Aminoglycoside administration in paediatrics: a literature search comparing international practices of intravenous injection or intravenous infusion

Abigail Manning , Anna Burgess

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/archdischild-2024-326924).

Welsh Medicines Advice Service, Cardiff and Vale University Health Board, Cardiff, UK

Correspondence to
Abigail Manning; Abigail.Manning@wales.nhs.uk

Received 26 January 2024
Accepted 15 March 2024
Published Online First 9 April 2024

To cite: Manning A, Burgess A. *Arch Dis Child Educ Pract Ed* 2024;**109**:242–246.

INTRODUCTION

Aminoglycosides are a class of broad-spectrum, bactericidal antibiotics of which amikacin, gentamicin and tobramycin are the most commonly prescribed. These antibiotics are frequently prescribed for children, usually for infections, which are caused by aerobic Gram-negative pathogens. [1]

Aminoglycosides are very poorly absorbed from the gastrointestinal tract, due to their lack of lipophilicity. Therefore, they must be administered parenterally. They are also concentration dependent, which means that the ratio between the peak concentrations (C_{max}) to the pathogen's minimum inhibitory concentration (MIC) is the pharmacokinetic-pharmacodynamic index, which is a marker for antimicrobial activity and effectiveness. To achieve an effective clinical response, a C_{max}/MIC ratio between 8 and 12 has been advised, although this is based on adult data.[1] Aminoglycosides have a narrow therapeutic margin, so therapeutic drug monitoring must be used to monitor for toxicity. High serum levels may result in ototoxicity and nephrotoxicity.[1]

Aminoglycosides are administered as once-daily or multiple-daily (previously known as 'standard dose') regimes. Once-daily regimens deliver a higher individual dose than multiple-daily doses. There are advantages and disadvantages of both methods, which have not been discussed in detail within this article.

Aminoglycoside use can result in rare cases of ototoxicity, even at normal serum levels. There is some evidence that suggests an association between mitochondrial mutations (particularly the m.1555A>G mutation, corresponding to a change of the *MT-RNR1* gene), leading to an increased risk of ototoxicity.[2] Within the UK, this occurrence is estimated at 1 in 500 patients. Currently, neonatal testing for the genetic variant is available through point of care testing for neonates with sepsis; however this is not commissioned nationally in the UK.[2]

Methods of administering intravenous medications include intermittent/or continuous intravenous infusions, or via slow

Key messages

- The suggested methods of aminoglycoside administration in paediatrics vary within the UK and internationally; however, there is more experience with intravenous infusion administration of aminoglycosides than for intravenous injection.
- There is no definitive guidance available suggesting what method of administration is most appropriate for gentamicin, amikacin or tobramycin in paediatric patients.
- Further studies are required to compare administration via intravenous injection and intravenous infusion, as well as pharmacodynamics changes, for example, the effects on time above the minimum inhibitory concentration when giving aminoglycosides via intravenous injection and how this affects both the clinical outcome and the incidence of adverse effects.
- There are multiple small studies/case reports highlighting the efficacy and safety of giving gentamicin one time per day via intravenous injection. Further research regarding the cost-saving and time-saving benefits would further the discussion and help to clarify optimal practice.

