

Nublic Health England



Pneumonia (hospitalacquired): antimicrobial prescribing

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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 <u>Yellow Card Scheme</u>.

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 <u>assess and reduce the environmental</u> <u>impact of implementing NICE recommendations</u> wherever possible.

Contents

Overview	4
Who is it for?	4
Recommendations	5
1.1 Managing hospital-acquired pneumonia	5
1.2 Choice of antibiotic	7
Terms used in the guideline	16
Summary of the evidence	17
Antibiotic prescribing strategies	17
Choice of antibiotics	19
Antibiotic course length, dosage and route of administration	26
Other considerations	28
Medicines adherence	28
Resource implications	28
Finding more information and committee details	29
Update information	30

Overview

This guideline sets out an antimicrobial prescribing strategy for hospital-acquired pneumonia. It does not cover ventilator-associated pneumonia. It aims to optimise antibiotic use and reduce antibiotic resistance.

For recommendations on identifying and treating hospital-acquired bacterial pneumonia secondary to COVID-19, see our <u>rapid guideline on managing acute COVID-19</u>.

Who is it for?

- Healthcare professionals
- People with hospital-acquired pneumonia, their families and carers

Recommendations

For recommendations on identifying and treating hospital-acquired bacterial pneumonia secondary to COVID-19, see our <u>rapid guideline on managing acute COVID-19</u>.

1.1 Managing hospital-acquired pneumonia

Treatment for adults, young people and children

- 1.1.1 For adults, young people and children with symptoms or signs of pneumonia starting within 48 hours of hospital admission, follow the <u>NICE guideline on</u> <u>community-acquired pneumonia</u>.
- 1.1.2 Offer an antibiotic(s) for adults, young people and children with hospital-acquired pneumonia. When choosing an antibiotic(s) (see the <u>recommendations on choice</u> <u>of antibiotic</u>), take account of:
 - the severity of symptoms or signs (at the time of publication, in September 2019, no validated severity assessment tools are available for hospitalacquired pneumonia, and severity of symptoms or signs should be based on clinical judgement)
 - the number of days in hospital before onset of symptoms
 - the risk of developing complications, for example, if the person has a relevant comorbidity such as severe lung disease or immunosuppression
 - local hospital and ward-based antimicrobial resistance data
 - recent antibiotic use
 - recent microbiological results, including colonisation with multidrug-resistant bacteria
 - recent contact with a health or social care setting before current admission
 - the risk of adverse effects with broad-spectrum antibiotics, such as

Clostridium difficile infection.

- 1.1.3 Start antibiotic treatment as soon as possible after establishing a diagnosis of hospital-acquired pneumonia, and certainly within 4 hours (within 1 hour if the person has suspected sepsis and meets any of the high risk criteria for this see the <u>NICE guideline on sepsis</u>).
- 1.1.4 Give oral antibiotics first line if the person can take oral medicines, and the severity of their condition does not require intravenous antibiotics.
- 1.1.5 If intravenous antibiotics are given, review by 48 hours and consider switching to oral antibiotics if possible.
- 1.1.6 Send a sample (for example, sputum sample, nasopharyngeal swab or tracheal aspirate) for microbiological testing.

Reassessment and specialist advice

- 1.1.7 When microbiological results are available:
 - review the choice of antibiotic(s) and
 - change the antibiotic(s) according to results, using a narrower-spectrum antibiotic, if appropriate.
- 1.1.8 Reassess adults, young people and children with hospital-acquired pneumonia if symptoms do not improve as expected or worsen rapidly or significantly.
- 1.1.9 Seek specialist advice from a microbiologist for adults, young people and children with hospital-acquired pneumonia if they have:
 - symptoms that are not improving as expected with antibiotics $\ensuremath{\text{or}}$
 - multidrug-resistant bacteria.
- 1.1.10 Follow the <u>NICE guideline on care of dying adults in the last days of life</u> when caring for adults with hospital-acquired pneumonia who are approaching their

end of life.

