

# Cough (acute): antimicrobial prescribing

NICE guideline

Published: 7 February 2019

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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 partially replaces CG69.

This guideline is the basis of QS210.

## Overview

This guideline sets out an antimicrobial prescribing strategy for acute cough associated with an upper respiratory tract infection or acute bronchitis in adults, young people and children. It aims to limit antibiotic use and reduce antibiotic resistance.

See a [2-page visual summary](#) of the recommendations, including tables to support prescribing decisions.

For treating coughs associated with other lower respiratory tract infections, see our [topic page on respiratory conditions](#).

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

## Who is it for?

- Healthcare professionals
- People with acute cough, their families and carers

# Recommendations

## 1.1 Managing acute cough

For guidance on managing acute cough in people with suspected or confirmed COVID-19, follow our [rapid guideline on managing COVID-19](#).

1.1.1 Be aware that an [acute cough](#):

- is usually self-limiting and gets better within 3 to 4 weeks without antibiotics
- is most commonly caused by a viral upper respiratory tract infection, such as a cold or flu
- can also be caused by [acute bronchitis](#), a lower respiratory tract infection, which is usually a viral infection but can be bacterial
- can also have other infective or non-infective causes.

1.1.2 For children under 5 with an acute cough and fever, follow the [NICE guideline on fever in under 5s: assessment and initial management](#).

1.1.3 For adults, children and young people with an acute cough and suspected pneumonia, follow:

- our [COVID-19 rapid guideline on managing COVID-19](#) for guidance on pneumonia secondary to COVID-19
- the [NICE guidelines on pneumonia \(community-acquired\): antimicrobial prescribing](#) and [pneumonia \(hospital-acquired\): antimicrobial prescribing](#) for guidance on pneumonia not secondary to COVID-19. **[amended 2021]**

## Referral and seeking specialist advice

1.1.4 Refer people with an acute cough to hospital, or seek specialist advice on further investigation and management, if they have any symptoms or signs suggesting a

more serious illness or condition (for example, sepsis, a pulmonary embolism or lung cancer).

## Treatment

1.1.5 Give general advice to people about:

- the usual course of acute cough (lasts up to 3 or 4 weeks)
- how to manage their symptoms with self-care (see the [recommendations on self-care](#))
- when to seek medical help, for example if symptoms worsen rapidly or significantly, do not improve after 3 to 4 weeks, or the person becomes systemically very unwell.

1.1.6 Do not offer the following treatments to people for an acute cough associated with an upper respiratory tract infection or acute bronchitis unless the person has an underlying airways disease, such as asthma:

- an oral or inhaled bronchodilator (for example, salbutamol) **or**
- an oral or inhaled corticosteroid.

1.1.7 Do not offer a mucolytic (for example acetylcysteine or carbocisteine) to treat an acute cough associated with an upper respiratory tract infection or acute bronchitis.

### Acute cough associated with an upper respiratory tract infection

1.1.8 Do not offer an antibiotic to treat an acute cough associated with an upper respiratory tract infection in people who are not systemically very unwell or at higher risk of complications (see [recommendation 1.1.15](#)). Give advice about why an antibiotic is not needed.

## Acute cough associated with acute bronchitis

- 1.1.9 Do not routinely offer an antibiotic to treat an acute cough associated with acute bronchitis in people who are not systemically very unwell or at higher risk of complications (see [recommendation 1.1.15](#)).
- 1.1.10 Be aware that:
- antibiotics do not improve the overall clinical condition of people with acute bronchitis
  - antibiotics make little difference to how long symptoms of acute bronchitis last (on average they shorten cough duration by about half a day)
  - antibiotics have possible adverse effects, particularly diarrhoea and nausea.
- 1.1.11 This recommendation has been removed.
- 1.1.12 When no antibiotic prescription is given, give advice about why an antibiotic is not needed.
- 1.1.13 If an antibiotic prescription is given, give advice about possible adverse effects of the antibiotic, particularly diarrhoea and nausea.

## Acute cough in people who are systemically very unwell or at higher risk of complications

- 1.1.14 For people with an acute cough who are identified as systemically very unwell (ideally at a face-to-face clinical examination), offer an immediate antibiotic prescription (for choice of antibiotic, see [recommendation 1.3.1](#)).
- 1.1.15 Be aware that people with an acute cough may be at higher risk of complications if they:
- have a pre-existing comorbidity, such as significant heart, lung, renal, liver or neuromuscular disease, immunosuppression or cystic fibrosis
  - are young children who were born prematurely

- are older than 65 years with 2 or more of the following criteria, or older than 80 years with 1 or more of the following criteria:
  - hospitalisation in previous year
  - type 1 or type 2 diabetes
  - history of congestive heart failure
  - current use of oral corticosteroids.

1.1.16 For people with an acute cough who are identified as at higher risk of complications (ideally at a face-to-face clinical examination), consider:

- an immediate antibiotic prescription (for choice of antibiotic, see [recommendation 1.3.1](#)) **or**
- a back-up antibiotic prescription.

1.1.17 When an immediate antibiotic prescription is given, give advice about possible adverse effects of the antibiotic, particularly diarrhoea and nausea.

1.1.18 When a back-up antibiotic prescription is given, give advice about:

- an antibiotic not being needed immediately
- using the back-up prescription if symptoms worsen rapidly or significantly at any time.

## Reassessment

1.1.19 Reassess people with an acute cough if their symptoms worsen rapidly or significantly, taking account of:

- alternative 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.

See the evidence and committee discussion on [bronchodilators](#), [corticosteroids](#), [mucolytics](#), [no antibiotic](#), [back-up antibiotics](#) and [choice of antibiotic](#).

## 1.2 Self-care

1.2.1 Be aware that some people may wish to try the following [self-care treatments](#), which have limited evidence of some benefit for the relief of cough symptoms:

- honey (in people aged over 1 year)
- pelargonium (a herbal medicine; in people aged 12 and over)
- over-the-counter cough medicines containing the expectorant guaifenesin (in people aged 12 and over)
- over-the-counter cough medicines containing cough suppressants, except codeine, (in people aged 12 and over who do not have a persistent cough, such as in asthma, or excessive secretions).

1.2.2 Be aware that limited evidence suggests that antihistamines, decongestants and codeine-containing cough medicines do not help cough symptoms.

See the evidence and committee discussion on [self-care](#).

## 1.3 Choice of antibiotic

1.3.1 When prescribing antibiotics for an acute cough follow:

- table 1 for adults aged 18 years and over
- table 2 for children and young people under 18 years.

**Table 1 Antibiotics for adults aged 18 years and over**

Treatment	Antibiotic, dosage and course length
<b>First choice</b>	<b>Doxycycline:</b> 200 mg on first day, then 100 mg once a day for 4 days (5-day course in total)
<b>Alternative first choices</b>	<b>Amoxicillin:</b> 500 mg three times a day for 5 days <b>Clarithromycin:</b> 250 mg to 500 mg twice a day for 5 days <b>Erythromycin:</b> 250 mg to 500 mg four times a day or 500 mg to 1,000 mg twice a day for 5 days

See the [BNF](#) for appropriate use and dosing in specific populations, for example, hepatic impairment, renal impairment, pregnancy and breast-feeding.

