MONOGRAPH

Tobramycin (intravenous) Monograph - Paediatric

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

QUICKLINKS

Dosage/Dosage Adjustments | Administration | Compatibility | Monitoring

DRUG CLASS

Aminoglycoside antibiotic.(1)

Tobramycin is a High Risk Medicine.

INDICATIONS AND RESTRICTIONS

Tobramycin is active against a broad range of gram-negative bacteria, including *Pseudomonas aeruginosa*.(2)

IV: Monitored (orange) antibiotic

- If the use is consistent with a standard approved indication, this must be communicated to ChAMP by documenting that indication on all prescriptions (inpatient and outpatient).
- The ChAMP team will review if ongoing therapy is required and/or if the order does not meet ChAMP Standard Indications
- If use is not for a standard approved indication, phone approval must be obtained from ChAMP before prescribing.

CONTRAINDICATIONS

- Hypersensitivity to tobramycin, any aminoglycoside (e.g. gentamicin or amikacin) or any component of the formulation.(3, 4)

PRECAUTIONS

- Use tobramycin with caution in patients with renal impairment, reduce the dose of tobramycin as recommended under 'dose adjustment' and seek Infectious Diseases/ChAMP/Pharmacy advice. Risk factors for nephrotoxicity include duration of treatment, high plasma concentrations, dehydration and treatment with other nephrotoxic medications.[1]
- Care should be taken in patients with a previous vestibular or auditory toxicity due to an aminoglycoside.[1] See 'monitoring' section.
- Use tobramycin with caution in patients with neuromuscular disease e.g. myasthenia gravis as the risk of muscle weakness and respiratory depression is increased.[1]
- Some brands contains sodium metabisulfite which may cause allergic reactions in susceptible people.[5]
- Clinically evident vestibular ototoxicity (nausea, vomiting, vertigo, nystagmus, difficulties with gait) and cochlear ototoxicity (noticeable hearing loss, tinnitus, a feeling of fullness in ear) occur in 2–4% of patients. Rates of both are higher if pure tone audiometry and electronystagmography are used to detect impairment (high frequency hearing loss in up to 26% of patients). Ototoxicity may be delayed in onset and is irreversible in about 50% of people; permanent deafness may occur.[1, 6]
- Ototoxicity can occur as an idiosyncratic reaction after single-dose aminoglycoside exposure in individuals who are genetically predisposed. This is associated with the A1555G gene (notably in Asian populations). Ototoxicity is more commonly the result of cumulative aminoglycoside exposure. Under certain circumstances, genetic testing *prior* to treatment with long course aminoglycosides or in children requiring repeated course may be considered following consultation with the infectious diseases team.[1]

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

- 80mg/2mL Vial
- 500mg/5mL Vial (kept in Pharmacy Compounding Service (PCS) unit and used only for Hospital in the Home (HiTH) tobramycin IV doses - preservative free.)

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: Refer to Neonatal Medication Protocols

Dosing in Overweight and Obese Children: Dosing should be based on adjusted body weight for overweight or obese children.

IV/IM:

General once daily dosing:

- **Children ≥ 1 month old to 10 years old:** 7.5mg/kg/dose (to a maximum of 320mg) ONCE daily.[1]
- **Children >10 years to 18 years :** 6-7mg/kg/dose (to a maximum of 560mg) ONCE daily.[1]

- No further dose increases should be made without consulting infectious diseases, ChAMP or clinical microbiology.

Cystic fibrosis patients:

- **1 month to 18 years initial dose:** 10mg/kg/dose (to a maximum of 750mg) ONCE daily. The dose can be increased based on AUC calculations to a maximum of 15mg/kg/dose or 750mg ONCE daily (whichever is less).[1, 3](

Inhalation:

Please refer to the separate inhaled Tobramycin monograph.

Renal impairment:

- eGFR calculator (Google Chrome®)
- Where possible, consider using a less nephrotoxic agent.
- Dosage adjustment may be required in cases of impaired renal function (with creatinine clearance of less than 60mL/min).[2]
- In cases where tobramycin is required, suggested initial dosing intervals are stated below. All future doses and intervals are to be determined based on therapeutic drug monitoring.
    - CrCl > 60mL/minute: 24 hourly dosing interval
    - CrCl 40-60mL/minute: 36 hourly dosing interval
    - CrCl < 40 mL/minute: consider alternative agents. If essential, give initial dose then contact Pharmacy for advice on monitoring and further doses.[2, 7]

Hepatic impairment:

- No dosage adjustment is required.[3]

ADMINISTRATION

NOTE: Inhalation formulations (e.g. Tobramycin 300mg/5mL solution for inhalation or Tobi Podhaler®) **MUST NOT** be administered via the intravenous or oral route.

