NHS
Cambridgeshire and Peterborough
Clinical Commissioning Group

Shared Care Guideline

Gentamicin for Nebulisation

For the long term prophylaxis of chronic lung infections in non–CF bronchiectasis

Executive Summary

Indication
Nebulised gentamicin is indicated in patients with chronic lung infection in non CF bronchiectasis. This is an unlicensed use.
Gentamicin is used 2nd line after the patient has failed to respond to (or failed to tolerate) appropriate oral antibiotic prophylaxis.

Dose
Doses used include:
Gentamicin 80mg/2ml + 1ml sodium chloride 0.9% nebulised twice daily
Gentamicin 160mg/4ml nebulised once or twice daily

Dose, nebuliser system and required consumables will be communicated to GP and patient by secondary care clinician

Adverse Reactions
Cough, bronchospasm
(Also potential for ototoxicity and nephrotoxicity if systemically absorbed)

Toxicity Monitoring (See Section 10)
Renal function to be checked regularly (at intervals dependent on baseline renal function).
Audiometry testing if suspicious of ototoxicity.

Efficacy Monitoring
Specific monitoring for efficacy to be carried out by secondary care

- The responsibilities of the hospital specialist, GP and patient for this Shared Care Guideline can be found within this document at section 11.

Sharing of care depends on communication between the specialist, GP and the patient or their parent/carer. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. The doctor/healthcare professional who prescribes the medication has the clinical responsibility for the drug and the consequences of its use. Further information about the general responsibilities of the hospital specialist and GP can be found here

1. Scope

Trust-wide and general practice for long term patients with chronic lung infection.

2. Aim

To provide guidance on the prescribing of nebulised gentamicin in patients with non-CF bronchiectasis.

3. Introduction

The targeted delivery of aerosolised antibiotics offers a real therapeutic option in patients with bronchiectasis by reducing bacterial burden and associated inflammation and promoting healing, limiting symptoms and improving quality of life. Nebulised gentamicin has been shown to reduce bacterial load and sputum volume and improve breathlessness and exercise capacity (Lin HC, 1997). These findings were supported in a randomised controlled trial of 12 months of nebulised gentamicin or normal saline in patients with non CF bronchiectasis and chronic lung infection including, but not exclusively, p*seudomonas aeruginosa*. There was a significant reduction in sputum bacterial density, 30% eradication of *pseudomonas* and 92% eradication of other organisms, greater exercise capacity, fewer exacerbations, increased time to first exacerbation and improvements in quality of life scores (Murray MP, 2011). Nebulised gentamicin is one of the treatment recommendations specified in the British Thoracic Society Non-CF bronchiectasis guidelines (Hill AT, 2011) (Pasteur MC, 2010).

- Hill AT, P. M. (2011). Primary care summary of the British Thoracic Society Guideline on the management of non-cystic fibrosis bronchiectasis. *Prim Care Respir J* , 135-140.
- Lin HC, C. H. (1997). Inhaled gentamicin reduces airway neutrophil activity and mucus secretion in patients with stable chronic bronchitis. *Am J Respir Crit Care Med* , 2024-2029.

- Murray MP, G. J. (2011). A randomised controlled trial of nebulized gentamicin in non-cystic fibrosis bronchiectasis. *Am J Respir Crit Care Med* , 491-499.
- Pasteur MC, B. D. (2010). British Thoracic Guideline for non-CF bronchiectasis. *Thorax* , i1-58.

4. Abbreviations

ADR – Adverse drug reaction
CCLI – Cambridge Centre for Lung Infection
CF – Cystic fibrosis
FEV1 – Forced expiratory volume in 1st second
FVC - Forced vital capacity
GFR – Glomerular filtration rate
GP – General practitioner
IV - intravenous

5. Dose and Administration

- The recommended doses are:
  - 80mg nebulised twice daily
  - 160mg nebulised once or twice daily
- The first dose of the medicine should be given under hospital supervision in case of bronchospasm.
- For an 80mg dose, 2ml (1 ampoule) of gentamicin 80mg/2ml injection solution should be mixed with 1ml sodium chloride 0.9%.
- For a 160mg dose, 4ml (2 ampoules) of gentamicin 80mg/ml injection should be used undiluted.
- Gentamicin is nebulised using a nebuliser.
- Gentamicin should not be mixed or diluted with any other medicines or solutions.
- There is no commercially available gentamicin nebuliser solution. Doses should be prepared from gentamicin 80mg/2ml solution for injection. This is an unlicensed use.

