

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

NICE guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should [assess and reduce the environmental impact of implementing NICE recommendations](#) wherever possible.

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This guideline replaces ESUOM25, ESUOM38 and ES12.

Overview

This guideline sets out an antimicrobial prescribing strategy for managing and preventing acute exacerbations of bronchiectasis (non-cystic fibrosis). It aims to optimise antibiotic use and reduce antibiotic resistance.

See a [3-page visual summary](#) of the recommendations, including tables to support prescribing decisions.

There is also a [NICE guideline on antimicrobial stewardship: systems and processes for effective antimicrobial medicine use](#).

Who is it for?

- Health professionals
- People with bronchiectasis, their families and carers

Recommendations

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

- 1.1.1 Be aware that an acute exacerbation of bronchiectasis is a sustained worsening of symptoms from a person's stable state.

Treatment

- 1.1.2 Obtain a sputum sample from people with an acute exacerbation of bronchiectasis and send for culture and susceptibility testing.
- 1.1.3 Offer an antibiotic to people with an acute exacerbation of bronchiectasis. When choosing an antibiotic (see the recommendations on choice of antibiotic), take account of:
- the severity of symptoms
 - previous exacerbation and hospital admission history, and the risk of developing complications
 - previous sputum culture and susceptibility results.
- 1.1.4 When results of sputum culture and susceptibility testing are 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).
- 1.1.5 With an antibiotic, give advice about:
- possible adverse effects of antibiotics, particularly diarrhoea

- seeking medical help if symptoms worsen rapidly or significantly at any time, or the person becomes systemically very unwell.

To find out why the committee made the recommendations, see the [rationale section on treatment of an acute exacerbation](#).

Reassessment

1.1.6 Reassess people with an acute exacerbation of bronchiectasis if their symptoms worsen rapidly or significantly at any time, taking account of:

- other possible diagnoses, such as pneumonia
- any symptoms or signs suggesting a more serious illness or condition, such as cardiorespiratory failure or sepsis
- previous antibiotic use, which may have led to resistant bacteria.

To find out why the committee made the recommendation, see the [rationale section on reassessment](#).

Referral and seeking specialist advice

1.1.7 Refer people with an acute exacerbation of bronchiectasis to hospital if they have any symptoms or signs suggesting a more serious illness or condition (for example, cardiorespiratory failure or sepsis).

1.1.8 Seek specialist advice for people with an acute exacerbation of bronchiectasis if they:

- have symptoms that are not improving with repeated courses of antibiotic treatment **or**
- have bacteria that are resistant to oral antibiotics **or**
- cannot take oral medicines (to explore locally available options for giving

intravenous antibiotics at home or in the community, rather than in hospital, where this is appropriate).

To find out why the committee made the recommendations, see the [rationale section on referral and seeking specialist advice](#).

1.2 Choice of antibiotic for treating an acute exacerbation of bronchiectasis

- 1.2.1 When prescribing antibiotic treatment for an acute exacerbation of bronchiectasis:
- follow table 1 for adults aged 18 years and over
 - follow table 2 for children and young people under 18 years.
- 1.2.2 Give oral antibiotics first line if the person can take oral medicines, and the severity of their condition does not require intravenous antibiotics.
- 1.2.3 Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible.

Table 1 Antibiotics for adults aged 18 years and over

Treatment	Antibiotic, dosage and course length
<p>First-choice oral antibiotics for empirical treatment in the absence of current susceptibility data (guided by most recent sputum culture and susceptibilities where possible)</p>	<p>Amoxicillin (preferred choice in pregnancy): 500 mg three times a day for 7 to 14 days</p> <p>Doxycycline: 200 mg on first day, then 100 mg once a day for a 7-day to 14-day course in total</p> <p>Clarithromycin: 500 mg twice a day for 7 to 14 days</p>
<p>Alternative choice oral antibiotics (if person at higher risk of treatment failure) for empirical treatment in the absence of current susceptibility data (guided by most recent sputum culture and susceptibilities where possible)</p>	<p>Co-amoxiclav: 500/125 mg three times a day for 7 to 14 days</p> <p>Levofloxacin(use is off label; with specialist advice if co-amoxiclav cannot be used; consider safety issues): 500 mg once or twice a day for 7 to 14 days</p>
<p>First-choice intravenous antibiotics (if unable to take oral antibiotics or severely unwell) for empirical treatment in the absence of current susceptibility data (guided by most recent sputum culture and susceptibilities where possible)</p>	<p>Co-amoxiclav: 1.2 g three times a day</p> <p>Piperacillin with tazobactam: 4.5 g three times a day, increased if necessary to 4.5 g four times a day</p> <p>Levofloxacin(use is off label; with specialist advice if co-amoxiclav or piperacillin with tazobactam cannot be used; consider safety issues): 500 mg once or twice a day</p>

Treatment	Antibiotic, dosage and course length
When current susceptibility data available, choose antibiotics accordingly	Consult a local microbiologist as needed

See the [BNF](#) for appropriate use and dosing in specific populations, for example, in hepatic impairment, renal impairment, pregnancy and breastfeeding, and when administering intravenous antibiotics.

