

Supporting guideline for the prescribing of nebulised colistimethate (Colomycin®) in the treatment of *Pseudomonas aeruginosa* lung infections in adult patients with non- Cystic Fibrosis Bronchiectasis

Background

Pseudomonas aeruginosa is a pathogen that causes severe lung damage in patients who become colonised and then chronically infected. Patients with Non-Cystic Fibrosis (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.

Licensed indication

Colistimethate (colistin) is only licensed for the treatment by inhalation of *Pseudomonas aeruginosa* lung infections in patients with cystic fibrosis (CF). The use of inhaled colistimethate for the treatment of infection in patients with non-CF Bronchiectasis is an unlicensed indication but common practice and recommended in BTS guidance.

Nottinghamshire APC status

Nebulised colistimethate is classified as **Amber 2** (specialist initiation) in the [Nottinghamshire Joint Formulary](#).

Place in therapy

This will be tailored to individual patients by secondary care, but long-term treatment with nebulised colistimethate will be considered in the following circumstances in line with BTS guidance:

- Patients chronically colonised with *P aeruginosa*
AND
- Patients having ≥ 3 exacerbations per year requiring antibiotic therapy or patients with fewer exacerbations that are causing significant morbidity.

The aim of treatment can be to either control infection and limit further lung damage or attempt to eradicate.

There is no clear evidence regarding the best way to eradicate pseudomonas and therefore a variety of regimens are used. For eradication, colistimethate is given for three months and ciprofloxacin 750mg twice daily can be co-administered (2).

Review

A review of the patient's condition and efficacy of treatment will initially be conducted at least every six months by secondary care. Once patients are stable, the frequency of review by secondary care may be reduced.

A treatment benefit is likely to not be seen until after six months of treatment. If patients are showing no benefit after this time, they should be reviewed in clinic where stopping treatment will be considered.

Responsibilities and Roles

Secondary Care Clinician Responsibilities:

1. To diagnose *Pseudomonas aeruginosa* infection in non - cystic fibrosis bronchiectasis patients based on a timely and comprehensive assessment.
2. To initiate colistin and ensure the first test dose is administered and patient is assessed 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 (ADRs) during the first test dose and the initiation period.
7. To liaise with the general practitioner (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 the GP when therapy may be stopped assuming no improvement is recognised in the patient's condition.
9. To review the patient's condition and efficacy of treatment three months after discharge from secondary care, and then as deemed necessary by the consultant, with consideration at each review as to whether treatment needs to continue.
10. To evaluate ADRs raised by the GP and evaluate any concerns arising from physical checks & reviews undertaken by the GP.
11. To advise the GP on related issues such as medication interactions etc.
12. To advise the GP on supply issues related to the prescribing of nebulised colistin.
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 Consultant Physician 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 colistin or on an alternative month on month off basis.
16. To advise the GP that the patient should be prescribed the **Colomycin®** brand of colistin.

GP Responsibilities:

1. To monitor the patient's overall health and wellbeing.
2. To observe the patient for evidence of ADRs or any abnormalities and raise with the secondary care clinician if necessary.

3. To prescribe **Colomycin®** after achievement of a stable dose regimen 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 facilitate 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.

Patient's role:

1. Report any adverse effects to their GP or consultant whilst using **Colomycin®** for nebulisation.
2. Take responsibility for their care and treatment and seek clarification if they have any questions regarding their condition/treatment.
3. Correctly store and administer the medicine.
4. Attend for follow-up appointments.

Dosage and Administration**a) Adult patients with non-CF bronchiectasis for maintenance treatment:**

- **Colomycin®** 1 or 2 million units nebulised twice daily.
- Dose should be diluted in water for injection or sodium chloride 0.9% to a volume between 2-4ml dependant on brand and nebuliser system employed.

b) Adult patients for eradication of first pulmonary colonisation:

- **Colomycin®** 2 million units nebulised twice daily for three months.
- Eradication is not always successful and should only be attempted once.
- Dose should be diluted in water for injection or sodium chloride 0.9% to a volume between 2-4ml dependant on brand and nebuliser system employed.
- **Ciprofloxacin 750mg twice daily is co-administered for three months.**

Special warning/advice to patient

Importance of adherence to the drug regime must be emphasised to patients as compliance to twice daily nebulisation of **Colomycin®** can be an issue for patients and may result in reduced efficacy of the drug (3).

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 **Colomycin®**.

The vials are for single use only and any remaining solution should be discarded. Patients should return any remaining solution to the supplying pharmacy where appropriate. The summary of product characteristics (SPC) advises that the solution should be used immediately after preparation. If this is not possible, the solution should not be stored for longer than 24hrs in a refrigerator.

Patients should be informed of potential side effects, including rash and hypersensitivity upon initiation. They should be advised to rinse their mouths with fresh water after inhaling the nebulised solution, to minimise localised exposure.

