BNSSG Health Community's Traffic Light System
Shared Care Guidance

Section 1: Heading

Trust: North Bristol NHS Trust and University Hospitals Bristol NHS Foundation Trust

Specialty / Department: Respiratory Medicine

Drug: ***nebulised*** Tobramycin

For the treatment / management of: Management of chronic respiratory infections / colonisation (not including cystic fibrosis patients)

Section 2: Treatment schedule

Tobramycin is available as; a generic preparation for injection, **Tobi**®300mg/5mL nebuliser solution and **Bramitob**®300mg/4mL nebuliser solution.
This shared care protocol specifically refers to the use of **Bramitob**® and full prescribing information can be located at *www.medicines.org.uk*

Bramitob® is available as a 300mg/4mL nebuliser solution of **tobramycin**

- **Bramitob**® is licensed for the management of chronic pulmonary infection with *Pseudomonas aeruginosa* in patients with cystic fibrosis aged 6 years or older.
- **Bramitob**® may be indicated in select patients with non-CF bronchiectasis with chronic respiratory infection/colonisation with *P. aeruginosa* on the advice of a respiratory consultant with specialist experience in managing this patient group.

The recommended dose for patients > 6 years of age is one-single dose container (300mg) inhaled via an appropriate nebuliser* twice a day (as close as possible to 12 hours apart) for 28 days followed by a 28 day break. ***Treatment should be with an alternating 28 day cycles with and without nebulised tobramycin unless indicated by the initiating consultant.***

Dose adjustments
No dose adjustments are required in; elderly patients (≥ 65 years), patients with renal or hepatic impairment or at extremes of weight. Elderly patients and patients with renal impairment (eGFR<50mL/min) may be at an increased risk of toxicity and this is discussed in the monitoring section below.

* **Bramitob**® should be administered using a either a; PARI LC PLUS reusable nebuliser equipped with PARI TURBO BOY compressor, *or* PARI LC SPRINT equipped with PARI BOY Sx compressor.

Section 3: Monitoring

Patients will require periodic assessment of renal function and additional investigations may be required in patients at high risk of nephro- or oto-toxicity. Due to the frequency of regular monitoring this can be carried out during normal follow up by secondary care. Where additional investigations are required these will be organised by secondary care, specifically;

Monitoring requirements (secondary care responsibilities)
For patients with a baseline eGFR>50mL/min U&E's should be carried out; prior to initiation, one and three months after initiation and yearly thereafter.

For patients with a baseline eGFR<50mL/min or who experience a decline in renal function after initial assessment (i.e. at either one and three month's) the frequency at which renal function monitoring is required and the requirement for periodic tobramycin therapeutic drug monitoring (TDM) will be determined by the secondary care team.

Periodic urinalysis should be carried out to examine for; protein, cells and casts

Initial and periodic audiometry in patients at high risk of ototoxicity.

Patients may be advised to perform pre- and post-nebulisation FEV_1 (forced expiratory volume) assessment and advised to contact the respiratory team if bronchospasm is present despite appropriate use of pre-treatment bronchodilators (see *Section 4: Side-effects* below for further details).

Monitoring requirements (primary care responsibilities)
Respond to suspected adverse effects as clinically indicated.

Of particular note the presence of auditory or vestibular toxicity (i.e. manifest as vertigo, ataxia, dizziness or tinnitus which is not transient) should be referred to the respiratory team who will advise(*see Section 4: Side-effects* for further details).

Section 4: Side-effects

See Bramitob® SPC section 4.8 - 'Undesirable Effects' at *www.medicines.org.uk* for full details.

Bronchospasm can occur following inhalation of medicinal products and has been reported with nebulised tobramycin. The first dose of nebulised tobramycin should be given under medical supervision, using a pre-nebulisation bronchodilator if this is already part of the current treatment regimen for the patient. FEV_1 should be measured before and after nebulisation. If there is evidence of therapy-induced bronchospasm in a patient not receiving a bronchodilator, the test should be repeated on a separate occasion, using a bronchodilator. Onset of bronchospasm in the presence of bronchodilator therapy may indicate an allergic reaction. Should an allergic reaction be suspected then treatment with nebulised tobramycin should be discontinued.

