only when IV route is not available.
Gentamicin is inactivated by penicillins and cephalosporins so should not be mixed in the same solution or administered simultaneously. Ensure the line is adequately flushed if administered consecutively.</td></tr>
<tr><td>Monitoring</td><td>Routine therapeutic drug monitoring for ≤ 48 hours duration of therapy is not necessary unless renal function is impaired.
For therapy > 48 hours, perform gentamicin concentration 22 hours after the 2nd dose and determine the dose interval as described in the dosage section.
Further gentamicin concentrations are not necessary unless renal function is impaired.
Renal impairment: Perform gentamicin concentration 22 hours after every dose to determine the dose interval.
Peak concentration may be important if an organism has a high minimum inhibitory concentration</td></tr>
</table>

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	(MIC) – speak with your microbiologist. Target peak concentration: 5–12 mg/L. Peak concentration should be drawn at 30 minutes post dose.
Contraindications	Concurrent therapy with other ototoxic or nephrotoxic drugs.
Precautions	CAUTION in patients with pre-existing renal impairment, auditory or vestibular impairment, hypocalcaemia, depressed neuromuscular transmission.
Drug Interactions	Gentamicin should not be mixed with penicillins parenterally as inactivation occurs. Ensure line is adequately flushed between antibiotics.
Adverse Reactions	Toxicity is rare in the newborn but can include: 1. Nephrotoxicity- Associated with excessive accumulation of gentamicin. The initial symptoms may be due to renal tubular concentrating defect. These include excessive losses of sodium, calcium and magnesium. This may progress to proteinuria, increased urea, oliguria, increased serum creatinine. Renal impairment is usually reversible. 2. Ototoxicity. Primarily vestibular but also auditory toxicity. Associated with excessive accumulation of gentamicin and duration of therapy. Effects often irreversible. 3. Neuromuscular blockade- Muscular paralysis and respiratory failure may occur particularly when used with other neuromuscular blockers such as pancuronium. 4. Hypersensitivity- Very rare – rash, urticaria, fever, laryngeal oedema, eosinophilia. NEPHROTOXICITY AND OTOTOXICITY ARE MORE PRONOUNCED WITH ADDITION OF OTHER NEPHROTOXIC/OTOTOXIC AGENTS SUCH AS FRUSEMIDE AND VANCOMYCIN.
Compatibility	Fluids: Glucose 5% , glucose 10%, Hartmann's, mannitol , sodium chloride 0.9% Y-Site: Amino acid solutions, amifostine, amiodarone, anidulafungin, atracurium, aztreonam, bivalirudin, caspofungin, ciprofloxacin, cisatracurium, dexmedetomidine, esmolol, fluconazole, foscarnet, granisetron, hydromorphone, labetalol, linezolid, magnesium sulfate, midazolam, morphine sulfate, palonosetron, pancuronium, pethidine, potassium chloride, remifentanil, tigecycline, vecuronium, zidovudine.
Incompatibility	Fluids: Fat emulsions. Y-site: Azathioprine, azithromycin, chloramphenicol, dexamethasone, flucloxacillin, folic acid, frusemide, ganciclovir, heparin sodium, indomethacin, pentamidine, propofol, teicoplanin.
Stability	Administer immediately, discard unused portion.
Storage	Protect from light. Store below 25°C
Evidence summary	Dosing: Dosage and intervals Extended interval dosing vs traditional multiple doses a day 1. Extended interval dosing for gentamicin in neonates is safe and effective with a superior pharmacokinetic profile when compared to traditional dosing [3,4,15] (Level I, Grade A). Term infants 1. Recommended dosing for term babies is 4–5 mg/kg 24 hourly [3,4,15] (Level II, Grade B). 2. HIE infants undergoing hypothermic therapy: Longer drug intervals of up to 36 hours may be more appropriate for cooled infants with moderate to severe HIE to avoid toxicity [5,6,7] (Level III, Grade C). Preterms: High dose versus low dose 1. Higher doses of 4–5 mg/kg at extended intervals of 36–48 hours confers a more favourable pharmacokinetic profile than low doses of 2.5 mg/kg 24 hourly [1,2,8-15] (Level II, Grade B). Monitoring: Target peak and trough concentrations 1. Target peak concentrations of 5–12 mg/L for efficacy [3,4,17,19] (Level II, Grade B). 2. Routine peak concentrations are not necessary as high dose extended interval dosing regimens are able to achieve target peak concentrations in the majority of infants [1-4,8-15] (Level II, Grade B). 3. Consider performing peak concentrations if there is poor clinical response in gram negative

	infections, oedema or macrosomia [16,18] (Level III, Grade C). 4. Target trough concentrations of < 2 mg/L to reduce risk of ototoxicity and nephrotoxicity. Levels of < 1 mg/L may be preferred in prolonged therapy beyond 3 doses [3,4,18,19] (Level II, Grade B). Timing of sampling: 1. A serum gentamicin concentration performed 22 hours after the 1st dose is useful to guide dosing intervals [1,2] (Level III, Grade C). 2. A trough concentration performed prior to the 3rd dose is useful to check for drug accumulation.[19] 3. A peak concentration, if required, can be performed after the 2nd or 3rd dose.[19]
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