# Bronchiectasis (non-cystic fibrosis), acute exacerbation: antimicrobial prescribing

## NICE guideline

## Draft for consultation, July 2018

1	This guideline sets out an antimicrobial prescribing strategy for managing
2	and preventing an acute exacerbation of bronchiectasis (non-cystic fibrosis). It
3	aims to optimise antibiotic use and reduce antibiotic resistance.
4	See a 3-page visual summary of the recommendations, including tables to
5	support prescribing decisions.
6	Who is it for?
7	Health professionals
8	<ul> <li>People with bronchiectasis, their families and carers</li> </ul>
9	The guideline contains:
10	the draft recommendations
11	<ul> <li>rationales explaining why the committee made their recommendations.</li> </ul>
12	Information about how the guideline was developed is on the guideline's page
13	on the NICE website. This includes the full evidence review, details of the
14	committee and any declarations of interest.

## 1 Recommendations

## Managing an acute exacerbation of bronchiectasis (non-cystic fibrosis)

- 4 1.1.1 Be aware that an <u>acute exacerbation of bronchiectasis</u> is a
- 5 sustained worsening of symptoms from a person's stable state.
- To find out why the committee made the recommendations on awareness of
  acute exacerbation of bronchiectasis, see the rationales.

#### 8 Treatment

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- 9 1.1.2 Obtain a sputum sample from people with an acute exacerbation of
   10 bronchiectasis and send for culture and susceptibility testing.
- 1.1.3 Consider an antibiotic (see the recommendations on <u>choice of</u>
   antibiotic) for people with an acute exacerbation of bronchiectasis
   taking account of:
- the limited evidence base for antibiotics
- the number and severity of symptoms
- previous exacerbation and hospital admission history, and the
   risk of developing complications
- previous sputum culture and susceptibility results.
- 19 1.1.4 When results of sputum culture and susceptibility testing are20 available:
- review the choice of antibiotic, and
- only change the antibiotic according to susceptibility results if
   bacteria are resistant and symptoms are not already improving
   (using a narrow spectrum antibiotic wherever possible).
- 25 1.1.5 When an antibiotic prescription is given, give advice about:
  - possible adverse effects of the antibiotic, particularly diarrhoea

1		seeking medical help if symptoms worsen rapidly or significantly	
2		at any time, or the person becomes systemically very unwell.	
3	To find o	out why the committee made the recommendations on treatment of an	
4	acute ex	acerbation see the rationales.	
5	Reasse	ssment	
6	1.1.6	Reassess the person if symptoms worsen rapidly or significantly at	
7		any time, taking account of:	
8		<ul> <li>other possible diagnoses, such as pneumonia</li> </ul>	
9		<ul> <li>any symptoms or signs suggesting a more serious illness or</li> </ul>	
10		condition, such as cardiorespiratory failure or sepsis	
11		<ul> <li>previous antibiotic use which may have led to resistant bacteria.</li> </ul>	
12	To find out why the committee made the recommendations on reassessment,		
13	see <u>the</u>	rationales.	
14	Referra	I and seeking specialist advice	
15	1.1.7	Refer people with an acute exacerbation of bronchiectasis to	
16		hospital if they have:	
17		<ul> <li>cardiorespiratory failure, or</li> </ul>	
18		<ul> <li>a severe systemic infection, or</li> </ul>	
19		<ul> <li>any of the high risk criteria for severe illness or death from the</li> </ul>	
20		NICE guideline on <u>sepsis</u> .	
21	1.1.8	Seek specialist advice for an acute exacerbation of bronchiectasis	
22		if the person:	
23		<ul> <li>has symptoms that are not improving with repeated courses of</li> </ul>	
24		antibiotic treatment	
25		<ul> <li>has bacteria that are resistant to oral antibiotics</li> </ul>	
26		<ul> <li>cannot take oral medicines (to explore locally available options</li> </ul>	
27		for giving intravenous antibiotics at home or in the community,	
28		rather than in hospital, where this is appropriate).	