See the evidence and committee discussions on <u>antibiotic prescribing strategies</u> and <u>choice of antibiotics</u>.

1.2 Choice of antibiotic

- 1.2.1 When prescribing an antibiotic(s) for hospital-acquired pneumonia:
 - follow table 1 for adults aged 18 years and over
 - follow table 2 for children and young people under 18 years.
- 1.2.2 Consider following the <u>NICE guideline on community-acquired pneumonia</u> for choice of antibiotic for adults, young people and children with symptoms or signs of pneumonia starting within days 3 to 5 of hospital admission who are not at higher risk of resistance. Higher risk of resistance includes relevant comorbidity (such as severe lung disease or immunosuppression), recent use of broadspectrum antibiotics, colonisation with multidrug-resistant bacteria, and recent contact with health and social care settings before current admission.

Table 1 Antibiotics for adults aged 18 years and over

Treatment	Antibiotic, dosage and course length
First-choice oral antibiotic if non-severe symptoms or signs, and not at higher risk of resistance (guided by microbiological results when available)	Co-amoxiclav : 500/125 mg three times a day for 5 days then review

Treatment	Antibiotic, dosage and course length
	Options include:
Alternative oral antibiotics if non-severe symptoms or signs, and not at higher risk of resistance, for penicillin allergy or if co-amoxiclav unsuitable (based on specialist microbiological advice and local resistance data)	Doxycycline:
	200 mg on first day, then 100 mg once a day for 4 days (5-day course) then review
	Cefalexin (caution in penicillin allergy):
	500 mg twice or three times a day (can be increased to 1 g to 1.5 g three or four times a day) for 5 days then review
	Co-trimoxazole (off-label use):
	960 mg twice a day for 5 days then review
	(see <u>BNF</u> for information on monitoring)
	Levofloxacin (only if switching from intravenous levofloxacin with specialist advice; off-label use; consider safety issues):
	500 mg once or twice a day for 5 days then review

Treatment	Antibiotic, dosage and course length
	Options include:
	Piperacillin with tazobactam:
	4.5 g three times a day (increased to 4.5 g four times a day if severe infection)
	Ceftazidime:
	2 g three times a day
	Ceftriaxone:
First-choice intravenous antibiotics if severe symptoms or signs (for example, symptoms or signs of sepsis) or at higher risk of resistance (based on specialist microbiological advice and local resistance	2 g once a day
	Cefuroxime:
	750 mg three times a day (increased to 750 mg four times a day or 1.5 g three or four times a day if severe infection) [amended October 2020]
	Meropenem:
	0.5 g to 1 g three times a day
	Ceftazidime with avibactam:
	2/0.5 g three times a day
	Levofloxacin (off-label use; consider safety issues):
	500 mg once or twice a day (use higher dosage if severe infection)

Freatment	Antibiotic, dosage and course length
	Vancomycin:
Antibiotics to be added if suspected or confirmed meticillin-resistant <i>Staphylococcus aureus</i> infection (dual therapy with a first-choice intravenous antibiotic)	 15 mg/kg to 20 mg/kg two or three times a day intravenously, adjusted according to serum vancomycin concentration (a loading dose of 25 mg/kg to 30 mg/kg can be used in seriously ill people); maximum 2 g per dose (see <u>BNF</u> for information on monitoring) Teicoplanin: Initially 6 mg/kg every 12 hours for 3 doses, then 6 mg/kg once a day intravenously (see <u>BNF</u> for information on monitoring) Linezolid (if vancomycin cannot be used; specialist advice only): 600 mg twice a day orally or intravenously (see <u>BNF</u> for information on monitoring)

See the <u>BNF</u> for appropriate use and dosing in specific populations, for example, hepatic impairment, renal impairment, pregnancy and breastfeeding, and administering intravenous (or, where appropriate, intramuscular) antibiotics.

Higher risk of resistance includes symptoms or signs starting more than 5 days after hospital admission, relevant comorbidity such as severe lung disease or immunosuppression, recent use of broad-spectrum antibiotics, colonisation with multidrug-resistant bacteria, and recent contact with a health or social care setting before current admission.

