South East London Integrated Guideline for the Use of Nebulised Antibiotics in the Management of *Pseudomonas aeruginosa* in Non-Cystic Fibrosis Bronchiectasis

This guideline has been developed by the South East London Responsible Respiratory sub-group – a sub-group of the SEL Integrated Medicines Optimisation Committee (SEL IMOC).

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South East London Integrated Medicines Optimisation Committee (SEL IMOC). A partnership between NHS organisations in South East London: South East London Clinical Commissioning Group (covering the boroughs of Bexley/Bromley/Greenwich/ Lambeth/Lewisham and Southwark) and GSTFT/KCH /SLaM/ Oxleas NHS Foundation Trusts and Lewisham & Greenwich NHS Trust

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This is a specialist pathway and all prescribing, supply and monitoring of treatment will be managed by the hospital team.

Aims, Diagnosis and Initial Treatment

- Nebulised antibiotics in non-cystic fibrosis (non-CF) bronchiectasis are indicated to minimise symptoms, reduce exacerbations and improve overall health. It should be considered for patients experiencing ≥3 infective exacerbations per year and those with significant associated morbidity, in spite of optimised management (including airway clearance - see below)
- Eradication antibiotic treatment should be offered to patients with a new growth of P. aeruginosa (first isolation or regrowth in the context of intermittently positive cultures):
  - **First line eradication treatment choice**: ciprofloxacin 500–750mg orally twice a day for 2 weeks;
  - **Second line eradication treatment choice**: IV antipseudomonal beta-lactam ± an IV aminoglycoside for 2 weeks
- Eradication with 3 months of nebulised antibiotic should almost always follow oral or IV treatment (as above)
- 1st line is colistin (Colomycin®); 2nd line is gentamicin.
- Suppression therapy with nebulised antibiotic may follow eradication
- Please refer to the British Thoracic Society Guideline For Bronchiectasis in Adults for further information

Patients must be adequately investigated and therapies optimised prior to initiation of nebulised antibiotics. This includes:

- Sputum clearance to reduce exacerbation rate
- Sputum culture (including a sputum AFB to test for non-tuberculous mycobacteria)
- Consideration of need for fungal investigations
- Lung function
- Radiological investigations

Considerations before Prescribing Nebulised Antibiotics

Good Antimicrobial Stewardship and Sensitivity Testing

- Prescribing nebulised antibiotics:
  - Initiation must be by a clinician experienced in the management of *Pseudomonas aeruginosa* in non-CF bronchiectasis
  - Counsel patients on potential major side effects of long-term antibiotics and advise patients to seek medical attention if side effects develop, e.g. ototoxicity with gentamicin or recurrence/worsening of symptoms suggestive of antimicrobial resistance
  - Nebulised antibiotics are not licensed to treat non-CF bronchiectasis and thus use for this indication is off-label
- Role of microbiology sensitivity testing:
  - Treatment should be guided by antibiotic sensitivity results, but where necessary may empirical based on previous sputum bacteriology
  - To identify resistance to acute or long-term antibiotic treatment
  - Some patients with an infective exacerbation may respond to antibiotic treatment despite resistance to that drug in vitro

Airway Clearance and Mucolytic Therapy

- Initial management includes airways clearance techniques, pulmonary rehabilitation, influenza and pneumococcal vaccinations, optimised oral mucolytic therapy (e.g. carbocisteine or acetylcysteine), and prompt and appropriate antibiotic treatment for acute exacerbations, alongside a self-management plan
- If a patient has ≥3 exacerbations a year, consider adding a nebulised mucolytic:
  - Hypertonic saline (3% or 7%). 3% up to four times daily, 7% up to twice a day
- Before initiating hypertonic saline a test dose of the nebulised drug needs to be administered
- Sodium chloride 0.9% (normal saline) is not routinely used in adults with non-CF bronchiectasis but may be used in the management of adults with COPD without non-CF bronchiectasis

Nebuliser Supply and Maintenance

Nebuliser equipment supply, servicing & repair: the hospital (e.g. lung function department or equipment store, depending on trust) issue all equipment including compressor, mouthpiece/mask, tubing, nebuliser chamber and filters. They carry out the annual service of *trust* issued compressors and can deal with any issues relating to nebuliser function or part replacement. The use of privately purchased equipment should be discouraged. Privately purchased nebuliser equipment also require maintenance and annual service. This cannot be provided by the trust, rather it is the patient's responsibility to arrange this independently.

Supporting Patient Literature: The patient should be provided with information (written and verbal) about nebuliser compressor equipment, servicing, and how to obtain ongoing advice or support regarding the maintenance of their nebuliser. They should also be offered the patient information leaflet on nebuliser use and maintenance, and the patient information leaflet, developed alongside this guideline, on the nebulised medication they are to be issued.