When a person is having antibiotic prophylaxis, treatment should be with an antibiotic from a different class.

Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics when possible for a total antibiotic course of 7 to 14 days.

Course length should be based on an assessment of the severity of bronchiectasis, exacerbation history, severity of exacerbation symptoms, previous culture and susceptibility results, and response to treatment.

People who may be at higher risk of treatment failure include people who have had repeated courses of antibiotics, a previous sputum culture with resistant or atypical bacteria, or a higher risk of developing complications.

In December 2018, the use of levofloxacin in recommendation 1.2.1 (table 1) was off label. See [NICE's information on prescribing medicines](#).

See the [Medicines and Healthcare products Regulatory Agency advice for restrictions and precautions for using fluoroquinolone antibiotics](#) because of very rare reports of disabling and potentially long-lasting or irreversible side effects affecting musculoskeletal and nervous systems. Warnings include: stopping treatment at first signs of a serious adverse reaction (such as tendonitis), prescribing with special caution in people over 60 years and avoiding co-administration with a corticosteroid (March 2019).

Table 2 Antibiotics for children and young people under 18 years

Treatment	Antibiotic, dosage and course length
First-choice oral antibiotics for empirical treatment in the absence of current susceptibility data (guided by most recent sputum culture and susceptibilities where possible)	Amoxicillin (preferred choice in pregnancy): 1 month to 11 months, 125 mg three times a day for 7 to 14 days 1 year to 4 years, 250 mg three times a day for 7 to 14 days 5 years to 17 years, 500 mg three times a day for 7 to 14 days Clarithromycin: 1 month to 11 years: Under 8 kg, 7.5 mg/kg twice a day for 7 to 14 days 8 kg to 11 kg, 62.5 mg twice a day for 7 to 14 days 12 kg to 19 kg, 125 mg twice a day for 7 to 14 days 20 kg to 29 kg, 187.5 mg twice a day for 7 to 14 days 30 kg to 40 kg, 250 mg twice a day for 7 to 14 days 12 years to 17 years, 250 mg to 500 mg twice a day for 7 to 14 days Doxycycline: 12 years to 17 years, 200 mg on first day, then 100 mg once a day for a 7-day to 14-day course in total

Treatment	Antibiotic, dosage and course length
Alternative choice oral antibiotics (if person at higher risk of treatment failure) for empirical treatment in the absence of current susceptibility data (guided by most recent sputum culture and susceptibilities where possible)	Co-amoxiclav: 1 month to 11 months, 0.25 ml/kg of 125/31 suspension three times a day for 7 to 14 days 1 year 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 to 14 days 6 years 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 to 14 days 12 years to 17 years, 250/125 mg three times a day or 500/125 mg three times a day for 7 to 14 days Ciprofloxacin (with specialist advice if co-amoxiclav cannot be used; consider safety issues): 1 year to 17 years, 20 mg/kg twice a day (maximum 750 mg per dose) for 7 to 14 days

Treatment	Antibiotic, dosage and course length
<p>First-choice intravenous antibiotics (if unable to take oral antibiotics or severely unwell) for empirical treatment in the absence of current susceptibility data (guided by most recent sputum culture and susceptibilities where possible)</p>	<p>Co-amoxiclav:</p> <p>1 month to 2 months, 30 mg/kg twice a day</p> <p>3 months to 17 years, 30 mg/kg three times a day (maximum 1.2 g three times a day)</p> <p>Piperacillin with tazobactam:</p> <p>1 month to 11 years, 90 mg/kg three or four times a day (maximum per dose 4.5 g four times a day)</p> <p>12 years to 17 years, 4.5 g three times a day, increased if necessary to 4.5 g four times a day</p> <p>Ciprofloxacin (with specialist advice if co-amoxiclav or piperacillin with tazobactam cannot be used; consider safety issues):</p> <p>1 year to 17 years, 10 mg/kg three times a day (maximum 400 mg per dose)</p>
<p>When current susceptibility data available, choose antibiotics accordingly</p>	<p>Consult a local microbiologist as needed</p>

See the [BNF for children](#) for appropriate use and dosing in specific populations, for example, in hepatic impairment and renal impairment, and when administering intravenous antibiotics.