Patients should be provided with written information regarding their treatment and use of the equipment from the specialist team when initiating treatment. For a full list of interactions and side-effects, please consult [the summary of product characteristics](#) or the British National Formulary (BNF).

Prescribing information

- **Colomycin®** is **supplied as an injection** and is available in 1 million and 2 million unit vials.
- **Colomycin® injection** is licensed for nebulisation and prescribers are reminded to also prescribe **5ml plastic vials** of diluent (either **0.9% sodium chloride or water for injection**).
- Each vial of **Colomycin®** should then be reconstituted with sodium chloride 0.9% or water for injection to an appropriate volume for nebulisation (usually 2-4mls).
- Please ensure that 0.9% sodium chloride or water for injection is prescribed **in plastic ampoules** and not glass ampoules **as the patients use a no needle technique** to prepare the **Colomycin®** for nebulisation.

NB. ***Colomycin® is the only brand of colistimethate that should be used in non-CF bronchiectasis.***

Relevant contraindications and precautions for colistimethate

Use with caution in renal impairment (Colomycin® is renally excreted). Dose adjustment is not considered necessary; however caution is advised in patients with renal impairment. Renal function monitoring should be performed at the start of treatment and regularly during treatment in all patients, as deemed necessary by the secondary care clinician.

Contra-indicated in patients with a hypersensitivity to colistimethate (colistin) or polymyxin B and in patients with myasthenia gravis.

Use with extreme caution in patients with porphyria.

Colistimethate 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. Advising patients and carers is the responsibility of the specialist service.

Colistimethate is excreted in breast milk. Its use in breast-feeding mothers should only proceed if the benefit to the mother outweighs the potential risk to the infant.

Side effects

Trans pulmonary absorption of colistimethate is generally considered to be negligible therefore, there is a low risk of systemic toxicity. Bronchospasm may occur on inhalation of

antibiotics (1) Due to the risk of bronchospasm with inhalation of Colomycin®, it is recommended the first dose should be administered under supervision in a hospital or clinic setting in secondary care where lung function before and after the initial dose, can be measured.

The SPC recommends that bronchospasm may be prevented or treated with appropriate use of beta2-agonists. If troublesome, treatment should be withdrawn (1). Sore throat or mouth has been reported and may be due to Candida albicans infection or hypersensitivity. Skin rash may also indicate hypersensitivity, if this occurs treatment should be withdrawn.

Drug interactions

As trans pulmonary absorption of colistimethate is generally considered to be negligible, there are no documented drug interactions when using the nebulised route.

Concomitant use of inhaled colistimethate sodium with other medicines that are nephrotoxic or neurotoxic should only be undertaken with the greatest caution. These include the aminoglycoside antibiotics such as gentamicin, amikacin and tobramycin. There may be an increased risk of nephrotoxicity if given concomitantly with cephalosporin antibiotics (1).

For further information on contraindications, precautions, side effects and drug interactions, refer to the BNF or the Summary of Product Characteristics.

Monitoring

Patients should be counselled to report any signs or symptoms of toxicity. Secondary care will ensure that regular sputum samples, CRP, respiratory function and renal function monitoring take place as appropriate for each patient.

As per [British Thoracic Society \(BTS\) guidance](#) (2), it is expected that ongoing support will be provided from the respiratory multidisciplinary team. The frequency of patient review and follow up should be communicated to primary care on initiation. Colomycin® should be used with caution in renal impairment - it is advisable to assess baseline renal function and to monitor during treatment (1). Because the frequency of renal monitoring during nebulised Colomycin® treatment has not been defined in the literature, this should be determined on an individual patient basis by the clinician initiating treatment.

Advice and support

Sherwood Forest Hospitals NHS trust:

Pharmacy Medicines helpline – Tel: 01623 672213;
Respiratory Nurse Specialist – Tel: 01623 622515 Ext 6831, 3541 and 6324.

Nottingham University Hospitals NHS trust:

Pharmacy Medicines helpline – Tel: 0115 9249924 Ext 64641;
Respiratory Nurse Specialist – Please contact the nurse responsible for your care.

References

1. Summary of Product Characteristics (SPC). Colomycin Injection[®] (Forest Laboratories UK limited); [accessed 25/04/17] via <https://www.medicines.org.uk/emc/search?q=%22Colomycin%22> revised 18/05/2016;
2. Pasteur MC, Bilton D, Hill AT. British Thoracic Society Guideline for non- CF Bronchiectasis. Thorax 2010; 65 Suppl 1;
3. Haworth C.S, Foweraker J.E, Wilkinson P et al. Inhaled Colistin in Patients with Bronchiectasis and Chronic Pseudomonas aeruginosa Infection Am J Respir Crit Care Med 2014 189;8:975-982.

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Updated by Laura Catt – Prescribing Interface Advisor March 2020

The updated guideline was circulated for comments with primary and secondary care representatives and this version reflects all the suggested changes.