The possibility of pregnancy should be considered in women of childbearing age. Doxycycline should not be used in pregnancy. Amoxicillin is the preferred antibiotic in pregnancy. Erythromycin is preferred if a macrolide is needed in pregnancy, for example, if there is true penicillin allergy and the benefits of antibiotic treatment outweigh the harms. See the [Medicines and Healthcare products Regulatory Agency \(MHRA\) Public Assessment Report on the safety of macrolide antibiotics in pregnancy](#).

**Table 2 Antibiotics for children and young people under 18 years**

Treatment	Antibiotic, dosage and course length
<b>First choice</b>	<b>Amoxicillin:</b> 1 month to 11 months, 125 mg three times a day for 5 days 1 year to 4 years, 250 mg three times a day for 5 days 5 years to 17 years, 500 mg three times a day for 5 days

Treatment	Antibiotic, dosage and course length
<p><b>Alternative first choices</b></p>	<p><b>Clarithromycin:</b></p> <p>1 month to 11 years:</p> <p>Under 8 kg, 7.5 mg/kg twice a day for 5 days</p> <p>8 kg to 11 kg, 62.5 mg twice a day for 5 days</p> <p>12 kg to 19 kg, 125 mg twice a day for 5 days</p> <p>20 kg to 29 kg, 187.5 mg twice a day for 5 days</p> <p>30 kg to 40 kg, 250 mg twice a day for 5 days</p> <p>12 years to 17 years, 250 mg to 500 mg twice a day for 5 days</p> <p><b>Erythromycin:</b></p> <p>1 month to 1 year, 125 mg four times a day or 250 mg twice a day for 5 days</p> <p>2 years to 7 years, 250 mg four times a day or 500 mg twice a day for 5 days</p> <p>8 years to 17 years, 250 mg to 500 mg four times a day or 500 mg to 1,000 mg twice a day for 5 days</p> <p><b>Doxycycline:</b></p> <p>12 years to 17 years, 200 mg on first day, then 100 mg once a day for 4 days (5-day course in total)</p>

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

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.

The possibility of pregnancy should be considered in women of childbearing age. Doxycycline should not be used in pregnancy. Amoxicillin is the preferred antibiotic in pregnancy. Erythromycin is preferred if a macrolide is needed in pregnancy, for example, if there is true penicillin allergy and the benefits of antibiotic treatment outweigh the harms. See the [MHRA Public Assessment Report on the safety of macrolide antibiotics in pregnancy](#).

See the [committee discussion on choice of antibiotic and antibiotic course length](#).

# Terms used in the guideline

## Acute cough

Acute cough is commonly defined as a cough that lasts less than 21 days (3 weeks). The average duration is 18 days, although it can sometimes last for up to 29 days (over 4 weeks). It is most commonly caused by an upper respiratory tract infection, such as a cold or flu, which are viral infections. It can also be caused by acute bronchitis, a lower respiratory tract infection, which is usually a viral infection but can be bacterial.

Other infective causes of cough include COVID-19, pneumonia, acute exacerbations of asthma, chronic obstructive pulmonary disease or bronchiectasis (which may also be non-infective exacerbations), and viral-induced wheeze, bronchiolitis, croup or whooping cough. Non-infective causes may include lung cancer, a foreign body, interstitial lung disease, pneumothorax, pulmonary embolism, heart failure, use of certain medicines (for example, an angiotensin-converting enzyme inhibitor), upper airway cough syndrome (post-nasal drip), or gastro-oesophageal reflux disease. ([NICE clinical knowledge summaries on cough](#), [chest infections – adult](#), [cough – acute with chest signs in children](#) and [Ebell et al. 2013](#)).

## Acute bronchitis

Acute bronchitis is a lower respiratory tract infection with temporary inflammation of the airways (the trachea and major bronchi) that causes cough and mucus production lasting for up to 3 weeks. It is usually caused by a viral infection, but may be caused by a bacterial infection. ([NICE clinical knowledge summary on chest infections – adult](#)).

## Self-care treatments

Self-care treatments available for acute cough include honey, herbal medicines and over-the-counter cough medicines (for example, expectorants and cough suppressants [also called antitussives]).

# Summary of the evidence

## Self-care

### Honey

- Honey significantly reduced the frequency and severity of cough at 1 day follow-up compared with placebo, no treatment or an antihistamine (diphenhydramine) by about 0.5 to 2 points on a carer-reported 7-point Likert scale in children and young people with an acute cough caused by an upper respiratory tract infection (low to moderate quality evidence). Carer responses about cough symptoms ranged from 'extremely' (6 points) to 'not at all' (0 points), but it was not clear how these responses were defined.
- However, honey did not reduce the frequency and severity of cough at 1 day follow-up compared with an antitussive (dextromethorphan; very low quality evidence).
- Honey significantly reduced bothersome cough by about 2 points on a 7-point Likert scale compared with placebo (moderate quality evidence), but not compared with no treatment or dextromethorphan (low quality evidence).
- Honey had no significant effect on children's or parents' sleep quality compared with placebo or dextromethorphan, but was significantly better compared with no treatment or diphenhydramine (by about 0.5 to 1 point on a 7-point Likert scale; low to moderate quality evidence).
- There was no data on the effect of honey on cough duration because follow-up was for 1 day only.
- There was no significant difference in gastrointestinal side effects with honey compared with placebo or dextromethorphan (very low to low quality evidence). There were also no significant differences in mild adverse effects (for example, nervousness, insomnia, hyperactivity and drowsiness) compared with dextromethorphan (very low quality evidence). No significant difference in sleepiness was found when honey was compared with diphenhydramine (very low quality evidence).
- Based on [Oduwole et al. \(2014\)](#), a [systematic review](#) and [meta-analysis](#) including 3 [randomised controlled trials](#) (RCTs) in 568 children and young people (aged 1 to

17 years) with acute cough caused by an upper respiratory tract infection.

- Honey should not be given to children until they are aged over 1 year because of concerns about infant botulism. It is also a sugar, and there are concerns about tooth decay. ([NHS – foods to avoid giving babies and young children](#))

## Herbal medicines

### Andrographis paniculata (A. paniculata)

- A. paniculata (as liquid or tablets) significantly reduced the frequency and severity of cough compared with placebo in people with acute cough as a symptom of upper respiratory tract infection or common cold (frequency: standardised mean difference [SMD]  $-1.00$ , 95% confidence interval [CI]  $-1.85$  to  $-0.15$ ; very low quality evidence; severity: SMD  $-0.57$ , 95% CI  $-1.01$  to  $-0.14$ ; very low quality evidence).
- No safety data for A. paniculata were reported.

Based on Wagner et al. (2015), a systematic review and meta-analysis of 6 RCTs with dosages of 31.5 mg to 200 mg for 3 to 10 days.

### Ivy, primrose or thyme

- Ivy, primrose or thyme as various combined or single preparations (as liquid or tablets) significantly reduced 'cough' (not defined and follow-up time was not reported) compared with placebo in people with an acute cough as a symptom of upper respiratory tract infection or common cold (77.4% versus 54.9%; very low quality evidence).
- No safety data for ivy, primrose or thyme were reported.

Based on Wagner et al. (2015), a systematic review and meta-analysis of 4 RCTs.

### Echinacea

- Echinacea significantly improved 'cough' (not defined) compared with placebo in people with an acute cough as a symptom of an upper respiratory tract infection or common cold (SMD  $-0.68$ , 95% CI  $-1.32$  to  $-0.04$ ; low quality evidence).

- However, this was a meta-analysis of just 2 studies, and the authors reported that most studies in the systematic review did not report any significant reduction in patients' cough symptoms. It is not clear if this was due to the absence of data for this outcome, or the lack of effectiveness for echinacea.
- No safety data for echinacea were reported.