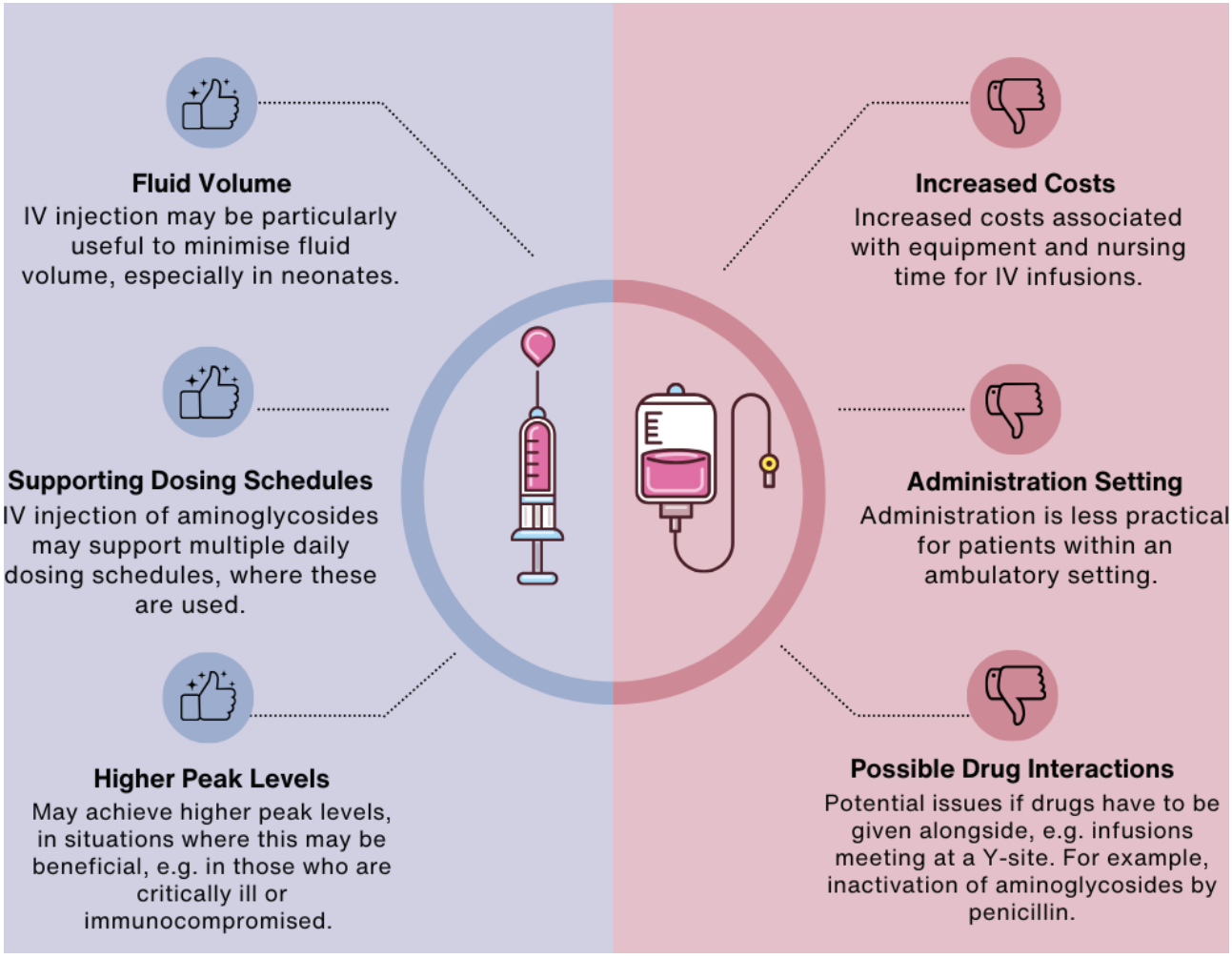

Figure 1 Examples of the advantages and disadvantages of IV injections and IV infusions.

intravenous injection (previously known as a bolus injection) (figure 1). Intravenous injection has the benefit of short administration time and minimal volume. This is particularly useful for patients who may be fluid restricted. The administration time may provide advantages due to the prompt time-to-first-dose, or a higher peak concentration.[3] Theoretical added benefits, include cost-savings, reduced nursing time and avoidance of drug incompatibilities, for example, the inactivation of aminoglycosides by β-lactam antibiotics.[4]

Despite these potential benefits, a review by *Spencer et al* states that aminoglycosides are not usually recommended for intravenous injection, due to the concerns that elevated peak levels after rapid administration may be a controllable risk factor for toxicity. However, this review acknowledges that intravenous injection of gentamicin and tobramycin has been reported frequently in the literature.[3]

AIM

The aim of this medicines update is to review the current practices and published evidence regarding the administration of aminoglycosides in paediatrics, via intravenous infusion or intravenous injection (specifically amikacin, gentamicin and tobramycin). This review will focus on current practices across the UK as well as the USA, New Zealand and Australia.

RESEARCH METHODS

A literature search of Medline and Embase databases was conducted between the dates of 15 July 2022 and 14 August 2023, as well as personal communications with specialist paediatric pharmacists in other UK health boards and internationally, to identify established local practices.