Cough may occur on inhalation of tobramycin. If troublesome or associated with haemoptysis then on-going treatment should be reviewed by an appropriate secondary care specialist.

Sore throat or mouth has been reported and may be due to *Candida albicans* infection (oral thrush) or hypersensitivity. Skin rash may also indicated hypersensitivity.
Oropharyngeal candidiasis should be treated if indicated.
If hypersensitivity occurs then treatment should be withdrawn.

Ototoxicity presenting as; dizziness, vertigo, ataxia, tinnitus, hearing loss or may be associated with nebulised tobramycin, particularly in patient at risk due to concomitant or previous use of ototoxic agents (see *Section 5: Drug interactions*) for more details.
Tinnitus may be transient and resolve without discontinuation of therapy or associated with permanent loss of hearing on audiogram.
If ototoxicity is suspected treatment continuation and the need for additional auditory assessments should be discussed with the patients respiratory Consultant or the respiratory team.

Section 5: Drug interactions

See Bramitob® SPC section 4.5 - 'Interactions with other medicinal products and other forms of interaction' at *www.medicines.org.uk* for full details.

Concomitant use with;other **aminoglycoside antibiotics** (such as **amikacin**and **gentamicin**), **amphotericin**, **colistimethate**, **ciclosporin**, **tacrolimus**, **polymixin** antibiotics (not included topical preparations) and/or **platinumcompounds** (**cisplatin** / **carboplatin**) may increase the risk of nephrotoxocity and should be avoided.

Concomitant use with **loop diuretics** (such as **furosemide** and **bumetanide**) increases the risk of ototoxicity and should be avoided unless strictly indicated. The risk of ototoxicity is also increased by concomitant use of **platinum compounds**.

Nebulised tobramycin should be used with extreme caution in Myasthenia gravis and may also antagonise the effect of **cholinesterase inhibitors** (such as **neostigmine** or **pyridostigmine**) used to treat this condition.

As an aminoglycoside tobramycin may enhance the effect of **non-depolarising muscle relaxants** or **suxamethonium** used during surgery.

Tobramycin may increase the effect of **botulinum toxin**.

Nebulised antibiotics should not be given within an hour of **dornase-alfa** (Pulmozyme®)

Section 6: Cautions and special recommendations

Administration of Bramitob® is contraindicated in all patients with hypersensitivity to **tobramycin**, to any other **aminoglycosides** or to any of the excipients.

It is also contraindicated in patients receiving potent diuretics, such as **furosemide** or **ethacrynicacid**, which have proved to be ototoxic.

Nephrotoxicity: nebulised tobramycin should be used with caution in patients with known or suspected renal dysfunction and serum concentrations of tobramycin should be monitored. Tobramycin levels need only to be measured in patients with known or suspected renal disease.

Ototoxicity: In patients with a predisposing risk due to previous prolonged, systemic aminoglycoside therapy, it may be necessary to consider audiological assessment before initiating, and during therapy with nebulised tobramycin.

Neuromuscular disorders: As aminoglycosides may aggravate muscle weakness due to a potential curare-like effect on neuromuscular function tobramycin should be used with caution in patients with neuromuscular disorders such as parkinsonism or other conditions characterised by myasthenia, including Myasthenia gravis.