Limited further information can be found in the gentamicin injection Summary of Product Characteristics.

6. Adverse Effects

Very common (≥ 1 in 10)

- Bronchospasm
- Nebulised gentamicin is generally well tolerated. The commonest adverse effects reported are coughing and bronchospasm. Bronchospasm can sometimes be controlled with a 2.5-5mg dose of nebulised salbutamol five minutes before nebulising gentamicin.
- There is a potential for the systemic absorption of gentamicin following nebulisation. Adverse effects of systemic therapy include:
    - Ototoxicity (vestibular damage, tinnitus, hearing loss)
    - Nephrotoxicity
- Other rare adverse effects from systemic therapy include pseudomembranous colitis and central neurotoxicity.

Limited further information can be found in the gentamicin injection Summary of Product Characteristics.

7. Cautions

- Gentamicin should be used with caution in patients with renal impairment or pre-existing vestibular or hearing impairment. Caution should also be exercised in patients with visual impairment due to the catastrophic consequences of hearing loss.

Special warning
Whilst on treatment, patients should continue with their standard treatments as clinically necessary. Where several different respiratory therapies are used, the following order is recommended: bronchodilator, sodium chloride 6% or 7% (hypertonic saline), chest physiotherapy, other inhaled medicines, and finally nebulised gentamicin.

Limited further information can be found in the gentamicin injection Summary of Product Characteristics.

8. Contraindications

Absolute & relative contraindications

- Nebulised gentamicin injection is contraindicated in any patient with a known hypersensitivity to gentamicin or a diagnosis of Myasthenia Gravis.

Limited further information can be found in the gentamicin injection Summary of Product Characteristics.

9. Interactions

- Concurrent and/or sequential use with other nephrotoxic or ototoxic medicines should be avoided. Some diuretics can enhance aminoglycoside toxicity.

Limited further information can be found in the gentamicin injection Summary of Product Characteristics.

10. Monitoring Standards & Actions to take in the event of abnormal test results/symptoms

- All specific monitoring for efficacy will be carried out by the Cambridge University Hospitals NHS Foundation Trust (CUHFT).

- For the initial test dose in hospital, the patient will have their pre-dose and post-dose FEV_1 and FVC measured and will also be monitored for post-dose wheeze and bronchoconstriction. If wheezing or bronchoconstriction occur, the test may be repeated 24 hours later with a dose of 2.5 – 5mg nebulised salbutamol prior to dosing with gentamicin.

- Ongoing efficacy monitoring:
  - Monitor respiratory function – FEV_1 and FVC
  - Monitor for reduction in frequency of IV and oral antibiotic treatment.
  - Monitor for improvement in subjective symptoms.

- Frequency of toxicity monitoring is dependent on the patient's underlying kidney function at baseline (as per appendix 1 (Page 8)). CUHFT will establish the frequency of monitoring and relay this to the GP.

- Contact respiratory specialist for advice if a gentamicin trough level is found to be greater than 1.0mg/ml.

- Contact respiratory specialist for advice if the patient's serum creatinine level rises above 1.25 times baseline value.

- Audiometry assessment is required if any symptoms of dizziness, imbalance or hearing impairment are reported by the patient.