GENTAMICIN

When comparing the two routes of administration, intravenous infusions have been associated with both subtherapeutic and excessive trough concentrations of gentamicin.[5] As shown in online supplemental appendix 1, intravenous infusion over 30 min to 2 hours (in 50–200 mL) is recommended in the USA. Conversely, in the UK, licensed product information recommends infusing over a maximum of 20 min to 30 min, in a limited fluid volume (100 mL) or a slow intravenous injection over 3 min.[6 7]

A literature search revealed only two studies conducted in paediatrics, the vast majority of the papers found were focused on adult patients.[8 9] Initial studies conducted by

the manufacturer mostly evaluated two routes of administration, intravenous infusion (30–60 min) and intramuscular injection. A review of multiple studies in adults showed gentamicin has been safely administered as an intravenous injection over 3–5 min.[3]

Robinson and Nahata retrospectively investigated intravenous injection (2–3 min) of gentamicin in paediatric patients (n=123; neonates n=11, age 31 days to 1 year n=71, 13 months to 12 years n=26, 12 years to adult n=15) at a single centre. Patients received a median of nine doses; with 42% receiving doses every 8 hours, 32% receiving doses every 24 hours, and the remainder at other intervals ranging from every 12 to 36 hours. The results did not show a significant elevation in peak serum gentamicin concentrations or renal function changes. In the neonatal population, no changes in auditory function were noted. Auditory data were not available for the older population. No other adverse effects were mentioned.[8]

Bromiker *et al* conducted a study in Israel to evaluate auditory and renal function in 30 infants (gestation age: 38.9±2.1 weeks, birth weight: 3057g±516g) who were treated with rapid intravenous gentamicin injection over 1 min at a dose of 2.5 mg/kg two times per day for 72 hours. Auditory evaluation was based on transient evoked otoacoustic emissions (TEOAEs) and behavioural observation audiometry. Initial auditory tests (n=25) produced normal findings bilaterally except for one patient whom normal TEOAE results were obtained from only one ear. Follow-up TEOAE examination of 24 out of 30 infants at 5 weeks or more after completion of therapy found normal results bilaterally in 23 infants, and one infant had a normal unilateral response. Data were not found to suggest intravenous injection caused an increase in adverse effects compared with intravenous infusion.[9]

Loewenthal and Dobson reported experiences in the use of gentamicin and tobramycin in an outpatient setting, between November 1995 and October 2010. These were administered as an intravenous injection over 3–5 min to children and adults aged 3–84 years, as 5593 doses (tobramycin n=3652 and gentamicin n=1941). One case of vestibular toxicity and hearing loss was reported in a middle-aged woman, with complex medical problems, 16 hours after the last dose of tobramycin.[10]

AMIKACIN

Usually amikacin is given via intravenous infusion (see online supplemental appendix 1); however, there are some indications for which intravenous injection is preferred, especially within the UK. One study conducted in adults (n=5) evaluated the administration of amikacin 7.5 mg/kg over 2 min; however, this resulted in potentially toxic peak serum concentrations (68–122 µg/mL).[3] A literature search identified two studies of amikacin in paediatrics; however, none used an intravenous injection method.[11 12]

Manufacturers of amikacin differ in their administration guidance. Pfizer confirmed that intravenous injection of amikacin in neonates and children ≤12 weeks would be outside of the product's license.[13]

Online supplemental appendix 1 summarises some of the international practices with regards to administering aminoglycosides. The Australasian Neonatal Medicines Formulary recommends preterm and term neonates should be given amikacin via intravenous infusion over 60 min.[14] American literature sources advise intravenous infusion over 30–60 min, or over 1–2 hours in infants, and do not recommend intravenous injection. However, these sources acknowledge that this practice is used. This is in contrast to UK sources, such as the British National Formulary for Children (BNFC), which recommend administering amikacin as an intravenous injection over 3–5 min, or via a slow intravenous infusion over 30–60 min, for the majority of indications.[15]

TOBRAMYCIN

The BNFC recommended tobramycin is given by slow intravenous injection over 3–5 min or by intravenous, infusion over 20–60 min (see online supplemental appendix 1). The NHS Injectable Medicines Guide (Medusa) recommends that the intravenous injection is restricted for multiple-dose regimens, while once-daily high-dose regimens should be given by intravenous infusion.[16] Tobramycin once-daily dosing has become common practice within the UK but is an unlicensed method of administration.[17 18]

