Bronchiectasis – Non CF Antibiotic Use UHL Guideline

University Hospitals of Leicester NHS
NHS Trust

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1. Introduction and who this guideline applies to

Bronchiectasis is a long-term condition where the airways of the lungs become abnormally widened, leading to a build-up of excess mucus that can make the lungs more vulnerable to infection. The severity of symptoms can vary widely. Some people have only a few symptoms that don't appear often, while others have wide-ranging daily symptoms.

These guidelines are for use in adult inpatients with an established diagnosis of bronchiectasis based on current or previous CT scan images of the lungs.

Specialist advice is available from the adult bronchiectasis team and from the microbiology team.

2. Guideline Standards and Procedures

2.1. Diagnosis and Antibiotic Treatment of exacerbations of non-CF Bronchiectasis

- **There are no precise, objective tests available to diagnose an exacerbation of bronchiectasis.**
- Patients with exacerbations will commonly NOT have new x-ray changes or raised inflammatory markers.

Patients may be considered to have an exacerbation with deterioration in THREE OR MORE key symptoms for at least 48 hours

- Cough
- Increased sputum volume and/or consistency
- Increased sputum purulence
- Breathlessness and/or reduced exercise tolerance
- Increased fatigue
- Haemoptysis

3 or more present

Assessment of exacerbation severity should be made by a senior clinical decision maker. Consider if any of the following are present

- Severe increase in respiratory symptoms
- Acute respiratory failure
- Failed response to oral antimicrobials
- Signs of Red Flag Sepsis
  (See UHL sepsis guideline for supportive management: B11/2014)

See Diagram 2.1: Empiric Antibiotic Treatment for Acute Exacerbations of Non-CF Bronchiectasis

- Antibiotic therapy is initiated based on previous bacterial isolates in sputum, if known.
- Antibiotic allergy or intolerance and previous toxicity should also guide the choice of antibiotic.
- Comorbidity is also common including renal impairment which may require the avoidance of some drugs and dose alteration of others.
- Antibiotic therapy is one part only of effective treatment; close attention should be paid to other elements of treatment, especially airway clearance and nutrition.

Diagram 2.1: Empiric Antibiotic Treatment for Acute Exacerbations of Non-CF Bronchiectasis

Before Prescribing Antibiotics

- Obtain sputum sample for culture and sensitivity
- Obtain viral swabs during seasonal viral outbreaks
- Obtain blood cultures if systemically unwell, febrile, or signs of sepsis.
- Check most recent sputum results
  - Base initial antibiotic choice on usual colonising organism +/- *in vitro* sensitivities.
- Check patients drug allergies or intolerances.

For all patients

- Refer to respiratory physiotherapy to maximise airway clearance
- Consider dietician referral if under or overweight
- Offer smoking cessation treatment.
- Offer pulmonary rehab referral to patients with breathlessness

For patients on long term prophylaxis

- Hold prophylaxis while receiving treatment for acute exacerbation.
- Ensure prophylaxis reviewed and re-initiated once exacerbation resolved.

Renal dosing

Many antibiotics require dose alteration based on renal function. Refer to the renal dosing guide on the antimicrobials intranet page or discuss with a pharmacist.

Unknown or no previous *Pseudomonas aeruginosa*

Mild to moderate exacerbation

- 1st Line: Oral co-amoxiclav 625 mg TDS for 10 days
- 2nd Line: Oral doxycycline 200mg OD for 10 days

Severe exacerbation or if oral route not appropriate

- 1st Line: IV co-amoxiclav 1.2g TDS
- 2nd Line (penicillin allergy): IV ceftriaxone 2g OD
- Alternative (if anaphylaxis to beta-lactams): IV levofloxacin 500 mg BD

Consider IV to Oral switch once clinically improving. Switch to oral option given above for mild to moderate. Maximum antibiotic duration is 10 days (IV and enteral combined).