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- 1 To find out why the committee made the recommendations on referral and
- 2 seeking specialist advice, see <u>the rationales</u>.

3	1.2	Choice of antibiotic for treating an acute exacerbation	
4		of bronchiectasis	
5	1.2.1	When prescribing antibiotic treatment for an acute exacerbation of	
6		bronchiectasis:	

- follow table 1 for adults aged 18 years and over
- follow table 2 for children and young people under 18 years.
- 9 1.2.2 Give oral antibiotics first line if the person can take oral medicines,
- and the severity of their condition does not require intravenousantibiotics.
- 12 1.2.3 Review intravenous antibiotics by 48 hours and consider stepping13 down to oral antibiotics where possible.

#### 14 Table 1. Antibiotics for adults aged 18 years and over

Antibiotic <sup>1</sup>	Dosage and course length		
First choice oral antibiotics <sup>2,3</sup>			
Amoxicillin	500 mg three times a day for 7 days then review <sup>4</sup>		
Clarithromycin	500 mg twice a day for 7 days then review <sup>4</sup>		
Erythromycin	500 mg four times a day for 7 days then review <sup>4</sup>		
Doxycycline	200 mg on first day, then 100 mg once a day for a 7-day course in total then review <sup>4</sup>		
Second choice oral antibiotics if severely unwell or higher risk of certain pathogens (guided by susceptibilities when available)			
Amoxicillin high-dose (if severe and colonised with <i>Haemophilus influenzae</i> [beta-lactamase negative])	1 g three times a day or 3 g twice a day for 7 days then review <sup>4</sup>		
Co-amoxiclav (if severe, and <b>not</b> colonised with <i>Pseudomonas aeruginosa</i> )	500/125 mg three times a day for 7 days then review <sup>4</sup>		
Ciprofloxacin (if colonised with <i>Pseudomonas</i> <i>aeruginosa</i> ; higher dose if severe)	500 mg or 750 mg twice a day for 7 days then review <sup>4</sup>		
First choice intravenous antibiotics (if unable to take oral antibiotics or			

severely unwell; guided by specialist advice and susceptibilities when
available) <sup>5</sup>

Ceftriaxone ( <b>not</b> if colonised with <i>Pseudomonas aeruginosa</i> )	2 g once a day		
Co-trimoxazole ( <b>not</b> if colonised with <i>Pseudomonas aeruginosa</i> ) <sup>6</sup>	960 mg to 1,440 mg twice a day		
Ceftazidime	2 g three times a day		
Piperacillin with tazobactam	<ul><li>4.5 g three times a day, increased if necessary to</li><li>4.5 g four times a day</li></ul>		
Ciprofloxacin	400 mg twice or three times a day		
Co-amoxiclav	1.2 g three times a day		
Second choice intravenous antibiotics or combined therapy			

Second choice intravenous antibiotics or combined therapy

Consult local microbiologist; guided by susceptibilities

<sup>1</sup>See <u>BNF</u> for appropriate use and dosing in specific populations, for example, hepatic impairment, renal impairment, pregnancy and breast-feeding.

<sup>2</sup>Empirical treatment or guided by most recent sputum culture and susceptibility.

<sup>3</sup>Amoxicillin or erythromycin are the preferred choices in women who are pregnant.

<sup>4</sup>Review treatment after 7 days and either stop the antibiotic if clinically stable or continue for a further 7 days as appropriate.

<sup>5</sup>Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible for a total antibiotic course of 7 to 14 days.

<sup>6</sup>Co-trimoxazole should only be considered for use in acute exacerbations of bronchiectasis when there is bacteriological evidence of sensitivity and good reason to prefer this combination to a single antibiotic (<u>BNF, June 2018</u>).

