THE SHEFFIELD AREA PRESCRIBING GROUP

Shared Care Protocol

For

Nebulised Colomycin®, gentamicin or tobramycin in adults with non-cystic fibrosis bronchiectasis

Issue 2

Shared care protocol developed by:

Dr Omar Pirzada, Consultant Respiratory Physician, STHFT
Linsey Abbott, Respiratory Pharmacist, STHFT
Hilde Storkes, Formulary Pharmacist, NHS SCCG

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Shared Care Protocol for nebulised Colomycin®, gentamicin or tobramycin in adults with non-cystic fibrosis bronchiectasis

Statement of Purpose

This shared care protocol (SCP) has been written to enable the continuation of care by primary care clinicians of adult patients initiated on nebulised Colomycin® (colistimethate sodium, colistin), gentamicin or tobramycin for non-cystic fibrosis bronchiectasis by the respiratory physicians at Sheffield NHS Teaching Hospitals Foundation Trust (STH). Primary care may be requested to take over prescribing of nebulised Colomycin®, gentamicin or tobramycin as an off-licence use, with details as outlined below.

This is an unlicensed therapeutic indication that has been reviewed by the STH Medicine Safety Committee. However nebulised colistimethate and tobramycin (as the nebulised solution) are licensed for *Pseudomonas aeruginosa* infection in cystic fibrosis bronchiectasis; all drugs are established in non-cystic fibrosis by common practice and consensus with STH physicians, the Northern bronchiectasis research group, BTS guideline for bronchiectasis and is standard UK practice.

Estimated usage will be between 25-40 patients per year.

Responsibilities of specialist clinician

- To discuss benefits and side effects of treatment with the patient/carer, including potential risk of bacterial resistance, and obtain informed consent. This is particularly important for off-label use.
- To initiate nebulised Colomycin®, gentamicin or tobramycin in appropriate patients.
- To carry out initial test dose.
- To prescribe the first month's supply of drug and diluent and ensure patient has all required equipment e.g. nebuliser. A month's supply of any required sundries e.g. needles / syringes will be supplied initially with ongoing issues being obtained from pulmonary function unit at NGH.
- To train patients and carers how to use and care for/maintain nebuliser, including, administration and infection control.
- To contact patient's primary care prescriber to request prescribing under shared care and send a link to or copy of the shared care protocol (see appendix).
- To advise the primary care prescriber regarding continuation of treatment, including the length of treatment.
- To discuss any concerns with the primary care prescriber regarding the patient's therapy and see patients ahead of routine appointment if necessary.
- To ensure nebuliser is serviced at appropriate intervals.
- The patient to remain under the specialist's care whilst ever the patient is being prescribed nebulised antibiotics.
- To conduct an annual review, including assessment of the efficacy of the treatment and to continue only where there is benefit.

Responsibilities of the primary care clinician

- To refer appropriate patients to secondary care for assessment.
- To agree to prescribe drug and diluent for patients in line with the shared care agreement.

- To report any serious adverse reaction to the MHRA and the referring specialist.
- To continue to prescribe drugs for the patient as advised by the specialist
- To undertake monitoring as per shared care protocol
- To inform the consultant if the patient discontinues treatment for any reason
- To seek the advice of the specialist if any concerns with the patient's therapy
- To conduct an annual face to face medication review or more frequent if required
- In the event that the primary care prescriber is not able to prescribe, or where the SCP is agreed but the specialist is still prescribing certain items e.g. hospital only product, the primary care prescriber will provide the specialist with full details of existing therapy promptly by fax on request.
- For medication supplied from another provider primary care prescribers are advised to follow recommendations for Recording Specialist Issued Drugs on Clinical Practice Systems

Responsibilities of Patients or Carers

- To attend hospital and primary care clinic appointments. Failure to attend will potentially result in the medication being stopped.
- Ensure adequate supply of usable tubing, mask etc. and re-order as necessary.
- Present rapidly to their primary care prescriber should their clinical condition significantly worsen so that appropriate action can be taken.
- Report any suspected adverse effects to their specialist or primary care prescriber whilst using nebulised antibiotics.
- To read the drug information given to them.
- To reconstitute and use medication as prescribed and as per training.
- Inform the specialist, primary care prescriber or community pharmacist dispensing their prescriptions of any other medication being taken – including over-the-counter medication.

Indication

For treatment of chronic *Pseudomonas aeruginosa* infection in non-cystic fibrosis bronchiectasis

Direct aerosol delivery of antibiotics to the lower airways has been shown to be effective in delivering high doses of bactericidal drugs directly to the airways with little risk of systemic toxicity. **Please note**: for gentamicin and tobramycin injection this is an unlicensed method of administration. Trial evidence has shown that nebulised anti-pseudomonal antibiotics can reduce the number of exacerbations, number of hospitalisations and the density of *Pseudomonas aeruginosa* within the sputum.

