**MONOGRAPH**

**Tobramycin (Inhaled) Monograph - Paediatric**

<table>
<thead>
<tr>
<th>Scope (Staff):</th>
<th>Medical, Nursing, Pharmacy</th>
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<td>Scope (Area):</td>
<td>Perth Children’s Hospital (PCH)</td>
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This document should be read in conjunction with this DISCLAIMER

### DESCRIPTION

- **High Risk Drug**

- 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 active against a broad range of gram-negative bacteria, including *Pseudomonas aeruginosa* *(PsA)*. \(^{(2)}\)
- Tobramycin is a **High Risk Medicine**.

### INDICATIONS AND RESTRICTIONS

Inhaled: 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.

**Drug and Therapeutics Committee Restrictions:**

- The Tobi\(^{\circledast}\) Podhaler brand of tobramycin for inhalation is restricted to patients with Cystic Fibrosis over 6 years who have a confirmed infection with *Pseudomonas* as per the Pharmaceutical Benefits Scheme (PBS) restrictions.

### CONTRAINDICATIONS

- Inhaled tobramycin is contraindicated in patients with a known hypersensitivity to any aminoglycoside or any components of the formulation. \(^{(3)}\)

### PRECAUTIONS

- In patients with a history of severe haemoptysis, there is a risk of further haemorrhage. \(^{(2)}\)
- Tobi\(^{\circledast}\) capsules are for inhalation only via the Podhaler device and should NOT be administered via any other route. \(^{(1)}\)

### FORMULATIONS

Available at PCH:

- 80mg/2mL Vial - may be used by IV or inhalation route
(contains preservative)

- 500mg/5mL Vial - (Tobra-Day®) kept in Pharmacy Compounding Service unit and to be used only for Hospital in the Home (HiTH) tobramycin IV doses - preservative free.
- 300mg/5mL ampoule – Tobramycin solution for inhalation (various brands) - preservative free.
- 28mg capsules for inhalation - Tobi® Podhaler (for children ≥ 6 years only as per PBS)

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<th>DOSAGE</th>
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<td>The doses listed below fall within the standard range.</td>
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<td>Higher doses may be prescribed for certain situations in consultation with an infectious diseases or microbiology consultant.</td>
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**Neonates (<1 month of age):**

- Inhaled tobramycin is not routinely used in neonates. Contact infectious disease or clinical microbiology consultant for advice.

**Inhalation (via nebuliser):**

**Children < 6 years old with Bronchiectasis:**

- 80mg twice daily (using the 80mg/2mL vial) for 28 days, followed by 28 days of no inhaled tobramycin therapy before considering another course of inhaled tobramycin.\(^{(4)}\)

**Children < 6 years old with Cystic Fibrosis:**

**Children ≥ 6 months to 2 years old:**

- 150mg twice daily (using Tobramycin 300mg/5mL solution for inhalation) for 28 days, followed by 28 days of no inhaled tobramycin therapy before considering another course of inhaled tobramycin.\(^{(5,6,7)}\)

**Children 2 to 6 years old:**

- 300mg twice daily (using Tobramycin 300mg/5mL solution for inhalation) for 28 days, followed by 28 days of no inhaled tobramycin therapy before considering another course of inhaled tobramycin.\(^{(6)}\)

**Children ≥ 6 years old with Bronchiectasis or Cystic Fibrosis:**

- 300mg twice daily (using Tobramycin 300mg/5mL solution for inhalation) for 28 days, followed by 28 days of no inhaled tobramycin therapy before considering another course of inhaled tobramycin.\(^{(1,2,8)}\)

- Doses should be administered as close to 12 hourly as possible, if this is not possible, doses must be separated by a minimum of 6 hours.\(^{(3)}\)
Inhalation (via Dry Powder Inhaler):

- **Note:** Tobi® capsules are for **INHALATION** route only via the Podhaler device.

**Children ≥ 6 years old:**

- 112mg (4 x 28mg capsules) administered twice daily for 28 days, followed by 28 days of no inhaled tobramycin therapy before restarting.\(^{(2,3,8)}\)

**IV:**

- Refer to the separate **IV tobramycin ChAMP monograph.**

### DOSAGE ADJUSTMENT

**Dosage adjustment required in renal impairment:**

- As systemic absorption of tobramycin following nebulisation or inhalation is low, dose adjustment is not routinely required. However, caution should be taken if inhaled tobramycin is used in patients with renal impairment or failure.\(^{(3)}\)
- Renal function monitoring is recommended prior to initiation of inhaled tobramycin treatment and annually thereafter.\(^{(2)}\) More frequent monitoring will be required for patients on other nephrotoxic medications.
- Refer to the **IV tobramycin monograph** for dosage adjustments required for systemic use.

### RECONSTITUTION

- Not applicable

### ADMINISTRATION

**Prior to Administration:**

- The first dose of inhaled tobramycin must be given in hospital under the supervision of a health care professional. If the patient has previously tolerated inhaled tobramycin then this is not necessary.
- Where possible it is recommended to measure lung function before and after the first dose of tobramycin and monitor for bronchospasm for 15 minutes post inhalation.\(^{(2)}\)
- Signs of bronchospasm include wheeze, cough, increased work of breathing or distress. In the event of bronchospasm in a child not using a bronchodilator, the test dose may be repeated using a bronchodilator.\(^{(2)}\)
- If there are other medications to be administered via the inhalation route, the other medications should be administered first, and the tobramycin administered last.\(^{(2,9)}\)

**Preparation:**

- The manufacturer recommends that Tobramycin 300mg/5mL solution for inhalation only be used with a PARI Pro-neb® or a PARI LC PLUS® nebuliser.\(^{(3,8)}\) In practice, alternative nebulisers have been used.
Administering a dose:

To administer a dose using the Tobramycin 300mg/5mL solution for inhalation:

The information below should be read in conjunction with Pari Nebuliser Administration.