The manufacturers state for paediatric patients, the dose should be infused over 20–60 min and it can be given as a direct intravenous injection. However, when given as an IV injection, serum levels may exceed 12 microgram/mL for a short period of time. While this is listed as a caution, slow intravenous injection is still a licensed method of administration.[17]

American literature sources do not recommend intravenous injection, despite acknowledging that this practice is used. The rationale for this is that infusion periods of less than 20 min may result in peak serum tobramycin concentrations exceeding 12 µg/mL.[18] There are concerns that these elevated peak levels after rapid administration may cause toxicity, such as ototoxicity.[3] The Australasian Neonatal Medicines Formulary also recommends that tobramycin 5 mg/kg/dose 24–48 hourly should be given as an intravenous infusion over 20–60 min (see online supplemental appendix 1).

The TOPIC study compared once-daily versus three-time daily regimens of tobramycin intravenous infusion in children (n=125) and adults (n=94) with cystic fibrosis. The pharmacokinetic modelling from this study showed equivalent efficacy for once-daily tobramycin, compared with, what was at the time, the conventional three-time daily treatment. A smaller rise in N-acetyl-β-D glucosaminidase in children in the once-daily group, compared with the three-time daily group suggests that the once-daily regimen may be less nephrotoxic than three-time daily regimen in children. As this safety and efficacy data were obtained following intravenous infusion, rather than

intravenous injection, this may explain the preference for the intravenous infusion method. There are limitations to this study, as toxic effects may be cumulative and could also contribute to the findings. None of the patients developed ototoxic effects.[19]

SUMMARY

There are multiple small studies or case reports highlighting the efficacy and safety of intravenous injection of gentamicin in paediatrics, especially for multiple daily dose regimens. Both methods of administration (intravenous injection and intravenous infusion) are licensed for gentamicin.[7] Therefore, as both methods of administration seem acceptable, intravenous injection may provide cost and time-saving benefits. Further investigation of the cost benefits would be needed; however, this is outside the scope of this review.

More quality research is needed to support the administration of tobramycin and amikacin via intravenous injection, although online supplemental appendix 1 shows that this practice is used within the UK and internationally.

Test your knowledge

MCQs

1. In what situation would it be beneficial to give a medicine via an intravenous infusion:
   a. For patients who are fluid restricted, for example, heart failure
   b. In an outpatient setting
   c. For medicines with a multiple daily dose schedule
   d. Where there are concerns regarding the rapid administration of a medicine
2. What bacteria are aminoglycosides most effective against?
   a. Gram-positive anaerobic bacteria
   b. Gram-negative aerobic bacteria
   c. Gram-positive aerobic bacteria
   d. Gram-negative anaerobic bacteria
3. Currently, which aminoglycoside has the most published data to support intravenous injection in paediatrics?
   a. Tobramycin
   b. Streptomycin
   c. Gentamicin
   d. Amikacin
4. What is the best marker of aminoglycoside antimicrobial activity and clinical effectiveness?
   a. C_{max}
   b. MIC
   c. C_{max}/MIC
   d. Trough level
5. What gene is responsible for rare cases of ototoxicity with aminoglycosides?
   a. MT-RNR4
   b. MT-RNR1
   c. MT-RNR2
   d. MT-RNR6

Answers to the quiz are at the end of the references.

Correction notice This paper has been corrected since it was first published. There was an error in figure 1.

Acknowledgements Thomas Wyllie (Specialist Clinical Pharmacist, Neonatology and Metabolic Disease) and Alexandra Leyshon (Specialist Antimicrobial Pharmacist) critically reviewed the piece of work, from a neonatal and microbiology perspective. Sana Junaid (Specialist Information Pharmacist) was involved in the research for an initial piece of work on the topic for NPPG. The NPPG committee should also be acknowledged.

Contributors AM is the main author of the Medicines Update. Contributions include writing the article, research, creation of figures and tables included. AB contributed to the paper by reviewing AM's work and undertaking initial research within the area.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer-reviewed.