If *Staphylococcus aureus* infection confirmed from new microbiology samples

Methicillin <u>sensitive</u> *S. aureus*

- 1st Line: Oral flucloxacillin 500 mg QDS
- 2nd Line: Oral doxycycline 200 mg OD

Methicillin <u>resistant</u> *S. aureus* (MRSA)

- 1st Line: Oral doxycycline 200 mg OD
- 2nd Line: Oral co-trimoxazole 960 mg BD
- Alternative: Oral linezolid 600 mg BD

<u>AND</u> Provide MRSA eradication therapy (see section 2.2.2)

Total duration for *S. aureus* infection is 14 days.

- **Review microbiology results after 48-72 hours** and amend treatment if necessary.
- **Assess clinical response at 5 days**, consider antibiotic change by day 7 if response poor.

In patients with no, or partial, clinical response consider:

- New or resistant organisms
- Non-tuberculous mycobacterial infection
- Viral infection or co-infection (e.g. influenza or RSV)
- Non-infectious complications (e.g.Allergic Bronchopulmonary Aspergillosis (ABPA) or Oesophageal reflux)
- Respiratory physiotherapy review to ensure optimal airway clearance and assess for Dysfunctional breathing patterns/ abnormal cough behaviour

Pseudomonas colonised

Mild to moderate exacerbation

- 1st line: Oral ciprofloxacin 500mg BD for 10 days
  - Up to 14 days under the advice of the bronchiectasis team
- 2nd line: Discuss with microbiology

Severe exacerbation or if oral route not appropriate

- 1st Line: IV ceftazidime 2g TDS
- 2nd Line (if intolerant or allergic to ceftazidime): IV piperacillin-tazobactam 4.5g TDS
- If 1st **<u>and</u>** 2nd line **not** appropriate **<u>and</u>** patient has **not** had recent treatment with a quinolone: IV ciprofloxacin 400 mg BD (may be increased to TDS in severe infections)

Consider IV to Oral switch once clinically improving. If switching to oral ciprofloxacin in severe exacerbations, use 750 mg BD.

Maximum antibiotic duration is 10 days of IV and enteral combined (up to 14 days under the advice of the bronchiectasis team).

Patients with severe disease may require a second antibiotic (such as tobramycin or colistimethate sodium) if recommended by microbiology or the bronchiectasis team.

In vitro sensitivity of Pseudomonas is a **<u>poor</u>** predictor of clinical response. In these patients, base antibiotic choice on previous clinical response, drug intolerance/allergy and any previous toxicity.

2.2. Eradication treatment for new isolates of specific organisms in Non-CF bronchiectasis

2.2.1. Pseudomonas aeruginosa

- The acquisition of chronic infection with Pseudomonas in Bronchiectasis is associated with poorer long term outcomes and increased exacerbation frequency.
- Pseudomonas eradication is most effective if carried out soon after acquisition. Distinction should be made between patients with new sputum isolates of Pseudomonas and previous negative sputum microbiology for Pseudomonas, and those patients with previous inadequate sampling who are more likely to have established long term infection. If in doubt please seek the advice of the bronchiectasis team.
- In a stable patient, three or more isolates (at least one-month apart) of Pseudomonas should be obtained before considering the patient chronically colonised.
- Patients with a new growth of pseudomonas and clinical deterioration should be treated as per the Acute Exacerbation section of this Guideline (section 2.1 and diagram 2.1)
- In patients who fail to eradicate pseudomonas despite an initial 2 week period of treatment, initiate a 3-month course of nebulised antibiotics. First line option is nebulised colistimethate sodium (Colomycin®) 1 million units BD (see prescribing advice in diagram 2.3).
- The risks and benefits of eradication therapy versus further monitoring and observation should be discussed with patients.

2.2.2. MRSA (methicillin resistant Staphylococcus aureus)

- Eradication is sometimes attempted in bronchiectasis patients with a new growth of MRSA in sputum. There is no evidence to guide this treatment and this should be discussed on an individual case basis with the bronchiectasis team and microbiology.

2.3. Antibiotic prophylaxis in non-CF Bronchiectasis

See Diagram 2.3: Antibiotic Guidelines for Antimicrobial Prophylaxis in Non-CF Bronchiectasis

- Long term antibiotics should only be considered in patients with confirmed bronchiectasis experiencing three or more exacerbations per year.
- All patients must be referred to a respiratory specialist for review before antimicrobials are prescribed.

