Pneumonia (hospital-acquired): antimicrobial prescribing

NICE guideline

Draft for consultation, February 2019

This guideline sets out an antimicrobial prescribing strategy for hospital-acquired pneumonia. It aims to optimise antibiotic use and reduce antibiotic resistance.

The recommendations in this guideline are for the use of antibiotics to manage hospital-acquired pneumonia in adults, young people and children who do not have ventilator-associated pneumonia. It does not cover diagnosis.

For managing other lower respiratory tract infections (including community-acquired pneumonia), see our web page on respiratory conditions.

See a 3-page visual summary of the recommendations, including tables to support prescribing decisions.

Who is it for?

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

The guideline contains:

- the draft recommendations
- summary of the evidence.

Information about how the guideline was developed is on the guideline's page on the NICE website. This includes the full evidence review, details of the committee and any declarations of interest.

Recommendations

1.1 Managing hospital-acquired pneumonia

Treatment for adults, young people and children

1.1.1 Offer an antibiotic(s) for adults, young people and children with hospital-acquired pneumonia within 4 hours of establishing a diagnosis. When choosing an antibiotic (see the recommendations on choice of antibiotic) take account of:

- the severity of symptoms or signs[1]
- the number of days in hospital before onset of symptoms
- the risk of developing complications, for example if the person has a co-morbidity (such as severe lung disease or immunosuppression)
- local hospital and ward-based antimicrobial resistance data
- recent antibiotic use
- recent microbiological results, including colonisation with multi-drug resistant bacteria
- recent healthcare exposure before current admission
- the risk of adverse effects with broad spectrum antibiotics.

[1] At the time of publication, no validated severity assessment tools are available for hospital-acquired pneumonia, and severity of symptoms or signs should be based on clinical judgement.

1.1.2 Give oral antibiotics first-line if the person can take oral medicines, and the severity of their condition does not require intravenous antibiotics.

1.1.3 Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics if possible.

1.1.4 Send a respiratory sample (for example, sputum sample, nasopharyngeal swab or tracheal aspirate) for microbiological testing.

Reassessment and specialist advice

1.1.5 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.

1.1.6 Reassess adults, young people and children with hospital-acquired pneumonia if symptoms do not improve as expected or worsen rapidly or significantly.

1.1.7 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, **or**
- multi-drug resistant bacteria.

1.1.8 Follow the NICE guideline on care of dying adults in the last days of life when caring for adults with hospital-acquired pneumonia who are approaching the end of life.

See the evidence and committee discussion on antibiotic prescribing strategies and choice of antibiotics.

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.

Table 1. Antibiotics for adults aged 18 years and over

Antibiotic[1]	**Dosage and course length[2]**
First choice antibiotic if non-severe symptoms or signs and not at higher risk of resistance (guided by microbiological results when available)[3,4]	
Co-amoxiclav	500/125 mg three times a day orally or 1.2 g three times a day IV[5] for 5 days in total then review[6]
Alternative antibiotic if non-severe symptoms or signs and not at higher risk of resistance, for penicillin allergy or if co-amoxiclav unsuitable (guided by microbiological results when available)[3,4]	
Levofloxacin[7]	500 mg once or twice a day orally or IV[5] for 5 days in total then review[6]
First choice antibiotics (given IV for at least 48 hours) if severe symptoms or signs (for example, symptoms or signs of sepsis) or at higher risk of resistance (guided by microbiological results when available)[4,5]	
Piperacillin with tazobactam	4.5 g three times a day (increased to 4.5 g four times a day if severe infection)
Levofloxacin[7]	500 mg once or twice a day (use higher dosage if severe infection)
Ceftazidime	2 g three times a day
Ceftriaxone	2 g once a day
Cefuroxime	750 mg three or four times a day (increased to 1.5 g three or four times a day if severe infection)
Meropenem (specialist advice only)	0.5 to 1 g three times a day
Ceftazidime with avibactam (specialist advice only)	2/0.5 g three times a day
Intravenous antibiotics to be added if suspected or confirmed MRSA infection (dual therapy with an IV antibiotic listed above)[5]	
Vancomycin	15 to 20 mg/kg two or three times a day (maximum 2 g per dose), adjusted according to serum-vancomycin concentration[8]
Linezolid (if vancomycin cannot be used; specialist advice only)	600 mg twice a day
Oral antibiotics (when IV antibiotics no longer required[5]; guided by microbiological results when available)	
Co-amoxiclav	500/125 mg three times a day for 5 days in total (including IV antibiotics) then review[6]