11. Shared Care Responsibilities

a. Hospital specialist:

1. To diagnose chronic infection likely to respond to nebulised gentamicin in Non-CF Bronchiectasis patients based on a timely and comprehensive assessment.
2. To discuss benefits and adverse effects of treatment with the patient and obtain consent from the patient for treatment
3. To initiate nebulised gentamicin and ensure a fully monitored test dose is carried out before a continuous prescription is requested.
4. To supply the initial 28 days treatment of gentamicin.
5. To train the patient/carer in the use of the nebuliser and preparation of the medication.
6. To advise the patient how and where to obtain the nebuliser system. Patients will usually be asked to purchase the Phillips InnoSpire™ Deluxe nebuliser with SideStream and filter holder from the Trust or are referred to the NARA-Breathing charity.
7. To co-ordinate servicing/maintenance of the nebuliser system purchased from the Trust. If obtained from the NARA-Breathing charity, they will arrange their own servicing.
8. To monitor for response and adverse drug reactions during the first test dose and the initiation period.
9. To liaise with the GP to share the patient's care when the test dose has been carried out and proven benefit has been established.
10. To outline to GP when therapy may be stopped assuming no improvement is recognised in the patient's condition.
11. To share baseline renal function details with GP and outline ongoing frequency of toxicity monitoring
12. To review the patient's condition and efficacy of treatment annually with consideration at each review as to whether treatment needs to continue.
13. To evaluate adverse drug reactions raised by the GP and evaluate any concerns arising from physical checks & reviews undertaken by the GP.
14. To advise the GP on related issues such as drug interactions etc.
15. To advise the GP on supply issues related to the prescribing of nebulised gentamicin

b. General Practitioner:

1. To monitor the patient's overall health and wellbeing. (Note that specific efficacy monitoring will be undertaken by tertiary care (see "Monitoring" section 10).
2. To monitor gentamicin trough level and creatinine levels as requested by hospital specialist (see "Monitoring" section 10)
3. To observe patient for evidence of adverse drug reactions or any abnormalities and raise with the tertiary care clinician if necessary.
4. To provide:
   a. Gentamicin 80mg/2ml injection solution
   b. Sodium Chloride 0.9% solution for nebulisation or Sodium Chloride 0.9% solution for injection (for patients prescribed 80mg dose)
   c. 5ml Syringes x 1 per dose
   d. Needle x 1 per dose
5. To arrange supply and disposal of sharps bins as required.
6. To ensure advice is sought from the tertiary care clinician if there is any significant change in the patient's physical health status.
7. To reduce and stop treatment in line with tertiary care clinician's original request.

c. Patient or parent/carer:

1. Report any adverse effects to their GP whilst using nebulised gentamicin.
2. Stop taking nebulised gentamicin immediately if they develop symptoms of tinnitus, dizziness, imbalance or hearing impairment.
3. Ensure they have a clear understanding of their treatment.
4. Correctly store and administer the nebuliser solution.

12. Contact numbers for advice and support

Cambridge University Hospitals NHS Foundation Trust		
Specialist	**Post**	**Telephone**
Dr Clare Sander	Respiratory Consultant	01223 217079
Respiratory SpR	Respiratory SpR	Via Switchboard
Jamie Forrester	Respiratory physiotherapist	01223 256634
Pharmacy Medicines Information Service		01223 217502
CUHFT Hospital Main Switchboard		01223 254151

13. Equality and Diversity Statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust Equality and Diversity statement.

14. Disclaimer

It is your responsibility to check that this printed out copy is the most recent issue of this document.

15. Document Management

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The information contained in this guideline is issued on the understanding that it is accurate based on the resources at the time of issue. For further information please refer to the most recent Summary of Product Characteristics

Appendix 1

Stage of kidney disease	Description	Baseline GFR (ml/min/1.73m^2)	Recommendation
1	Normal or raised GFR	≥90	Check U&E and gentamicin trough level at 1 month and 6 monthly thereafter
2	Mild decrease in GFR – normal range for young adult	60-89	Check U&E and gentamicin trough level at 1 month and 6 monthly thereafter
3A	Mild - moderately lowered GFR	45-59	Check U&E and gentamicin trough level at 2 weeks, 1 month and 3 monthly thereafter
3B	Moderately – severely lowered GFR	30-44	Consider alternative prophylactic regime. If prescribed then check U&E and gentamicin trough level at 1 week, 2 weeks, 1 month and 3 monthly thereafter
4	Severely lowered GFR	15-29	Consider alternative prophylactic regime and discuss with nephrologist
5	Kidney failure	<15	Consider alternative prophylactic regime and discuss with nephrologist