Review treatment after a total of 5 days of antibiotics and consider stopping antibiotics if clinically stable. Review intravenous antibiotics by 48 hours and consider switching to oral antibiotics for a total of 5 days, then review.

For <u>off-label</u> use, the prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the <u>General Medical Council's good practice in prescribing and managing medicines and devices</u> for further information.

See <u>Medicines and Healthcare products Regulatory Agency (MHRA) advice</u> 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 for people over 60 years and avoiding coadministration with a corticosteroid (March 2019).

Treatment	Antibiotic, dosage and course length
Choice for children under 1 month	Antibiotic choice based on local resistance data and specialist microbiological advice
First choice oral antibiotic for children aged 1 month and over if non-severe symptoms or signs and not at higher risk of resistance (guided by microbiological results when available)	Co-amoxiclav: 1 month to 11 months, 0.5 ml/kg of 125/ 31 suspension three times a day for 5 days, then review 1 year to 5 years, 10 ml of 125/31 suspension (or 5 ml of 250/62 suspension) three times a day, or 0.5 ml/kg of 125/31 suspension three times a day for 5 days, then review 6 years to 11 years, 10 ml of 250/62 suspension three times a day or 0.3 ml/ kg of 250/62 suspension three times a day for 5 days, then review 12 years to 17 years, 500/125 mg three times a day for 5 days, then review

Treatment	Antibiotic, dosage and course length
	Clarithromycin:
Alternative oral antibiotic for children aged 1 month and over if non-severe symptoms or signs and not at higher risk of resistance, for penicillin allergy or if co-amoxiclav unsuitable (other options may be suitable based on specialist microbiological advice and local resistance data)	1 month to 11 years:
	Under 8 kg, 7.5 mg/kg twice a day for 5 days, then review
	8 kg to 11 kg, 62.5 mg twice a day for 5 days, then review
	12 kg to 19 kg, 125 mg twice a day for 5 days, then review
	20 kg to 29 kg, 187.5 mg twice a day for 5 days, then review
	30 kg to 40 kg, 250 mg twice a day for 5 days, then review
	12 years to 17 years, 500 mg twice a day for 5 days, then review

Treatment	Antibiotic, dosage and course length
	Options include:
	Piperacillin with tazobactam:
	1 month to 11 years, 90 mg/kg three or four times a day (maximum 4.5 g per dose four times a day)
	12 years to 17 years, 4.5 g three times a day (increased to 4.5 g four times a day if severe infection)
First-choice intravenous antibiotics if severe	Ceftazidime:
symptoms or signs (for example, symptoms or signs of sepsis), or at higher risk of resistance (antibiotic choice should be based on specialist microbiological advice and local resistance data)	1 month to 17 years, 25 mg/kg three times a day (50 mg/kg three times a day if severe infection; maximum 6 g per day)
	Ceftriaxone:
	1 month to 11 years (up to 50 kg), 50 mg/kg to 80 mg/kg once a day (use dose at higher end of range if severe infection; maximum 4 g per day)
	9 years to 11 years (50 kg and above), 2 g once a day
	12 years to 17 years, 2 g once a day

Treatment	Antibiotic, dosage and course length
	Teicoplanin:
	1 month, initially 16 mg/kg for 1 dose, then 8 mg/kg once daily, subsequent dose to be given 24 hours after initial dose (doses given by intravenous infusion)
	2 months to 11 years, initially 10 mg/kg every 12 hours intravenously for 3 doses, then 6 mg/kg to 10 mg/kg once daily intravenously
	12 years to 17 years, initially 6 mg/kg every 12 hours intravenously for 3 doses, then 6 mg/kg once daily intravenously
Antibiotics to be added if suspected or	(see <u>BNF for children</u> for information on monitoring)
confirmed meticillin-resistant	Vancomycin:
Staphylococcus aureus infection (dual therapy with a first-choice intravenous antibiotic)	1 month to 11 years, 10 mg/kg to 15 mg/kg four times a day intravenously, adjusted according to serum-vancomycin concentration
	12 years to 17 years, 15 mg/kg to 20 mg/kg two or three times a day intravenously, adjusted according to serum vancomycin concentration (a loading dose of 25 mg/kg to 30 mg/kg can be used in seriously ill people); maximum 2 g per dose
	(see <u>BNF for children</u> for information on monitoring)
	Linezolid (if vancomycin cannot be used; off-label use; specialist advice only):
	3 months to 11 years, 10 mg/kg three times a day orally or intravenously