Based on Wagner et al. (2015), a systematic review and meta-analysis including 8 RCTs with dosages of 0.3 g to 6 g daily for 1 to 12 weeks.

## Pelargonium

- *Pelargonium sidoides* (*P. sidoides*, as a liquid) significantly reduced 'failure to resolve all symptoms' by day 7 (61.0% versus 95.3%; very low quality evidence), 'failure to resolve cough' by day 7 (very low quality evidence) and 'failure to resolve sputum' by day 7 (very low quality evidence) compared with placebo in adults with acute bronchitis.
- *P. sidoides* tablets (any dosage) significantly reduced 'failure to resolve all symptoms' by day 7 (92.7% versus 99.0%; low quality evidence) and 'failure to resolve cough' by day 7 (low quality evidence) compared with placebo in adults with acute bronchitis, although, individually, only the 30-mg dose achieved a significant reduction for 'failure to resolve cough' (low quality evidence).
- *P. sidoides* (as a liquid) significantly reduced 'failure to resolve all symptoms' by day 7 (79.9% versus 97.1%; low quality evidence), 'failure to resolve cough' by day 7 (low quality evidence) and 'failure to resolve sputum' by day 7 (very low quality evidence) compared with placebo in children or young people with acute bronchitis.
- *P. sidoides* tablets (any dosage) did not significantly reduce 'failure to resolve all symptoms' by day 7 (low quality evidence) or 'failure to resolve sputum' by day 7 (very low quality evidence) compared with placebo in children or young people with acute bronchitis. Only *P. sidoides* tablets of 20 mg significantly reduced 'failure to resolve cough symptoms' by day 7 (low quality evidence) compared with placebo.
- *P. sidoides* (as a liquid or tablet) significantly increased the number of people (adults, young people and children) with adverse events (19.5% versus 15.1%; very low quality evidence) compared with placebo, which were mainly gastrointestinal. However, there was no significant difference in the number of people with adverse events which led to withdrawal (0.5% versus 1.0%; very low quality evidence).

- Based on 2 systematic reviews and meta-analyses, Wagner et al. (2015) and [Timmer et al. \(2013\)](#), in adults, young people or children with an acute cough or acute bronchitis.

## Non-steroidal anti-inflammatory drugs (NSAIDs)

- NSAIDs (naproxen or ibuprofen) were not significantly different to placebo for a cumulative cough score at follow-up in adults with a common cold (very low quality evidence). NSAIDs significantly reduced associated individual symptoms scores for headache (very low quality evidence), joint and muscle pain (low quality evidence), earache (very low quality evidence) and sneezing (low quality evidence).
- NSAIDs were not significantly different to placebo for overall symptom score, severity of illness, duration of illness, throat irritation or hoarseness, malaise or fatigue, chilliness, nasal irritation, pain on swallowing, eye itching, rhinorrhoea, nasal obstruction or dryness, number of nose blows, total weight of mucous, tissue count, sense of smell or adverse effects in adults with a common cold (very low to low quality evidence).

Based on [Kim et al. \(2015\)](#), a systematic review and meta-analysis of 9 RCTs of NSAIDs in adults with a common cold.

NSAIDs are associated with cardiovascular and gastrointestinal risks ([Drug Safety Update, October 2012](#) and [Drug Safety Update, December 2007](#)).

## Over-the-counter expectorants

- Guaifenesin significantly reduced patient reported cough frequency and intensity compared with placebo in 1 RCT in adults and young people over 12 years with an acute cough or upper respiratory tract infection (75% said guaifenesin was helpful compared with 31% in the placebo group,  $p < 0.01$ ; low quality evidence). There was no significant difference in cough frequency or severity in another RCT, but guaifenesin significantly reduced sputum thickness compared with placebo ( $p = 0.001$ ; low quality evidence). Extended-release guaifenesin reduced symptom severity scores at 4 days ( $p = 0.04$ ) but not at 7 days compared with placebo in 1 RCT (low quality evidence).
- In 2 RCTs reporting adverse events, there was no difference between guaifenesin and placebo (no  $p$  values reported; very low quality evidence).



Based on [Smith et al. \(2014\)](#), a systematic review including 3 RCTs of adults and young people over 12 years with an acute cough or upper respiratory tract infection.

Over-the-counter cough medicines containing the expectorant guaifenesin are subject to MHRA advice on how to use cough and cold medicines safely for children under 12 years ([Drug Safety Update, April 2009](#)).

## Over-the-counter cough suppressants (antitussives)

### Codeine

- Codeine was no more effective than placebo, either as a single dose of 30 mg or in a total daily dose of 120 mg (30 mg four times a day), in reducing cough symptoms in adults with acute cough (low quality evidence). A single dose of codeine (50 mg) was no more effective than placebo in reducing cough symptoms at 90 minutes in adults with acute cough (low quality evidence).
- Codeine as a single dose at bedtime (10 mg in 5 ml plus guaifenesin) for 3 nights was no more effective than placebo in reducing cough score on day 3 in children with acute cough ( $p=0.70$ , low quality evidence).
- No safety data for codeine were reported for adults. In children, adverse effects (mainly drowsiness, diarrhoea and hyperactivity) were not significantly different between codeine and placebo (very low quality evidence).

### Dextromethorphan

- Dextromethorphan (as a single 30-mg dose) was no more effective than placebo for reduction in cough frequency or reduction in cough severity in 1 RCT of adults with acute cough (very low quality evidence). However, in another RCT, a single 30-mg dose of dextromethorphan significantly reduced cough counts (not further defined) in adults (mean changes of cough counts between dextromethorphan and placebo varied from 19% to 36%,  $p<0.05$ ; very low quality evidence). A third RCT found that a single 30-mg dose of dextromethorphan significantly reduced cough bouts (average treatment difference 12% to 17%,  $p=0.004$ ), cough components ( $p=0.003$ ), cough effort ( $p=0.001$ ) and cough latency ( $p=0.002$ ) compared with placebo in adults with acute cough (very low quality evidence).

- Oral dextromethorphan with salbutamol was no more effective than placebo or dextromethorphan alone in reducing cough frequency (very low quality evidence) or daytime cough severity (low quality evidence) in 1 RCT of adults with acute cough. Dextromethorphan with salbutamol was superior to placebo or dextromethorphan alone in relieving cough at night (mean symptom score 0.19 versus 0.67 and 0.44, respectively on day 4,  $p < 0.01$ ; low quality evidence). However, more tremors were reported in the dextromethorphan with salbutamol group than in the placebo group (no figures given,  $p < 0.05$ ; low quality evidence).
- Dextromethorphan was no more effective than placebo (in 4 RCTs) or diphenhydramine (in 1 RCT) in reducing various cough outcomes in children with an acute cough, a night cough or an upper respiratory tract infection (very low quality evidence). In 2 RCTs, there were no differences between the groups in adverse effects, which were generally mild. In another RCT, adverse events (mainly gastrointestinal and dizziness) were reported in 34% of the dextromethorphan group and 5% of the placebo group (p value not reported).

Based on [Smith et al. \(2014\)](#), a systematic review including 11 RCTs of adults, young people and children with an acute cough, with or without a related upper respiratory tract infection.

- Over-the-counter cough medicines containing the cough suppressant dextromethorphan are subject to MHRA advice on how to use cough and cold medicines safely for children under 12 years ([Drug Safety Update, April 2009](#)). Cough medicines containing codeine have restricted use in children ([Drug Safety Update, April 2015](#)).