- Just prior to use, remove one ampoule from the foil packaging by gently pulling apart one of the attached ampoules at the bottom tab. Return the remaining ampoules to their foil packaging and keep in the refrigerator.
- Open the Tobramycin 300mg/5mL solution for inhalation ampoule by holding the bottom tab with one hand and twisting off the top with your other hand.
- For 300mg doses squeeze the entire contents of the ampoule into the nebuliser cup and replace the nebuliser top.
- For 150mg doses use a syringe to remove 2.5mL (150mg) and put in the nebuliser cup. Replace the nebuliser top and discard the remainder of the ampoule.
- Refer to Pari Nebuliser Administration for further information. For information on home administration, refer to the product information.
- The contents of any ampoule remaining after use must be discarded immediately; opened ampoules should never be stored for re-use. (3)

To administer a dose using the tobramycin 80mg/2mL vial:

- Flip off the plastic seal of the tobramycin vial.
- Using a needle and syringe withdraw the required volume of the tobramycin solution and dilute with sodium chloride 0.9% solution to produce a final volume of 4mL.
- Place this solution in the nebuliser bowl.
- Once fully assembled, turn on the nebuliser compressor and ensure a steady mist is being produced. Refer to Pari Nebuliser Administration for further information.
- Sitting or standing in an upright position, place the mouthpiece between the patient’s teeth and the top of the tongue and instruct the patient to breathe normally through the mouth until there is no longer a mist being produced.
- If using a facemask in a younger child, breathe normally through the mouth until there is no longer a mist being produced. This generally takes 10 to 15 minutes.
To administer a tobramycin 112mg dose using Tobi® dry powder for inhalation:

- Holding the body of the inhaler, unscrew and remove the mouthpiece from the inhaler body.
- Insert a single capsule into the inhaler chamber, replace the mouthpiece and screw it on firmly.
- Holding the inhaler with the mouthpiece down, press the blue button on the base firmly to pierce the capsule and then release.
- Fully exhale, and position the inhaler with the mouthpiece towards you, place mouth over the mouthpiece creating a tight seal. Inhale the powder deeply with a single continuous inhalation.
- Remove the inhaler from mouth, hold your breath for 5 seconds and exhale normally.
- Repeat this process to ensure all the contents of the capsule have been administered.
- Unscrew the mouthpiece and remove the empty capsule from the chamber (it should appear empty). If there is powder still contained in the capsule, repeat steps 2 to 7 until it is empty
- Repeat the above process for the remaining 3 capsules until the full 112mg dose has been administered.
- Wipe the mouthpiece of the inhaler device, but do not wash with water. Discard the device after 7 days.\(^{(3,9)}\)

**MONITORING**

- Although there is limited absorption of tobramycin if administered via the inhalation route, renal function should be monitored before treatment and annually throughout treatment.\(^{(2)}\) More frequent monitoring will be required for patients on other nephrotoxic medications.

**ADVERSE EFFECTS**

- **Common:** cough, bronchospasm, dysphonia, taste disturbances, pharyngitis, mouth ulcers, salivary hypersecretion, laryngitis, haemoptysis, epistaxis, throat pain, transient tinnitus (without hearing loss).\(^{(1,2)}\)
- For additional adverse effects seen with systemic therapy refer to the [IV tobramycin monograph](#).

**COMPATIBLE FLUIDS**

- Tobramycin 300mg/5mL solution for inhalation ampoules – Not applicable
- Tobi® dry powder for inhalation – Not applicable
- Tobramycin 80mg/2mL vial– sodium chloride 0.9%
- Tobramycin 500mg/5mL vial – sodium chloride 0.9%
**STORAGE**

- 80mg/2mL ampoule (DBL brand) should be protected from light and stored below 25°C.\(^{(3)}\)
- 500mg/5mL vial (Tobra-Day\(^{®}\)) should be protected from light and stored between 2 and 8°C.\(^{(4)}\)
- Tobramycin 300mg/5mL solution for inhalation should be stored between 2 and 8°C away from direct light.\(^{(3)}\)
- If refrigeration is not possible, the Tobramycin 300mg/5mL solution for inhalation pouches (opened or sealed) may be stored at room temperature (up to a maximum of 25°C) for up to 28 days.\(^{(3)}\)
- Tobramycin 300mg/5mL solution for inhalation may darken if not stored in the refrigerator, this does not indicate a change in quality.\(^{(3)}\)
- Tobi\(^{®}\) capsules for inhalation should be stored at room temperature (less than 30°C) and protected from moisture and humidity.\(^{(3)}\)
- The capsules should be kept in the original packaging until ready to be administered. Each Podhaler device should be discarded after 7 days.\(^{(3)}\)

**INTERACTIONS**

Inhaled tobramycin may interact with other medications; please consult PCH approved references (e.g. *Clinical Pharmacology*), your ward pharmacist or Pharmacy on extension 63546 for more information.

- There have not been any drug interaction studies performed with tobramycin solution for inhalation or podhalers.
- Due to minimal systemic absorption, interactions are considered to be unlikely. However caution should be taken with concurrent use of other nephrotoxic or ototoxic medications.
- The nebuliser bowl should be thoroughly cleaned between the administration of different nebulising solutions.

**COMMENTS**

- Tobramycin 300mg/5mL solution for inhalation should not be mixed with any other liquids or medication prior to being administered.\(^{(9)}\)

**MANUFACTURER SAFETY DATA SHEET (SDS)**

- To access to the Manufacturer SDS for this product, use the following link to ChemAlert.
Related internal policies, procedures and guidelines

- Antimicrobial Stewardship Policy
- ChAMP Empiric Guidelines

References