Selection of patients

As per British Thoracic Society (BTS) guidelines:
Patients having >3 exacerbations per year requiring antibiotic therapy **or** patients with fewer exacerbations that are causing significant morbidity should be considered for long-term nebulised antibiotics.
In such patients, long-term nebulised antibiotics should be considered if chronically colonised with *Pseudomonas aeruginosa*. Colomycin® would normally be used first line with gentamicin as the preferred 2nd line choice (BTS guidelines). At STH, tobramycin is also used as a 2nd line choice as it achieves greater sputum concentration than gentamicin, although the trial data for both is limited; choice is often governed by current supply issues.

Dosage and administration

Patients should have an initial supervised test dose with pre and post dose monitoring of lung function (secondary care responsibility).

Colomycin®: 1 – 2 mega units twice daily. All patients would have had test doses and reconstitution training at STH.

Hypertonic solutions of Colomycin® (colistimethate sodium) can cause bronchospasm. In order to avoid this, each dose is made up with 2ml water for injections and 2ml sodium chloride 0.9% for injections.

Each vial of Colomycin® (colistimethate sodium) can be reconstituted with 2.5 mg/2.5ml of salbutamol if the above solutions have caused bronchoconstriction. This would be on advice from secondary care post initiation as mixing of products is not recommended by the manufacturer.

Gentamicin: 80mg twice daily is usual dose, occasionally 160mg twice daily, diluted with sodium chloride 0.9% to a volume of 4ml, and administer via a nebuliser (off label use).

Tobramycin: 80mg - 240 mg twice daily (prescribed as 80mg/2ml vials). If the dose is less than 160mg (i.e. 4ml) dilute with sodium chloride 0.9% to a volume of 4ml

Tobramycin injection (phenol free) (**not** Nebcin® Flynn brand as this contains phenol) should be used and administered via a nebuliser (off label use). **Supply should be made only using the 80mg/2ml vials as this is the most cost effective option.**

Please note: only cystic fibrosis patients can be prescribed the tobramycin solution for nebulisation (300mg/5ml), e.g. TOBI®, and this preparation is **not** covered within this guideline.

Prior to administration of gentamicin and tobramycin, the patient should receive a bronchodilator e.g. salbutamol either using a MDI or nebuliser, as this will reduce the risk of coughing and bronchospasm.

Patients with excess secretions should be given their nebulised antibiotics after chest clearance.

Prior to shared care, all patients will have been trained by the specialist team in reconstitution, dilution and administration, including infection control.

Nebulisers may act as a source of bacterial contamination. The ideal standards and methods for cleaning nebulisers have not yet been well established. Patients should follow the manufacturer's recommendations. In general, patients should be advised to:

- wash hands before and after use
- rinse the nebuliser and dry thoroughly after every use.

Contra-indications

Colomycin®

- Hypersensitivity to colistimethate sodium (colistin) or to polymixin B

Gentamicin and tobramycin

- Hypersensitivity to any aminoglycoside, or any of the excipients listed within the product summary product characteristics (SmPC)
- Avoid using if creatinine clearance <30ml/min
- Caution if significant hearing loss, needs hearing aids or has significant balance issues

Side–effects

The details below are not a complete list and the current BNF and the SmPC remain authoritative.

Inhalation may induce coughing or bronchospasm; if troublesome treatment should be withdrawn after discussion with specialist.
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.
Transpulmonary absorption of Colomycin®, gentamicin and tobramycin is considered to be negligible therefore, there is a low risk of systemic toxicity.

Any suspected adverse reactions should be reported via the Yellow Card Scheme: https://yellowcard.mhra.gov.uk/

Monitoring

No routine monitoring is required.

Patients on nebulised gentamicin or tobramycin do not routinely require drug levels due to limited systemic absorption. If the patient is suspected to be experiencing aminoglycoside toxicity, e.g. ototoxicity or nephrotoxicity, then levels may be taken. This should be a trough level.

Routine respiratory clinic follow up under initiating consultant as required; at least annual review but more frequently if needed.

Interactions

The details below are not a complete list and the current BNF and the SmPC remain authoritative.

Colomycin®

- Neuromuscular blocking drugs and ether should be used with extreme caution in patients receiving colistimethate sodium.

BNF colistimethate interactions

Gentamicin and tobramycin

- Concomitant use with other medicinal products of neurotoxic and/or nephrotoxic potential should be avoided. These include the aminoglycoside antibiotics such as gentamicin, amikacin, netilmicin and tobramycin. There may be an increased risk of nephrotoxicity if given concomitantly with cephalosporin antibiotics.