## Over-the-counter antihistamines and decongestants

- Loratadine in combination with pseudoephedrine for 4 days was no more effective than placebo in reducing a composite cough symptom score in 1 RCT of adults with a common cold (very low quality evidence). Adverse effects (including dry mouth, headache and insomnia) were not significantly different between groups (reported in 30% of the loratadine with pseudoephedrine group compared with 21% of the placebo group; very low quality evidence).
- Clemastine for 3 days was no more effective than placebo or chlorpheniramine in reducing cough scores in 1 RCT of children under 5 years with a common cold (very low quality evidence). Drowsiness and sleepiness was reported in 20% of children,

with no difference between groups (p values not reported).

- Diphenhydramine (as a single dose at night) was no more effective than placebo in reducing composite symptom scores, cough frequency or sleep disturbance in children and their parents in 1 RCT of children and young people aged 2 to 18 years with acute cough due to an upper respiratory tract infection (low quality evidence). No safety data were reported.
- Promethazine for 3 days was no more effective than placebo in reducing a composite cough symptom scores in 1 RCT of children and young people aged 1 to 22 years with acute cough due to an upper respiratory tract infection (low quality evidence). Adverse events were reported in 32% of the promethazine group and 5% of the placebo group (p value not reported; low quality evidence).

Based on 4 RCTs from 1 systematic review ([Smith et al. 2014](#)) in adults, young people and children with cough related to a common cold or upper respiratory tract infection.

Over-the-counter cough medicines containing the antihistamines diphenhydramine and promethazine are subject to MHRA advice on how to use cough and cold medicines safely for children under 12 years ([Drug Safety Update, April 2009](#)).

### **Committee discussion on self-care**

- Overall, the committee recognised that the quality of the evidence on self-care treatments for cough was limited. In many studies it was not clear what outcomes were being measured, or these measures were subjective. The sweet, glycerine-like consistency of many cough remedies, rather than the 'active ingredients' themselves may also have an effect, and the placebo effect of taking something rather than nothing to ease symptoms could be marked. However, promoting the role of self-care may help to reduce the amount of antibiotic prescriptions, and repeated or future consultations in general practice.

### **Honey**

- The committee agreed that there was some evidence that suggests honey reduced cough symptoms in children and young people with an acute cough caused by an upper respiratory tract infection. The clinical significance of the benefit of honey on cough symptoms is unclear, particularly because follow-up was for 1 day only.
- Honey was well tolerated in the studies, and is readily available. However, it should not be given to children under 1 year of age because of concerns about infant botulism. It also contains sugars, and the committee discussed concerns about tooth decay.
- In the studies, honey was given as a single 10-g dose in 1 trial, and 2 trials reported that honey was given before bedtime. A range of types of honey were used, with no studies using the same variety.
- Based on evidence, the committee agreed that that limited evidence suggests that honey may have some benefit on cough symptoms and people over 1 year of age may wish to try this for the treatment of acute cough.

### **Herbal medicines**

- The committee found that the evidence for many of the herbal medicines was limited by poorly defined populations, outcomes, length of follow-up and a lack of safety data or data on adverse outcomes.

- The committee reviewed evidence for several herbal products: *Andrographis paniculata*, ivy, primrose and thyme as a combined product, echinacea, and pelargonium.
- The committee agreed that there was some evidence that suggests ***Andrographis paniculata*** (*A. paniculata*) reduced cough symptoms. However, as the clinical significance of this benefit is unclear, safety data was not available, and no *A. paniculata* product has been granted a traditional herbal registration with the MHRA, the committee agreed that no recommendation on its use for the treatment of acute cough could be made.
- The committee agreed that there was some evidence that suggests **ivy, primrose or thyme** as various combined or single products reduced cough symptoms. However, as the clinical significance of this benefit is unclear and safety data was not available, the committee agreed that no recommendation on the use of these herbal products for the treatment of acute cough could be made. Several combined products containing ivy, primrose or thyme have been granted traditional herbal registrations with the MHRA to relieve coughs and catarrh associated with the common cold based on traditional use only.
- Most studies in a systematic review of **echinacea** did not report a benefit on cough symptoms, and no safety data was available. Therefore, the committee agreed that no recommendation on the use of echinacea for the treatment of acute cough could be made. Numerous echinacea products have been granted traditional herbal registrations with the MHRA to relieve the symptoms of the common cold and influenza type infections based on traditional use only.
- The committee agreed that there was some evidence that suggests **pelargonium** (*Pelargonium sidoides*, *P. sidoides*) reduced cough symptoms in people with acute bronchitis, with a liquid preparation being more beneficial than a tablet preparation. However, *P. sidoides* increased the number of people with adverse events (mainly gastrointestinal). The clinical significance of the benefit of *P. sidoides* on cough symptoms is unclear, and the committee noted that all the RCTs were conducted in Russia or Ukraine and were initiated and funded by a single manufacturing company. However, several *P. sidoides* products have been granted traditional herbal registrations with the MHRA to relieve symptoms of the common cold, sore throat, cough and blocked or runny nose.

- The committee agreed that limited evidence suggests that pelargonium may have some benefit on cough symptoms and people over 12 years may wish to try it for the treatment of acute cough. Because of the limited evidence of benefit, and possible adverse effects, the committee agreed not to recommend pelargonium for children.

### NSAIDs

- Based on evidence, the committee agreed that NSAIDs did not benefit cough symptoms and no recommendation for their use to treat acute cough should be made. Paracetamol or ibuprofen are often used to manage any associated pain.

### Cough expectorant medicines

- The committee agreed that there was some evidence that suggests **guaifenesin** reduced cough symptoms in adults and young people with an acute cough or upper respiratory tract infection, with no increase in adverse effects. The clinical significance of any benefit is unclear, but the committee agreed that people over 12 years may wish to try cough medicines containing guaifenesin for the treatment of acute cough.
- Over-the-counter cough medicines containing the expectorants guaifenesin and ipecacuanha are subject to [MHRA advice](#). They should not be used in children under 6 years of age and are only available in pharmacies for use in children from 6 to 12 years where advice can be given.

### Cough suppressant (antitussive) medicines

- The committee agreed that the evidence for **dextromethorphan** was mixed. There was some evidence that suggests a single, high dose reduced cough symptoms in adults with an acute cough but other evidence that it had no effect, and it may increase adverse effects (mainly gastrointestinal and dizziness). The clinical significance of any benefit it may have is unclear.
- Based on evidence, the committee agreed that **codeine** had no benefit on cough symptoms.

- The systematic review of over-the-counter cough medicines did not include evidence specifically on **pholcodine**. However, the committee recognised that a RCT comparing pholcodine with dextromethorphan is available.
- Taking all the evidence, and their experience, into account the committee agreed that some people over 12 years may wish to try cough medicines containing cough suppressants (apart from codeine) for the treatment of acute cough.
- Over-the-counter cough medicines containing the cough suppressants dextromethorphan and pholcodine are subject to [MHRA advice](#). They should not be used in children under 6 years of age (pholcodine) or 12 years of age (dextromethorphan) and pholcodine is only available in pharmacies for use in children from 6 to 12 years where advice can be given. Over-the-counter cough medicines containing codeine should not be used in children under 12 years and are not recommended for young people under 18 years with breathing problems ([MHRA advice](#)).