#### 1 Table 2. Antibiotics for children and young people under 18 years

Antibiotic <sup>1</sup>	Dosage and course length <sup>2</sup>
First choice oral antibiotics <sup>3,</sup>	4
Amoxicillin	1 to 11 months, 125 mg three times a day for 7 days then review <sup>5</sup>
	1 to 4 years, 250 mg three times a day for 7 days then review <sup>5</sup>
	5 to 17 years, 500 mg three times a day for 7 days then review $^{5}$
Clarithromycin	1 month to 11 years:
	Under 8 kg, 7.5 mg/kg twice a day for 7 days then review <sup>5</sup>
	8 to 11 kg, 62.5 mg twice a day for 7 days then review <sup>5</sup>
	12 to 19 kg, 125 mg twice a day for 7 days then review <sup>5</sup>
	20 to 29 kg, 187.5 mg twice a day for 7 days then review5
	30 to 40 kg, 250 mg twice a day for 7 days then

	review <sup>5</sup>	
	or	
	12 to 17 years, 250 mg to 500 mg twice a day for 7 days then review $^{5}$	
Erythromycin	1 month to 1 year, 125 mg four times a day or 250 mg twice a day for 7 days then review <sup>5</sup>	
	2 to 7 years, 250 mg four times a day or 500 mg twice a day for 7 days then review⁵	
	8 to 17 years, 250 mg to 500 mg four times a day or 500 mg to 1,000 mg twice a day for 7 days then review <sup>5</sup>	
Doxycycline	12 to 17 years, 200 mg on first day, then 100 mg once a day for a 7-day course in total then review <sup>5</sup>	
Second choice oral antibiotic pathogens (guided by susce	cs if severely unwell or higher risk of certain ptibilities when available)	
Amoxicillin high-dose (if severe and colonised with <i>Haemophilus influenzae</i>	1 month to 11 years, 30 mg/kg (maximum 1g per dose) three times a day for 7 days then review <sup>5</sup> 12 to 17 years, 1 g three times a day for 7 days	
[beta-lactamase negative])	then review <sup>5</sup>	
Co-amoxiclav (if severe and <b>not</b> colonised with	1 to 11 months, 0.25 ml/kg of 125/31 suspension three times a day for 7 days then review <sup>5</sup>	
Pseudomonas aeruginosa)	1 to 5 years, 5 ml of 125/31 suspension three times a day or 0.25 ml/kg of 125/31 suspension three times a day for 7 days then review <sup>5</sup>	
	6 to 11 years, 5 ml of 250/62 suspension three times a day or 0.15 ml/kg of 250/62 suspension three times a day for 7 days then review <sup>5</sup>	
	12 to 17 years, 250/125 mg three times a day or 500/125 mg three times a day for 7 days then review <sup>5</sup>	
Ciprofloxacin (on specialist advice if colonised with	1 to 11 years, 20 mg/kg twice daily (maximum 750 mg per dose) for 7 days then review⁵	
<i>Pseudomonas aeruginosa</i> ; higher dose if severe)	12 to 17 years, 500 mg or 750 mg twice a day for 7 days then review⁵	
First choice intravenous antibiotics (if unable to take oral antibiotics or severely unwell; guided by specialist advice and susceptibilities when available) <sup>6</sup>		
Ceftriaxone ( <b>not</b> if colonised with <i>Pseudomonas</i>	1 month to 11 years (up to 50 kg), 50 to 80 mg/kg once a day (maximum 4 g per day)	
aeruginosa)	9 to 11 years (50 kg and above), 1 to 2 g once a day	
	12 to 17 years, 1 to 2 g once a day	
Co-trimoxazole ( <b>not</b> if colonised with <i>Pseudomonas aeruginosa</i> ) <sup>7</sup>	6 weeks to 17 years, 18 mg/kg to 27 mg/kg twice a day (maximum 1440 mg per dose)	
Ceftazidime	From 1 month, 25 to 50 mg/kg three times a day (maximum 6 g per day)	
Piperacillin with tazobactam	1 month to 11 years, 90 mg/kg three or four times	

	a day (maximum per dose 4.5 g four times a day)
	12 to 17 years, 4.5 g three times a day, increased if necessary to 4.5 g four times a day
Ciprofloxacin	1 to 11 years, 10 mg/kg three times a day (maximum 400 mg per dose)
	12 to 17 years, 400 mg twice or three times a day
Co-amoxiclav	1 to 2 months, 30 mg/kg twice a day
	3 months to 17 years, 30 mg/kg three times a day (maximum 1.2 g three times a day)

Second choice intravenous antibiotic or combined therapy

Consult local microbiologist; guided by susceptibilities

<sup>1</sup>See <u>BNF for children</u> for appropriate use and dosing in specific populations, for example hepatic impairment and renal impairment.