Levofloxacin[7]	500 mg once or twice a day for 5 days in total (including IV antibiotics) then review[6]
Cefuroxime	500 mg twice a day for 5 days in total (including IV antibiotics) then review[6]
[1]See BNF and MHRA advice for appropriate use and dosing in specific populations, for example, hepatic impairment, renal impairment, pregnancy and breast-feeding, and administering intravenous antibiotics. [2]Oral doses are for immediate-release medicines. [3]Give oral antibiotics first-line if the person can take oral medicines. [4]Higher risk of resistance includes onset of symptoms more than 5 days after hospital admission, relevant co-morbidity (such as severe lung disease or immunosuppression), recent (within last 3 months) antibiotic use, colonisation with multi-drug resistant bacteria, and recent healthcare exposure before current admission. [5]Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics if possible. [6]Review treatment after 5 days and consider stopping the antibiotic if the person is clinically stable. [7]Levofloxacin is not licensed for hospital-acquired pneumonia, so use would be off label. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information. [8]Therapeutic drug monitoring and assessment of renal function is required. A loading dose of 25 to 30 mg/kg (maximum per dose 2 g) can be used in seriously unwell people to facilitate rapid attainment of the target trough serum-vancomycin concentration (BNF, December 2018).	
Abbreviations: IV, Intravenous; MRSA, Methicillin-resistant *Staphylococcus aureus*	

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

Antibiotic[1]	**Dosage and course length[2]**
Children under 3 months	
Refer to paediatric specialist and treat with intravenous antibiotics in line with the NICE guideline on fever in under 5s.	
Children aged 3 months and over	
First choice antibiotic if non-severe symptoms or signs and not at higher risk of resistance (guided by microbiological results when available)[3,4]	
Co-amoxiclav	Oral doses: 3 to 11 months, 0.5 ml/kg of 125/31 suspension three times a day for 5 days then review[5] 1 to 5 years, 10 ml of 125/31 suspension three times a day or 0.5 ml/kg of 125/31 suspension three times a day for 5 days then review[5] 6 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[5] 12 to 17 years, 500/125 mg three times a day for 5 days then review[5]

	IV dose: 3 months to 17 years, 30 mg/kg three times a day (maximum 1.2 g per dose)[6]
Alternative antibiotic if non-severe symptoms or signs and not at higher risk of resistance, for penicillin allergy or if co-amoxiclav unsuitable (guided by microbiological results when available)[3,4]	
Clarithromycin	Oral doses, 3 months to 11 years: Under 8 kg, 7.5 mg/kg twice a day for 5 days then review[5] 8 to 11 kg, 62.5 mg twice a day for 5 days then review[5] 12 to 19 kg, 125 mg twice a day for 5 days then review[5] 20 to 29 kg, 187.5 mg twice a day for 5 days then review[5] 30 to 40 kg, 250 mg twice a day for 5 days then review[5] IV dose, 3 months to 11 years: 7.5 mg/kg twice a day (maximum 500 mg per dose) 12 to 17 years, 500 mg twice a day orally or IV[6] for 5 days in total then review[5]
First choice antibiotics (given IV for at least 48 hours) if severe symptoms or signs (for example, symptoms or signs of sepsis) or at higher risk of resistance (guided by microbiological results when available)[4,6]	
Piperacillin with tazobactam	3 months to 11 years, 90 mg/kg three or four times a day (maximum 4.5 g per dose four times a day) 12 to 17 years, 4.5 g three times a day (increased to 4.5 g four times a day if severe infection)
Ceftazidime	3 months 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	3 months to 11 years (up to 50 kg), 50 to 80 mg/kg once a day (use dose at higher end of range if severe infection; maximum 4 g per day) 9 to 11 years (50 kg and above), 2 g once a day 12 to 17 years, 2 g once a day
Cefuroxime	3 months to 17 years, 20 mg/kg three times a day (maximum 750 mg per dose), increased to 50 to 60 mg/kg three or four times a day if severe infection (maximum 1.5 g per dose)
Intravenous antibiotics to be added if suspected or confirmed MRSA infection (dual therapy with an IV antibiotic listed above)[6]	
Vancomycin	3 months to 11 years, 10 to 15 mg/kg four times a day, adjusted according to serum-vancomycin concentration[7] 12 to 17 years, 15 to 20 mg/kg two or three times a day (maximum 2 g per dose), adjusted according to serum-vancomycin concentration[7]
Linezolid[8] (if vancomycin cannot be used; specialist advice only)	3 months to 11 years, 10 mg/kg three times a day (maximum 600 mg per dose) 12 to 17 years, 600 mg twice a day