BNF gentamicin interactions
BNF tobramycin interactions

Re-Referral guidelines

All patients will be seen at least annually, but if any of the following occur please re-refer sooner or seek advice;

- See under monitoring section above.
- Deterioration of disease

Financial implications

Colomycin® (Teva)
Injection, powder for reconstitution, colistimethate sodium,
Costs as per Drug Tariff May 2021:
1 million-unit vial = £1.80; 2 million-unit vial = £3.20
Cost range of £1314 - £2336 per year (1mega unit BD – 2mega unit BD)

Gentamicin (non-proprietary)
Injection, gentamicin (as sulfate) 40mg/ml (2ml ampoules/vials)
Cost as per Drug Tariff May 2021: £6.88 x 5
Cost range of £1,004 to £2,008 per year (80mg bd to 160mg bd)

Tobramycin (non-proprietary)
Injection, tobramycin (as sulfate) 40 mg/mL, Costs as per Drug Tariff May 2021
2-mL (80-mg) vial = £5.37; [6-mL (240-mg) vial = £19.20 is available but note **not** recommended for prescribing]
Cost range of £3920 - £11760 per year (80mg BD – 240mg BD) based on 80mg/2ml vials

Ordering information

Colomycin®, gentamicin and tobramycin injection and diluents are available through regular pharmaceutical wholesale chains

Tubing and other accessories to be obtained by the patient via pulmonary function unit at NGH: 0114 2269800

Support, education and information

Brearley Outpatients NGH: 0114 2269800 or email: sth.brearleyopd@nhs.net

References

Colomycin® injection (Teva) SmPC, accessed via
https//www.medicines.org.uk/emc/product/1094/smpc

Gentamicin 40mg/ml injection SmPC, accessed via
https://www.medicines.org.uk/emc/search?q=gentamicin+injection

Tobramycin 40mg/ml injection SmPC, accessed via
https://www.medicines.org.uk/emc/product/1425/smpc

British Thoracic Society guideline for non CF bronchiectasis (December 2018), accessed via
https://www.brit-thoracic.org.uk/quality-improvement/guidelines/bronchiectasis-in-adults/

Babu K.S. et al. Role of long term antibiotics in chronic respiratory diseases. Resp Med 2013;107(6):800-15
http://www.antimicrobe.org/hisphoto/history/RespirMed-Babu-antibiotics%20respiratory-2013.pdf

NICE Evidence Summary ES12. Non-cystic fibrosis bronchiectasis: inhaled tobramycin (4 April 2017)
https://www.nice.org.uk/advice/es12/chapter/Key-points

NICE NG117 Bronchiectasis (non-cystic fibrosis), acute exacerbation: antimicrobial prescribing (18 Dec 2018)
https://www.nice.org.uk/guidance/ng117/resources/bronchiectasis-noncystic-fibrosis-acute-exacerbation-antimicrobial-prescribing-pdf-66141603457477

BNF online access via
https://bnf.nice.org.uk

Version history

Issue 2 updated from:
Shared Care Guideline for nebulised Colomycin® or tobramycin in adults with non-cystic fibrosis bronchiectasis
Developed by: Dr Omar Pirzada, Consultant Respiratory Physician, STHFT; Nick Gunn, Respiratory Pharmacist, STHFT; and Isobel Bancroft, Clinical Practice Pharmacist, NHS Sheffield CCG.
Approved by: Sheffield APG July 2018

Appendix - **Request for Shared Care – Nebulised Antibiotics in adults with non CF Bronchiectasis**

Dear Doctor

RE: …….. DOB: …… NHS No. ……..

Address: ……..

Your patient is being started on treatment with (enter medication):

This treatment can be prescribed by GPs under the Traffic Light System under the 'shared care' arrangements. The shared care protocol has been approved by the Sheffield Area Prescribing Group.
http://www.intranet.sheffieldccg.nhs.uk/medicines-prescribing/shared-care-protocols.htm

Drug: ……..…….. Dose:……..

As part of shared care arrangements please can you monitor adherence, response and side effects to therapy at annual medication review. Will you also please undertake to prescribe for your patient?

Please acknowledge you are happy to take on shared care by returning the slip below to above address or by email to BOPD – sth.brearleyopd@nhs.net

Do not hesitate to contact us if you have any concerns.

Yours sincerely

Clinician's Name

Clinician's Title

IMPORTANT REMINDER

The prescribing doctor is responsible for monitoring *the patient on the medication being prescribed*

Please tear here, return to address or email sth.brearleyopd@nhs.net

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RE: …….. DOB: …….. NHS:……..

Address: ……....

☐ I AGREE to take on shared care of this patient

☐ I DO NOT AGREE to take on shared care of this patient

Signed ……
GP Practice……
Date……