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.

When a person is having antibiotic prophylaxis, treatment should be with an antibiotic from a different class.

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.

Course length should be based on an assessment of the severity of bronchiectasis, exacerbation history, severity of exacerbation symptoms, previous culture and susceptibility results, and response to treatment.

People who may be at higher risk of treatment failure include people who have had repeated courses of antibiotics, a previous sputum culture with resistant or atypical bacteria, or a higher risk of developing complications.

See the [Medicines and Healthcare products Regulatory Agency advice for restrictions and precautions for using fluoroquinolone antibiotics](#) because of very rare reports of disabling and potentially long-lasting or irreversible side effects affecting musculoskeletal and nervous systems. Warnings include: stopping treatment at first signs of a serious adverse reaction (such as tendonitis), prescribing with special caution in people over 60 years and avoiding co-administration with a corticosteroid (March 2019).

To find out why the committee made the recommendations, see the [rationale section on choice and duration of antibiotics for managing an acute exacerbation](#).

1.3 Preventing acute exacerbations of bronchiectasis (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.
- 1.3.2 Seek specialist advice about options for preventing exacerbations in people with repeated acute exacerbations, which may include a trial of antibiotic prophylaxis.
- 1.3.3 Only start a trial of antibiotic prophylaxis (with oral or inhaled antibiotics) in

people with repeated acute exacerbations on the advice of a specialist. To ensure shared decision making, discuss the following with the person:

- the potential benefits of antibiotics for reducing exacerbations (taking into account the uncertain evidence of benefit for inhaled antibiotics)
- the risks of antimicrobial resistance with long-term antibiotics, which may mean fewer effective antibiotics for future exacerbations
- the possible adverse effects of long-term antibiotics, such as:
 - diarrhoea, cardiac events, hearing loss or tinnitus with macrolide antibiotics
 - bronchospasm with inhaled antibiotics
- the possible interactions of macrolide antibiotics with other medicines
- the need to regularly review prophylaxis.

To find out why the committee made the recommendations, see the [rationale section on preventing acute exacerbations of bronchiectasis](#).

Terms used in this guideline

Acute exacerbation of bronchiectasis

An acute exacerbation of bronchiectasis is characterised by an acute deterioration of normal symptoms and signs usually over several days. It presents with worsening local symptoms (such as cough, increased sputum volume, change of sputum viscosity, or increased sputum purulence) with or without increased wheeze, breathlessness or haemoptysis. Fever or pleurisy may also be present (British Thoracic Society's 2010 guideline on non-cystic fibrosis bronchiectasis).

Bronchiectasis is defined as persistent or recurrent bronchial sepsis related to irreversibly damaged and dilated bronchi (British Thoracic Society's 2010 guideline on non-cystic fibrosis bronchiectasis).

Rationales

Treatment

Recommendations 1.1.2 to 1.1.5

Why the committee made the recommendations

The committee agreed, based on their experience, that people with an acute exacerbation of bronchiectasis presenting with worsening local symptoms (such as cough, increased sputum volume, change of sputum viscosity or increased sputum purulence) with or without increased wheeze, breathlessness, haemoptysis, fever or pleurisy, should receive an antibiotic. Choice should take account of the severity of their symptoms, their previous exacerbation and hospital admission history, their risk of developing complications, and previous sputum culture and susceptibility results.

The committee discussed the limited evidence base for antibiotics for treating an acute exacerbation of bronchiectasis. No evidence was found comparing antibiotics with placebo from systematic reviews or randomised controlled trials from the search, which went back to 2006. However, the committee were aware of older, heterogeneous, head-to-head studies comparing different antibiotic regimens (which may not reflect current practice).

Based on experience, the committee agreed that although in the first instance, antibiotic treatment for an acute exacerbation may be empirical, a new sputum sample should be sent for culture to confirm susceptibility of the bacteria. The committee discussed that for empirical treatment, antibiotics should be chosen initially based on the most recent sputum culture and susceptibility results. People with bronchiectasis are likely to have previous sputum samples, and because pathogenic bacteria are reasonably static in this population, antibiotics that worked previously are a good starting point to treat new exacerbations. However, pathogenic bacteria can change and a new sputum sample should be sent for culture when people present with a new exacerbation of bronchiectasis, and this new susceptibility data used to review antibiotic choice. The committee discussed the importance of all prescribers having access to microbiology results, with hospital managers ensuring that primary care teams have easy access to microbiology results.