<sup>2</sup>The age bands apply to children of average size and, in practice, the prescriber will use the age bands in conjunction with other factors such as the severity of the condition and the child's size in relation to the average size of children of the same age.

<sup>3</sup>Empirical treatment or guided by most recent sputum culture and susceptibility.

<sup>4</sup>Amoxicillin or erythromycin are the preferred choices in young women who are pregnant.

<sup>5</sup>Review treatment after 7 days and either stop the antibiotic if clinically stable or continue for a further 7 days as appropriate.

<sup>6</sup>Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible for a total antibiotic course of 7 to 14 days.

<sup>7</sup>Co-trimoxazole should only be considered for use in acute exacerbations of bronchiectasis when there is bacteriological evidence of sensitivity and good reason to prefer this combination to a single antibiotic (<u>BNF for children, June 2018</u>).

- 1 To find out why the committee made the recommendations on choice and
- 2 duration of antibiotics for managing an acute exacerbation, see the rationales.

1	1.3	Preventing acute exacerbations of bronchiectasis
2		(non-cystic fibrosis)

- 1.3.1 Do not routinely offer antibiotic prophylaxis to prevent acute
   exacerbations of bronchiectasis. Give advice about seeking
   medical help if symptoms of an acute exacerbation develop.
- 6 1.3.2 Only consider antibiotic prophylaxis (see the recommendations on
   7 <u>choice of antibiotic</u>) for adults with repeated acute exacerbations of
   8 bronchiectasis, taking account of evidence that antibiotics can:
- 9 reduce exacerbations

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- increase antimicrobial resistance
  - cause adverse effects, particularly diarrhoea.
- 12 **1.3.3** Before antibiotic prophylaxis is given, give advice about:
- the risk of antimicrobial resistance with long-term antibiotics,
   which may mean fewer effective antibiotics for future
   exacerbations
- possible adverse effects of long-term antibiotics, particularly
   diarrhoea, but also less common cardiac events with macrolide
   antibiotics
- possible interactions of macrolide antibiotics with other
   medicines
  - returning for review after 3 months, or other agreed time.

- 1.3.4 When prescribing antibiotics to prevent acute exacerbations of
   bronchiectasis follow table 3 for adults aged 18 years and over.
- 3 1.3.5 Do not offer nebulised dornase alfa to prevent acute exacerbations
  4 of bronchiectasis.
- 5 1.3.6 Do not offer inhaled corticosteroids (with or without a long-acting
  6 beta2 agonist) for the sole purpose of preventing acute
  7 exacerbations of bronchiectasis.
- 8 To find out why the committee made the recommendations on preventing
- 9 acute exacerbations of bronchiectasis, see the rationales.

#### 10 **1.4** Choice of antibiotic for preventing acute

#### 11 exacerbations

#### 12 Table 3. Antibiotic prophylaxis for adults aged 18 years and over

Antibiotic <sup>1,2</sup>	Dosage and course length <sup>3</sup>		
First choice oral antibiotics <sup>4</sup>	First choice oral antibiotics <sup>4</sup>		
Azithromycin	500 mg three times a week or 250 mg daily		
Clarithromycin	250 mg twice day		
Erythromycin	500 mg twice a day		
<sup>1</sup> See <u>BNF</u> for appropriate use and dosing in specific populations, for example, hepatic impairment, renal impairment, pregnancy and breast-feeding			
<sup>2</sup> Choose antibiotics according to recent sputum culture and susceptibility results where possible. Select a different antibiotic for prophylaxis if treating an acute exacerbation of bronchiectasis.			
<sup>3</sup> Doses given are by mouth using immediate release medicines, unless otherwise stated.			