Nebulised Treatment for *Pseudomonas aeruginosa* (eradication and suppression)

The 1st dose must be administered by a trained respiratory physiotherapist, respiratory physiologist or lung function technician

First line treatment

Colistin (Colomycin®) (Off-label Indication)

- **Dose**: **2 million International Units (IU) nebulised twice a day**
- **Presentation**: 2 million IU powder for reconstitution in glass vial with 'flip off' lilac cap
- **Diluent:** 4mL water for injection OR 4mL sodium chloride 0.9% OR 2.5mL salbutamol 2.5mg/2.5mL
- **Additional equipment:** syringe
- **Administration:**
  - Prepare a clean surface, wash and dry hands before mixing the dose
  - Each vial of Colomycin® is 2 million IU = one vial per dose
  - Pull back the lid on the vial, peel off the metal ring around the top of the vial and remove the rubber bung
  - Add the diluent (chosen from options above) to the vial of Colomycin®
  - DO NOT SHAKE THE VIAL. This causes the solution to froth and adversely affects its nebulisation. Rather, gently roll the vial until the powder in the vial is dissolved
  - Pour the solution within the vial into the medication chamber of the SideStream® Plus device
  - Safely dispose of the diluent syringe, metal cap and vial
- **Potential side effects:** wheezing, chest tightness, bronchospasm, skin reactions, sore throat, sore mouth, oral candidiasis, increased cough.
- **Prior to prescribing, consider the following cautions to colistin use:**
  - Myasthenia gravis, porphyria, renal impairment, pregnancy or breast-feeding
- **Monitoring:**
  - Sputum cultures (after 3 months of eradication treatment and otherwise as advised by respiratory specialist)
  - Efficacy of treatment
  - Signs or symptoms of toxicity (e.g. nephrotoxicity and neurotoxicity (colistin specific)
  - Renal function - perform at the start of treatment and then repeat regularly during treatment in all patients

Refer to the Colomycin® Summary of Product Characteristics for further information

Second line treatment

Gentamicin (Off-label Indication)

- **Dose: 80mg nebulised twice a day**
- **Presentation:** 80mg in 2mL solution in glass ampoule
- **Diluent:** none required for vial reconstitution. Sodium chloride ampoule 0.9% for dilution
- **Additional equipment:** needle, syringe, sharps bin
- **Administration:**
  - Prepare a clean surface, wash and dry hands before mixing the dose
  - Attach a needle to the syringe
  - Each ampoule of gentamicin contains 80mg in 2mL. Use one ampoule for each dose
  - Open the plastic ampoule of sodium chloride 0.9%
  - Carefully snap open the glass gentamicin ampoule
  - Draw up the contents of the gentamicin ampoule vial using the needle and syringe
  - Draw up 2mL sodium chloride 0.9% from the ampoule into the syringe. This dilutes the gentamicin to make a total volume of 4mL
  - Put the contents of the syringe into the nebuliser chamber of the SideStream® Plus
  - Safely dispose of the needle, syringe and glass ampoule in your sharps bin
- **Potential side effects:** Cough, bronchospasm. Ototoxicity and nephrotoxicity.
- **Prior to prescribing, consider the following cautions to colistin use:**
  - creatinine clearance <30mL/min, concomitant nephrotoxic medications, patient needing a hearing aid or with considerable balance issues, pregnancy or breast-feeding
- **Monitoring:** As for colistin, plus audiometry testing if suspicion of ototoxicity

Other information:

- For maximum effect, a nebulised antibiotic should be administered after chest physiotherapy and other nebulised therapies or inhaled bronchodilators. Prior use with bronchodilators is not necessary if reconstituting with salbutamol
- Nebulised antibiotics should not be mixed other than the diluents listed above

Nebuliser Trial/Test Dose

A trial dose is administered to confirm the patient's tolerance of nebulised treatment and to ensure there is no deterioration in lung function. The test dose is deemed unsuccessful if the patient experiences a drop in FEV_1 of $\geq$15%, a significant increase in respiratory rate, a decrease in SpO_2 or they develop a wheeze or signs of distress. The healthcare professional administering the test dose must document the details and outcome of the trial in the medical notes.

Initial Prescription: Following the test dose, the first month of nebulised antibiotic is prescribed by the hospital respiratory team. It will include the medication, diluent and necessary ancillaries

Subsequent Prescriptions: Follow up prescriptions can written by the hospital respiratory team for dispensing and delivery directly to the patient by a homecare company. **The hospital team remain responsible for the prescribing, supply and monitoring of medication.**