1. Purpose and scope

To facilitate the safe and effective use of amikacin in the Neonatal Intensive Care Unit (NICU).

2. Drug

Drug	**Amikacin**
Drug action	Bacteriocidal aminoglycoside antibiotic which inhibits bacterial protein synthesis.[1] Active against a wide variety of pathogenic gram negative and gram positive bacteria, including, *Klebsiell*a, *Citrobacter*, *Escherichia coli*, Enterobacter spp, *Pseudomonas aeruginosa*, Proteus spp, Serratia spp, Staphylococcus spp (including penicillin and methicillin resistant strains).[2] Displays concentration-dependent killing.[1] Poorly absorbed by the oral route but rapid absorption from intramuscular injection sites. Amikacin is highly hydrophilic and distributes primarily into the extracellular fluid. It has poor penetration into the blood brain barrier, even when the meninges are inflamed, 12% penetrates bronchial secretions. Low binding (<11%) to human plasma protein. 94-98% excreted unchanged in the urine with a half-life of 7 hours in low birth weight infants and 4-5 hours in full term infants over 7 days old.[1]
Indications	• Suspected or proven neonatal sepsis[2] resistant to other aminoglycosides.[3]
Description	Amikacin vial 500mg/2ml. Clear to pale yellow solution. Sodium content: 0.64mmol per 500mg amikacin pH: 3-5.5.5 [4]
Route	Intravenous infusion **over 1-2 hours**[1,3,5,6] (preferred) IM
Dose	**Age 0-7 days: Initial dose,** see table below[7] **Gestation (weeks)** / **Dose (mg/kg/)** / **Interval (hours)** ≤ 29* / 18 / 48 30 – 34 / 18 / 36 ≥ 35 / 15 / 24 ***Or** significant asphyxia, patent ductus arteriosus (PDA), or treatment with indomethacin Dosage should be based on actual weight unless the patient has hydrops fetalis.[1] Measure serum concentrations when treating for more than 48 hours or 24 hours for serious infections or changing fluid or renal status.[7] **Age > 7 days** – Initial dose 15mg/kg, then draw blood for serum levels 30 minutes after end of infusion (peak) and another 12-24 hours later, **Serum levels:** Aim for: • Peak: 20 – 30 micrograms/ml (30 mins after end of infusion or 1 hour after IM injection)

	• Trough: 2-5 micrograms/ml (immediately pre-dose) Refer to the aminoglycoside dosing programme for further dosing instructions. Once on a stable dose, monitor levels every 3-5 days as required.[2]
Contraindications & Precautions	• Known hypersensitivity to amikacin, sulfites or other aminoglycosides[2] • Impaired renal function[2] • Myasthenia gravis[8] • Previous ototoxicity or vestibular toxicity to any aminoglycoside[5] • Concurrent use of other nephrotoxic and/or ototoxic medications may increase adverse effects.[1] • Caution in concurrent therapy with cephalosporins, potent diuretics such as frusemide and neuromuscular blocking agents[2] • Treatment should not usually exceed 7 days[9] • Correct dehydration before starting[9]
Compatibilities & Incompatibilities	• Compatible with glucose 5%, glucose 10%, Lactated ringer's (Hartmann's) and sodium chloride 0.9%, glucose/sodium chloride combinations[4] • Incompatible with amphotericin B, amoxicillin, cefotaxime, ceftazidime, chlorothiazide, dexamethasone, heparin (concentrations >1unit/ml), phenytoin and propofol[7,10] • Do not mix with other drugs[4], blood or blood products[2] • Amikacin is inactivated by solutions containing penicillins or cephalosporins, administer separately (at least 1 hr apart) at different sites[4]
Adverse effects	• Transient and reversible renal tubular dysfunction resulting in urinary losses of sodium, calcium and magnesium[7] • Vestibular and auditory ototoxicity (irreversible) • Gastrointestinal (nausea, vomiting and diarrhoea)[5], antibiotic-associated colitis, stomatitis[9] • Injection site pain (IM)[5] • Central nervous system: Neurotoxicity[1] • Renal:Nephrotoxicity[1] • Allergic reactions – dyspnoea, eosinophilia,[1] hypersensitivity[11] • Hepatotoxicity[2] • Laboratory test interference[2] (see data sheet) • Can cause neuromuscular blockade and potentiate the effects of neuromuscular blockers[6]

3. Administration

Competency for administration	This procedure is carried out This procedure is carried out by, or under, the direct supervision of a registered nurse who holds current Waikato DHB Generic Medicines Management and Neonatal specific certifications NCV/NAC, as well as Guardrails competency
Preparation & Administration	1. Draw up 1ml (=250mg) from vial and dilute with 4ml of sodium chloride 0.9% (making a solution of 50mg/ml). 2. Draw up prescribed dose. 3. IV: Dilute to 10mg/ml or weaker and administer via a Guardrails profiled syringe driver over **1-2 hours**.[12] IM: Inject dose deep into large muscle mass (using 50mg/ml solution). Avoid injecting into a blood vessel.[4] NOTE: Flush before and after giving IV infusion with sodium chloride 0.9%. The flush should be administered at the same rate as the amikacin.