<sup>4</sup>Erythromycin is the preferred choice in women who are pregnant.

- 13 To find out why the committee made the recommendations on choice of
- 14 antibiotics for preventing acute exacerbations of bronchiectasis, see the
- 15 <u>rationales</u>.

## 1 Terms used in this guideline

#### 2 Acute exacerbation of bronchiectasis

3 An acute exacerbation of bronchiectasis is characterised by an acute

- 4 deterioration of normal symptoms and signs usually over several days. It
- 5 presents with a worsening cough (with increased sputum volume, viscosity, or
- 6 purulence) with or without increased wheeze, breathlessness or haemoptysis;
- 7 and/or fever or pleurisy. The presence of mucopurulent or purulent sputum
- 8 alone without a deterioration in symptoms is not necessarily an acute
- 9 exacerbation (NICE clinical knowledge summary bronchiectasis, British
- 10 Thoracic Society guideline on non-cystic fibrosis bronchiectasis 2010).

### 11 2 Rationales

#### 12 Awareness of acute exacerbation of bronchiectasis

13 Recommendation 1.1.1

#### 14 Why the committee made the recommendations

- 15 Based on experience, the committee agreed that an acute exacerbation is a
- 16 sustained worsening of symptoms from a person's stable state. The
- 17 committee agreed with the definition of an acute exacerbation in the BTS
- 18 guideline on non-cystic fibrosis bronchiectasis 2010.
- 19 Return to the <u>recommendations</u>.

#### 20 Treatment

21 Recommendations 1.1.2 to 1.1.5

#### 22 Why the committee made the recommendations

- 23 Based on consensus, the committee agreed that although in the first instance
- 24 antibiotic treatment will be empirical or based on the most recent sputum
- culture, a new sputum sample should be sent for culture to confirm
- 26 susceptibility of the bacteria. The committee discussed that people with
- 27 bronchiectasis are likely to have previous sputum samples, and because

1 pathogenic bacteria are reasonably static in this population, antibiotics that

2 worked previously are a good starting point to treat new exacerbations.

3 However, pathogenic bacteria can change and a new sputum sample should

- 4 be sent for culture when people present with a new exacerbation of
- 5 bronchiectasis.

6 The committee discussed the limited evidence base for antibiotics for treating 7 an acute exacerbation of bronchiectasis. No evidence was found comparing 8 antibiotics with placebo from systematic reviews or randomised controlled 9 trials from the search, which went back to 2006. The committee was aware of 10 UK guidelines that make recommendations for the antimicrobial treatment of 11 acute exacerbations based on older, heterogeneous, head to head studies 12 comparing different antibiotic regimens (often of intramuscular or intravenous 13 antibiotics in hospitalised patients, which may not reflect current practice) and 14 expert consensus. The committee agreed, based on their experience, that 15 people with an acute exacerbation may benefit from antibiotic treatment, but 16 this should be considered on an individual patient basis, based on the number 17 and severity of their symptoms, their previous exacerbation and hospital 18 admission history, their risk of developing complications, and previous sputum 19 culture and susceptibility results. The committee noted that exacerbations 20 could also be due to a viral infection or environmental factors rather than a 21 bacterial infection.

Based on consensus, the committee agreed that when results of sputum cultures are available, if they suggest the bacteria are not susceptible, the person should be contacted to assess symptoms. However, the antibiotic should only be changed according to susceptibility results if symptoms are not already improving. In line with good antimicrobial stewardship, narrow spectrum antibiotics should be used wherever possible.

The committee agreed that when an antibiotic is given, people should be advised about possible adverse effects and also be given safety netting advice.

31 Return to the <u>recommendations</u>.

#### 1 Reassessment

2 Recommendation 1.1.6

#### 3 Why the committee made the recommendations

- 4 Based on experience, the committee agreed that, for safety netting,
- 5 reassessment was needed if symptoms of the acute exacerbation worsen
- 6 rapidly or significantly at any time.
- 7 Return to the <u>recommendations</u>.