Based on experience, 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.

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Reassessment

[Recommendation 1.1.6](#)

Why the committee made the recommendation

Based on experience, the committee agreed that, for safety netting, reassessment was needed if symptoms of the acute exacerbation worsen rapidly or significantly at any time.

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Referral and seeking specialist advice

[Recommendations 1.1.7 and 1.1.8](#)

Why the committee made the recommendations

Based on experience, the committee agreed that, for safety netting, people with an acute exacerbation of bronchiectasis should be referred to hospital if they have any symptoms or signs suggesting a more serious illness or condition (for example, cardiorespiratory failure or suspected sepsis).

- The committee discussed that some people who are severely ill or have resistant bacteria (particularly *Pseudomonas aeruginosa*) may need intravenous antibiotics, particularly if their symptoms are not responding to several courses of oral antibiotics for the same episode, or if several sputum samples show resistance to oral antibiotics.

The committee discussed that specialist advice should be sought for people needing intravenous antibiotics, to discuss local options for giving intravenous antibiotics at home or in the community, rather than in hospital, if this is appropriate for the person.

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Choice of antibiotic for treating an acute exacerbation of bronchiectasis

[Recommendations 1.2.1 to 1.2.3, and tables 1 and 2](#)

Why the committee made the recommendations

Antibiotic choice

Very limited evidence was identified to guide the choice of antibiotic for treating an acute exacerbation of bronchiectasis. Based on experience, common pathogens in acute exacerbations, the susceptibility of these to various classes of antibiotics, the risks of resistance and good antimicrobial stewardship, the committee agreed the following antibiotic choices for empirical treatment in the absence of current susceptibility data. Choice should be guided by the most recent sputum culture and susceptibilities where possible. Several oral and intravenous antibiotics were recommended to enable antibiotics to be selected based on the severity of illness and previous antibiotic use.

First-choice **oral antibiotics** for empirical treatment are:

- **amoxicillin** (a penicillin), which has good activity against common pathogens, such as *Streptococcus pneumoniae* and *Haemophilus influenzae*
- **clarithromycin** (a macrolide)
- **doxycycline** (a tetracycline; adults and young people over 12 years only).

Alternative choice **oral antibiotics** for empirical treatment for people who are at higher risk of treatment failure (which may include people who have had repeated courses of antibiotics, a previous sputum culture with resistant or atypical bacteria, or people at higher risk of developing complications) are:

- **co-amoxiclav**, a broad-spectrum antibiotic which combines a penicillin with a beta-lactamase inhibitor, making it active against beta-lactamase-producing bacteria that are resistant to amoxicillin alone **or**
- a fluoroquinolone: **levofloxacin** in adults or **ciprofloxacin** in children (only on specialist advice because fluoroquinolones are generally not recommended in children or young people who are growing), which have good activity against atypical bacteria, particularly *Pseudomonas aeruginosa*.

The committee was aware of the [European Medicines Agency's Pharmacovigilance Risk Assessment Committee recommendation to restrict the use of fluoroquinolone antibiotics](#) following a review of disabling and potentially long-lasting side effects mainly involving muscles, tendons and bones and the nervous system (press release October 2018). This includes a recommendation to not use them for mild or moderately severe infections unless other antibiotics cannot be used. The committee discussed that fluoroquinolones are appropriate as an alternative option for people who may be at a higher risk of treatment failure. However, the committee was keen to point out that fluoroquinolone safety concerns should be taken into account on an individual patient basis.

First-choice **intravenous antibiotics** for empirical treatment in people who are unable to take oral antibiotics or are severely unwell are:

- **co-amoxiclav** (a penicillin with a beta-lactamase inhibitor)
- **piperacillin with tazobactam** (an antipseudomonal penicillin with a beta-lactamase inhibitor)
- **levofloxacin** (in adults) or **ciprofloxacin** (in children [on specialist advice only]), which are fluoroquinolones.

When current susceptibility data are available, antibiotics should be chosen and modified accordingly, consulting local microbiologists as needed.

The committee discussed evidence from a randomised controlled trial, which showed that adding nebulised tobramycin to oral ciprofloxacin did not improve the resolution of exacerbation symptoms, and increased wheeze.

Antibiotic course length

Very limited evidence was identified to guide the duration of antibiotics for treating an

acute exacerbation of bronchiectasis. The 1 randomised controlled trial identified, which compared a nebulised antibiotic plus an oral antibiotic with an oral antibiotic alone, used a 14-day course, which is current practice.