Oral antibiotics (when IV antibiotics no longer required[6]; guided by microbiological results when available)	
Co-amoxiclav	See oral doses above; for 5 days in total (including IV antibiotics) then review[5]
Clarithromycin	See oral doses above; for 5 days in total (including IV antibiotics) then review[5]
Cefuroxime	3 months to 1 year, 10 mg/kg twice a day (maximum 125 mg per dose) for 5 days in total (including IV antibiotics) then review[5] 2 to 11 years, 15 mg/kg twice a day (maximum 250 mg per dose) for 5 days in total (including IV antibiotics) then review[5] 12 to 17 years, 500 mg twice daily for 5 days in total (including IV antibiotics) then review[5]
[1]See BNF for children and MHRA advice for appropriate use and dosing in specific populations, for example, hepatic impairment, renal impairment, pregnancy and breast-feeding, and administering intravenous antibiotics. Not all antibiotics are licensed for hospital-acquired pneumonia. [2]Oral doses are for immediate-release medicines. 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. [3]Give oral antibiotics first-line if the person can take oral medicines. [4]Higher risk of resistance includes onset of symptoms more than 5 days after hospital admission, relevant co-morbidity (such as severe lung disease or immunosuppression), recent (within last 3 months) antibiotic use, colonisation with multi-drug resistant bacteria, and recent healthcare exposure before current admission. [5]Review treatment after 5 days and consider stopping the antibiotic if the person is clinically stable. [6]Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible. [7]Therapeutic drug monitoring and assessment of renal function is required; see summary of product characteristics (BNF, December 2018). [8]Linezolid is not licensed in children and young people under 18 years, so use would be off label. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.	
Abbreviations: MRSA, Methicillin-resistant *Staphylococcus aureus*; IV, Intravenous	

See the evidence and committee discussion 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 the time of 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 (occurring within 4 days of hospital admission) is usually caused by *Streptococcus pneumoniae* and late-onset hospital-acquired pneumonia 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 (NICE guideline on pneumonia [2014]: final scope).
- The recommendations in this guideline are based on the evidence identified and the experience of the committee. The evidence specifically included antibiotics for managing hospital-acquired pneumonia in adults without ventilator-associated pneumonia. 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; Herer et al. 2009). Bronchoscopy was carried out within 24

hours after clinical diagnosis and gram stain results (available 4 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[2] 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 multi-drug resistant bacteria was significantly worse 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 discussed the evidence for antibiotic prescribing strategies in adults with hospital-acquired pneumonia.
- They noted that the bronchoscopy 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. Due to 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.

[2] For the purposes of this guideline, empirical antibiotics is defined as prescribing an antibiotic without knowledge of the causative pathogen.