#### 8 **Referral and seeking specialist advice**

9 Recommendation 1.1.7 and 1.1.8

#### 10 Why the committee made the recommendations

- 11 Based on experience, the committee agreed that, for safety netting, people
- 12 with an acute exacerbation of bronchiectasis should be referred to hospital if
- 13 they have cardiorespiratory failure, a severe systemic infection or suspected
- 14 sepsis.
- 15 The committee discussed that some people with resistant bacteria
- 16 (particularly *Pseudomonas aeruginosa*) may need intravenous antibiotics,
- 17 particularly if they are not responding to several courses of oral antibiotics for
- 18 the same episode, or if several sputum samples show resistance to oral
- 19 antibiotics. The committee discussed that specialist advice should be sought
- 20 for people needing intravenous antibiotics, to discuss local options for giving
- 21 intravenous antibiotics at home or in the community, rather than in hospital,
- 22 where this is appropriate for the individual.
- 23 The committee agreed, based on experience, that it may be necessary to use
- 24 alternative antibiotics or combine antibiotics in the care of certain people who
- are severely unwell or have particular pathogens, but this should be done
- according to local policy on the advice of a microbiologist.
- 27 Return to the <u>recommendations</u>.

#### 1 Choice of antibiotic for treating an acute exacerbation of

#### 2 bronchiectasis

3 Recommendations 1.2.1 to 1.2.3 and tables 1 and 2

#### 4 Why the committee made the recommendations

#### 5 Antibiotic choice

- 6 Very limited evidence was identified to guide the choice of antibiotic for
- 7 treating an acute exacerbation of bronchiectasis.
- 8 Based on experience, common pathogens in acute exacerbations, the
- 9 susceptibility of these to various classes of antibiotics, the risks of resistance,
- 10 and good antimicrobial stewardship, the committee agreed the following
- 11 antibiotic choices. Several oral and intravenous antibiotics were
- 12 recommended to enable antibiotics to be selected based on the severity of
- 13 illness and antibiotic susceptibilities from culture results when available.

#### 14 First-choice **oral antibiotics** are:

- **amoxicillin** (a penicillin) at the usual dose of 500 mg three times a day for
- 16 adults (with corresponding usual doses in children), which has good activity
- against common pathogens, such as *Streptococcus pneumoniae* and
- 18 Haemophilus influenzae
- clarithromycin or erythromycin (macrolides; erythromycin is preferred in
   women who are pregnant) at usual doses
- doxycycline (a tetracycline; adults and young people over 12 years only)
   at the usual dose.
- Second-choice oral antibiotics for people who are more severely unwell or are
  at higher risk of certain pathogens (guided by susceptibilities when available)
  are:
- high-dose amoxicillin (1 g three times a day or 3 g twice a day for adults;
- 27 with corresponding doses in children), if severely ill and colonised with
- 28 beta-lactamase negative *Haemophilus influenzae*

co-amoxiclav (500/125 mg three times a day for adults; with
 corresponding doses in children), if severely ill and colonised with
 pathogens other than *Pseudomonas aeruginosa* (this broad-spectrum
 antibiotic combines a penicillin with a beta-lactamase inhibitor, making it
 active against beta-lactamase-producing bacteria that are resistant to
 amoxicillin alone)