Pneumonia (hospital-acquired): antimicrobial prescribing (NG139)

Treatment	Antibiotic, dosage and course length
	(maximum 600 mg per dose)
	12 years to 17 years, 600 mg twice a day orally or intravenously
	(see <u>BNF for children</u> for information on monitoring)

See the <u>BNF for children</u> for appropriate use and dosing in specific populations, for example, hepatic impairment, renal impairment, pregnancy and breastfeeding, and administering intravenous (or, where appropriate, intramuscular) 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 being treated and the child's size in relation to the average size of children of the same age.

Higher risk of resistance includes symptoms or signs starting more than 5 days after hospital admission, relevant comorbidity such as severe lung disease or immunosuppression, recent use of broad-spectrum antibiotics, colonisation with multidrug-resistant bacteria, and recent contact with a health or social care setting before current admission.

Review treatment after a total of 5 days of antibiotics and consider stopping antibiotics if clinically stable. Review intravenous antibiotics by 48 hours and consider switching to oral antibiotics for a total of 5 days, then review.

For off-label use, the prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the <u>General Medical Council's good practice in prescribing and managing medicines and devices</u> for further information.

See the evidence and committee discussions on choice of antibiotic and antibiotic course length, dosage and route of administration.

Terms used in the guideline

Hospital-acquired pneumonia

Pneumonia that develops 48 hours or more after hospital admission and that was not incubating at hospital admission. When managed in hospital, the diagnosis is usually confirmed by chest X-ray. For the purpose of this guideline, pneumonia that develops in hospital after intubation (ventilator-associated pneumonia) is excluded from this definition.

Summary of the evidence

This is a summary of the evidence. For full details, see the evidence review.

Hospital-acquired pneumonia is a lower respiratory tract infection that may be life threatening.

- Early-onset hospital-acquired pneumonia (less than 5 days after admission to hospital) is usually caused by *Streptococcus pneumoniae* and late-onset (more than 5 days after admission to hospital) is usually caused by microorganisms that are acquired in hospital, most commonly methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa* and other non-pseudomonal gram-negative bacteria.
- No evidence from systematic reviews or randomised controlled trials (RCTs) was identified in children or young people under 18 years.

Antibiotic prescribing strategies

- An antibiotic prescribing strategy (guided by results of immediate bronchoscopy with protected specimen brush sample culture) was not significantly different from immediate antibiotics for clinical cure and mortality up to 28 days in adults with hospital-acquired pneumonia (non-ventilated; <u>Herer et al. 2009</u>). Bronchoscopy was carried out within 24 hours of clinical diagnosis and gram-stain results (available 4 hours to 6 hours after bronchoscopy) were used to modify treatment.
- The total costs (antibiotics and bronchoscopy) of each strategy were not significantly different overall.
- An antibiotic prescribing strategy of using antibiotics with very broad antimicrobial cover (imipenem with cilastatin plus vancomycin) followed by de-escalation to a broad-spectrum antibiotic based on culture results was significantly better than empirical antibiotics for achieving adequate initial antimicrobial cover. However, there were no significant differences in clinical outcomes, including mortality up to 28 days (Kim et al. 2012). This study included non-ventilated adults with hospital-acquired pneumonia and a small proportion of adults with ventilator-associated pneumonia (8.3%).

• The overall incidence of multidrug-resistant bacteria was significantly higher with very broad antimicrobial cover followed by de-escalation, compared with empirical antibiotics.