Diagram 2.3: Antibiotic Guidelines for Antimicrobial Prophylaxis in Non-CF Bronchiectasis

All patients must be referred to a respiratory specialist for review before antimicrobials are prescribed

Criteria
Long term antibiotics should only be considered in patients with confirmed bronchiectasis experiencing three or more exacerbations per year.

Optimise airway clearance, nutritional status and ensure pulmonary rehabilitation has been offered before starting long term antibiotics.

In all patients

- Ensure patient receives annual, seasonal, influenza vaccination through GP or other primary care service (e.g. community pharmacy).
- Patients should also receive the pneumococcal PPV23 vaccine from their GP. This should be given every 5 years in those with no spleen, dysfunctional spleen, or chronic renal disease.

Unknown or no previous *Pseudomonas aeruginosa*

First line
Oral azithromycin 250 mg three times a week (e.g. Mondays, Wednesdays, and Fridays)

Second line
Oral doxycycline 100 mg OD

Alternative
Nebulised gentamicin 80 mg BD

Pseudomonas colonised

First line
Oral azithromycin 250 mg three times a week (e.g. Mondays, Wednesdays, and Fridays)

Second line
Nebulised colistimethate sodium (Colomycin®) 1 million units BD

If monotherapy proves insufficient
Oral azithromycin 250 mg three times a week
AND
Nebulised colistimethate sodium 1 million units BD

Alternative
Nebulised gentamicin 80 mg BD may be used in place of nebulised colistimethate sodium

Assess clinical response to all prophylactic therapies after 6 months.

Stop/amend treatments that have not produced objective/subjective reduction in exacerbations

Prescribing Notes

Long term doxycycline

- Take with a full glass of water and remain in an upright position for 30 minutes
- Avoid taking at same time as calcium, magnesium, iron, zinc, etc., including medicines (e.g. antacids) and food (e.g. dairy) that contain these.
- Warn patients about photosensitivity reaction. Advise to avoid sun lamps. Advise to avoid sunlight, ensure to stay covered up and wear high SPF sun cream.
- Avoid in women who may become pregnant.

Long term Azithromycin

- Screen for non-tuberculous mycobacteria before starting therapy.
- Perform ECG on patients before commencing. Do not use in patients with unstable cardiac arrhythmias or prolonged QT.
- Warn patients of signs of hearing damage and consider performing hearing tests.
- The effects of azithromycin are maintained for several months after stopping treatment, stable patients may stop treatment during summer months
- 250 mg three times per week is a starting dose. This may be increased in line with response, under a respiratory specialist.

Nebulised colistimethate sodium and gentamicin

- These agents require a supervised test dose to exclude drug-induced bronchospasm
- Monitor renal function before and during use. Caution in those whose creatinine clearance is less than 30 mL/min due to increased risk of toxicity.
- A shared care agreement is needed to enable the GP to prescribe colistimethate [http://bit.ly/LMSGSCA].
- Nebulised gentamicin is prescribed and dispensed in UHL only.

3. Education and Training

None

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Prescribing antimicrobial therapy in line with the guideline	Trust-wide antimicrobial prescribing audits	Antimicrobial Pharmacists	Annual	To CMG and Trust boards

5. Supporting References

1. Hill AT, Sullivan AL, Chalmers JD, et al., (2019) British Thoracic Society Guideline for bronchiectasis in adults, *Thorax*, **74** (Suppl 1):1–69x
2. NICE, (2019) Bronchiectasis (non-cystic fibrosis), acute exacerbation: antimicrobial prescribing, *National Institute for Health and Care Excellence*. [available online: https://www.nice.org.uk/guidance/ng117].
3. Martinez-Garcia MA, et al. (2014) Multidimensional approach to non-cystic fibrosis bronchiectasis: the FACED score. *Eur Respir J*, **43**(5):1357-67.
4. Schelstraete P, et al., (2013) Eradication therapy for Pseudomonas aeruginosa colonization episodes in cystic fibrosis patients not chronically colonized by P. aeruginosa, *J Cystic Fibrosis*, **12**:1-8

6. Key Words

- Bronchiectasis
- Exacerbation of Bronchiectasis
- Nebulised antibiotics
- Nebulised colistimethate

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