#### **Antihistamines and decongestants**

- The committee agreed that, from the limited evidence found, **antihistamines** (loratadine, clemastine, diphenhydramine and promethazine) and **decongestants** (pseudoephedrine) had no benefit on cough symptoms, and increased adverse effects (including drowsiness and dry mouth).
- Over-the-counter cough medicines containing the antihistamines diphenhydramine and promethazine are subject to [MHRA advice](#) on how to use cough and cold medicines safely for children under 12 years.

## **Bronchodilators**

### **Beta-2 agonists**

- Beta-2 agonists (salbutamol syrup) did not significantly reduce the presence of cough at 7 days, or mean cough score at days 1 to 7, compared with placebo in children with acute cough or acute bronchitis (low to moderate quality evidence). There were no significant differences in adverse effects (shaking or tremor or other adverse effects)



between groups (very low quality evidence).

- Beta-2 agonists (salbutamol tablets, salbutamol inhaler or fenoterol inhaler [not available in the UK]) did not significantly reduce the presence of cough at 7 days, productive cough after 7 days, night cough after 7 days, not working by day 7 or mean cough score at days 1 to 7, compared with placebo in adults with acute cough or acute bronchitis (very low to moderate quality evidence).
- There was a significant increase in adverse effects (shaking, tremor or nervousness) in adults with acute cough or acute bronchitis treated with beta-2 agonists compared with placebo or other treatment (55.2% versus 11.3%, number needed to harm [NNH] 2 [range 1 to 3]; very low quality evidence), but not in other adverse effects.
- Beta-2 agonists (salbutamol syrup) were significantly better than erythromycin ethylsuccinate syrup for cough after 7 days (41.2% versus 88.2%; number needed to treat [NNT] 3 [range 2 to 6]; low quality evidence), productive cough after 7 days (35.7% versus 76.5%; NNT 2 [range 2 to 12]; low quality evidence) but not night cough after 7 days (very low quality evidence) in adults with acute cough or acute bronchitis.
- Based on Becker et al. (2015), a systematic review and meta-analysis of 7 RCTs in adults and children with an acute cough or acute bronchitis.

### **Committee discussion on bronchodilators**

- Based on evidence, the committee agreed that bronchodilators, such as oral or inhaled salbutamol, did not benefit cough symptoms and increased adverse events, such as tremor. The committee agreed that there may be instances when people with an acute cough and an underlying airways disease, such as asthma, require bronchodilators. Therefore, they agreed that bronchodilators should not be offered to people (adults or children) with an acute cough unless they had underlying airways disease, such as asthma.
- The committee discussed the evidence for oral salbutamol plus dextromethorphan but no recommendation was made because no such product is available in the UK.



## Corticosteroids

### Inhaled corticosteroids

- Inhaled corticosteroids (fluticasone proprionate) significantly reduced the mean cough score at the end of the second week of treatment compared with placebo in adults with acute or subacute cough following respiratory tract infection (mean difference [MD]  $-0.50$ , 95% CI  $-0.55$  to  $-0.45$ ; very low quality evidence) but not at 4 weeks.
- Inhaled corticosteroids (fluticasone proprionate) significantly reduced the mean cough score by at least 50% reduction at the end the second week in non-smoking adults with acute or subacute respiratory tract infection compared with placebo (53.5% versus 80.5%; NNT 4 [range 3 to 13]; very low quality evidence). The mean difference in the average daily cough score in the second week in non-smoking adults was  $-0.9$  (95% CI  $-1.3$  to  $-0.4$ ; very low quality evidence). There was no difference in smokers. One RCT found that additional treatment sought after 2 weeks of study treatment was significantly lower with fluticasone proprionate compared with placebo (43.1% versus 62.7%, NNT 6 [range 3 to 35]; very low quality evidence).
- There were no significant differences found for mean symptom scores (cough, cough frequency, symptoms associated with cough, night-time cough or the frequency of taking cough medicines), and the outcomes of little or no improvement at 7 to 14 days, severe symptoms at 11 days, and adverse effects (hoarseness) during the treatment period (very low quality evidence).

Based on [El-Gohary et al. \(2013\)](#), a systematic review of 4 RCTs in adults with an acute or subacute respiratory tract infection.

Systemic effects (mineralocorticoid and glucocorticoid) may occur with inhaled corticosteroids, including a range of psychological or behavioural effects (particularly in children; [Drug Safety Update, September 2010](#)).

### Committee discussion on corticosteroids

- The committee agreed that the evidence for inhaled corticosteroids was mixed. There was some evidence that it reduced cough symptoms in adults with an acute or subacute cough (particularly in non-smokers) but other evidence that it had no effect. No evidence for oral corticosteroids was found.
- Corticosteroids have well-recognised systemic (mineralocorticoid and glucocorticoid) effects, including a range of psychological or behavioural effects (particularly in children) and the committee agreed that, weighing up the potential risks and benefits, oral or inhaled corticosteroids should not be offered for people (adults or children) with an acute cough (including acute bronchitis).
- The committee discussed the evidence that inhaled corticosteroids reduced additional treatments being sought, and they could reduce the prescribing of antibiotics for acute cough. However, any prescribed alternatives to antibiotics have workload implications as people are likely to re-consult and expect similar treatments in the future, sending the wrong message that prescribed treatment is needed for a largely self-limiting condition.
- The committee agreed that there may be instances when people with an acute cough and an underlying airways disease, such as asthma, require corticosteroids. Therefore, they agreed that an oral or inhaled corticosteroid should not be offered to people (adults or children) with an acute cough unless they had an underlying airways disease, such as asthma.

## Mucolytics

- Mucolytics (oral acetylcysteine and oral carbocysteine) were significantly better than placebo for reducing cough at 6 to 7 days in children with acute upper and lower respiratory tract infection (4.1% versus 13.8%; very low quality evidence), but not at the end of treatment (28 days; very low quality evidence).
- There were no significant differences between mucolytics and placebo for the outcomes of productive cough and expectoration at end of treatment (at 7 days), pulmonary function at day 3, febrile state at 6 days, dyspnoea at 6 to 7 days, bad general condition after 6 to 7 days, and appetite trouble (not defined) at the end of

treatment (5 to 9 days) in children with acute upper and lower respiratory tract infection (very low quality evidence). There was also no significant difference for the outcome of abnormal chest signs (for example wheezing or rattling) after 5 days, but there was a significant difference for this outcome at the end of treatment (28 days; 2% versus 16%; very low quality evidence).

Based on [Chalumeau and Duijvestijn \(2013\)](#), a systematic review and meta-analysis of 6 RCTs in children with acute upper and lower respiratory tract infections.

### **Committee discussion on mucolytics**

- The committee agreed that the evidence for mucolytics (acetylcysteine and carbocysteine) was mixed. There was some evidence that a mucolytic reduced cough symptoms in children with acute upper and lower respiratory tract infections but other evidence that it had no effect.
- The clinical significance of any benefit of mucolytics is unclear, and the committee agreed that they should not be offered for people (adults or children) with an acute cough. Any prescribed alternatives to antibiotics have workload implications as people are likely to re-consult and expect similar treatments in the future, sending the wrong message that prescribed treatment is needed for a largely self-limiting condition.

## **No antibiotic**

- Acute cough associated with an upper respiratory tract infection or acute bronchitis is usually a self-limiting infection caused by a viral infection. Most upper respiratory tract infections, such as a common cold or flu, are viral. Acute bronchitis has been estimated to be viral in 85% to 95% of cases, although this is difficult to estimate. ([NICE clinical knowledge summary on chest infections – adult and Worrall, 2008](#)).