ORCID iD

Abigail Manning http://orcid.org/0009-0000-3512-3033

REFERENCES

1 Germovsek E, Barker C, Sharland M. What do I need to know about aminoglycoside antibiotics? archives of disease in childhood. *Education and Practice* 2017;102:89–93.
2 Implementing pharmacogenomic testing for aminoglycosides – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice 2023, Available: https://www.sps.nhs.uk/articles/implementing-pharmacogenomic-testing-for-aminoglycosides/ [Accessed 6 Dec 2023].
3 Spencer S, Ipema H, Hartke P, *et al*. Intravenous push administration of antibiotics: literature and considerations. *Hosp Pharm* 2018;53:157–69.
4 Miller J, ed. *Aminoglycosides General Statement. In: AHFS Drug Information (online)*. Bethesda, MD: American Society of Health-System Pharmacists, Inc, Available: https://www.medicinescomplete.com
5 Miller J. Tobramycin sulfate. In: *In: AHFS drug information (online*. American Society of Health-System Pharmacists, Inc, Available: https://www.medicinescomplete.com [accessed 1 Dec 2023].
6 Sweetman S S. Gentamicin sulfate. In: *In: Martindale:The Complete Drug Reference*. Michigan, USA: Merative: London:The Royal Pharmaceutical Society of Great Britain. Ann Arbor, Available: https://www.micromedexsolutions.com/
7 Summary of product characteristics - gentamicin Paediatric 20Mg/2Ml. Zentiva. Date of revision of the text: 16 Feb 2021. Available: https://www.medicines.org.uk/emc/product/4186/smpc [Accessed 7 Oct 2023].
8 Robinson RF, Nahata MC. Safety of intravenous bolus administration of gentamicin in pediatric patients. *Ann Pharmacother* 2001;35:1327–31.

9 Bromiker R, Adelman C, Arad I, *et al*. Safety of gentamicin administered by intravenous bolus in the nursery. *Clin Pediatr (Phila)* 1999;38:433–5.
10 Loewenthal MR, Dobson PM. Tobramycin and gentamicin can safely be given by slow push. *J Antimicrob Chemother* 2010;65:2049–50.
11 Cleary TG, Pickering LK, Kramer WG, *et al*. Amikacin pharmacokinetics in pediatric patients with malignancy. *Antimicrob Agents Chemother* 1979;16:829–32.
12 Howard JB, McCracken GH. Pharmacological evaluation of amikacin in neonates. *Antimicrob Agents Chemother* 1975;8:86–90.
13 Pfizer medical information. In: *Personal communication*. 2023.
14 Australian medicines Handbook. In: *Adelaide:Australian Medicines Handbook Pty Ltd*. 2023.
15 Paediatrics Formulary committee. BNF for children (online). London:BMJ Group, Pharmaceutical Press, and RCPCH Publications. Available: https://www.medicinescomplete.com [Accessed 8 Oct 2023].
16 Tobramycin intravenous - CHILD. In: *In: NHS Injectable Medicines Guide (Medusa) 2021 Available from*. Available: https://www.medusaimg.nhs.uk/
17 Summary of product characteristics - tobramycin 40Mg/ml injection. Hospira UK Ltd. Date of revision of the text: Aug 2022. Available: https://www.medicines.org.uk/emc/product/1425/smpc [Accessed 7 Nov 2023].
18 Miller J, ed. Tobramycin sulfate. In: *In: AHFS Drug Information (online)*. Bethesda, MD: American Society of Health-System Pharmacists, Inc, Available: https://www.medicinescomplete.com [accessed 1 Dec 2023].
19 Smyth A, Tan KH-V, Hyman-Taylor P, *et al*. Once versus three-times daily regimens of tobramycin treatment for pulmonary exacerbations of cystic fibrosis—the TOPIC study: a randomised controlled trial. *Lancet* 2005;365:573–8.

Answer to the multiple choice questions

1. d
2. b
3. c
4. c
5. b

Medicines Update

Appendix 1 – International Practices of Aminoglycoside Administration (IV infusion and IV injection)