Based on experience, the committee agreed that the shortest course that is likely to be effective should be prescribed to reduce the risk of antimicrobial resistance and minimise the risk of adverse effects.

The committee agreed that a course of 7 to 14 days was required to treat an acute exacerbation, based on an assessment of the person's severity of bronchiectasis, their exacerbation history, the severity of their exacerbation symptoms, previous culture and susceptibility results, and response to treatment.

Oral antibiotics should be used first line where possible, in line with the [NICE guideline on antimicrobial stewardship](#).

The committee agreed that the use of intravenous antibiotics should be reviewed by 48 hours (taking into account the person's response to treatment and susceptibility results from sputum culture) and switched to oral treatment where possible. This aligns with the NICE guideline on antimicrobial stewardship and [Public Health England's 'Start smart – then focus' toolkit](#).

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Preventing acute exacerbations of bronchiectasis (non-cystic fibrosis) and choice of antibiotic

[Recommendations 1.3.1 to 1.3.3](#)

Why the committee made the recommendations

Prophylactic antibiotics

The committee discussed the evidence for prophylactic antibiotics. Overall, antibiotics reduced exacerbation rates, hospitalisations and the number of people with an exacerbation. However, there was a significant increase in antibiotic resistance and adverse effects.

Most of the studies were in populations who had experienced multiple exacerbations in the previous year, and the committee thought the findings could not be generalised to everyone with bronchiectasis.

Based on evidence and experience, the committee agreed that people should not routinely be offered antibiotic prophylaxis to prevent acute exacerbations, because of the balance of risks and benefits in the overall population.

For people with repeated exacerbations, where the benefits of prophylaxis may outweigh the risks, specialist advice should be sought on various management options, which may include a trial of antibiotic prophylaxis (with oral or inhaled antibiotics).

The committee noted it was difficult to give a precise definition of 'repeated exacerbations' and clinical judgement would be needed to define this on an individualised patient basis.

The committee agreed that a trial of antibiotic prophylaxis should only be started in people with repeated acute exacerbations on the advice of a specialist, because it is important to consider antibiotic prophylaxis alongside other management options. Shared decision making is important for taking into account the risks and benefits of prophylaxis on an individualised patient basis. This includes discussing the potential benefits of antibiotics for reducing exacerbations, but also the harms of long-term antibiotics. There is an increased risk of resistance with long-term antibiotics, which impacts at both a population and an individual level, and people should be advised that this can mean fewer antibiotics may work for their exacerbations in the future. People should also be advised about possible adverse effects. With macrolides, diarrhoea is common but there are also less common cardiac events, hearing loss and tinnitus, and the potential to interact with other medicines. Bronchospasm is a possible adverse effect with inhaled antibiotics and a challenge test is needed. The committee discussed that people being considered for antibiotic prophylaxis would also need to return for regular review.

The committee discussed that most evidence for prophylactic antibiotics was 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. The limited evidence in children and young people found prophylactic oral macrolide antibiotics did not significantly reduce exacerbations but increased antimicrobial resistance.

- The evidence for nebulised or inhaled antibiotics was particularly limited, and not all products studied are available in the UK. As a class, prophylaxis with nebulised or inhaled antibiotics did not significantly reduce exacerbations in adults. In 1 trial of nebulised colistimethate sodium in people with chronic *Pseudomonas aeruginosa* infection, exacerbations were significantly reduced in an adherent population, but not in the intention-to-treat population, which was the primary end point. In another trial of nebulised tobramycin, a non-significant increase in exacerbations, and adverse events such as dyspnoea, chest pain and wheeze were seen.

The committee were unable to make specific recommendations on the choice of antibiotic for prophylaxis, because this will be an individualised decision based on the clinical needs of the person, their preferences and advice from a specialist.

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See the [full evidence review](#) for a summary of the evidence and more information.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the [NICE topic page on antimicrobial stewardship](#).

For full details of the evidence and the guideline committee's discussions, see the [evidence review](#). You can also find information about [how the guideline was developed](#), including [details of the committee](#).

NICE has produced [tools and resources to help you put this guideline into practice](#). For general help and advice on putting our guidelines into practice, see [resources to help you put NICE guidance into practice](#).

Update information

Minor changes since publication

September 2019: Minor wording changes were made and footnotes were updated in tables 1 and 2 to reflect new restrictions and precautions for the use of fluoroquinolone antibiotics.

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