Observations and management	• Observe for adverse effects • Urinalysis, urine output, electrolytes, serum creatinine, serum concentrations[1] • Monitor IV site regularly and rotate injection site to reduce risk of local irritation and pain • Correct dehydration before initiation therapy and maintain adequate hydration throughout[4] • Audiology testing is recommended for longer term treatment where possible (CPAP and ventilation are too noisy to evaluate hearing), and on discharge from NICU
Storage	• Store vials at room temperature (<25°C) until opened • Store diluted solutions at room temperature for up to 12 hours. Discard any unused solution[4]
Special considerations	• Increased risk of nephrotoxicity and ototoxicity with concomitant frusemide or vancomycin. • Possible increase in amikacin levels and potentiation of toxicity with indomethacin[2]

4. Guardrails Information[13]

Note that if infusions are run over 2 hours, you may get an alarm saying it is below the soft minimum. This value will be adjusted in the next guardrails download.

Guardrails Drug Name	**Amikacin***			
Pump	CC			
	0.4-1kg	**1-2kg**	**2-3kg**	**3-5kg**
Concentration (mg/ml)				
Minimum	1.25	3.12	6.25	9.38
Maximum	15.7	31.3	46.9	50
Default	3.75	9.38	18.7	28.1
Administration Rate (mg/kg/hr)				
Soft minimum	10	10	10	10
Default	30	30	30	30
Soft maximum	40	40	40	40
Hard maximum	50	50	50	50

5. Associated Documents

- Waikato DHB Service Specific to NICU Procedure #4360 “To give slow infusion/Intermittent infusion”

6. References

1 Ped & Neonatal Dosage Handbook, 21st edition. Taketomo et al.
2 Auckland NICU Drug Protocols – Amikacin, June 2013. Available from: http://www.adhb.govt.nz/newborn/DrugProtocols/Default.htm Last accessed 24 August 2016.
3 The New Zealand Medicines and Medical Devices Safety Authority (Medsafe): Gentamicin, Data sheet -New Zealand. Last accessed 8 April 2015. Available from http://www.medsafe.govt.nz/profs/datasheet/a/Amikacininj.pdf
4 New Zealand Hospital Pharmacists Association: Notes on Injectable Drugs, 7th Edition, Amikacin. Published 2015, Wellington NZ.
5 MIMs Gateway Amikacin profile. Last accessed 24 August 2016. Available from http://www.mimsgateway.co.nz/

6 Phelps SJ, Hak EB, Crill CM, editors. Teddy Bear Book: Pediatric Injectable Drugs. 10th Edition. Amikacin Sulfate. Bethesda, MD: American Society of Health-System Pharmacists; 2013

7 Micromedex® 1.0 (Healthcare Series), (electronic version). Paediatrics and Neofax - Amikacin. Truven Health Analytics, Greenwood Village, Colorado, USA. Last accessed 24 August 2016. Available from : http://www.micromedexsolutions.com/

8 British National Formulary for Children. 2011-2012. Pharmaceutical Press, London, 2011.

9 The New Zealand Formulary Editorial Team. New Zealand Formulary for Children (electronic version – v50 – 01 Aug 2016). Amikacin. New Zealand Formulary, NZ. Last accessed 24 August 2016. Available from http://nzfchildren.org.nz/nzf_31

10 Handbook on injectable drugs, 18th edition, American Society of Health-system Pharmacists 2015.

11 UpToDate® Amikacin: Paediatric drug information accessed on 24 August 2016. Available from: http://www.uptodate.com/contents/amikacin-drug-information?source=search_result&search=amikacin&selectedTitle=1%7E100

12 The Royal Children's Hospital Melbourne: Paediatric Injectable Guidelines 5th edition, Amikacin. Accessed on 24 August 2016. Available from: http://pig.hcn.com.au/monographs/Amikacin-3.html

13 Guardrails Data Sheets, Waikato Hospital, Hamilton, NZ, August 2016