Aminoglycoside Administration – IV Infusion				
	United Kingdom	**United States**	**Australia**	**New Zealand**
Gentamicin	• BNFC [1] – infuse over 20-30 minutes or over 60 minutes for once daily regimens • Medusa Injectable Medicines Guide [2] – infuse over 30 minutes or 60 minutes for once daily regimens. • Alder Hey Children's NHS Foundation Trust [3] – infuse over 20 minutes • PIER network (Wessex) – infuse over 30 minutes. [4]	• Pediatric Injectable Drugs: the teddy bear book – infuse over 30 – 120 minutes. [5] • Lexicom – infuse over 30 – 120 minutes (usual infusion time is 30 – 60 minutes). Longer infusion times (60 -120 minutes) with high doses. [6]	• Queensland Children's Hospital – infuse over 30 minutes. [7] • Perth Children's Hospital – infuse over 30 minutes [8] • The Children's Hospital at Westmead – infuse over 30 minutes. [9] • Australian Medicines Handbook – infuse over 15-30 minutes. [10] • Sydney Children's hospital – may be given as a 30 minute infusion. [11]	• Starship Child Health – infuse over 30 minutes for once daily dosing. [12] • Notes on Injectable Drugs – for once daily dose regimes infuse over 30 minutes (preferred method). [13]
Amikacin	• BNFC [1] • Medusa Injectable Medicines Guide [2] • Scottish perinatal network [14] – for neonates. • Great Ormond Street Hospital – for 20-30 mg/kg once daily doses, infuse over 30 minutes.[15] • Leeds Centre for Cystic Fibrosis (adult and paediatric) [16] – infuse over 30-60 minutes. • Alder Hey Children's NHS Foundation Trust [3] – infuse over 20 minutes.	• Pediatric Injectable Drugs: the teddy bear book – infuse over 30 – 60 minutes. [17] • Lexicomp – Infuse over 30 – 60 minutes, 20 minutes has been reported in neonates (1st line). [6]	• Perth Children's Hospital – infuse over 30 -60 minutes. [18] • The Children's Hospital at Westmead – infuse over 30-60 minutes in children and 1-2 hours in infants. [9] • Australian Medicines Handbook – infuse over 15-30 minutes. [10] • Queensland Children's Hospital – infuse over 30 minutes – 1 hour, or 1-2 hours in neonates and infants. [7] •	• Australasian Neonatal Medicines Formulary – infuse over 60 minutes. [19] • Starship Child Health – infuse over 30 minutes for once daily dosing. [12] • Notes on Injectable Drugs – infuse over 30 – 60 minutes (children) or 60 – 120 minutes in infants (preferred method).[20]
Tobramycin	• BNFC [1] • Medusa Injectable Medicines Guide – once daily regimens [2] • UK Cystic Fibrosis (CF) Trust antibiotic working group guidelines [21] – for 10 mg/kg once daily, infuse over 30 minutes • Leeds Centre for Cystic Fibrosis (adult and paediatric) [16] – infuse over 30 minutes • Alder Hey Children's NHS Foundation Trust [3] – for 7mg/kg once daily or 10mg/kg once daily in CF, infuse over 20 minutes.	• Pediatric Injectable Drugs: the teddy bear book – infuse over 20 – 60 minutes. [22] • Lexicomp – Infuse over 20 to 60 minutes. [6]	• Perth Children's Hospital – infuse over 20 – 40 minutes. [23] • The Children's Hospital at Westmead – infuse over 30 minutes. [9] • Australian Medicines Handbook – infuse over 15-30 minutes. [10] • Sydney Children's hospital – may be given as a 30 minute infusion. [11] • Queensland Children's Hospital – infuse over 30 minutes. [7]	• Australasian Neonatal Medicines Formulary – infuse over 30 minutes (20-60 minutes). [24] • Starship Child Health – infuse over 30 minutes for once daily dosing. [12] • Notes on Injectable Drugs – for once daily dose regimen infuse diluted over 20 – 60 minutes, preferably 60 minutes (preferred method). (25)