- or ciprofloxacin (500 mg or 750 mg twice a day; with corresponding doses
   in children [only on specialist advice because quinolones are generally not
   recommended in children or young people who are growing], a quinolone
   which should be reserved for people colonised with *Pseudomonas aeruginosa* only.
- First-choice intravenous antibiotics at usual doses for treating acute
  exacerbations in people who are severely unwell, not responding to or unable
  to take oral antibiotics (guided by specialist advice and susceptibilities when
  available) are:
- ceftriaxone (a third generation cephalosporin), which is suitable for people
   not colonised with *Pseudomonas aeruginosa*
- co-trimoxazole (trimethoprim plus a sulphonamide), which is suitable for
   people not colonised with *Pseudomonas aeruginosa*
- 20 **ceftazidime** (a third generation cephalosporin)
- piperacillin with tazobactam (an antipseudomonal penicillin with a betalactamase inhibitor)
- 23 ciprofloxacin (a quinolone)
- **co-amoxiclav** (a penicillin with a beta-lactamase inhibitor).
- 25 The committee discussed that some people with resistant bacteria
- 26 (particularly *Pseudomonas aeruginosa*) may need intravenous antibiotics,
- 27 particularly if they are not responding to several courses of oral antibiotics for
- the same episode, or if several sputum samples show resistance to oral
- antibiotics.
- 30 The committee discussed that specialist advice should be sought for people
- 31 needing intravenous antibiotics, to discuss which antibiotics are suitable and

- 1 the local options for giving intravenous antibiotics at home or in the
- 2 community, rather than in hospital, where this is appropriate for the individual.

The committee agreed, based on experience, that it may be necessary to use alternative antibiotics or combine antibiotics in the care of certain people who are severely unwell or have particular pathogens, but this should be done according to local policy on the advice of a microbiologist.

- 7 The committee discussed evidence from a randomised controlled trial which
- 8 showed that adding nebulised tobramycin to oral ciprofloxacin did not improve
- 9 the resolution of exacerbation symptoms, and increased wheeze. The
- 10 committee agreed that combining a nebulised antibiotic with an oral antibiotic
- 11 for the treatment of an acute exacerbation added no additional benefit and
- 12 should not be routinely offered.

#### 13 Antibiotic course length

- 14 Very limited evidence was identified to guide the duration of antibiotics for
- 15 treating an acute exacerbation of bronchiectasis. The 1 RCT identified, which
- 16 compared a nebulised antibiotic plus an oral antibiotic with an oral antibiotic
- 17 alone, used a 14-day course. However, the committee were aware of the
- 18 British Thoracic Society guideline on non-cystic fibrosis bronchiectasis 2010
- 19 which includes older head to head studies comparing different oral,
- 20 intravenous or intramuscular antibiotic regimens, which used 7-day, 10-day or
- 21 14-day courses.
- 22 Based on consensus, the committee agreed that the shortest course that is
- 23 likely to be effective should be prescribed to reduce the risk of antimicrobial
- 24 resistance and minimise the risk of adverse effects.
- 25 The committee agreed that a minimum of a 7-day course of all the
- recommended antibiotics was required to treat an acute exacerbation. At
- 27 7 days, treatment should be reviewed, and either stopped if the person is
- clinically stable or continued for a further 7 days as appropriate.

- 1 Oral antibiotics should be used first-line where possible, in line with the NICE
- 2 guideline on <u>antimicrobial stewardship</u>. The committee discussed that some
- 3 people with resistant bacteria (particularly *Pseudomonas aeruginosa*) may
- 4 need intravenous antibiotics, particularly if they are not responding to several
- 5 courses of oral antibiotics for the same episode, or if several sputum samples
- 6 show resistance to oral antibiotics.
- 7 The committee agreed that the use of intravenous antibiotics should be
- 8 reviewed by 48 hours (taking into account the person's response to treatment
- 9 and susceptibility results from sputum culture) and switched to oral treatment
- 10 where possible. This aligns with the NICE guideline on antimicrobial
- 11 stewardship and <u>Start smart then focus</u>.
- 12 Return to the <u>recommendations</u>.