- The committee discussed evidence from Kim et al. (2012) suggesting no difference in clinical outcomes between a prescribing strategy of very broad spectrum antibiotics with de-escalation, compared with empirical antibiotics. However, the committee was concerned that the rate of emergence of multi-drug resistant bacteria was significantly higher with the very broad spectrum antibiotics followed by de-escalation strategy.
- The committee were 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, which is current practice.
- The committee agreed that when microbiological results are available, the antibiotic should be reviewed and changed according to results (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) (Schmitt et al. 2006)
  - cephalosporin with beta-lactamase inhibitor (ceftazidime with avibactam) compared with a carbapenem (meropenem) (Torres et al. 2017)
  - tetracycline (tigecycline) compared with a carbapenem (imipenem with cilastatin) (Freire et al. 2010 and Ramirez et al. 2013)

  - fluoroquinolone (moxifloxacin) compared with a cephalosporin (ceftriaxone followed by cefuroxime) (Hoffken et al. 2007)
  - cephalosporin (ceftobiprole) compared with cephalosporin plus oxazolidinone (ceftazidime plus linezolid) (Awad et al. 2014)
  - glycopeptide (telavancin) compared with glycopeptide (vancomycin) (Rubinstein et al. 2011 reported in Rubinstein et al. 2014).

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 a 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 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).
- Tendon damage (including rupture) has been reported rarely in people receiving fluoroquinolones (BNF, December 2018), and the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (press release October 2018) has recommended restricting the use of these antibiotics following a review of disabling and potentially long-lasting side effects mainly involving muscles, tendons and bones and the nervous system.
- Fluoroquinolones may be associated with a small increased risk of aortic aneurysm and dissection, particularly in older people (MHRA Drug Safety Update, November 2018).
- Loading and maintenance doses of vancomycin are calculated on the basis of the person's weight and renal function, with adjustments made according to serum-vancomycin concentrations.

- 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 a fluoroquinolone (moxifloxacin) compared with a cephalosporin (ceftriaxone with cefuroxime; 30% versus 16%, number needed to harm [NNH] 7, [range 3 to 84]).
- Significantly more people discontinued treatment due to adverse events with a glycylcycline (tigecycline) compared with a carbapenem (imipenem with cilastatin; 10.9% versus 6.6%, NNH 23, [range 12 to 150]).
- See the summaries of product characteristics for information on contraindications, cautions, drug interactions and adverse effects of individual medicines.

Committee discussion on choice of antibiotics

- The committee agreed by consensus that prompt antibiotic treatment should be offered to all people diagnosed with hospital-acquired pneumonia.
- The committee discussed the timing of antibiotic treatment and was aware of current practice to offer antibiotics within 4 hours. As no systematic reviews or RCTs were identified, the committee agreed by consensus that there was no reason to change current practice. However, they noted that the timing should be based on 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 their experience in children and young people 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 3 months), the committee agreed that these children should be managed by a

paediatric specialist and treated with intravenous antibiotics in line with the NICE guideline on fever in under 5s.

- 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.
- Based on their experience, the committee agreed that there are a number of factors that need to be taken into account when choosing an antibiotic, including the severity of symptoms or signs. The committee was not aware of any validated tools for assessing the severity of hospital-acquired pneumonia, and therefore this should be based on clinical judgement.
- They recognised that *Streptococcus pneumoniae* is the most common cause in people who develop the infection within 5 days of hospital admission. The risk of having a multi-drug resistant infection with *Pseudomonas 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.
- The committee also agreed that some people are at higher risk of developing complications, for example people with a relevant co-morbidity (such as severe lung disease or immunosuppression).
- The committee recognised that local antimicrobial resistance data is an important consideration in hospital-acquired pneumonia, including at hospital and ward-based level (particularly in intensive care units and in high-risk wards, such as haematology or oncology), where these data are available.
- The committee also agreed that recent antibiotic use (within the last 3 months) and recent healthcare exposure 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 their 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 resistant organisms.
- The committee agreed that people who may be at a higher risk of resistance includes people with onset of symptoms more than 5 days after hospital admission, relevant co-morbidity (such as severe lung disease or immunosuppression), recent (within last 3 months) antibiotic use, colonisation with multi-drug resistant bacteria and recent healthcare exposure before current admission.
- For people with severe symptoms or signs or who are at a higher risk of resistance, the committee noted that many broad spectrum antibiotics are likely to be appropriate, if following expert microbiological advice. They agreed that recommending a range of antibiotic options would allow antibiotic choice to be determined by local resistance data and an individual person's risk of resistance (for example, due to recent exposure to a particular antibiotic).
- Based on their experience, the committee recommended **co-amoxiclav** as **first-choice 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 *Streptococcus pneumoniae* and *Haemophilus influenzae.* The committee

also recognised the extensive clinical experience of its effectiveness in this population.