Evidence for antibiotic prescribing strategies is based on 2 RCTs (Herer et al. 2009 and Kim et al. 2012).

Committee discussion on antibiotic prescribing strategies

- The committee noted that the bronchoscopy antibiotic prescribing strategy used by Herer et al. (2009) was not consistent with clinical practice in the UK; culture results are not usually available within 24 hours and sputum cultures are more common than gram staining of bronchoscopy samples.
- The committee noted that overall there were no significant differences in clinical outcomes between the 2 prescribing strategies. Because of the lack of applicability to UK practice, and the small sample size, the committee agreed that there was insufficient evidence to show that the prescribing strategies were equivalent.
- The committee discussed evidence from Kim et al. (2012) suggesting no difference in clinical outcomes between a prescribing strategy of very-broadspectrum antibiotics with de-escalation, compared with empirical antibiotics. However, the committee was concerned that the rate of emergence of multidrugresistant bacteria was significantly higher with the very-broad-spectrum antibiotics followed by de-escalation strategy.
- The committee was concerned about the risk of antimicrobial resistance from using very-broad-spectrum antibiotics for longer than necessary, as well as the high rates of adverse effects in some of the included studies. Therefore, the committee concluded that a respiratory sample (for example, sputum sample, nasopharyngeal swab or tracheal aspirate) should be taken and sent for microbiological testing if possible. This reflects current practice.

The committee agreed that when microbiological results are available, the antibiotic should be reviewed and changed accordingly (for example, if bacteria are found to be resistant), using a narrower-spectrum antibiotic, if appropriate.

Choice of antibiotics

Efficacy of antibiotics

- Overall, there were no differences in the clinical effectiveness (clinical cure or mortality) in a range of antibiotic comparisons in adults with hospital-acquired pneumonia:
 - penicillin with beta-lactamase inhibitor (piperacillin with tazobactam) compared with a carbapenem (imipenem with cilastatin; <u>Schmitt et al. 2006</u>)
 - cephalosporin with beta-lactamase inhibitor (ceftazidime with avibactam)
 compared with a carbapenem (meropenem; <u>Torres et al. 2017</u>)
 - tetracycline (tigecycline) compared with a carbapenem (imipenem with cilastatin;
 <u>Freire et al. 2010</u> and <u>Ramirez et al. 2013</u>)
 - fluoroquinolone (moxifloxacin) compared with a cephalosporin (ceftriaxone followed by cefuroxime; <u>Hoffken et al. 2007</u>)
 - cephalosporin (ceftobiprole) compared with cephalosporin plus oxazolidinone (ceftazidime plus linezolid; <u>Awad et al. 2014</u>)
 - glycopeptide (telavancin) compared with glycopeptide (vancomycin; <u>Rubinstein</u> <u>et al. 2011</u> reported in <u>Rubinstein et al. 2014</u>).

Evidence for efficacy of antibiotics is based on 6 RCTs (Schmitt et al. 2006, Torres et al. 2017, Freire et al. 2010, Ramirez et al. 2013, Hoffken et al. 2007 and Awad et al. 2014) and 1 post-hoc analysis of an RCT (Rubinstein et al. 2014).

Safety of antibiotics

- About 10% of the general population claim to have a penicillin allergy; this is often because of a skin rash that occurred while taking a course of penicillin as a child.
 Fewer than 10% of people who think they are allergic to penicillin are truly allergic. See the <u>NICE guideline on drug allergy</u> for more information.
- People with a history of immediate hypersensitivity to penicillins may also react to cephalosporins and other beta-lactam antibiotics (<u>BNF, August 2019</u>).