## **Efficacy of antibiotics**

### **Antibiotics for clinical improvement in acute bronchitis**

- Antibiotics (doxycycline, co-trimoxazole, erythromycin, cefuroxime, azithromycin,

amoxicillin and co-amoxiclav) were not significantly better than placebo (or no active treatment) for clinical improvement at follow-up in people with acute bronchitis (11 RCTs, n=3,841, 73.2% versus 66.5%; low quality evidence). Clinical improvement was measured by a global assessment of improvement by clinicians at follow-up.

- In subgroup analysis by antibiotic, there was no significant difference in clinical improvement between doxycycline and placebo (3 RCTs), erythromycin and placebo (2 RCTs) or amoxicillin and placebo (2 RCTs; low to moderate quality evidence). However, cefuroxime significantly increased clinical improvement at follow-up in adults with acute bronchitis compared with placebo (1 RCT, n=343, 92.4% versus 79.1%; low quality evidence).
- Antibiotics (erythromycin, cefuroxime, doxycycline or co-amoxiclav) did not significantly reduce the number of adults and children with acute bronchitis without improvement at physician follow-up compared with placebo (very low quality evidence). When a subgroup of people with non-purulent tracheo-bronchitis from an upper respiratory tract infection study was omitted, antibiotics were significantly better than placebo (5 RCTs, n=816, 7.7% versus 17.6%; NNT 11 [7 to 19]; moderate quality evidence). However, only 1 RCT in this analysis of cefuroxime versus placebo (accounting for 35.5% of the weight in the meta-analysis) showed a significant improvement compared with placebo.
- Antibiotics (erythromycin, cefuroxime or doxycycline) were significantly better than placebo for improving abnormal lung examination at follow-up in adults with acute bronchitis (5 RCTs, n=613, 18.5% versus 34.8%, NNT 7 [5 to 11]; moderate quality evidence). However, only 1 RCT in this analysis of cefuroxime versus placebo (accounting for 77.8% of the weight) had a significant reduction for this outcome in the antibiotic group.
- Antibiotics (erythromycin, doxycycline or amoxicillin) significantly reduced the mean number of days feeling ill compared with placebo or no active treatment in adults and children with acute bronchitis (5 RCTs, n=809; moderate quality evidence). However, the significant effect was not maintained when a study of antibiotics compared with no active treatment (no placebo) was omitted. A subgroup analysis of RCTs of doxycycline versus placebo showed a significant reduction in the mean number of days feeling ill by about half a day compared with placebo (3 RCTs, n=383; high quality evidence).

## Antibiotics for reduction of cough in acute bronchitis

- Antibiotics (erythromycin or doxycycline) significantly reduced cough at follow-up in adults with acute bronchitis compared with placebo (4 RCTs, n=275, 32.9% versus 50.8%, NNT 6 [4 to 16]; moderate quality evidence). This significant reduction was seen in a subgroup of RCTs of doxycycline compared with placebo (2 RCTs, n=210, 22.9% versus 42.6%, NNT 6 [4 to 14]; moderate quality evidence) but not erythromycin compared with placebo (low quality evidence).
- Antibiotics (erythromycin, cefuroxime or doxycycline) significantly reduced night cough at follow-up in adults with acute bronchitis compared with placebo (4 RCTs, n=538, 29.5% versus 44.6%, NNT 7 [5 to 15]; low quality evidence). This significant reduction was seen in a subgroup analysis of cefuroxime compared with placebo (1 RCT, n=340, 36.8% versus 56.8%; low quality evidence) but not for erythromycin or doxycycline compared with placebo (low quality evidence). Antibiotics did not make any significant difference to the presence of productive cough at follow-up in adults and children with acute bronchitis (moderate quality evidence).

## Antibiotics for duration of cough in acute bronchitis

- Antibiotics (erythromycin, amoxicillin or doxycycline) significantly reduced the mean number of days of cough in adults and children with acute bronchitis compared with placebo or no active treatment by about half a day (7 RCTs, n=2,776; moderate quality evidence). This significant reduction was also seen in studies that compared antibiotics with placebo only (6 RCTs, n=2,350; moderate quality evidence). No significant differences were found for individual antibiotics in subgroup analyses.
- Antibiotics made no significant difference to the mean number of days of productive cough in adults and children with acute bronchitis compared with placebo or no active treatment. When a subgroup of people with non-purulent tracheo-bronchitis from an upper respiratory tract infection study was omitted, antibiotics did significantly reduce the mean number of days of productive cough by about half a day (5 RCTs, n=535; moderate quality evidence). The significant difference was maintained in a subgroup of studies comparing doxycycline with placebo (4 RCTs, n=444; moderate quality evidence) but not in 2 RCTs of amoxicillin or erythromycin compared with placebo or no treatment (moderate quality evidence).

## **Antibiotics for moist cough of greater than 10 days duration in children**

- Antibiotics (erythromycin or co-amoxiclav) significantly reduced the number of children with clinical failure (not cured or substantially improved) at follow-up in children with prolonged moist cough compared with placebo or no treatment (2 RCTs, n=140, 34.3% versus 72.6%, NNT 3 [2 to 5]; moderate quality evidence). However, this became non-significant when children with *Bordetella pertussis* were excluded and in an intention-to-treat analysis using those not lost to follow-up (very low quality evidence). Antibiotics significantly reduced the need for additional treatment due to illness compared with placebo or no treatment (2 RCTs, n=125, 5.1% versus 36.4%, NNT 4 [3 to 6]; moderate quality evidence).

## **Antibiotics for preventing suppurative complications from undifferentiated upper respiratory tract infections**

- Antibiotics (co-amoxiclav) had no significant effect on the development of acute otitis media in children with undifferentiated acute respiratory tract infection compared with placebo or no treatment (3 RCTs; very low quality evidence), or in a subgroup of children from high-income countries (2 RCTs; very low quality evidence). Antibiotics (ampicillin) had no significant effect on the development of pneumonia in children aged under 11 months or those aged 12 to 58 months with undifferentiated acute respiratory infection compared with placebo or no treatment (1 RCT; very low quality evidence).

## **Antibiotics for subgroups in acute lower respiratory tract infection**

- In 1 RCT in adults with an acute cough, for the outcome of resolution of symptoms rated moderately bad or worse, no pre-specified subgroup (green sputum, current smokers, significant past medical history, people with symptoms for longer than 7 days at baseline, fever at baseline or minor chest signs) was significantly more likely to benefit from antibiotics (amoxicillin). People with significant past medical history compared with those without significant past medical history (n=438, MD -0.28, 95% CI -0.46 to -0.09; very low quality evidence) had a significantly lower mean symptom severity score on days 2 to 4 after consultation. People with symptoms for less than 7 days at baseline compared with those who had symptoms for more than 7 days at baseline had a significantly lower mean symptom severity score on days 2 to 4 after consultation (n=711, MD -0.16, 95% CI -0.27 to -0.06; very low quality evidence). Non-current smokers compared with current smokers had a significantly lower mean

symptom severity score on days 2 to 4 after consultation (n=483, MD -0.12, 95% CI -0.22 to -0.03; very low quality evidence). No subgroups were identified that were significantly more likely to develop new or worsening symptoms.