Medicines Update

Aminoglycoside Administration – IV injection				
	United Kingdom	**United States**	**Australia**	**New Zealand**
Gentamicin	• BNFC [1] • Medusa Injectable Medicines Guide [2] • Alder Hey Children's NHS Foundation Trust [3] – for neonates and patients on multiple daily dosing regimens • Oxford University Hospitals NHS Trust [26] – for neonates • PIER network (Wessex) [4]	• Lexicomp – not 1st line but it has been reported in paediatric patients receiving ≤4mg/kg/dose [6]	• Sydney Children's hospital- may be administered as a slow push over 3-5 minutes. [11] • Perth Children's hospital – doses ≤ 120mg (higher doses may be given to those who are critically unwell) [8] • The Children's Hospital at Westmead (preferred method) [9] • Australian Medicines Handbook – doses <120mg may be given as an IV injection over 3-5 minutes, although it acknowledges that bolus administration of all doses is widely used in clinical practice without evidence of clinical toxicity. [10]	• Australasian Neonatal Medicines Formulary – over 5 minutes. [27] • Notes on Injectable Drugs – only if intermittent intravenous infusion is not possible – for once daily and multiple daily dose regimen (undiluted or in up to 20ml NaCl 0.9% over at least 3 minutes). [13]
Amikacin	• BNFC [1] • Medusa Injectable Medicines Guide [2] – for doses ≤15 mg/kg • UK Cystic Fibrosis Trust antibiotic working group guidelines [21] – for 10mg/kg 8 hourly • Alder Hey Children's NHS Foundation Trust [3] – for neonates but short infusion usually preferred • Great Ormond Street Hospital – for 10-15 mg/kg once daily doses [15]	• Lexicomp – some reports of slow injection (over 1 -5 minutes) but not 1st line. [6]	• Australian Medicines Handbook - Doses <500mg can be given as an IV injection over 3-5 minutes. [10]	• Notes on Injectable Drugs – for multiple daily dose regimen administer undiluted or dilute in compatible fluid over 3 – 5 minutes (IV infusion is preferred). [19]
Tobramycin	• BNFC [1] • Medusa Injectable Medicines Guide – multiple-dose regimens [2] • UK Cystic Fibrosis Trust antibiotic working group guidelines [21] – for 3.3 mg/kg 8 hourly • Alder Hey Children's NHS Foundation Trust [3] – for neonates on extended interval dosing	• Lexicomp – some reports of slow injection (≤5 minutes) but not 1st line. [6]	• Sydney Children's hospital – may be administered as a slow push over 3-5 minutes. [11] • Perth Children's Hospital - doses ≤ 120mg [23] • Australian Medicines Handbook – doses <120mg may be given as IV injection over 3-5 minutes. [10]	• Notes on Injectable Drugs – for multiple daily dose regimes administer undiluted over 3 – 5 minutes. [24]