- Macrolides (for example, clarithromycin) should be used with caution in people with a predisposition to QT interval prolongation (<u>BNF, August 2019</u>).
- Tetracyclines (for example, doxycycline), can deposit in growing bone and teeth (by binding to calcium) causing staining and occasionally dental hypoplasia. They should not be given to pregnant or breastfeeding women, and use in children under 12 years is either contraindicated or cautioned for use in severe or life-threatening infections where there are no alternatives (<u>BNF, August 2019</u>).
- Co-trimoxazole is associated with rare but serious side effects including blood disorders and Stevens–Johnson syndrome. It is cautioned for use in older people because there is an increased risk of serious adverse effects, and in those with a predisposition to hyperkalaemia. Monitoring of blood counts is recommended with prolonged treatment (<u>BNF, August 2019</u>).
- Fluoroquinolones have restrictions and precautions around their use because of rare reports of disabling and potentially long-lasting or irreversible side effects affecting musculoskeletal and nervous systems (<u>MHRA Drug Safety Update, March 2019</u>). They may also be associated with a small increased risk of aortic aneurysm and dissection, particularly in older people (<u>MHRA Drug Safety Update, November 2018</u>).
- Glycopeptide (for example, vancomycin and teicoplanin) doses are based on body weight. Therapeutic drug monitoring and monitoring of various patient parameters including blood count, urinalysis, auditory function, hepatic function and renal function is recommended depending on the particular glycopeptide (<u>BNF, August 2019</u>).
- Severe optic neuropathy can occur with linezolid, particularly if used for longer than 28 days. Blood disorders have also been reported and weekly full blood counts are recommended (<u>BNF, August 2019</u>).
- Overall, there were no significant differences in adverse effects in the studies between antibiotics or classes of antibiotics in people with hospital-acquired pneumonia.
- Treatment-related adverse events were significantly higher with moxifloxacin compared with a cephalosporin (intravenous ceftriaxone then oral cefuroxime; 30% versus 16%, number needed to harm [NNH] 7 [range 3 to 84]).
- Significantly more people stopped treatment because of adverse events with tigecycline than with imipenem with cilastatin (10.9% versus 6.6%, NNH 23 [range 12 to 150]).

• See the <u>summaries of product characteristics</u> for information on contraindications, cautions, drug interactions and adverse effects of individual medicines.

Committee discussion on choice of antibiotics

- The committee agreed that prompt antibiotic treatment should be offered to everyone with hospital-acquired pneumonia.
- The committee discussed the definition of hospital-acquired pneumonia. Because it includes people with pneumonia that develops 48 hours or more after hospital admission and that was not incubating at hospital admission, the committee agreed that the <u>NICE guideline on community-acquired pneumonia</u> should be followed for people with symptoms or signs of pneumonia starting on days 1 or 2 after hospital admission.
- The committee discussed the timing of antibiotic treatment and was aware of current practice to offer antibiotics within 4 hours. No systematic reviews or RCTs were identified, and the committee agreed that there was no reason to change current practice. However, they noted that the timing should be within 4 hours of an established diagnosis to avoid inappropriate use of broad-spectrum antibiotics.
- The committee noted that evidence was identified in adults only, and for a limited number of head-to-head antibiotic comparisons. They agreed that recommendations for children and young people should be based on its experience and extrapolation of evidence in adults, taking account of any relevant medicines safety concerns.
- Given the clinical expertise needed for assessing and managing hospital-acquired pneumonia in very young children (under 1 month), the committee agreed that the choice of antibiotic in these children should be based on local resistance data and specialist microbiological advice.
- Overall, the limited evidence showed no differences in clinical effectiveness between different broad-spectrum antibiotics or classes of antibiotics, with some small differences in the rates of adverse effects. The committee noted the high rates of adverse events for many broad-spectrum antibiotics included in the studies.
- The committee discussed the most common causes of hospital-acquired pneumonia. They agreed that cause is often uncertain because many people do

not have a microbiological diagnosis.