Haemoptysis: Inhalation of nebulised solutions may induce a cough reflex. The use of nebulised tobramycin in patients with active, severe haemoptysis should be undertaken only if the benefits of treatment are considered to outweigh the risks of inducing further haemorrhage

Section 7: Advice to the patient

The secondary care team will provide information on the appropriate use and care of the nebuliser. This will include advice on;

- Nebulised antibiotics should be used regularly
- The solution is for single use only and any remaining solution should be discarded.
- The manufacturer's instruction should be followed for the operation and care of the nebuliser and compressor.
- If a reliever inhaler or nebuliser (salbutamol, ipratropium or combination) is part of the patients normal regimen this should be used at least 20 minutes before inhaling the antibiotic.
- If you are carrying out breathing exercises (i.e. Active Cycle of Breathing Technique – ACBT) this should be done after using the reliever but before nebulising colistimethate.
- The nebuliser should be used in conjunction with an exhaust filter to prevent others being exposed to the medication and to prevent a sticky deposit from forming. A new filter should be used for each dose. The procedure should be done in a well-ventilated room.
- After drug administration is completed (which may take up to 20 minutes) rinse your mouth, gargle with water and then spit out. This will reduce the risk of side-effects such as thrush or mouth ulcers.
- After each use the nebuliser should be cleaned as per manufacturer's directions.
- Do not mix tobramycin with other nebuliser solutions.

You should check your lung function using a peak flow meter before and after using nebulised tobramycin. If there is bronchospasm after treatment, indicated by a lower FEV_1 measurement or wheeze, despite using a reliever inhaler or nebuliser then you should contact the respiratory team who will advise on what you should do.

Nebulised tobramycin has been associated with permanent or temporary hearing loss and damage to associated structures. This may present as; dizziness, vertigo, feeling off balance and an unsteady gait, tinnitus or deafness. If this occurs contact the respiratory team who will advise on the need to withhold treatment or organise any tests.

Section 8: Responsibilities for Secondary Care

1. Prescribing responsibility remains with specialist for initial 3 months of treatment.
2. Initiate therapy after discussion with the patient about treatment options and possible side effects.
3. Arrange for an initial test dose to be administered in hospital under appropriate supervision.
4. Arranging the provision of appropriate training for the patient via the nurse specialist.
5. Seek agreement from primary care to continue prescribing under the shared care guideline.
6. Promptly notify primary care to inform them of any dose changes or following treatment discontinuation.
7. If tobramycin levels are indicated secondary care will organise for these to be taken and interpreted and advise the patient and primary care of the outcome.
8. Organise on-going review as clinically indicated, typically;
    - Review the patient after 6 months and continue treatment if FEV_1 has improved or there is a reduced rate of FEV_1 decline and the patient is compliant with treatment.
    - On-going review thereafter, at 6 monthly intervals, with continuation of treatment if rate of FEV1 decline is consistently improved and the patient remains compliant with treatment.
    - U&E's will be assessed at each follow-up.

Section 9: Responsibilities for Primary Care

1. In patients with stable renal function after initial 3 months of treatment under specialist care assume prescribing responsibility.
2. Refer promptly to secondary care if lack of clinical efficacy is suspected or any concerns arise,

including suspected adverse drug reactions.
3. Report adverse events to secondary care physician.

Section 10: Contact details

Name	Organisation	Telephone number	E-mail address	Availability
Respiratory specialist nurses	NBT	0117 323 2387		NBT patients – working hours
Respiratory pharmacist	NBT	Via switchboard 0117 950 5050		NBT patients – working hours
Respiratory on-call Registrar	NBT	Via switchboard 0117 950 5050		NBT patients – 24 hours
Dr Nabil Jarad	UHBristol	0117 342 2620	Nabil.Jarad@uhbristol.nhs.uk	
Respiratory specialist nurses	UHB	0117 3424101		

Section 11: Document details

Date prepared:	November 2012
Prepared by:	Philip Lloyd Mayers (Pharmacist)on behalf of North Bristol Lung Centre
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Document identification:	NEBULISED TOBRAMYCIN SCP NBT

Section 12: Collaboration

Draft will be circulated to interested parties including;
NBT formulary pharmacist and other senior member of the NBT and UBHT pharmacy departments,
NBT Respiratory Consultants and Specialist nurses.

Section 13: References

1. Summary of Product Characteristics: Tobramycin nebuliser solution - Bramitob®.Chiesi Limited. September 2012. Accessed via *www.medicines.org.uk*last updated02/11/2011.