IV Injection:

- For doses ≤ 120mg, the dose may be diluted to a suitable final volume (up to 20mL) with compatible fluid and administered over 3 to 5 minutes.[5]

IV infusion:

- Dilute to a suitable volume (up to 100mL) with compatible fluid to allow infusion over 20 to 60 minutes. [5, 6, 8]

IM injection:

- If IV access is not available this medication may be given by IM injection into a large muscle mass. However the IV route is preferred for patients with suspected shock or sepsis.
- IM injection is NOT suitable for premature neonates.[3]
- Refer to Intramuscular (IM) injections for further information.

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Sodium chloride 0.9%
- Glucose 5%
- Glucose 10% (if final concentration of tobramycin is <6mg/mL)
- Glucose/sodium chloride solutions
- Hartmann's[5]

Compatible at Y-site:

Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

MONITORING

Therapeutic drug monitoring:

Monitoring for patients with normal pharmacokinetics:

- Trough level should be taken immediately prior to the 4th dose and should be below the limit of detection (<0.6mg/L).
- If the trough level is greater than or equal to 0.6mg/L, contact Pharmacy for advice as this indicates reduced clearance of tobramycin and cessation or dose adjustment is required.
- Follow-up levels should be performed twice weekly unless the clinical situation dictates otherwise (e.g. impaired renal function and concurrent use of nephrotoxic drugs where levels should be collected more frequently).

Patients with altered pharmacokinetics:

- Include patients with Cystic fibrosis, oncology patients, patients with severe burns or patients with impaired renal function.
- These patients should have therapeutic drug monitoring completed with the **SECOND** dose of tobramycin.
- Monitoring should be based on calculating the drug concentration in the body relative to time, monitoring area under the curve (AUC).
- AUC measurement involves a mathematical calculation that requires the recording of the drug concentration at two specific times.
- Refer to the form MR860.91 Gentamicin and Tobramycin AUC reporting form for the specific times required.
- This form should be kept in the patients notes on the ward and it will be collected and interpreted by the ward pharmacist who will then calculate the AUC. The target AUC level for Cystic fibrosis patients is 70-100mg/L.hr.
- **ALL** patients (including those on HiTH) require ongoing monitoring of their tobramycin AUC levels at a minimum of once weekly AND/OR following any dose adjustment.

HiTH patients (excluding those with altered pharmacokinetics):

- Require weekly monitoring of their trough levels and renal function monitoring.
- Trough levels should remain below the limit of detection (<0.6mg/L).
- If the trough level is greater than or equal to 0.6mg/L, contact Pharmacy for advice as this indicates reduced clearance of tobramycin and cessation or dose adjustment is required.

Process of therapeutic drug monitoring:

- Blood samples for therapeutic drug monitoring (TDM) for tobramycin may be collected via a capillary blood sample OR via accessing a central venous access device (CVAD) line.
- A capillary blood sample (i.e. finger prick or heel prick for infants <6months) should be used if there is no CVAD in-situ.
- For patients with a CVAD in-situ (especially Cystic Fibrosis patients) the following process should be used:[9]
    - Stop all fluids running through the CVAD line.
    - Flush the line with sodium chloride 0.9%. The volume used is three times the internal line-filling volume of the CVAD device (as per table below).
    - Collect an initial blood sample to be **discarded.** The volume taken is three times the internal line-filling volume of the CVAD device PLUS the additional volume of the IV tubing, injection caps and connectors (as per table below). This is to ensure there is no residue tobramycin in the line which may falsely elevate levels.
    - Collect a **therapeutic drug level monitoring sample** of blood to send to PathWest for determination of the AUC.
    - Administer another flush of sodium chloride 0.9% (volume as per table below) to ensure line does not clot after blood sample is taken.
    - Recommence fluids if required

Line type	Approximate internal fill volume of CVAD and line	Flush and discard volume
PICC and Non-tunnelled CVC	1mL	3mL
Tunnelled line (broviac) and Implanted (port)	2mL	6mL

Collection tube:

- **Paediatric -** Lithium Heparin (Green top) 600microlitre (PST gel) or Serum (Red top clot) 600microlitre (No Gel) or Lithium Heparin (Dark Green Top) 1mL (no gel)[10]
- **Neonatal -** Lithium Heparin (Green top) 600microlitre (PST gel) or Serum (Red top clot) 600microlitre (No Gel)[10]
- **Minimum volume required:** 300microlitres[10]

For further information, refer to the PathWest test directory.