- They recognised that *S. pneumoniae* is the most common cause in people who develop hospital-acquired pneumonia within 5 days of hospital admission. The risk of having a multidrug-resistant infection with *P. aeruginosa*, MRSA or extended-spectrum beta-lactamases (ESBLs) increases in people who develop the infection after more than 5 days of being in hospital, although resistance rates vary locally.
- Therefore, the committee agreed that for people with symptoms or signs of pneumonia starting on days 3 to 5 after hospital admission who are not at high risk of resistance, it may be appropriate to follow the NICE guideline on community-acquired pneumonia for recommendations on the choice of antibiotic, based on their clinical judgement. This would give the option to treat some people with amoxicillin, which is a narrower-spectrum antibiotic with activity against *S. pneumoniae*.
- Based on experience, the committee agreed that there are several factors that need to be taken into account when choosing an antibiotic, including the severity of symptoms or signs. The committee did not know of any validated tools for assessing the severity of hospital-acquired pneumonia, and therefore agreed that this should be based on clinical judgement.
- The committee also agreed that some people are at higher risk of developing complications, for example, people with a comorbidity such as severe lung disease or immunosuppression.
- The committee recognised that, when available, local antimicrobial resistance data are an important consideration in hospital-acquired pneumonia, including at hospital and ward-based level (particularly in high-risk areas such as intensive care, high-dependency units, haematology or oncology).
- The committee also agreed that recent use of broad-spectrum antibiotics and recent contact with healthcare services before the current hospital admission were also highly likely to increase the risk of resistant pathogens.
- The committee agreed that taking account of these factors would optimise the appropriate use of broad-spectrum antibiotics and minimise the risk of

antimicrobial resistance.

- The committee agreed that an antibiotic should be started empirically, so as not to delay treatment for an infection with a high-mortality risk.
- The committee agreed that the choice of antibiotic should be based on its experience of which antibiotics are effective against likely pathogens and cause the least harm, with the narrowest spectrum possible to minimise the risk of antimicrobial resistance and adverse effects. However, the committee discussed that people with severe symptoms or signs and those at higher risk of resistance will need broad-spectrum antibiotics with high activity against likely organisms.
- Based on its experience, the committee recommended co-amoxiclav as firstchoice antibiotic for people with non-severe symptoms or signs who are not at higher risk of resistance; co-amoxiclav is a broad-spectrum antibiotic that combines a penicillin with a beta-lactamase inhibitor and has good activity against common pathogens, such as *S. pneumoniae* and *Haemophilus influenzae*. The committee also recognised the extensive clinical experience of its effectiveness in this population.
- For adults with non-severe symptoms or signs who are not at higher risk of resistance, with penicillin allergy or in whom co-amoxiclav is unsuitable (for example, because of local resistance data), the committee agreed that the choice of an alternative antibiotic should be based on local resistance data and specialist microbiological advice only. They agreed that options include:
 - doxycycline (a tetracycline)
 - cefalexin (a cephalosporin; not suitable if there is a risk of penicillin-resistant pneumococci)
 - co-trimoxazole (trimethoprim plus a sulfonamide)
 - levofloxacin (a fluoroquinolone; only to be used when switching from IV antibiotics, following specialist advice).
- Co-trimoxazole and levofloxacin are not licensed for hospital-acquired pneumonia, so use would be off-label.

- In children and young people with penicillin allergy or in whom co-amoxiclav is unsuitable, the alternative antibiotic is clarithromycin (a macrolide); this has good activity against common pathogens and is appropriate for use in children and young people. However, the committee recognised that other options may be suitable based on local resistance data and specialist microbiological advice.
- The committee agreed that specialist advice should be sought for young women who are pregnant with penicillin allergy or in whom co-amoxiclav is unsuitable, because they were not able to specify an alternative antibiotic for this population.
- Based on its experience, the committee recognised that many broad-spectrum antibiotics would be appropriate as first-choice intravenous antibiotics for people with severe symptoms or signs, or who are at higher risk of resistance. It agreed that the choice should be based on local resistance data and following specialist microbiological advice. Options include:
 - piperacillin with tazobactam (an antipseudomonal penicillin with a betalactamase inhibitor)
 - **ceftazidime** (a third-generation cephalosporin)
 - **ceftriaxone** (a third-generation cephalosporin)
 - **cefuroxime** (a second-generation cephalosporin; in adults)
 - **meropenem** (a carbapenem; in adults)
 - ceftazidime with avibactam (a third-generation cephalosporin with a betalactamase inhibitor; in adults)
 - levofloxacin (in adults).
- These antibiotics have good activity against common pathogens in this population, including multidrug-resistant *P. aeruginosa*, ESBLs and some carbapenemase-producing gram-negative bacteria.
- The committee discussed that a small number of people with hospital-acquired pneumonia may have suspected or confirmed infection with MRSA. Therefore, based on their experience, the committee agreed that for these people, 1 of the

