**Tobramycin (intravenous) Monograph - Paediatric**

| Scope (Staff): | Medical, Nursing, Pharmacy |
| Scope (Area):  | Perth Children’s Hospital (PCH) |

This document should be read in conjunction with this DISCLAIMER

### DESCRIPTION

- Tobramycin is an aminoglycoside antibiotic that inhibits bacterial protein synthesis by irreversibly binding to the 30S ribosomal subunit, resulting in cell membrane damage.\(^1\)

- 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**

- Prescription and use consistent with a standard approved indication must be communicated to ChAMP by documenting the 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.

- Refer to the inhaled tobramycin monograph for further restrictions and information related to inhaled tobramycin.

### CONTRAINDICATIONS

- Tobramycin is contraindicated in patients with a history of allergy or hypersensitivity (via any route) to tobramycin or other aminoglycoside e.g. gentamicin and amikacin, or any component of the formulation.\(^3,4\)

### PRECAUTIONS

- Use aminoglycosides with caution in patients with renal impairment and reduce the dose of aminoglycoside as recommended under ‘dose adjustment’ and seek Infectious diseases/ChAMP/Pharmacy advice. Risk factors for nephrotoxicity include length 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.\(^1\)
- Use aminoglycoside 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 contain sodium metabisulfite which may cause allergic reactions in susceptible people.\(^{(5)}\)

**FORMULATIONS**

**Available at PCH:**
- 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.)

**Other formulations available**
- Nil

**DOSAGE**

- The doses listed below fall within the standard range.
- Higher doses may be prescribed for certain situations in consultation with an infectious diseases or clinical microbiology consultant.

**Dosing should be based on the ideal body weight for overweight or obese children.**

Please refer to: [Guidelines For Drug Dosing in Overweight and Obese Children](#)

**Neonates (<1 month of age):**
- Please refer to [neonatal clinical care drug protocols](#) for dosing in infants <1 month of age.

**IV/IM:**

**General once daily dosing:**
- **Children ≥ 1 month old to 10 years old:** 7.5mg/kg/dose ONCE daily to a maximum of 320mg.\(^{(1)}\)
- **Children >10 years to 18 years:** 6-7mg/kg/dose ONCE daily to a maximum of 560mg.\(^{(1)}\)
- 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 ONCE daily (maximum of 750mg), can be increased based on AUC calculations to a maximum of 15mg/kg/dose or 750mg ONCE daily (whichever is less).\(^{(1, 4)}\)
**Oncology patients:**
- Contact Pharmacy for advice, gentamicin is preferred in oncology patients at PCH.

**Inhalation:**
- Please refer to the separate inhaled Tobramycin monograph.

### DOSAGE ADJUSTMENT

**Dosage adjustment required in renal impairment (once daily dosing):**
- 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).\(^{(2, 6)}\)

\[
eGFR\text{ (mL/min/1.73m}^2\text{)} = 36.5 \times \text{height (in cm)}
\]

Serum creatinine (micromol/L)

- 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.\(^{(2, 6)}\)

**Dose adjustment required in overweight or obese patients:**
Dosing should be based on the ideal body weight for overweight or obese children.

Please refer to: Guidelines For Drug Dosing in Overweight and Obese Children

**Dosage adjustment required in hepatic impairment:**
- No dosage adjustment is required.\(^{(4)}\)

### RECONSTITUTION

Not applicable

### ADMINISTRATION

**NOTE:** Inhalation formulations (e.g. 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
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<table>
<thead>
<tr>
<th><strong>IV infusion:</strong></th>
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<tbody>
<tr>
<td><strong>Dilute to a final concentration of 40mg/mL or weaker with compatible fluid and infuse over 20 to 60 minutes.</strong> (5, 6, 9-11)</td>
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<table>
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<tr>
<th><strong>IM injection:</strong></th>
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<tr>
<td><strong>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.</strong></td>
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<td><strong>IM injection is NOT suitable for premature neonates.</strong> (4)</td>
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<td><strong>Refer to Intramuscular (IM) injections for further information.</strong></td>
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### MONITORING

| **A capillary blood sample is preferred for drug levels wherever possible (i.e. finger prick or heel prick for infants <6 months).** |
| **If unable to obtain via this method a venous sample can be used.** |
| **Note:** levels should NOT be taken from a CVAD lumen used to administer tobramycin. |

**Collection tube:**

- **Paediatric** - Lithium Heparin (Green top) 600 microlitre (PST gel) or Serum (Red top clot) 600 microlitre (No Gel) or Lithium Heparin (Dark Green Top) 1 mL (no gel) (12)
- **Neonatal** - Lithium Heparin (Green top) 600 microlitre (PST gel) or Serum (Red top clot) 600 microlitre (No Gel) (12)
- **Minimum volume required:** 300 microlitres (12)
- **For further information, refer to the PathWest test directory.**

**Monitoring in Neonates:**

Please refer to Neonatal Medication Protocols

**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 (<0.6 mg/L).**
- **If the trough level is greater than or equal to 0.6 mg/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).**

**HIITH patients:**

- **Require weekly monitoring of their trough levels and renal function monitoring.**
- **Trough levels should remain below the limit of detection.**
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- 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.

**Patients with altered pharmacokinetics:**
- Cystic fibrosis
- Oncology
- Severe burns
- Impaired renal function
- These patients should have therapeutic drug monitoring completed with the **FIRST** dose of tobramycin.

**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.

**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.\(^1\,\,11\)
- **Rare:** Anaphylaxis, bronchospasm, oliguria, peripheral neuropathy and neuromuscular blockade, electrolyte disturbances, nausea, vomiting.\(^1\,\,11\)

**COMPATIBLE FLUIDS**
- Sodium chloride 0.9%
- Glucose 5%
- Glucose 10% (if final concentration of tobramycin is <6mg/mL)
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#### 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.\(^{(5, 9)}\)

#### Interactions
Tobramycin interacts with other medications; please consult PCH approved references (such as Clinical Pharmacology), your ward pharmacist or Pharmacy on 60190 for more information

- IV aminoglycoside antibiotics are inactivated by IV penicillins and cephalosporins. Aminoglycoside antibiotics are rapidly bactericidal and should be administered first. The line should then be flushed well with a compatible fluid and the penicillin or cephalosporin administered. In patients with renal impairment, the two agents should be separated by several hours.\(^{(3, 5)}\)

- There is an increased risk of ototoxicity and/or nephrotoxicity when tobramycin is used with other ototoxic or nephrotoxic agents (e.g. loop diuretics and vancomycin), especially in patients with pre-existing renal impairment.\(^{(1, 6, 13)}\)

- Aminoglycosides prolong the effect of neuromuscular blockers (both non-depolarising and depolarising). A dose reduction may be required and patients should be monitored closely for respiratory insufficiency.\(^{(1)}\)

- Tobramycin used in conjunction with IV magnesium sulphate has an additive neuromuscular blocking effect and should be used with caution.\(^{(1)}\)

#### Comments
- 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.\(^{(1)}\)

- Under certain circumstances, genetic testing prior to treatment with long course aminoglycosides or in children requiring repeated course can be considered following consultation with the infectious diseases team.\(^{(1)}\)

**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 internal policies, procedures and guidelines**
<table>
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<tr>
<td>6. Micromedex 2.0 [Internet]. Truven Health Analytics. 2016 [cited 12/01/2020].</td>
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