## Safety of antibiotics

- Antibiotic-associated diarrhoea is estimated to occur in 2% to 25% of people taking antibiotics, depending on the antibiotic used ([NICE clinical knowledge summary on diarrhoea – antibiotic associated](#)).
- About 10% of the general population claim to have a penicillin allergy; this has often been because of a skin rash that occurred during a course of penicillin in childhood. Fewer than 10% of people who think they are allergic to penicillin are truly allergic. See the [NICE guideline on drug allergy: diagnosis and management](#) for more information.
- People with a history of immediate hypersensitivity to penicillins may also react to cephalosporins and other beta-lactam antibiotics ([BNF, December 2018](#)).
- Macrolides should be used with caution in people with a predisposition to QT interval prolongation. Nausea, vomiting, abdominal discomfort, and diarrhoea are the most common side effects of macrolides. These are less frequent with clarithromycin than with erythromycin ([BNF, December 2018](#)).
- Tetracyclines, including doxycycline, can deposit in growing bone and teeth causing staining and occasionally dental hypoplasia. Their use is cautioned in children under 12 years, for use only in acute, severe or life-threatening infections when there are no adequate alternatives, and they should not be given to pregnant or breast-feeding women. Common side effects include nausea, vomiting, diarrhoea, dysphagia, and oesophageal irritation ([BNF, December 2018](#)).
- See the [summaries of product characteristics](#) for information on contraindications, cautions and adverse effects of individual medicines.
- Antibiotics significantly increased the overall number of adverse effects compared with placebo or no active treatment in people with acute bronchitis (12 RCTs, n=3,496, 22.6% versus 18.7%, NNH 25 [range 15 to 84]; low quality evidence). The most commonly reported adverse effects included gastrointestinal symptoms such as nausea, vomiting, or diarrhoea. There were no significant differences in adverse effects for subgroups of different antibiotics (erythromycin, amoxicillin or co-amoxiclav, or doxycycline) versus placebo or no active treatment (very low to low



quality evidence).

- There were no significant differences between antibiotics and placebo or no treatment for adverse effects (vomiting, rash or diarrhoea) in children with moist cough for longer than 10 days duration.

Based on 3 systematic reviews and meta-analyses, Smith et al. (2017) which included adults and children with acute bronchitis from 17 RCTs, Marchant et al. (2005) which included children with a moist cough lasting longer than 10 days from 2 RCTs and [Alves et al. \(2016\)](#) which included children with undifferentiated acute respiratory infection from 4 RCTs; and 1 RCT in adults with an acute cough ([Moore et al. 2014](#)).

## Back-up antibiotics

- Two RCTs included in a systematic review of adults and children with acute cough did not report data for back-up versus immediate antibiotics. However, the systematic review states that there was no difference in reported clinical outcomes.
- One RCT included in a systematic review compared a back-up antibiotic prescription (either at the time of visit or requiring collection) with immediate antibiotics and a no antibiotic prescribing strategy in adults with acute cough. A back-up antibiotic prescription was not significantly different to an immediate antibiotic or no antibiotic for the outcomes of cough duration, pain duration or fever duration (low quality evidence).

Based on Spurling et al. (2017), a systematic review and meta-analysis of 11 RCTs of back-up antibiotic prescriptions for respiratory infections (including acute otitis media, pharyngitis, sore throat, common cold and other respiratory tract infections) in adults and children, 3 RCTs were in an acute cough population.



## **Committee discussion on no antibiotics, back-up antibiotics and immediate antibiotics**

- The committee discussed that acute cough, either associated with an upper respiratory tract infection or acute bronchitis, is usually a self-limiting infection. It is often a viral infection, and antibiotics are not usually needed.

### **Acute cough associated with an upper respiratory tract infection**

- No evidence was found for antibiotics to treat an acute cough specifically associated with an upper respiratory tract infection, which is usually a viral infection. Based on the lack of evidence and experience, the committee agreed that antibiotics should not be offered to people (adults or children) with an acute cough associated with an upper respiratory tract infection. People should be given advice that an acute cough can last up to 3 or 4 weeks and does not need an antibiotic. They should also be given safety netting advice to seek medical help if symptoms worsen rapidly or significantly, do not improve after 3 or 4 weeks, or they become systemically very unwell.

### **Acute cough associated with acute bronchitis**

- Based on evidence and experience, the committee agreed that antibiotics should not routinely be offered to people (adults or children) with an acute cough associated with acute bronchitis. Antibiotics had a beneficial effect on some outcomes, but not others, and any benefit from antibiotics needs to be weighed up against their potential to cause adverse effects. Even where statistically significant effects were seen, these were often difficult to interpret and may not be clinically meaningful for many people.
- Antibiotics did not improve the overall clinical condition of people with acute bronchitis, or the number of people with improvement at physician follow-up. Antibiotics did improve abnormal lung examination at follow-up, but the committee agreed this was not an important patient-orientated outcome for people with acute bronchitis, and this outcome was heavily influenced by 1 study of cefuroxime.
- Antibiotics reduced the number of people who had 'any cough' or 'night cough' at follow-up, with a number needed to treat of 6 or 7. However, the timing of follow-

up is unclear, varying between studies from 2 to 18 days after treatment started.

- Antibiotics made little difference to how long the symptoms of acute bronchitis lasted. They reduced the mean number of days of cough by about 0.5 days (range 0 to 1 day), which the committee agreed may not be clinically meaningful for many people when an acute cough lasts up to 3 or 4 weeks.
- Antibiotics have possible adverse effects, particularly diarrhoea and nausea. In people with acute bronchitis, antibiotics increased adverse effects, with a NNH of 25.
- Based on experience, the committee discussed that withholding antibiotics in acute cough is unlikely to lead to complications in people who are not systemically very unwell or at higher risk of complications. However, they acknowledged the limited evidence base, which was solely for no increased risk of acute otitis media or pneumonia in children with acute undifferentiated respiratory tract infection.
- The committee recognised the usefulness of back-up antibiotic prescriptions in managing self-limiting illnesses. However, from the evidence, back-up antibiotics were not significantly different to immediate antibiotics or no antibiotics for how long a cough lasts.
- Based on evidence, experience and the principles of antimicrobial stewardship, the committee recommended a no antibiotic prescribing strategy (routinely) for people with acute cough associated with acute bronchitis. They recognised that antibiotics may be an option for some people on an individual patient basis, but this should not be routine practice. For most people with an acute cough (which is a condition that can persist for some weeks) they felt a back-up antibiotic prescribing strategy sent the wrong message that antibiotics may be needed at some point.

#### **Acute cough in people who are systemically very unwell or at higher risk of complications**

- Based on evidence and experience, the committee agreed that an immediate antibiotic prescription should be offered to people (adults or children) with an

acute cough (associated with an upper respiratory tract infection or acute bronchitis) who are identified as systemically very unwell (ideally at a face-to-face clinical examination), because these people require prompt treatment with an antibiotic.