Medicines Update

References - Appendix 1

1) Paediatrics Formulary Committee. BNF for Children (online). London: BMJ Group, Pharmaceutical Press, and RCPCH Publications. Available from: https://www.medicinescomplete.com/#/ [Accessed 8 Oct 2023].
2) NHS Injectable Medicines Guide (Medusa), 2020. Available from: https://www.medusaimg.nhs.uk/ [Accessed 8 Nov 2023].
3) Alder Hey Children's NHS Foundation Trust Medicines Information. Personal communication. 2023.
4) Paediatric Innovation, Education and Research (PIER) Network. Gentamicin dosing in children, 2018. Available from:https://www.piernetwork.org/uploads/4/7/8/1/47810883/pier_gentamicin_guidelines_final_feb_2018_copy.pdf [Accessed 1 Dec 2022].
5) Phelps SJ, Hageman TM, Lee KR, *et al*. Gentamicin Sulfate. In: Pediatric injectable drugs: the teddy bear book. Bethesda: American Society of Health-System Pharmacists; 2018. p 438–41.
6) Post T, editor. Pediatric drug information. Lexicomp®. In: UpToDate. Waltham, MA: Wolters Kluwer Health. Available from: http://www.uptodate.com/ [Accessed 8 Nov 2022].
7) Children's Health Queensland Hospital and Health Service. Intravenous Aminoglycoside therapy (Amikacin, Gentamicin and Tobramycin). Paediatric Medication Guideline 2023. Available from: https://www.childrens.health.qld.gov.au/__data/assets/pdf_file/0031/176917/paed-tobramycin-gentamicin-therapeutic-drug-monitoring.pdf [Accessed 6 Dec 2023].
8) Perth Children's Hospital. Children's Antimicrobial Management Programme (ChAMP). Gentamicin (intravenous) Monograph – Paediatric 2022. Available from: https://pch.health.wa.gov.au/~/media/Files/Hospitals/PCH/General-documents/Health-professionals/ChAMP-Monographs/Gentamicin.pdf [Accessed 6 Dec 2023].
9) The Children's hospital at Westmead. Aminoglycoside dosing and Monitoring 2021. Available from: https://www.schn.health.nsw.gov.au/_policies/pdf/2011-8018.pdf [Accessed 6 Dec 2023].
10) *Australian Medicines Handbook.* Adelaide: *Australian Medicines Handbook Pty Ltd*; 2023.
11) Sydney Children's Hospital. Aminoglycoside Therapy – Practice Guideline. 2021. Available from: https://www.schn.health.nsw.gov.au/_policies/pdf/2012-7008.pdf [Accessed 6 Dec 2023].
12) Starship Hospital, Auckland. Aminoglycosides Clinical Guideline 2021. Available from: https://starship.org.nz/guidelines/aminoglycosides/ [Accessed 8 Nov 2023].
13) New Zealand Hospital Pharmacists' Association (Inc.). *Notes on Injectable Drugs*. Gentamicin. 2020.
14) West of Scotland NEONATAL Parenteral Drug Monographs. Amikacin. 2019; Available from: https://www.perinatalnetwork.scot/wp-content/uploads/2022/06/Amikacin-WoS_PI.pdf [Accessed 6 Dec 2023].
15) Great Ormond Street Hospital for Children NHS Foundation Trust. Amikacin Guidelines, 2014. Available from: https://goshintensivecare.files.wordpress.com/2017/08/amikacin.pdf [Accessed 7 Nov 2023].
16) Leeds Centre for Cystic Fibrosis & Leeds Children's Hospital. INTRAVENOUS Antibiotic Guidelines for Patients with Cystic Fibrosis at Leeds Cystic Fibrosis Units (Adult and Paediatric), 2019. Available from: http://www.leedsformulary.nhs.uk/docs/5.1CysticFibrosisAntibioticIVdoses.pdf [Accessed 7 Nov 2023].
17) Phelps SJ, Hageman TM, Lee KR, *et al*. Amikacin Sulfate. In: *Pediatric injectable drugs*: the teddy bear book. Bethesda: American Society of Health-System Pharmacists; 2018. p42–5.
18) Perth Children's Hospital. Children's Antimicrobial Management Programme (ChAMP). Amikacin Monograph – Paediatric, 2022. Available from: https://pch.health.wa.gov.au/~/media/Files/Hospitals/PCH/General-documents/Health-professionals/ChAMP-Monographs/Amikacin.pdf [Accessed 6 Dec 2023].
19) Australasian Neonatal Medicines Formulary Consensus Group. Amikacin 2021. Available from: https://www.anmfonline.org/wp-content/uploads/2021/06/amikacin-18022021-2.0.pdf [Accessed 8 Dec 2023].
20) New Zealand Hospital Pharmacists' Association (Inc.). *Notes on Injectable Drugs*. Amikacin 2020.
21) UK Cystic Fibrosis Trust Antibiotic Working Group. Antibiotic Treatment for cystic fibrosis. 3rd edition 2009. Available from: https://www.cysticfibrosis.org.uk/sites/default/files/2020-11/Anitbiotic%20Treatment.pdf [Accessed 1 Dec 2023].
22) Phelps SJ, Hageman TM, Lee KR, *et al*. Tobramycin Sulfate. In: Pediatric injectable drugs: the teddy bear book. Bethesda: American Society of Health-System Pharmacists; 2018. p 830–3.
23) Perth Children's Hospital. Children's Antimicrobial Management Programme (ChAMP). Tobramycin (intravenous) Monograph – Paediatric, 2022. Available from: https://pch.health.wa.gov.au/~/media/Files/Hospitals/PCH/General-documents/Health-professionals/ChAMP-Monographs/Tobramycin.pdf [Accessed 6 Dec 2023].

Medicines Update

24) Australasian Neonatal Medicines Formulary Consensus Group. Tobramycin 2020. Available from: https://www.anmfonline.org/wp-content/uploads/2021/06/tobramycin-29102020-1.0.pdf [Accessed 8 Dec 2023].
25) New Zealand Hospital Pharmacists' Association (Inc.). *Notes on Injectable Drugs*. Tobramycin 2020.
26) Oxford University Hospitals NHS Trust. Gentamicin Injection - Monograph Neonatal 2014. Available from: accessed via NPPG discussion forum.
27) Australasian Neonatal Medicines Formulary Consensus Group. Gentamicin 2021. Available from: https://www.anmfonline.org/wp-content/uploads/2021/06/gentamicin-18022021-3.0.pdf [Accessed 8 Dec 2023].