- The **alternative antibiotic** for people with non-severe symptoms or signs who are not at higher risk of resistance is **levofloxacin** in adults – a fluoroquinolone that provides broad spectrum cover for hospital-acquired pneumonia. Because of safety concerns with fluoroquinolones, the committee agreed that it should only be given to people with penicillin allergy, or in whom co-amoxiclav is unsuitable (for example, because of local resistance data). Ciprofloxacin should not be used because it does not provide adequate cover against *Streptococcus pneumoniae*.
- 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.
- 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, as they were not able to specify an alternative antibiotic for this population.
- Based on their experience, the committee recommended the following **first-choice intravenous antibiotics** for people with severe symptoms or signs, or who are at higher risk of resistance:
  - **piperacillin with tazobactam** (an antipseudomonal penicillin with a beta-lactamase inhibitor)
  - **levofloxacin** (in adults)
  - **ceftazidime** (a third-generation cephalosporin)
  - **ceftriaxone** (a third-generation cephalosporin)
  - **cefuroxime** (a third-generation cephalosporin)
  - **meropenem** (a carbapenem; in adults following specialist advice only)
  - **ceftazidime with avibactam** (a third-generation cephalosporin with a with a beta-lactamase inhibitor; in adults following specialist advice only).
- These broad spectrum antibiotics have good activity against common pathogens in this population, including multi-drug resistant *Pseudomonas*

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 one of the following **intravenous antibiotics** with activity against MRSA should be added to the treatment regimen:
  - **vancomycin** (a glycopeptide)
  - **linezolid** (an oxazolidinone; if vancomycin cannot be used, following specialist advice only).
- Based on their experience, the committee recommended the following **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:
  - **co-amoxiclav**
  - **levofloxacin** (in adults) or **clarithromycin** (in children and young people)
  - **cefuroxime** (a third-generation cephalosporin with a similar spectrum of activity to alternative options).
- The committee recognised that hospital-acquired pneumonia requires careful monitoring. They 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 was aware that the NICE guideline on care of dying adults in the last days of life should be followed, if appropriate.
- The committee agreed that for people with symptoms that are not improving as expected with antibiotics, or who are known to have multi-drug resistant bacteria, specialist advice from a microbiologist should be sought. They noted that ceftazidime with avibactam and linezolid should only be given after specialist advice. The committee also

agreed based on their experience that meropenem should also only be given after specialist advice.

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 that requires effective treatment.
- Based on their experience and extrapolation of evidence for people with community-acquired pneumonia (see the NICE antimicrobial prescribing guideline on community-acquired pneumonia), the committee agreed by consensus 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 their experience, the committee agreed that usual BNF and BNF for children doses for hospital-acquired pneumonia, or severe susceptible infections should be used.
- The committee was aware that most antibiotics used in the studies were given intravenously for the total course duration, or in some cases stepped down to oral antibiotics. For people with severe symptoms or signs or at higher risk of resistance, the committee agreed by consensus that intravenous antibiotics should always be given for at least the first 48 hours. For other people, intravenous antibiotics may be needed if the person is unable to take oral medicines, for example if they are vomiting.
- In line with the NICE guideline on antimicrobial stewardship and Start smart – then focus, the committee agreed that if intravenous antibiotics are used initially, this should be reviewed by 48 hours (taking into account the person's response to treatment and microbiological results) and switched to oral treatment where possible.

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 NICE guideline on medicines adherence).

Resource implications

- Recommended antibiotics (except ceftazidime with avibactam) are available as generic formulations. See Drug Tariff for costs.

See the evidence review for more information.