

BRONCHIECTASIS (non-cystic fibrosis), nebulised antibiotics

The Pan Mersey Area Prescribing Committee recommends the prescribing of nebulised colistimethate (Colomycin®), gentamicin or tobramycin for adult non- cystic fibrosis bronchiectasis patients

AMBER patient retained by specialist

The BTS guideline for bronchiectasis treatment in adults recommends considering long term nebulised antibiotics in patients with non-cystic fibrosis (CF) bronchiectasis colonised with pseudomonas aeruginosa (PsA) who experience three or more exacerbations per year. Nebulised aminoglycosides (gentamicin and tobramycin) may be considered as a second line alternative to colistimethate in those patients intolerant of colistimethate or who continue to exacerbate with colistimethate¹. Colomycin® brand is preferable to Promixin® due to cost. Nebulisation of colistimethate, gentamicin or tobramycin injections in non- CF bronchiectasis is an off-label use. Tobramycin is often favourable to gentamicin due to its better side effect profile and its availability as nebulisers rather than glass ampoules for ease of administration.

Each 1 mega-unit (mu) of Colomycin® should be reconstituted with 2ml of 0.9% sodium chloride prior to nebulisation² and gentamicin should be diluted with 2ml 0.9% sodium chloride. They should be nebulised with a compressor with a flow rate of 8-10l/min and a breath enhanced open vent nebuliser e.g. Sidestream Plus®. An expiratory filter or corrugated tubing to vent out of a window should be used to prevent exposure to other household members. All nebulising equipment including expiratory filters/corrugated tubing will be supplied and patients will be trained in its use by the specialist clinic. Syringes and needles must be provided by the specialist centre or district nurses. Where gentamicin is the treatment selected the patient will need to be provided with filter needles to prevent the nebulisation of glass particulate.

Nebulisers will be maintained by the specialist trust's medical engineering team.

Treatment should be initiated by a chest physician with access to specialist respiratory nursing/physiotherapist services with expertise in performing a nebulised antibiotic challenge test. Patients will be trained how to reconstitute and administer during the challenge test. Following a successful challenge test outcome, the first month of treatment should be prescribed by the chest physician.

Drug for nebulisation	Adult dose	Cost per month of drug (BNF)	Cost per month of plastic ampoule Sodium chloride 0.9% (BNF)
Colomycin®	1-2 mu twice a day reconstituted with 2-4ml sodium chloride 0.9% (2ml for each mega unit)	£108 x 1mu £194 x 2mu	5ml (Advanz) £21.45 5ml (B Braun) £26.58
Gentamicin ampoules	80mg twice a day diluted with 2ml sodium chloride 0.9%	£82.56	2ml (Advanz) £21.45
Tobramycin nebuliser solution	300mg twice a day. Use the 300mg/5ml solution	£780.00	

The BTS guideline for bronchiectasis recommends that azithromycin or erythromycin be considered as alternatives to inhaled antibiotics (e.g. in patients who do not tolerate inhaled antibiotics) for patients with bronchiectasis and chronic PsA infection.¹ They may also be considered as an additive treatment for patients using inhaled antibiotics who continue to have a high exacerbation frequency.

Recommended doses are: erythromycin 250mg twice daily or azithromycin 250mg to 500mg three times weekly.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

Effectiveness

Haworth et al³ studied 144 bronchiectasis patients with chronic PsA infection treated with colistimethate or 0.45% sodium chloride over 6 months. Although the study did not reach significance at its primary endpoint of time to next exacerbation (165 days vs 111 days ($p = 0.11$)), there was significance in a predetermined 'compliant' population (those who took their medication for greater or equal to 80% of the time (168 vs 103 days $p=0.028$)). The whole group also demonstrated a significant reduction in PsA colony forming unit count at 12 weeks and a significant improvement in SGRQ total score at 26 weeks. The incidence of adverse effects was low and similar in both groups.

A study of 65 patients comparing inhaled gentamicin 80mg twice daily vs 0.9% sodium chloride demonstrated a significant improvement in time to next exacerbation at 3 month follow up (61.5 days vs 120 days $p=0.02$) and the exacerbation number was also reduced (0 (0-1) vs 1.5 (1-2) $p = <0.0001$).⁴ Quality of life measures improved, sputum became less purulent and exercise capacity improved. Although 7/32 in the gentamicin arm reported bronchoconstriction, this only led to 2 withdrawals.

Safety

Nebulised colistimethate is usually well tolerated post-test dose trial. Potential side effects include arthralgia, asthenia, tinnitus and balance impairment, chest discomfort, dysphonia, dyspnoea, fever, haemorrhage, headache, nausea and taste alterations.⁵ It should be stopped and reviewed in secondary care in patients who develop severe haemoptysis or renal impairment. It should be avoided in patients with myasthenia gravis. Whilst neurotoxicity and nephrotoxicity are rare with inhaled colistimethate, use cautiously with other medications that are nephrotoxic or neurotoxic.²

Gentamicin/Tobramycin:

Usually well tolerated post-test dose trial. Avoid in renal impairment. Potential side effects include dysphonia and aphonia.

Advise patients to rinse mouth after antibiotic nebulisation to prevent oral candida.

Annual cost (basic NHS price including NaCl 0.9%)⁵

Colomycin[®] 1mu = £1,553.40-1614.96

Colomycin[®] 2mu = £2590.20-2651.76

Gentamicin 80mg = £1,248.12

Tobramycin 300mg (Teva, Mylan) = £10,140.00

Patient factors

Colistimethate: Vials can be opened without requiring needle insertion; foil seal can be peeled off and rubber bung removed. Patients can reconstitute two doses at a time each with sodium chloride and store one dose in the fridge. The refrigerated dose should be used within 24 hours. Neurotoxicity, characterized by dizziness, confusion or visual disturbances has been reported following parenteral administration of colistimethate sodium. If these effects occur, patients should be warned against driving or operating machinery.

Prescribing information

As described on page 1.

Implementation notes

Initial first month supply shall be supplied by the specialist respiratory centre (antibiotic and sodium chloride ampoules). Subsequent prescriptions including sodium chloride ampoules should be provided by the G.P. The size of sodium chloride ampoules required will be made clear by the specialist centre.

References

1. Hill AT, Welham SA, Sullivan AL, et al. Updated BTS Adult Bronchiectasis Guideline 2018: a multidisciplinary approach to comprehensive care. *Thorax* 2019;74:1-69 https://thorax.bmj.com/content/thoraxjnl/74/Suppl_1/1.full.pdf
2. Colomycin[®] Summary of Product Characteristics. <https://www.medicines.org.uk/emc/product/9664> [Accessed 7/3/19]
3. Haworth et al. [Inhaled Colistin in Patients with Bronchiectasis and Chronic Pseudomonas aeruginosa Infection](#). *Am J Respir Crit Care Med*. 2014 Apr 15; 189(8): 975–982
4. Murray et al. A randomised controlled trial of nebulized gentamicin in non-cystic fibrosis bronchiectasis. *Am J Resp Crit Care Med*. 2011; 183: 491-9
5. Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press <<http://www.medicinescomplete.com>> [Accessed on 29/2/19]