Monitoring in Neonates:

- Please refer to Neonatal Medication Protocols

Additional monitoring:

- Renal function and electrolytes should be performed weekly whilst on treatment.
- Patients receiving treatment > 2 weeks (e.g. for Cystic Fibrosis exacerbation) with tobramycin must be monitored for hearing loss and vestibular toxicity every 1 to 2 weeks.[1]

ADVERSE EFFECTS

Common: Nephrotoxicity (usually reversible, but can be anticipated if treatment extends beyond 7-10 days, or if pre-existing renal impairment), vestibular and cochlear toxicity.[1, 6]

Infrequent: nausea, vomiting, skin reactions[6]

Rare: Anaphylaxis, bronchospasm, oliguria, peripheral neuropathy and neuromuscular blockade, electrolyte disturbances, diarrhoea, dizziness.[1, 6]

STORAGE

- 80mg/2mL ampoule should be protected from light and stored below 25˚C.
- 500mg/5mL Vial should be protected from light and refrigerated between 2 and 8˚C.[5]

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of **tobramycin (intravenous)**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

Antimicrobial Stewardship Policy

ChAMP Empiric Guidelines and Monographs

KEMH Neonatal Medication Protocols

References

1. Rossi S, editor. Australian Medicines Handbook. Adelaide, S. Aust.: Australian Medicines Handbook; 2021.
2. Antibiotic Writing Group. eTG complete. West Melbourne: Therapeutic Guidelines Ltd; 2021. Available from: https://tgldcdp-tg-org-au.pklibresources.health.wa.gov.au/etgAccess.
3. Clinical Pharmacology [Internet]. Elsvier BV. 2021 [cited 8/07/2021]. Available from:

http://www.clinicalpharmacology-ip.com.pklibresources.health.wa.gov.au/default.aspx.
4. MIMS Australia. MIMS online [full product information]. St Leonards, N.S.W: CMP Medica Australia.; 2021. p. 1v. (various pagings).
5. Symons K. Ermer J. (editors). Australian injectable drugs handbook. Collingwood: The Society of Hospital Pharmacists of Australia; 2020.
6. Paediatric Formulary Committee. BNF for Children: 2020. London: BMJ Group Pharmaceutical Press; 2021.
7. IBM Micromedex [Internet]. Truven Health Analytics. 2021 [cited 11/05/2021]. Available from: http://www-micromedexsolutions-com.pklibresources.health.wa.gov.au/micromedex2/librarian.
8. Pediatric Injectable Drugs. Maryland: American Society of Health -System Pharmacists; 2020.
9. Lichliter RL, Tremewan LE, Shonka NM, Mehnert JE, Brennan L, Thrasher JM, et al. Therapeutic antibiotic serum concentrations by two blood collection methods within the pediatric patient: A comparative effectiveness trial. J Spec Pediatr Nurs. 2018;23(2):e12212.
10. PathWest. PathWest - test directory Perth2020 [cited 2020. Available from: http://www.pathwest.com.au/testdirectory/.

This document can be made available in alternative formats on request for a person with a disability.

File Path:	W:\Paediatrics\PMH\ChAMP\Monographs\FINALISED\00 Current version 00		
Document Owner:	Head of Department – Infectious Diseases		
Reviewer / Team:	Children's Antimicrobial Management Program Pharmacist		
Date First Issued:	April 2013	**Last Reviewed:**	July 2021
Amendment Dates:	December 2017	**Next Review Date:**	July 2024
Approved by:	Medication Safety Committee	**Date:**	August 2021
Endorsed by:	Drugs and Therapeutics Committee	**Date:**	September 2021
Standards Applicable:	NSQHS Standards:  NSMHS: N/A Child Safe Standards: N/A		

Printed or personally saved electronic copies of this document are considered uncontrolled

Healthy kids, healthy communities

Compassion | Excellence | Collaboration | Accountability | Equity | Respect

Neonatology | Community Health | Mental Health | Perth Children's Hospital