#### 13 **Preventing acute exacerbations of bronchiectasis (non-cystic**

#### 14 fibrosis) and choice of antibiotic

15 Recommendations 1.3.1 to 1.3.6 and table 3

#### 16 Why the committee made the recommendations

#### 17 **Prophylactic antibiotics**

- 18 The committee discussed the evidence for prophylactic antibiotics. Overall,
- 19 antibiotics reduced exacerbation rates, hospitalisations and the number of
- 20 people with an exacerbation. However, there was a significant increase in
- 21 antibiotic resistance and adverse effects.
- 22 The majority of the studies were in populations who had experienced multiple
- 23 exacerbations in the previous year and the committee thought the findings
- 24 could not be generalised to everyone with bronchiectasis.
- 25 Based on evidence and experience, the committee agreed that all people
- 26 should not routinely be offered antibiotic prophylaxis to prevent acute
- 27 exacerbations, because of the risk/benefit balance in the overall population.
- However, although routine antibiotic prophylaxis is not recommended, this

1 could be considered for adults with repeated exacerbations, where the

2 benefits of prophylaxis may outweigh the risks.

The committee discussed that most evidence was found for oral macrolide antibiotics in adults, where they reduced exacerbation rates and the number of people with an exacerbation. However, they also increased antibiotic resistance and adverse effects. Nebulised or inhaled prophylactic antibiotics had no effect on exacerbations in adults. In 1 small trial of nebulised tobramycin, a non-significant increase in exacerbations, and adverse events such as dyspnoea, chest pain and wheeze were seen.

10 The majority of the studies were in populations who had experienced multiple 11 exacerbations in the previous year. However, the populations had a variety of 12 exacerbation histories with no clear benefit seen in a specific population. The committee felt it was, therefore, difficult to give a precise definition of 13 14 'repeated exacerbations'. Clinical judgement would be needed to define this on an individualised patient basis, taking into account the frequency and 15 16 severity of exacerbations, and the individualised risks and benefits of long-17 term antibiotics.

18 The limited evidence in children and young people found prophylactic oral

19 macrolide antibiotics had no effect on exacerbations but increased

20 antimicrobial resistance, and no recommendation for prophylaxis in children

and young people was made.

22 The committee agreed that before antibiotic prophylaxis is given, people 23 should be advised about the harms of long-term antibiotics. There is an 24 increased risk of resistance with long-term antibiotics, which impacts at both a 25 population and an individual level. People should be advised that this can 26 mean fewer antibiotics may work for their exacerbations in the future. People 27 should also be advised about possible common adverse effects, such as 28 diarrhoea, but also about less common cardiac adverse events. They should 29 also be advised about the potential for macrolide antibiotics, in particular, to 30 interact with other medicines. The committee agreed that anyone being

1 offered antibiotic prophylaxis should return for a review after 3 months, or

2 other agreed time.

3 The committee discussed that the evidence of benefit for antibiotic prophylaxis

- 4 was with oral macrolides (which included azithromycin, clarithromycin,
- 5 erythromycin and roxithromycin [not available in the UK]). They discussed that
- 6 macrolides may have anti-inflammatory or intracellular effects which is why
- 7 they may show benefit over other antimicrobials. Nebulised or inhaled
- 8 antibiotics (not all of which are available in the UK) had no effect on
- 9 exacerbations. However, the evidence base was limited with low patient
- 10 numbers in all studies.
- 11 Based on the evidence, the committee recommended azithromycin (500 mg
- 12 three times a week or 250 mg daily), clarithromycin 250 mg twice day or
- 13 erythromycin 500 mg twice a day where antibiotic prophylaxis was considered
- 14 appropriate. Nebulised or inhaled antibiotics were not recommended.

#### 15 Non-antimicrobial interventions

Evidence showed that nebulised dornase alfa increased exacerbation rates in adults with bronchiectasis, and resulted in more people using antibiotics and steroids. Therefore the committee agreed that nebulised dornase alfa should not be offered to prevent acute exacerbations of bronchiectasis.

- 20 Evidence showed that inhaled corticosteroids (with or without a long-acting
- 21 beta2 agonist) had no effect on acute exacerbations of bronchiectasis in
- 22 adults. Based on experience, the committee also discussed the potential for
- 23 adverse effects with inhaled corticosteroids. Therefore the committee agreed
- 24 that inhaled corticosteroids should not be offered solely to prevent acute
- 25 exacerbations.
- 26 Return to the <u>recommendations</u>.
- 27 See the full evidence review for more information.