- Based on evidence and experience, the committee agreed that an immediate antibiotic prescription or a back-up antibiotic prescription could be considered for people with an acute cough (associated with an upper respiratory tract infection or acute bronchitis) who are identified as at higher risk of complications (ideally at a face-to-face clinical examination).
- The committee recognised that the previous NICE guideline on upper respiratory tract infections noted that people with acute cough are likely to be at higher risk of developing complications because of pre-existing comorbidity (significant heart, lung, renal, liver or neuromuscular disease, immunosuppression, cystic fibrosis, and young children who were born prematurely) or because of older age and the presence of certain criteria (type 1 or type 2 diabetes, congestive heart failure, use of oral corticosteroids, hospitalisation in previous year). The committee agreed that for some of these people an immediate antibiotic may not be clinically required, and a back-up antibiotic could be considered.
- The committee recommended that ideally antibiotics should only be considered after people have been assessed face-to-face but this may not always be possible.
- The committee agreed that a back-up antibiotic prescription could be used if symptoms worsen rapidly or significantly at any time. Giving safety netting advice is also important to ensure people seek medical help if symptoms worsen rapidly or significantly despite taking the antibiotic, or they become systemically very unwell.
- Based on experience, the committee agreed that people with acute cough who present with any symptoms or signs suggesting a more serious illness or condition (for example, sepsis, a pulmonary embolism or lung cancer) should be referred to hospital, or specialist advice should be sought on further investigation and management.

### **Antibiotics for moist cough of greater than 10 days duration in children**

The committee discussed the evidence for antibiotics reducing clinical failure in children with a prolonged moist cough. However, they noted the limitations with this evidence base and did not make a recommendation specifically for this population. Many children had a cough for over 3 weeks at baseline, and therefore did not have an acute cough. Also, there was no benefit of antibiotics when children with *Bordetella pertussis* were excluded (9% of all children), and in an intention-to-treat analysis using those not lost to follow-up.

## **Choice of antibiotic**

- No systematic reviews and RCTs met the inclusion criteria for this section.

### Committee discussion on choice of antibiotic

- There was no evidence directly comparing different antibiotics. However, subgroup analysis from a systematic review in people with acute bronchitis did find some differences between antibiotics compared with placebo.
- Individually, doxycycline compared with placebo showed a significant reduction in the following outcomes: mean number of days feeling ill, cough at follow-up and mean number of days of productive cough, where other antibiotics (amoxicillin and erythromycin) did not.
- Individually, cefuroxime also showed benefit over placebo for the following outcomes: clinical improvement at follow-up, improvement at physician follow-up and night cough at follow-up, where other antibiotics did not. This was based on a trial of over 300 people, which contributed much of the weight in meta-analyses. The committee discussed this finding and had some concerns that the study design of the cefuroxime study in particular influenced this result.
- Cefuroxime is a broad-spectrum antibiotic (a second generation cephalosporin). The committee discussed that, if an antibiotic is needed to treat an infection that is not life-threatening, a narrow-spectrum antibiotic should generally be first choice. Indiscriminate use of broad-spectrum antibiotics creates a selective advantage for bacteria resistant even to these 'last-line' broad-spectrum agents, and also kills normal commensal flora leaving people susceptible to antibiotic-resistant harmful bacteria such as *Clostridium difficile*.
- Based on evidence, their experience and resistance data, the committee agreed to recommend **doxycycline** at usual dose, as the first-choice antibiotic for adults with acute cough (including acute bronchitis), where an antibiotic is appropriate. This is a tetracycline, which is only suitable for non-pregnant adults and, for acute cough, in young people over 12 years. Doxycycline was preferred over amoxicillin because there was limited evidence from subgroup analyses that showed benefits on some outcomes where amoxicillin did not. But more importantly, they agreed that amoxicillin should be reserved, when possible, for use in more serious infections where bacterial infection is more common, for example pneumonia. This is because of concerns that amoxicillin drives resistance not just in pneumococci but also in gram-negative organisms. The committee was aware of evidence that the risk of resistance to amoxicillin is significantly increased in urinary isolates of

*Escherichia coli* following a course of amoxicillin. These effects are greatest in the first month after use, but are detectable for up to 12 months. There is a concern that using amoxicillin in conditions such as acute cough, where the benefits of antibiotics are marginal, drives resistance without adding benefit.

- Alternative first-choice antibiotics (at usual doses) for adults unable to take doxycycline, which have good activity against common causal bacteria, are:
  - **amoxicillin** (a penicillin)
  - **clarithromycin** or **erythromycin**, which are macrolides.
- The committee agreed that because the evidence of benefit of doxycycline over amoxicillin, clarithromycin or erythromycin is limited, these antibiotics should be offered as alternative first choices. This also reflects concerns that doxycycline is contraindicated in pregnancy, and this should be considered when choosing antibiotics for women of childbearing age.
- The committee also discussed the [MHRA Public Assessment Report on the safety of macrolide antibiotics in pregnancy](#). This found that the available evidence is insufficient to confirm with certainty whether there is a small increased risk of birth defects or miscarriage when macrolides are taken in early pregnancy. They agreed with the [UK Teratology Information Service monograph on the use of macrolides in pregnancy](#). They decided that there should be an informed discussion of the potential benefits and harms of treatment. Then, after such a discussion, macrolides can be used if there is a compelling clinical need and there are no suitable alternatives with adequate pregnancy safety data. Erythromycin is the preferred choice if a macrolide is needed during pregnancy, for example, if there is true penicillin allergy and the benefits of antibiotic treatment outweigh the harms. This is because there is more documented experience of its use than for other macrolides.
- For children and young people, **amoxicillin** is recommended as the first-choice antibiotic, with **clarithromycin**, **erythromycin** or **doxycycline** (in young people aged 12 to 17 years only) as alternative choices.

## Antibiotic course length

- No systematic reviews and RCTs met the inclusion criteria for this section.

### Committee discussion on antibiotic course length

- There was no evidence directly comparing different antibiotic course lengths. From a systematic review in people with acute bronchitis, antibiotic course length varied from 5 to 10 days typically depending on the antibiotics used.
- The committee agreed that, when an antibiotic is appropriate, the shortest course that is likely to be effective should be prescribed.
- Based on evidence, their experience and resistance data, the committee agreed that a 5-day course for all the recommended antibiotics was sufficient to treat acute cough, where an antibiotic was appropriate. This takes into account the overall efficacy and safety evidence for antibiotics, and minimises the risk of resistance. Studies in the evidence review for specific antibiotics in acute bronchitis sometimes had course lengths of more than 5 days.

## Other considerations

### Medicines adherence

- Medicines adherence may be a problem for some people taking medicines that need frequent dosing or longer treatment duration (for example, antibiotics). See the [NICE guideline on medicines adherence](#).

### Resource implications

- Respiratory tract infections, including acute cough, are a common reason for consultations in primary care and for potential antibiotic prescribing. In a 2011 survey of UK primary care ([Gulliford et al. 2014](#)), consultations for 'cough and bronchitis' accounted for 39% of all consultations for respiratory tract infections, and the median practice issued an antibiotic prescription in 48% of these.
- There is potential for resource savings if a no antibiotic or a back-up antibiotic prescription strategy is used. One systematic review ([Spurling et al. 2017](#)) found significantly lower antibiotic use with a back-up antibiotic prescribing strategy compared with immediate antibiotics, both when the back-up antibiotic prescription was given at the time of consultation (38.4% versus 86.8%; very low quality evidence) and when the prescription had to be collected on a separate visit (27.3% versus 95.3%; very low quality evidence).
- Recommended antibiotics are all available as generic formulations, see [Drug Tariff](#) for costs.



## Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the [NICE topic pages on respiratory conditions](#) and [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

**January 2022:** We made minor wording changes to reflect updated advice on the use of macrolides in pregnancy.

**May 2021:** We clarified the use of our pneumonia guidelines for people with acute cough and suspected pneumonia in recommendation 1.1.3. We removed recommendation 1.1.11 because this is no longer relevant.

ISBN: 978-1-4731-3263-4