following **antibiotics** with activity against MRSA should be added to the treatment regimen:

- vancomycin (a glycopeptide)
- teicoplanin (a glycopeptide)
- linezolid (an oxazolidinone; if vancomycin cannot be used, following specialist advice only). Linezolid is not licensed in children and young people under 18 years, so use would be off-label.
- Based on its experience, the committee recommended the same oral antibiotics (discussed above) for people with severe symptoms or signs or at higher risk of resistance who have initially received intravenous antibiotics, to complete the antibiotic course when intravenous antibiotics are no longer required.
- The committee recognised that hospital-acquired pneumonia requires careful monitoring. It agreed by consensus that a person's condition should be reassessed if symptoms do not improve as expected or worsen rapidly or significantly at any time.

The committee agreed that for people with symptoms that are not improving as expected with antibiotics, or who are known to have multidrug-resistant bacteria, specialist advice from a microbiologist should be sought.

Antibiotic course length, dosage and route of administration

• No systematic reviews or RCTs were identified that compared antibiotic course lengths, dosage or route of administration.

Committee discussions on antibiotic course length, dosage and route of administration

- The committee agreed that the shortest course that is likely to be effective should be prescribed to reduce the risk of antimicrobial resistance and adverse effects from broad-spectrum antibiotics. However, hospital-acquired pneumonia is a serious infection with a high-mortality risk and needs effective treatment.
- Based on its experience and extrapolation of evidence for people with community-acquired pneumonia (see the <u>NICE guideline on community-acquired</u> <u>pneumonia</u>), the committee agreed that a total course of 5 days of antibiotics was the minimum required.
- The committee agreed that antibiotic treatment should be reviewed at 5 days. Stopping the antibiotic should be considered on an individual basis if the person is judged to be clinically stable.
- Based on its experience, the committee agreed that usual BNF and BNF for children doses for hospital-acquired pneumonia, or severe susceptible infections should be used.
- In line with the <u>NICE guideline on antimicrobial stewardship</u> and Public Health England's <u>Start smart – then focus</u>, oral antibiotics should be given first line if the person can take them, and if the severity of their infection does not require intravenous antibiotics. The use of intravenous antibiotics should be reviewed by 48 hours (taking into account the person's response to treatment and any microbiological results) and switched to oral treatment where possible.

For people with severe symptoms or signs or at higher risk of resistance, the committee agreed that intravenous antibiotics should always be given initially.

Other considerations

Medicines adherence

Medicines adherence may be a problem for some people taking antibiotics that need frequent dosing or longer treatment duration (see the <u>NICE guideline on medicines</u> <u>adherence</u>).

Resource implications

Recommended antibiotics (except ceftazidime with avibactam) are available as generic formulations. See the <u>Drug Tariff</u> and the <u>BNF</u> for costs.

See the evidence review for more information.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the <u>NICE</u> topic page on pneumonia.

For full details of the evidence and the guideline committee's discussions, see the <u>evidence review</u>. You can also find information about <u>how the guideline was</u> <u>developed</u>, including <u>details of the committee</u>.

NICE has produced <u>tools and resources to help you put this guideline into practice</u>. For general help and advice on putting our guidelines into practice, see <u>resources to help you</u> <u>put NICE guidance into practice</u>.

Update information

9 October 2020: We amended the cefuroxime dosage for adults in line with the summaries of product characteristics.

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