Shared Care Guideline

Inhaled colistimethate sodium for the treatment of *Pseudomonas aeruginosa* lung infections in non-cystic fibrosis bronchiectasis

Executive Summary

Indication:

- Eradication or long term prophylaxis for patients with pseudomonal lung infection and non-CF bronchiectasis

Usual dose:

- Eradication: 1 – 2 million units nebulised twice daily for 3 months
- Prophylaxis: 1 – 2 million units nebulised twice daily on either a continuous or alternate month basis.

Please ensure the prescribing of diluents (1 – 4 ml water for injection or sodium chloride 0.9% - volume dependent on nebuliser system used).

The responsibilities of the hospital specialist, GP and patient for this Shared Care Guideline can be found within this document in 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

Prescribing and monitoring by hospital specialist consultants and General Practitioners

2. Aim

To outline the details of prescribing and the responsibilities for each health care practitioner caring for a patient who is treated with inhaled colistimethate sodium.

3. Introduction

Pseudomonas aeruginosa is a pathogen that causes severe lung damage in patients who become colonised and then chronically infected. Patients with non-CF bronchiectasis are at risk of significant morbidity and mortality from the damage caused by this pathogen. Nebulised *antipseudomonal* antibiotic treatment has been shown to improve lung function, slow the rate of respiratory decline and reduce the frequency of exacerbations of infection in these patients. Nebulised antibiotics are able to achieve high local concentrations with low systemic absorption and toxicity as opposed to intravenous antibiotics, where there is high risk of developing adverse effects from systemic absorption.
Use of Colomycin® and Promixin® in patients with non-CF bronchiectasis is off-label but the use of these products is supported by British Thoracic Society recommendations.
https://www.brit-thoracic.org.uk/guidelines-and-quality-standards/bronchiectasis-guideline/

4. Abbreviations

ADRs – adverse drug reactions
GP – General practitioner
CF – Cystic fibrosis

5. Dose and Administration

Colistimethate sodium is used in the long-term treatment of chronic *Ps. aeruginosa* infection or may be used as part of an eradication regime to treat new *Ps. aeruginosa* colonisation

Eradication regime:
Colistimethate sodium 1- 2 million units nebulised twice daily for three months
The dose should be diluted in water for injection or sodium chloride 0.9% to a volume of between 1ml – 4ml dependant on brand and nebuliser system employed.
(For some patients ciprofloxacin 750mg twice daily is also co-administered for six weeks)

Chronic treatment:
Colistimethate sodium 1 - 2 million units nebulised twice daily.
The dose should be diluted in water for injection or sodium chloride 0.9% to a volume of between 1ml – 4ml dependant on brand and nebuliser system employed.

In some patients colistimethate sodium is used on an alternate month basis with other nebulised antipseudomonal antibiotics e.g. inhaled aminoglycoside. If this regime is employed it will be communicated to the GP.

Nebuliser systems:
Colistimethate sodium can be administered through a wide variety of nebuliser systems.

Papworth patients on Colomycin® branded colistimethate sodium will usually be using Pari Boy™ compressors coupled with Pari LC Plus™ nebuliser systems, or Portaneb™ compressors with Ventstream™ nebuliser kits, or Pari e-Flow™ compressor-nebuliser systems.

Promixin® is exclusively nebulised via an I-neb hand-held nebuliser which is provided by the manufacturer. Ongoing use of the I-neb requires activation "discs" that are present in each pack of Promixin

Note that generic colistimethate sodium injection is not licensed for nebulisation.

Further information can be found in the Summary of Product Characteristics
Colomycin: http://www.medicines.org.uk/emc/medicine/1590
Promixin: http://www.medicines.org.uk/emc/medicine/13495

6. Adverse Effects

Transpulmonary absorption of colistimethate sodium is generally considered to be negligible therefore there is a low risk of systemic toxicity.
Inhaled colistimethate sodium causes bronchoconstriction in some patients which may lead to discontinuation. This may be relieved in some patients by using an inhaled bronchodilator (e.g. salbutamol) prior to nebulisation.

Very common (≥ 1 in 10)

- Cough, chest tightness, bronchoconstriction or bronchospasm

Unknown rarity

- Sore throat, sore mouth
- Hypersensitivity reactions (e.g. rash)

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Promixin: http://www.medicines.org.uk/emc/medicine/13495

7. Cautions

- Should be used with extreme caution in patients with porphyria
- Caution in patients with haemoptysis
- Transpulmonary absorption can be variable in some patients and may depend on the aerosol particle size, nebuliser system and lung status. Studies have reported serum levels from nil to potentially therapeutic concentrations of 4mg/l or more. The possibility of systemic absorption should be considered when treating patients by inhalation although systemic adverse effects are rare.

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8. Contraindications

- Colistimethate sodium is contra-indicated in patients with a hypersensitivity to colistimethate sodium or polymyxin B
- Contra-indicated in patients with myasthenia gravis
- Colistimethate sodium crosses the placental barrier and there may be a risk of foetal toxicity if repeated doses are given to pregnant patients. Exposure to pregnant carers during nebulisation should be minimised. Use of colistimethate sodium in pregnant patients requires a careful risk/benefit analysis (poorly controlled lung infection is also a risk in pregnancy) which will be the responsibility of the specialist centre.
- Colistimethate sodium is excreted in breast milk. Use in pregnant or breast-feeding mothers should only proceed if the benefit to the mother outweighs the potential risk to the foetus and infant. Each patient will be individually assessed by the specialist centre and informed whether or not to continue treatment.

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9. Interactions

Concomitant use of inhaled colistimethate sodium with other medicines that are potentially nephrotoxic or neurotoxic, such as aminoglycosides, or neuromuscular blocking products, such as curariform agents should be undertaken with caution.

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Promixin: http://www.medicines.org.uk/emc/medicine/13495

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

Regular monitoring during treatment is essential to detect adverse reactions at an early stage and patients should be counselled about the risk factors and to report all signs and symptoms of toxicity. Through the hospital consultant, regular sputum samples / respiratory function monitoring will take place

Signs of renal dysfunction or neurotoxicity (including apnoea, transient sensory disturbances (such as facial paraesthesia and vertigo), vasomotor instability, slurred speech, visual disturbances, confusion or psychosis) should be reported immediately to the specialist team.

11. Shared Care Responsibilities

a. Hospital specialist:

1. To diagnose *Pseudomonas aeruginosa* infection in non-CF bronchiectasis patients based on a timely and comprehensive assessment.
2. To initiate colistimethate sodium and ensure the first test dose is carried out before a continuous prescription is requested.
3. To supply the initial 28 days treatment
4. To provide the nebuliser system and train the patient/carer in the use of the nebuliser and preparation of the medication.
5. To co-ordinate servicing/maintenance of the nebuliser system
6. To monitor for response and adverse drug reactions during the first test dose and the initiation period
7. 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
8. To outline to GP when therapy may be stopped assuming no improvement is recognised in the patient's condition.
9. To review the patients condition and efficacy of treatment 6 months after discharge from secondary care, and then annually thereafter, with consideration at each review as to whether treatment needs to continue.
10. To evaluate ADRs raised by the GP and evaluating any concerns arising from physical checks & reviews undertaken by GP.
11. To advise GP on related issues such as drug interactions etc.
12. To advise the GP on supply issues related to the prescribing of nebulised
13. In relation to eradication therapy, secondary care will supply the patient with sputum collection pots and advise the patient to send the specimens to their GP for processing in the laboratory.
14. The hospital specialist will follow up results of the sputum cultures after the three months eradication therapy, and relay any information to the GP
15. In relation to prophylactic therapy, advise the GP if the patient is on continuous treatment with colistimethate sodium or on an alternate" month on month off" basis.
16. To advise the GP if the patient should be prescribed Colomycin® or Promixin® brand of colistimethate sodium if it is deemed necessary to have medicine delivered via the I-neb nebulizer.

b. General Practitioner:

1. To monitor the patient's overall health and well being
2. To observe patient for evidence of ADRs or any abnormalities and raise with the secondary care clinician if necessary
3. To prescribe colistimethate sodium after achievement of a stable dose regime by secondary care
4. To ensure advice is sought from the secondary care clinician if there is any significant change in the patient's physical health status
5. To reduce and stop treatment in line with secondary care clinicians original request
6. For eradication therapy, GP should ensure sputum samples from the patient are sent for processing two weeks after patient has completed the three month eradication therapy, and send any further samples for processing if requested to.

c. Patient or parent/carer:

1. Report any adverse effects to their GP whilst using colistimethate sodium for nebulisation
2. Ensure they have a clear understanding of their treatment.
3. Correctly store and administer the medicine.

Special advice to patient:

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, inhaled mucolytic's e.g. sodium chloride 3%, 6% or 7% (hypertonic saline), chest physiotherapy, other inhaled medicines, and finally nebulised colistimethate sodium.

12. Contact numbers for advice and support

Papworth Hospital NHS Foundation Trust		
Specialist	**Post**	**Telephone**
Specialist Nurses	CCLI Specialist Nurses	01480 364079/364456
Dr Charles Haworth	CCLI Consultant	01480 364656
Dr.Helen Barker	CCLI Consultant	10480 364697
Dr.Nadia Shafi	CCLI Consultant	01480 364793
Dr Christopher Johnson	CCLI Consultant	01480 366009
Dr Mike Harrison	CCLI Consultant	01480 366234
Dr Uta Hill	CCLI Consultant	01480 366042
Siobhan Singh	CCLI Lead Physiotherapist	01480 364215
Duncan Grady	Thoracic Directorate Pharmacist	01480 364179
Pharmacy Medicines Information Service		01480 364179
Pharmacy Medicines Helpline (answerphone)		01480 364739
Papworth Hospital Main Switchboard		01480 830541

13. Equality and Diversity Statement

This document complies with the Papworth Hospital NHS Foundation Trust service 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

Document ratification and history

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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:
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